HUMAN TECHNOPOLE

Activity Report
2020-2021

INDEX

METHODOLOGICAL NOTE

This report has been drawn up based on the contents of public documents concerning the Human Technopole Foundation, including the Management Reports, the Integrated Financial Statements, and the Strategic Plan, of which entire parts are reported.

The document, as required by Article 1, paragraph 275(a) of Law 160/2019, includes data for the years 2020 and 2021 but also tracks previous work and, in some cases, information for the year 2022, to provide a broader and more comprehensive picture of the activities carried out and planned, especially with reference to their impact on the national research system.

Version completed in September 2022.

1. INTRODUCTION

An investment in knowledge always pays the best interest.

– Benjamin Franklin

On October 31, 2015, the Universal Exposition closed in Milan, an event that – by bringing together the best skills and competencies of institutions, businesses, the third sector and civil society as a whole – had shown the world the best of Made in Italy.

In the aftermath of its closure, to pick up its legacy and enhance its achievements, national and local institutions decided to transform the area that had hosted the Expo into a new hub of research, knowledge, and innovation within a large urban park dedicated to scientists, doctors, students and entrepreneurs. The heart of this innovation district would be a new research institute for life sciences, inspired by major international centres, with cutting-edge technology platforms, capable of engaging the country's entire scientific community and attracting investments and talents from around the world.

This is how Human Technopole was born, established by Law 232 of December 11, 2016, precisely with the aim of creating a multidisciplinary, nationally significant, integrated scientific and research complex in the fields of health, genomics, data and decision science, capable of acting as a leverage effect to attract other crucial players to the area for the establishment of a life sciences innovation ecosystem.

The approval of the Statute of Human Technopole in March 2018 marked the beginning of a visionary project that in just 4 years would go from 0 to 300 people including researchers, professionals, and collaborators involved from 27 different countries; from 500sqm of office space to 30,000sqm of laboratories and workspaces[1]. All under the guidance of Prof. Iain Mattaj, the first Director of Human Technopole, a Scottish biochemist, former Director of the European Molecular Biology Laboratory in Heidelberg, and President of the RNA Society, chosen on the basis of a rigorous selection process carried out by an international Search Committee led by the Nobel Prize winner in Chemistry 2008, Martin Chalfie.

Within a few years, Human Technopole not only succeeded in an extraordinary operation of "brain drain," selecting for the scientific leadership of the genomics, neurogenomics, structural biology, computational biology, and health data science centres researchers of international stature, with professional backgrounds carried out predominantly abroad, but also initiated the construction of its own campus with cutting-edge research infrastructures.

In 2027, once completed, the Campus will house not only the laboratories and facilities envisioned by the Human Technopole Strategic Plan, but also the National Platforms envisioned by the additional activities entrusted to the Institute by Law 160/2019. In fact, among Human Technopole's missions is to design, build, and manage high-tech infrastructures and make them accessible in a competitive manner to meet the needs of the national scientific community in the life sciences sector. The Platforms will be identified through consultations with the entire scientific

[1] July 2022 data

community and will complement the facilities of Human Technopole for the benefit of Italian research.

Despite the institute's young age and the need to focus its initial efforts on recruiting staff and building the necessary infrastructure to support its mission, numerous activities have already been carried out in support of the national scientific community and stakeholders. From the funding of the Early Career Fellowship Programme – an initiative aimed at supporting the professional development of deserving researchers, helping them start their own independent research activities in Italy, now at its second edition – to training activities, and technology transfer support for the life sciences supply chain. Not to mention the countless outreach activities aimed at strengthening the confidence of our fellow citizens towards science.

Meanwhile, around Human Technopole, the innovation district has been growing. The MIND – Milano Innovation District area, whose urban reconversion project is the result of a major public-private partnership between Arexpo, the majority-public company that owns the area, and Lendlease, an Australian multinational, is being populated. Following the relocation of the IRCCS Ospedale Galeazzi-Sant'Ambrogio to the district, construction work on the Milan State University Science Campus has also begun. These public "anchors," together with the development of Human Technopole, have already fostered the attraction of numerous private companies in the life sciences sector, which are settling in the district.

Seven years after the closing of Expo Milano 2015, the gamble of that all-important legacy has thus been taken up and is in full realisation and expression. At the heart of this ambitious project, a large science and innovation park that seemed almost visionary, Human Technopole is a beating heart in constant evolution. This report, following up on the provisions of Law 160/2019, aims to summarise, for the benefit of the founding Ministries and Chambers, the activities carried out and planned in the biennium 2020-2021.

2. VISION AND TARGETS

Scientific excellence is the guiding principle of all Human Technopole (HT) activities. HT's vision is that of an internationally competitive research institute applying the highest standards in biomedical research. Human Technopole staff are recruited through open international calls and rigorous, merit-based selection procedures carried out by experts, internal and external, in their respective fields of expertise. The goal is to attract the best scientific talents by providing them with an optimal environment to pursue their research, as well as to help them create a dynamic, constantly evolving environment that allows for the continuous renewal of the institute's expertise and scientific profile. At the same time, another objective of Human Technopole is to generate a pool of highly qualified researchers who, after their time at the institute, will be able to enrich the national scientific community, exerting a beneficial, long-term cascading effect on the country's system.

Human Technopole, besides the aim of becoming an internationally competitive research institute, aspires to serve the community by providing access to high-level technology platforms and offering the best training opportunities also through collaborations of research and coordination in specific areas.

In addition, Human Technopole's research vision is based on a mix of fundamental and translational. Human Technopole expresses broad expertise in basic research in areas relevant to the understanding of human biology and physiology. Translational research, more medically oriented, will instead be conducted largely in collaboration with external organisations and industrial and clinical-hospital partners.

Human Technopole thus aims to enrich and contribute to the improvement of the national system, setting itself as a reference point for the Italian life sciences academic community.

In summary, our mission is as follows:

- Carrying out **frontier research in the life sciences**, aimed at developing innovative approaches for personalised and preventive medicine.
- Realise and manage **high-tech scientific services and facilities** to be **made available to the national scientific community**, responding to the needs of national and international life sciences researchers.
- Organise and provide **development and career opportunities** for the next generation of scientists.
- Driving innovation and progress by promoting **technology transfer** and engaging in relationships with industry to foster the transformation of scientific discoveries into tangible applications that benefit patients and society.
- **Disseminating scientific activities and results** to reinforce the message that science is a public good.

A section of this Report is devoted to each of these aspects.

3. OUR RESEARCH

3.1 The scientific context

People's health, aging, and quality of life are decisively influenced by a combination of internal factors – principally linked to the genetics of each individual – and external ones – such as lifestyle and the environment. Contemporary scientific research must take these into account in the identification of treatments that are increasingly targeted to the individual patient and his/her peculiarities, with the twin goals of providing better care and containing healthcare costs.

Scientists can now take advantage of the technological advances of the past decade, which have made possible:

- the investigation of the human genome and numerous other aspects of biology, including the epigenome (the changes to the genome that often occur in response to the environment)
- the transcriptome (all RNAs transcribed from the genome)
- the proteome (all the proteins produced by RNAs)
- the metabolome (all the metabolites present in a cell, organ, tissue, or organism)

In parallel, digital technologies and advanced computational analysis offer tools to study datasets related to a multitude of information about increasing numbers of individuals.

Thanks to these new tools, critical biological questions, directly related to human health, can be addressed as never before by studying directly human subjects or, if necessary, by using model organisms and other investigative systems.

The integration and exploitation of information from the use of new technologies and available tools have increased the possibilities for scientists to develop layered approaches and better strategies, more focused on fighting or preventing diseases in a "personalised" approach to health, where information about the genetic composition of individuals, or of their diseased tissue, is used to select the most appropriate interventions.

Moreover, the current availability of innovative data and technologies has opened unexplored scenarios for scientists in the study of new strategies for public health or for improving the management of healthcare systems.

3.2 Research at Human Technopole

Research goals and activities for the five-year period 2020/2024 were detailed in the Human Technopole multi-year Strategic Plan, drafted by the Institute's scientific leadership, assessed by its Scientific Advisory Board, and approved by the Supervisory Board in October 2020. The Strategic Plan represents the central axis of Human Technopole's strategy to contribute to research in the life sciences with a comprehensive and interdisciplinary approach to the study of human biology, aimed at understanding the fundamental mechanisms that regulate physiology and disease.

Indeed, Human Technopole's research aims at advancing our understanding and developing new therapeutic strategies for various groups of chronic and degenerative diseases, such as: cancer and cardiovascular diseases and their intermediate phenotypes; neurodegenerative and

neurodevelopmental disorders, such as autism and intellectual disabilities; rare and orphan diseases, such as primary ciliary dyskinesia; respiratory diseases, such as cystic fibrosis.

Five major areas, complementary and functional to biomedical and health research, form the basis of Human Technopole's research strategy, represented by the five research centres:

- Genomics
- Neurogenomics
- Structural Biology
- Computational Biology
- Health Data Science

3.3 The Research Centres

The Research Centre for Genomics

Genomics is an essential component of modern biomedicine. Research in this field aims to identify the mechanisms that regulate gene expression and how inherited genetic information give rise to differences between individuals that are relevant for health and well-being.

Genomics research at Human Technopole consists of two complementary research programmes: one in functional genomics led by Dr. Piero Carninci, and the other in medical and population genomics led by Prof. Nicole Soranzo. The goal is to help characterise the genetic variability and the uniqueness of the environment of Italian population to improve the understanding of genetic causes of several diseases prevalent in the population, thus generating additional potential for both research and clinical purposes.

The Research Centre for Genomics consists of seven research groups:

- Bienko Group
- Calviello Group
- Carninci Group
- Domínguez Conde Group
- Glastonbury Group
- Soranzo Group
- Soskic Group

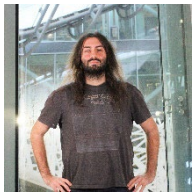
Bienko Group

Magda Bienko, Research Group Leader
Magda Bienko graduated in Biotechnology from the Jagiellonian University in Krakow in 2005. She then joined the Dikic Lab at Goethe University in Frankfurt, Germany, where she obtained her PhD in Biochemistry and Molecular Biology in 2011. During her PhD, she analyzed the role of ubiquitin in the regulation of DNA damage and pioneered the discovery of ubiquitin-binding domains involved in the regulation of translesion synthesis. In 2015, she was appointed Associate Professor at the Karolinska Institute and Fellow at the Science for Life Laboratory in Stockholm, Sweden, where she started her own laboratory. Winner of an ERC Starting Grant, she helped develop a novel sequencing method for mapping DNA double-strand breaks along the genome.

The Bienko Group aims at understanding the design principles and mechanisms shaping the spatial arrangement of DNA, RNA, and proteins in the mammalian cell nucleus. The Group

analyses how the three-dimensional genome architecture instructs and/or is instructed to perform fundamental processes such as DNA replication, transcription, or repair. In particular, the research is focused on understanding how chromatin constituents are arranged and what factors and mechanisms mediate the spatial organisation of chromatin in the nucleus. Furthermore, research seeks to understand how mutations and genomic alterations associated with prevalent disorders such as cancer generate in the context of the 3D genome and, in turn, how they disrupt the structure and functions of the 3D genome to exert their pathogenic effects. To this end, going beyond the cutting-edge, new sequencing and microscopy methods are being developed (at single cell), as well as new mathematical modelling approaches.

Calviello Group



Lorenzo Calviello, Research Group Leader
Lorenzo Calviello obtained a Master's degree in Molecular Biology at the University of Pisa and in 2017 obtained a PhD at the Berlin Institute for Medical Systems Biology at MDS Berlin during which he developed computational methods for the analysis of RNA-sq and Ribo-seq datasets, focusing on the discovery of translated Open Reading Frames, quantification of translation on alternative transcript isoforms and integration with tandem mass spectrometry data. From 2018 to 2021, he was a Postdoc at the University of California at San Francisco in Stephen Floor's lab to study translational control by RNA helicases and the consequences of their misregulation in disease, with a focus on neurodevelopmental disorders.

The Calviello Group studies post-transcriptional gene regulation, employing computational and experimental methods that revolve around the omics of translation, a fundamental process that determines the functions of the transcribed genome and influences the cytoplasmic fate of mRNAs and proteins. Some areas of investigation include:

- Quantifying the control of translation between cell types and states. RNA cis-regulatory elements and RNA-binding proteins (RBPs) can modulate protein synthesis from mRNA, providing an additional mode of control of gene expression. Decades of detailed molecular investigations into protein synthesis have uncovered multiple connections between mRNA maturation, translation, and degradation. Despite the enormous amount of data that can illustrate these processes at the transcriptome level with great accuracy, an analytical framework capable of quantifying and predicting gene regulation that considers these different steps in the gene expression cascade is lacking.
- Characterising the role of heterogeneous RNPs and their dynamics along the mRNA. The action of multiple ribonucleoprotein (RNP) complexes orchestrates the tight control of cytoplasmic gene expression. An important example is the human ribosome, which undergoes drastic changes as it scans mRNA and mediates protein synthesis. Recent advances in the analysis of RNP complexes have revealed hundreds of regulatory factors that interact with the ribosome during the translation cycle. However, our knowledge of the functions of different ribosomal complexes remains very limited.
- Alternative RNA processing and its contribution to protein synthesis and cell physiology. RNA sequencing (RNA-seq) data have allowed researchers to quantify the expression of thousands of genes, from more canonical examples of protein-coding genes to transcripts with unknown functions. Furthermore, different isoforms of transcripts from the same genes often show other and often tissue-specific parts, highlighting the need for deeper investigation into gene regulation. For many genes, computational analysis of ribosome profiling data (Ribo-seq) has provided evidence for marked diversity in the translation and degradation of different isoforms from the same genes, providing an essential window

into the cytoplasmic fate of thousands of transcripts. However, the physiological relevance of the presence of many transcripts for the same gene is largely unknown.

- Proteogenomics applications between RNA and protein. RNA sequencing technologies are essential for detecting expressed transcripts and identifying synthesized proteins. As several studies have shown, careful analysis of Ribo-seq profiles can reveal protein synthesis events with high confidence and aid the discovery of new proteins translated from upstream Open Reading Frames (uORFs), long non-coding RNAs (lncRNAs) and different transcript isoforms. Despite these recent promising results, integrating transcriptomics with the complex world of proteome dynamics, considering regulation by post-translational modifications, the presence of protein isoforms, and the subcellular localisation and function of proteins remains an open challenge in the post-genomic era.

Carninci Group

Piero Carninci, Head of Genomics Research Centre – Functional Genomics
Piero Carninci is a geneticist, currently Team Leader of the Laboratory for Transcriptome Technology and Deputy Director of the RIKEN Centre for Integrative Medical Sciences in Yokohama, Japan. Graduate and PhD student at the University of Trieste, Piero Carninci has lived in Japan for over 20 years and is responsible for the creation and development of several new technologies for DNA and RNA sequencing and analysis. He has participated in and led numerous large-scale national and international initiatives, such as FANTOM, ENCODE and the Human Cell Atlas. Piero Carninci holds 50 patents and has won numerous awards.

In recent years, genomic studies have identified multiple functions for the non-coding genome and transcriptome, including regulating gene expression in all cells, tissues, and organs. However, there are still many aspects to be investigated. Adequate gene regulation, such as the dosage of gene expression in each cell, is a crucial factor in both health and disease conditions. To fully understand genome regulation, it is necessary to understand how non-coding regions act together in all the different cells and tissues of the human body.

The genome produces a wide variety of long non-coding RNAs (lncRNAs). The relatively few well-studied lncRNAs are engaged in numerous activities, including interactions with chromatin; other RNAs and proteins may have regulatory or structural roles. Along with lncRNAs, many proteins regulate the genome, including transcription factors, epigenome modifiers, and other proteins interacting with the DNA. All these molecules generally form complexes that interact with and regulate chromatin, promoters, and enhancers in the human body that have high cellular specificity in different genetic backgrounds under both physiological and pathological conditions.

To address these challenges, the Carninci Group strives to develop and use a wide range of technologies to comprehensively study the non-protein-coding portion of the genome, its function, and the set of its interactions (interactome).

Some objectives of the group are:

- Study the role, structure, modifications, and interactome of the SINE elements incorporated in antisense lncRNAs involved in the regulation of translation of the gene on which they act. These RNAs, called SINEUPs, are the first class of lncRNAs known to positively regulate protein synthesis and reveal fundamental aspects of RNA biology.
- Development and standardisation of transcript profiling technologies such as cap-analysis gene expression (CAGE) to develop a universal and finely quantitative transcriptome technology to be used ultimately to profile single cell populations in tissues.

- Further development of approaches used to detect the interactomes of molecules, such as RADICL-seq technology, which detects RNA interactions with chromatin globally and identifies RNAs that are likely to regulate gene activity.

Domínguez Conde Group

Cecilia Domínguez Conde, Research Group Leader
After training as a pharmacist at the University of Seville, Cecilia Domínguez Conde completed a PhD in immunology at the Research Centre for Molecular Medicine (CeMM) in Vienna, where her work focused on dissecting the genetic cause of molecularly undiagnosed primary immunodeficiencies using exome sequencing. In 2019, Cecilia joined the Teichmann lab at the Wellcome Sanger Institute, where she focused on analyzing the diversity of human immune cell types in lymphoid and non-lymphoid tissues as part of the Human Cell Atlas initiative.

The Domínguez Conde Group seeks to understand human immunity in children's early childhood and immune-mediated diseases in children, using state-of-the-art genomic and computational methods.

The Group harnesses the unprecedented power of single-cell multimodal technologies to identify cellular phenotypes associated with specific development stages. The studies focus on adaptive immune responses, which constitute the long-term immunological memory mediated by somatically recombined antigen-specific receptors expressed by lymphocyte lineage of T and B lymphocytes, dissecting the phenotypic changes T and B cells undergo through development and human tissues. Tracking unique antigen receptors will reveal the dynamic changes in antigen-specific receptor repertoires in connection with clinical outcomes such as viral infections or symptoms of autoimmunity.

Rare genetic conditions that impair immune development lead to congenital errors of immunity that manifest as early-onset immunodeficiency, autoimmunity, or immune dysregulation. Recent advances in genome sequencing have led to a wealth of genetic data that has improved our understanding of the genetics of rare diseases. However, a detailed understanding of the functional impact of individual genetic variants is still lacking. To address this challenge, in-depth phenotyping of primary patient material will be combined with molecular characterisation of specific genes and genetic variants using genome engineering.

The Group's approaches include cutting-edge genomic technologies including single-cell RNA sequencing (scRNA-seq) combined with receptor sequencing of single-cell T and B cells; single-cell chromatin sequencing assay accessible to transposase (scATAC-seq); short- and long-read genome sequencing and engineering of the CRISPR genome.

Glastonbury Group

Craig Glastonbury, Research Group Leader
Craig Glastonbury is a geneticist with expertise in the use of machine learning applied to biology. After completing his PhD at King's College London, Craig Glastonbury was a Postdoc at the Big Data Institute (BDI) and the University of Oxford and was Lead Machine Learning Researcher at BenevolentAI in London, leading the genetics team in the Precision Medicine team.

The Glastonbury Group develops and applies machine learning methods to understand the genetic basis of a broad spectrum of complex diseases. With the advent of population-scale biobanks, it's possible to collect datasets on hundreds of thousands of individuals. One type of data is imaging data, a high-dimensional and information-rich modality for human phenotyping.

The Glastonbury Group is interested in applying machine learning techniques to any discovery related to human genetics (Variant → Gene → Phenotype). One of the Group's key objectives is to extract cellular and disease phenotypic mechanisms from histopathological images. Daily use of Whole Slide Imaging (WSI) of tissue sections diagnoses various conditions, such as inflammatory bowel disease, oncological and neurological post-mortem diseases.

With supervised and unsupervised machine learning techniques, it is possible to extract very precise cell and tissue phenotypes and use them to characterise the causes and consequences of an underlying disease. By combining such images derived from phenotypes with genetic information (e.g., genotyping, exome, whole-genome sequencing), it is possible to begin to distinguish mechanistically how a genetic variant contributes to increased disease risk and how that risk is shared between diseases and phenotypes

Soranzo Group

Nicole Soranzo, Head of Genomics Research Centre - Population & Medical Genomics
Nicole Soranzo has been Professor of Human Genetics at the Medical School of the University of Cambridge since 2015 and Senior Group Leader at the Wellcome Sanger Institute in Hinxton (UK) since 2017. She graduated in biology from the University of Milan in 1994 and received a PhD in genetics and biotechnology from the University of Dundee in the UK in 1999. Between 1999 and 2002, she carried out research at the University of Milan and between 2002 and 2005 at University College London, applying genetic analysis to the study of human evolution. Between 2005 and 2007, she worked in the pharmaceutical industry in the USA, applying human genetics to drug improvement. Back in the UK, she set up her own research group at the Wellcome Trust Sanger Institute in Hinxton in 2009. For her work, she has been awarded several honours including, in 2016, "Italy's Most Influential Researcher and Scientist" by the National Observatory on Women's Health (ONDA).

A significant challenge in modern biology and medicine is understanding how genetic variations influence human traits and diseases. The Soranzo Group uses high-resolution, population-scale genomic analysis of phenotypes representing different hierarchical levels of gene regulation, cellular and organismic phenotypes to unravel these complex relationships.

The Group also investigates the aetiology of complex diseases and uses the power of certain genomic technologies (e.g., transcriptomics and epigenomics) to foster a better understanding of molecular and functional fundamentals of the blood and immune system. By exploiting multi-omic technologies, the Soranzo Group also intends to contribute to the prioritisation of therapeutic targets in human diseases. Indeed, mapping changes in metabolic function associated with disease loci provides information on understanding the pathophysiological and molecular components of the disease and can be used to prioritise new biological targets in programmes for new drug discovery and repositioning of existing drugs. Current efforts use a rare variation with loss of function (LoF) to study the phenotypic impact of inactivation of target genes of certain drugs (www.opentargets.org). In a healthy individual, these variants can provide evidence of safe modulation of that target to reduce the risk of disease.

Soskic Group

Blagoje Soskic, Research Group Leader
After completing his studies in molecular biology at the University of Belgrade, Blagoje Soskic obtained a PhD in Immunology at University College London in 2016. From 2016 to 2022, he was a postdoctoral fellow at the Wellcome Sanger Institute in Cambridge, UK, where he worked on studying the impact of genetic variation on T-lymphocyte function.

Immune-mediated diseases are chronic and disabling conditions that affect large numbers of people. Genome association studies (Genome wide associations studies, GWAS) have mapped hundreds of DNA positions (loci) associated to the risk of developing immune-mediated diseases, opening enormous potential for discovering new disease mechanisms and identifying new therapeutic targets. However, disease variants remain hard to study, for they are often located in non-coding regions of the genome and their activity is evident in specific cell types or states.

The Soskic Group uses a wide range of genomic and immunological experiments to study variations at the level of the human immune system to understand how disease variants affect cellular processes and cell-cell interactions. The Group focuses on understanding the interaction between T and B cells, which is central for protective immunity and is involved in a wide range of immune diseases. By studying variations in gene expression, chromatin activity, and cellular phenotypes, we seek to understand the molecular and genetic control of B-cell activation and antibody production. This study is critical for understanding the genetics of autoimmune diseases, infections, and vaccine responses.

3.3.2 The Research Centre for Neurogenomics

The Research Centre for Neurogenomics studies the underlying mechanisms of human neuropsychiatric and neurological diseases, ranging from neurodevelopmental to neurodegenerative disorders, combining basic and translational research through different experimental systems and computational approaches (brain organoids, animal models and epidemiological cohorts) to probe the structure, function and development of the nervous system at multiple levels of resolution.

The Head of the Research Centre for Neurogenomics is Prof. Giuseppe Testa, and the Centre consists of five research groups:

- Davila-Velderrain Group
- Harschnitz Group
- Kalebic Group
- Taverna Group
- Testa Group

Davila-Velderrain Group

Jose Davila-Velderrain, Research Group Leader
Jose Davila-Velderrain is a Mexican-born computational systems biologist interested in developing a deeper understanding of the diversity and dynamic behaviour of human brain cells. Jose has worked as a postdoctoral researcher at the Massachusetts Institute of Technology, the Broad Institute of MIT and Harvard.

The research conducted by the Davila-Velderrain Group involves combining theoretical and computational tools with genomic measurements on single cells to characterise and study the cellular complexity of the brain and its vulnerabilities. The ultimate aim is to understand how brain cells acquire functional identities during development and why neuropathologies can compromise cell circuit functionality, despite the robustness and plasticity achieved through the evolutionary process.

The Group studies the human brain to reveal fundamental concepts about the mechanisms that regulate cell identity and the dynamics of the cellular state. Other organisms' brains are analyzed to identify the properties of human brain preserved or diversified during the evolutionary process.

From a methodological point of view, the interest lies in developing and using computational technologies that integrate tools and concepts from machine learning, network theory, and statistical physics to produce conceptually intuitive resources for the benefit of the life sciences community.

Harschnitz Group

Oliver Harschnitz, Research Group Leader
Oliver Harschnitz received his medical degree from Maastric University (The Netherlands) in 2009 and completed his PhD in the groups of Leonard van den Berg and Jeroen Pasterkamp at Utrecht University Medical Centre (The Netherlands) in 2017. During his PhD, Oliver developed pluripotent human stem cell models to study inflammatory neuropathies and motor neuron diseases. From 2017 to 2021, he continued his postdoctoral research in Lorenz Studer's lab at the Sloan Kettering Institute (USA) studying host-virus interactions in the central nervous system using human pluripotent stem cell models and forward genetic screens

Neuro-immunological disorders, such as viral and autoimmune encephalitis, are potentially fatal if left untreated and can cause severe neurological deficits in survival patients. In the past, studies on human neuro-immunological diseases have mainly relied on autopsy or biopsy material, and the lack of continuous access to primary cells of the human central nervous system has precluded most mechanistic studies. Guided differentiation of human pluripotent stem cells (hPSCs) into the three germ layers allows the derivation, analysis, and disruption of – at least potentially – any in vitro human cell type. Consequently, hPSC technology offer an exciting approach to studying neurological and neuro-immunological diseases.

The Harschnitz Group is particularly interested in the molecular and cellular mechanisms underlying susceptibility to viral and autoimmune diseases of the human nervous system and the molecular mechanisms driving chronic neuroinflammation. The hPSC technology is used to establish state-of-the-art in vitro models to study neuro-inflammation directly in disease-relevant human cells.

The Group implements a multidisciplinary approach, combining state-of-the-art human stem cell models with chemical or genetic tests, single-cell analysis, and advanced live cell imaging technology. In this way, human stem cell-based disease models can be improved and contribute to a deeper understanding of the neuro-immunological disease. The aim is to identify therapeutic targets with direct translational implications for patients suffering from viral or autoimmune encephalitis.

Kalebic Group

Nereo Kalebic, Research Group Leader
After graduating in Molecular Biology from the University of Zagreb in Croatia, Nereo Kalebic completed his PhD in Molecular Biology at the European Molecular Biology Laboratory (EMBL) and the University of Heidelberg. During his PhD, he studied the role of post-translational modifications of microtubules in the development and function of the nervous system. From 2013 to 2019, he performed postdoctoral research in Wieland Huttner's group at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden studying the development and evolution of the human neocortex.

The neocortex is the part of the brain involved in several higher cognitive functions, including language, and is considered the basis of the unparalleled cognitive abilities of humans. During

the evolution of the human brain, the neocortex has undergone a significant expansion. Cognitive disorders often result from an alteration in the size or shape of the neocortex caused by defects in the proliferation of neural stem cells in the early stages of brain development. In the adult brain, tumour cells can exploit the same molecular mechanisms, causing uncontrolled proliferation. However, our knowledge of the mechanisms underlying these processes is still minimal.

The Kalebic Group's research focuses on the molecular and cellular mechanisms underlying the development of the human neocortex and their implications in neurodevelopmental disorders and brain tumours. In the context of neurodevelopment, the molecular and cellular characteristics of neural stem cells are being studied, which, if impaired, can lead to an alteration in the size and shape of the neocortex, leading to intellectual disabilities, including Down syndrome. In the context of brain tumours, interest is directed at the biology molecular and cellular biology of glioblastoma stem cells to identify new targets associated with cancer proliferation and invasiveness.

The Group implements a multidisciplinary approach across all biological scales, combining state-of-the-art molecular and genetic techniques, CRISPR/Cas9 genome editing, advanced live imaging, and computational tools. These techniques are applied to various model systems, including primary human samples, brain organoids, and animal models.

Taverna Group

Elena Taverna, Research Group Leader
After graduating in Biology from the University of Milan and obtaining a PhD in Pharmacology and Toxicology from the CNR Institute of Neuroscience in Milan, Elena Taverna worked for 15 years for the Max Planck Society, where she developed a technique for tracking and manipulating single neural stem cells in tissues during her post-doctoral studies and subsequently served as Senior Staff Scientist and Project Leader. She also developed a robot for high-throughput analysis of single neural stem cells in the tissues.

The neurons forming our brain are produced from neural stem cells during embryonic development. Stem cells and neurons must be produced at the right time for the brain to achieve its correct size and structure development. This spatiotemporal coordination is particularly interesting when placed in the clinical context, as changes in the composition, size, and complexity of the neural stem cell assembly are associated with neurodevelopmental disorders.

The Taverna Group's research aims to uncover the cellular and molecular logic underlying brain development and synapse formation regarding physiology, disease, and evolution. A multidisciplinary approach that combines robotics and developmental neuroscience, multicellular multi-omics, and cell biology is adopted.

There are three main directions of research:

- Stem cells meet robotics: to achieve a comprehensive definition of cell identity in the development of the brain, a fully automated robot will be developed for single-cell manipulation and multimodal analysis of neural stem cells and neurons in primary brain tissue and human brain organoids.
- Stem cell identity in brain development: the study of how basic cellular processes occurring within the cell can influence neural stem cells behaviour and brain development under physiological and pathological conditions. In particular, the focus will be on cell polarity and the organelles that generate polarity.

- Time and the cell biology of neurons: the study of the role of time in the regulation of synapse formation and the ruling of neuronal function during the developmental process and in some human pathologies.

Testa Group

Giuseppe Testa, Head of Neurogenomics Research Centre
Giuseppe Testa is a clinician, Professor of Molecular Biology at the Università Statale di Milano and Director of the High-Definition Disease Modelling Lab: Stem Cell and Organoid Epigenetics at the European Institute of Oncology. After graduating from the University of Perugia, a PhD at the European Molecular Biology Laboratory and a post-doctoral fellowship at the Max Planck Institute for Cell Biology and Genetics, Giuseppe Testa continued his studies by completing a master's programme in health ethics and law at the University of Manchester. Subsequently, he held various academic positions at top institutions in Europe and the United States. Giuseppe Testa has authored numerous publications in prestigious international journals, including Science and Nature. In 2022, he was appointed as a member of EMBO, the European Molecular Biology Organisation.

The Testa Group exploits the unprecedented potential of cellular reprogramming to study the molecular basis of human neuropsychiatric and neurological diseases (NPDs), analyzing the dynamics of their unfolding in pathophysiologically relevant models and straddling multiple scales of analysis: from single-cell resolution to organism function.

One of the most tangible results of somatic cell reprogramming has been a paradigm shift in our ability to model human disease, which has hitherto been characterised by some fundamental limitations: the limited availability of diseased primary tissues, particularly for disorders of the nervous system, and the difficulty of reconstructing developmental and patient-specific trajectories during the unfolding of diseases.

The Group is pursuing the modelling of NPDs with human induced pluripotent stem cells (iPSCs) coupled with differentiation into relevant lineages through many complementary experimental paradigms, including:

- glutamatergic neurons by inducing the expression of neurogenin-2 (NGN2)
- neural crest stem cells and three-dimensional brain organoids to recapitulate some salient stages of early brain development, including the diversity of cell populations that is unique to the human brain level

This allows the genetic and environmental components of NPD pathogenesis to be distinguished by means of several large-scale "omics" approaches at single cell resolution integrated with high-processivity imaging and functional assays in vitro and in vivo.

The Testa Group focuses on a number of highly informative syndromes that occur with intellectual disability and autism spectrum disorders that are caused by mutations or alterations in the dosage of the epigenetic regulators and transcription factors, including Williams-Beuren syndrome and 7q11 .23 micro-duplication syndrome, Kabuki syndrome, autism spectrum disorders ADNP-related, Weaver syndrome, Gabriel-Head-DeVries syndrome, as well as on paradigmatic environmental factors that negatively impact neurodevelopment – i.e., endocrine disrupting chemicals.

Finally, the spectrum of human neurodevelopmental disorders also allows to investigate the logic of gene regulatory networks underlying the evolution of the modern human face and brain, integrating the analysis of craniofacial dysmorphologies and brain alterations to shed light on the evolutionary and developmental trajectories underlying the current human condition.

3.3.3 The Research Centre for Structural Biology

The Research Centre for Structural Biology aims to contribute to the knowledge of the structure of macromolecules and macromolecular complexes in order to understand their functioning.

The Centre features a state-of-the-art technology platform for Cryo-Electron Microscopy, which uses "single particle analysis" (SPA) and electron cryo-tomography to obtain high-resolution structures of macromolecules, both isolated and in their cellular context. Complementary approaches, such as X-ray crystallography, fluorescent single-molecule microscopy, native or cross-linking-coupled mass spectrometry, and a wide range of biophysical analysis, are also used to obtain details on the mechanisms of the functioning of macromolecules.

Dr. Alessandro Vannini and Dr. Gaia Pigino are, respectively, Head and Associate Head of the Centre.

The Research Centre for Structural Biology is divided into five research groups:

- Casañal Group
- Coscia Group
- Erdmann Group
- Pigino Group
- Vannini Group

Casañal Group

Ana Casañal, Research Group Leader
After completing her Master's degree in Advanced Biotechnology at the University of Malaga-International University of Andalucia, Ana Casañal completed her PhD in Biotechnology at the Department of Molecular Biology and Biochemistry, University of Malaga. From 2014 to 2020, she was a postdoctoral researcher and EMBO Long Term Fellow at the MRC-Laboratory of Molecular Biology, Cambridge, UK. The focus of her research is the study of the characterisation of multi-protein complexes involved in mRNA polyadenylation.

Gene expression can be regulated at several levels, allowing organisms to respond rapidly to specific cellular stimuli while maintaining a stable internal environment. This regulation is often achieved through chemical signals on DNA and proteins. Recently, signals on RNA have also been described as critical regulators of gene expression: they are involved in essential cellular roles, such as development and stress, and their deregulation is linked to human disorders, including cancer, infertility, and depression.

Despite their fundamental importance, the mechanisms that determine how these signals are added to the RNA and regulated, remain poorly understood.

The Casañal Group combines cryo-EM technology with biochemical and biophysical methods to determine the three-dimensional structure of the macromolecular machinery that adds and reads signals on RNA. This approach will help understand how RNA modifications work within the cell and how they affect disease, helping to discover new therapeutic targets for drug development.

Coscia Group

Francesca Coscia, Research Group Leader
Francesca Coscia graduated in Chemistry from the University of Naples, where she also obtained a Master's degree in Biostructures. She subsequently completed her PhD at the Institute of Structural Biology in Grenoble. For her work, she received the Brenner Prize for Research at MRC-LMB in 2020 and the European Thyroid Association Lecture in 2021, and most recently, the Thyroid Pathophysiology Prize from the Accademia Nazionale dei Lincei. In 2022, she received an ERC Starting Grant for the THYROMOL project, to study the regulation of thyroid hormone from atoms to organoids using advanced molecular imaging techniques.

The thyroid gland is a natural bioreactor where rare dietary iodine is stored and used to synthesize thyroid hormones, iodine molecules essential for metabolism and development in all vertebrates. In humans, thyroid dysfunction severely affects cardiovascular homeostasis, metabolism, development and brain function, with an increasing incidence worldwide. At present, the understanding of the molecular events underlying thyroid hormone synthesis and major thyroid diseases is far from complete.

At the MRC Laboratory of Molecular Biology (Cambridge, UK), Francesca Coscia used Cryo-EM technology to study the structure of human thyroglobulin, the precursor protein of thyroid hormones. This work is the starting point for answering many questions about the levels and action of thyroid hormones, which the Group in Human Technopole aims to address through multiple approaches such as structural biology, biochemistry, and cell biology. This research seeks to advance knowledge on thyroid biology and progress towards studying specific thyroid diseases, such as autoimmune diseases, congenital hypothyroidism, and thyroid tumours.

Erdmann Group

Philipp Sebastian Erdmann, Research Group Leader
Philipp S. Erdmann is a chemical biologist and microscopist. After graduating in chemistry in Würzburg, he completed his doctorate in biochemistry at the Ludwig Maximilian University in Munich, developing projects in optogenetics. He then worked at the Massachusetts Institute of Technology in Boston and was Group Leader at the Max Planck Institute for Biochemistry in Martinsried, Germany.

The Erdmann Group focuses on and analyses the effects of liquid-liquid phase separation (LLPS) using cryo-electron tomography. LLPS is often involved in crucial processes of communicable and non-communicable diseases, including viral infections and neurodegenerative diseases.

Compartmentalisation is a feature of cellular organisation. It separates incompatible chemical reactions, enables the creation of specialised microenvironments, and can make chemical reactions more efficient by limiting the molecular actors to partial volumes. Traditionally, it refers to membrane-bound compartments such as the endoplasmic reticulum (ER), Golgi apparatus, or mitochondria. Membranes in these organelles not only represent separating interfaces but can also serve as two-dimensional platforms for organizing reaction pathways.

In recent years, a new concept of cytoplasmic organisation has emerged: membrane-free compartments resulting from liquid-liquid phase separation (LLPS). Examples of such compartments in eukaryotes include the Cajal bodies and the nucleolus. It is becoming increasingly evident that LLPS is of great importance for understanding the pathogenesis of various communicable diseases, neurodegenerative disorders, and aging. Consequently, methods to study liquid-liquid phase separation within intact cells ("in situ") are needed.

To meet this need, the Erdmann Group uses a combination of cryo-fluorescence microscopy (FLM), cryo-lift out (LO), cryo-focalised ion beam milling (FIB), and cryo-electron tomography (ET) to study the liquid-liquid phase in separate compartments within vitrified cells and tissues. A constant effort is put on improving the accuracy of this pipeline by developing new software and hardware.

Pigino Group

Gaia Pigino, Associate Head of Structural Biology Research Centre
Gaia Pigino is a biologist. She completed her PhD at the University of Siena, and subsequently worked as Post Doc in Takashi Ishikawa's group at ETH Zurich and since 2012 as Group Leader at the Max Planck Institute for Molecular Cell Biology and Genetics in Dresden. Gaia Pigino is the author of more than 30 publications and has received international awards and research funding, including the Keith R. Porter Fellow Award for Cell Biology in 2018, a European Research Council (ERC) Consolidator grant in 2018 and a German Research Foundation (DFG) grant in 2019. In 2022, she was appointed as a member of EMBO, the European Molecular Biology Organisation.

Cilia are hair-like organelles that extend from the surface of almost all polarised cell types in the human body. They are crucial for various motor and sensory functions during development, morphogenesis, and homeostasis. Sensory cilia act as cellular antennae, detecting environmental and morphogenic signals. Mobile cilia, on the other hand, are used to propel cells themselves or to move fluids on epithelia (e.g., in our lungs). Cilia-related disorders (known as ciliopathies) affect many tissues and organs in various ways.

Ciliary dysfunction is the cause of an increasing number of single-organ diseases and complex syndromic forms, including hydrocephalus, infertility, airway diseases, polycystic kidney, liver, or pancreas diseases, as well as retinal diseases, hearing and smell defects.

The Pigino Group investigates the 3D structure of the molecular components of cilia in their native cellular context and isolation, seeking to understand how they orchestrate specific cilia functions. The work is typically positioned at the interface between structural biology and molecular cell biology. The latest tools and methodologies from both fields are thus combined, from cryo-electron tomography, correlative light and fluorescence microscopy (CLEM) to in vitro reconstituted dynamic systems, genetics, biochemistry, image analysis methods and the more classical cell biology.

The ultimate goal of the Pigino Group is to understand the molecular causes underlying ciliary function and dysfunction to develop possible therapeutic strategies for ciliopathies.

Vannini Group

Alessandro Vannini, Head of Structural Biology Research Centre
Alessandro Vannini is a biochemist. With a degree in Biological Sciences from Roma Tre University and a PhD in Biochemistry and Molecular Biology from Tor Vergata University and Merck, he worked as a specialist in Patrick Cramer's laboratory at Ludwig Maximilian University. In 2012, he moved to the Institute of Cancer Research in London where he served as Principal Investigator and Deputy Head of Division. Alessandro Vannini is the recipient of several awards, including the Wellcome Trust Investigator (2016), and international fundings.

Gene transcription is the first step that regulates the expression of genetic information encoded in a genome and is the basis of cell differentiation and organism development. Eukaryotic gene transcription occurs in the context of highly structured and organised genomes and coordinates numerous events in the nucleus. Eukaryotic transcription relies on three different RNA polymerases: RNA polymerase I (Pol I) transcribes ribosomal RNA, RNA polymerase II (Pol II)

synthesizes messenger RNAs, and RNA polymerase III (Pol III) produces short, untranslated RNAs, including the entire pool of tRNAs, which are essential for cell growth.

For a long time, it has been assumed that only Pol II was regulated, and that Pol I and Pol III didn't require such control, being dedicated to housekeeping genes. However, it is now clear that RNA polymerase III transcription is tightly regulated and is a crucial determinant for the growth of an organism. Deregulation of Pol III has been observed in various forms of cancer, and genetic mutations in Pol III cause severe neurodegenerative diseases.

In addition, Pol III and its associated factors play a vital role in the structure and organisation of the genome. These "extra-transcriptional roles" are played through interactions with other cellular components such as transposons, SMC (Structural Maintenance of Chromosomes) complexes, and specific chromatin remodellers.

The Vannini Group uses an Integrative Structural Biology approach, combining state-of-the-art cryo-microscopy analysis, X-ray diffraction data, cross-linking, and native mass spectrometry. Structural data are integrated with molecular and cellular biology techniques to comprehensively view these fundamental processes and how their misregulation can lead to oncological and neurodegenerative diseases.

3.3.4 The Research Centre for Computational Biology

Human Technopole's Research Centres generate enormous amounts of data. Therefore, close integration with research in computational biology using statistical, computational, and bioinformatics approaches is required to develop solutions for the analysis, management and integration of large-scale data in support of all other research areas.

Through the Centre for Computational Biology, led by Dr. Andrea Sottoriva, Human Technopole intends to develop, host and manage software tools and data resources accessible to the broader biomedical community. The aim is to provide a service to the external community and link international, publicly accessible biomolecular data with national health data.

The Research Centre for Computational Biology is divided into four research groups:

- Iorio Group
- Jug Group
- Pinheiro Group
- Sottoriva Group

Iorio Group

Francesco Iorio, Research Group Leader
Franceso Iorio is a bioinformatician and has been team leader at the Wellcome Sanger Institute in Hixton (UK). Francesco mainly works on bioinformatics methods for drug-genomics, therapeutic target discovery, drug repositioning and big-data analysis in the biomedical field. His work focuses on cancer, rare diseases and neurodegenerative disorders such as Alzheimer's and Parkinson's.

The Iorio Group works between biology, machine learning, statistics, and information theory with the aim of understanding and predicting the role of genomic alterations and molecular traits

derived from other omics in disease processes, in the rewiring of biological circuits, and their impact on therapeutic response in human cancers and other diseases.

The research aims to improve human health by developing algorithms, computational tools, and new analytical methods for integrating and analysing pharmacogenomics and functional genomics datasets to identify new therapeutic targets, biomarkers, and opportunities for drug repositioning.

The Group is contributing to creating a comprehensive map of all genetic dependencies and vulnerabilities in human cancers and developing a computational infrastructure to translate this map into guidelines for early-stage drug development and precision medicine.

It develops, implements, and manages bioinformatic methods and novel tools for the evaluation of preclinical models, pre-processing, analysis, and visualisation of data from genome-editing screenings, for the in-silico correction of specific biases in such data, and for the optimisation of single-guide RNA libraries for aggregated CRISPR-Cas9 screenings and other experimental settings.

The Group's interest also lies in big-data analysis, developing biomedical predictive models based on non-biomedical data, and efficient computer strategies for constrained randomisation useful for testing combinatorial properties in biological networks and large-scale genomic data.

Jug Group

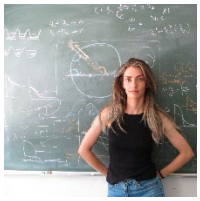
Florian Jug, Research Group Leader and Head of Image Analysis Facility
Florian Jug holds a PhD in computational neuroscience from the Institute of Theoretical Computer Science at the ETH Zurich. His research aims to push the boundaries of what artificial intelligence and machine learning can do to better analyse and quantify biological data. His team makes a strong contribution to the Fiji software (around 100,000 active users) and collaboratively develops methods such as CARE, Noise2Void, PN2V, DivNoising etc. It organises scientific conferences (e.g., the I2K conference), workshops (e.g., the BIC workshops at high-level computer vision conferences) and various practical training courses on machine learning for bio-image analysis (e.g., DL@MBL at Woods Hole) or microscopy (e.g., Quantitative Imaging at Cold Spring Harboe).

Research conducted by the Jug Group is pushing the boundaries of what image analysis and machine learning can do to quantify biological (image) data. The common denominator of these projects is the unquestionable need to analyse large amounts of optical microscopy data without causing impossible amounts of manual data handling and processing to life sciences researchers (i.e., our users and collaborators).

From a computational point of view, the Group is interested in noise reduction and image restoration, object segmentation and tracking, and analysis modules for tasks such as object detection, registration/deformation of nD images, etc.

Besides developing new algorithmic and machine learning solutions, the Jug Group also strongly focuses on merging these methods into modular and reusable software packages. This work develops primarily in the context of Fiji software and Python programming, which is constantly evolving. We strongly believe in the power and flexibility of the image.sc community and their rich universe of open-source solutions are of value and utility to the life sciences community that can hardly be underestimated.

Pinheiro Group



Fernanda Pinheiro, Research Group Leader
Fernanda Pinheiro has a Bachelor's degree in Molecular Sciences and a Specialist degree in Physics from the University of São Paulo, Brazil. She received her PhD in Physics from Stockholm University in 2015, where she worked on collective phenomena in quantum many-body systems with applications to quantum simulation.

The Pinheiro Group's research combines data from laboratory evolution experiments, statistical physics approaches, and mathematical models to map systems biology with the ultimate goal of predicting ecological and evolutionary dynamics.

The most pressing challenges in modern medicine require knowledge of the evolutionary processes of pathogens. Predicting evolution, however, is a theoretical challenge. Evolutionary dynamics depend on cell metabolism and ecological resources. The complexity of this interaction gives rise to solid non-linearities generated by interactions that are often not captured by modelling individual parts but require system-level modelling. Predicting evolutionary dynamics presents additional challenges: we need to do systems biology among genetically diverse organisms and integrate stochastic processes that operate at different scales.

The Pinheiro Group integrates experimental and theoretical research to develop a predictive framework for evolutionary processes under ecological complexity based on models of cellular metabolism. The laboratory is hybrid, theoretical and experimental, with a strong interest in understanding the evolution of antibiotic resistance in microbial communities. It uses systems biology approaches, evolutionary models, computational methods, data analysis, and data from evolutionary experiments, building a solid dialogue between theory and experiment. It uses theory to identify interesting regimes that can optimise experimental designs and biology to motivate new theoretical methods.

Sottoriva Group

Andrea Sottoriva, Head of Computational Biology Research Centre
Andrea Sottoriva is a computational biologist with a background in computer science and physics. After graduating in computer science from the University of Bologna in 2006, Sottoriva received a master's degree in computational science from the University of Amsterdam in 2008. He did research at the National Institute of Nuclear and High Energy Physics (NIKHEF) in the Netherlands where he worked on the ANTARES neutrino telescope experiment. In 2012, he obtained a PhD in computational biology from the University of Cambridge, where he worked at the Cancer Research UK research centre. After postdoctoral work at the University of Southern California, he set up his own lab at the Institute of Cancer Research in London in 2013, where he became Deputy Director of the Centre for Evolution and Cancer in 2018 and then Director in 2020. He has authored numerous studies published in prestigious scientific journals including Science, Nature Genetics and Cancer Discovery. In 2016 Cancer Research UK awarded him the prestigious Future Leaders in Cancer Research award.

The Sottoriva Group deals with deciphering cancer dynamics in patients in terms of growth, progression, and treatment resistance through mathematical and computational approaches applied to multi-omics cancer data, with the aim of predicting the future course of the disease. The Group approaches cancer as a complex system, using rational tissue sampling and integrative genomics as the basis for data generation. It combines laboratory-generated data with mathematical models of tumour evolution and machine learning methods to formulate clinically driven hypotheses and test their impact on cancer treatments.

The Group's work rests on ideas from the field of theoretical population genetics. For decades, population geneticists have developed mathematical tools to make sense of complex genetic data. The Sottoriva Group combines classical evolutionary theory with modern computational and machine learning methods, multi-omics profiling of patient samples, and experimental methods to study tumour evolution quantitatively. The research focuses on:

- Measuring cancer evolution in patients: using intra-tumour heterogeneity to quantify tumour evolution in human malignancies
- Predicting cancer evolution: observing temporal evolution and spatial genomic profiling to predict the disease course
- Designing evolution-informed treatments: developing model systems for evolutionary testing to identify new treatment strategies

The Group has also contributed significantly to the debate between neutral evolution and selection in cancer.

3.3.5 The Health Data Science Centre

The Health Data Science Centre at Human Technopole aims to become a reference institution in the national landscape for health data analysis. The Centre seeks to collect data and information from various sources to integrate clinical data with socio-economic, environmental, and molecular risk factors to identify vulnerability profiles and stimulate targeted prevention strategies. In addition, the Centre will work to promote new solutions for data analysis, developing and integrating new analytical methods with clinical epidemiology and health research in collaboration with national and international partners.

Prof. Emanuele Di Angelantonio, and his Associate Head Prof. Francesca Ieva, lead the Centre. It is the most recently established and has two research groups:

- Di Angelantonio & Ieva Group
- Zuccolo Group

The Health Data Science Centre promotes a Ph.D. programme in Data Analytics and Decision Sciences (DADS) through a collaboration with the Politecnico di Milano.

Di Angelantonio & Ieva Group

Emanuele Di Angelantonio, Head of Health Data Science Centre
Emanuele Di Angelantonio is Professor of Clinical Epidemiology in the Department of Public Health and Primary Care at the University of Cambridge. After graduating in medicine and specialising in internal medicine in Italy and France, he obtained an MSc in medical statistics from the London School of Hygiene and Tropical Medicine and a PhD in epidemiology from the University of Cambridge. During his career he has held important positions at the University of Cambridge, NHS Blood and Transplant (UK equivalent of the National Blood Centre), the European Society of Cardiology (ESC), and the World Health Organisation (WHO). Emanuele Di Angelantonio was awarded the Fellow of the Royal College of Physicians of London (2018) and the Viviane Conraads Achievement Award from the European Association of Preventive Cardiology (2019). He is the author of more than 200 studies published in prestigious journals, including Lancet, JAMA and New England Journal of Medicine.

Francesca Ieva, Associate Head of Research Centre
Francesca Ieva is Associate Professor of Statistics at Politecnico of Milano. She obtained her PhD in Mathematical Models and Methods for Engineering at the Politecnico in 2012, then she was hosted at the MRC Biostatistic Unit in Cambridge before becoming a junior researcher at the Università Statale di Milano (Department of Mathematics) in 2013 and a tenured professor at MOX – Modelling and Scientific Computing lab, within the Department of Mathematics of the Politecnico di Milano, in 2016.

In the Di Angelantonio & Ieva Group, epidemiologists, statisticians, and data scientists work together to bridge the knowledge gap between genotype and phenotype by studying various levels of molecular data to investigate the health status of individuals and populations. To achieve this goal, the Group develops innovative studies that integrate biomolecular data with data from medical records, imaging, and portable medical devices. Both existing and new data generated by population studies are used and analysed using new analytical methods, integrating clinical epidemiology with health research to improve data analysis and interpretation.

The Group aims to generate valuable advances in biology, disease aetiology, risk prediction, early diagnosis, and therapeutic targeting. The methods developed will see application in personalised medicine, with benefits for individual patient health, as well as in population studies using large-scale data, with significant advances in public health, health data analysis, and targeted health policy development.

The Group's research focuses on the development and use of biostatistics and artificial intelligence to investigate risk factors that cause disease and to develop risk prediction models for the development of chronic diseases using different levels of data, including omics, genetics, and from medical records.

Zuccolo Group

Luisa Zuccolo, Research Group Leader
Luisa Zuccolo is an epidemiologist with expertise in causal inference applied to population health. After graduating in Physics, she was awarded a fellowship at the University of Turin in Epidemiology and Cancer Surveillance, which was followed by a pre-doctoral fellowship from the UK Medical Research Council to complete a Master in Epidemiology (London School of Hygiene and Tropical Medicine) and a PhD in Genetic Epidemiology at the University of Bristol where she subsequently obtained a tenure-track position in 2018.

In the Zuccolo Group, epidemiologists, statisticians, and data scientists analyse complex, high-dimensional data to improve our understanding of maternal and child health, focusing on intergenerational effects. New data pipelines and phenotype acquisitions develop while applying state-of-the-art methods for inference to inform knowledge translation. It describes trends and trajectories of health and behaviour emerging in contemporary populations, studies their determinants, identifies predictors of vulnerability and risk, and investigates how families, and in particular parent-child interactions, shape the health and well-being of individuals. The resulting evidence will help prioritise and aid the design of family- or parent-level interventions to support maternal, child, and adolescent health.

Dr. Zuccolo's research includes the causal effects of alcohol on health, particularly prenatal alcohol exposure, through methods and designs that improve causal inference. More recently, she has been focused on maternal and child health, studying the barriers and effects of prolonged breastfeeding, the impact of COVID-19 on fertility and pregnancy outcomes, and misinformation in public health messages on social media.

4. OUR FIRST RESULTS

Although we completed our first laboratories in the first half of 2021, in the two years covered by this report, the researchers recruited by Human Technopole have already published dozens of scientific articles, including publications in prestigious journals such as Nature and Science.

Among these, three have earned the covers of Science, Trends in Neurosciences, and MolecularCell.

4.1 Publications

There were 27 publications with Human Technopole affiliation in 2020 and 54 in 2021.

Below is a summary divided by affiliation centre:

Publications – 2020		
		Neurogenomics
Title	Authors	Journal
Serotonin Receptor 2A Activation Promotes Evolutionarily Relevant Basal Progenitor Proliferation in the Developing Neocortex	Xing L., **Kalebic N.**, Namba T., Vaid S., Wimberger P., Huttner W.	Neuron
Autism spectrum disorder at the crossroad between genes and environment: contributions, convergences, and interactions in ASD developmental pathophysiology	Cheroni C., Caporale N., **Testa G.**	Molecular autism
Thinking "ethical" When designing an international, cross-disciplinary biomedical research consortium	Torres Padilla M. E., Bredenoord A. L., Jongsma K. R., Lunkes A,. Marelli L., Pinheiro I., **Testa G.**	The EMBO journal
LifeTime and improving European healthcare through cell-based interceptive medicine	Rajewsky N., Almouzni G., Gorski S. A., Aerts S., Amit I., Bertero M. G., Bock C., Bredenoord A. L., Cavalli G., Chiocca S., Clevers H., De Strooper B., Eggert A., Ellenberg J., Fernández X. M., Figlerowicz M., Gasser S. M., Hubner N., Kjems J., Knoblich J., A., Krabbe G., Lichter P., Linnarsson S., Marine J. C., Marioni J., Marti-Renom M. A., Netea M. G., Nickel D., Nollmann M., Novak H. R., Parkinson H., Piccolo S., Pinheiro I., Pombo A., Popp C., Reik W., Roman-Roman S., Rosenstiel P., Schultze J. L., Stegle O., Tanay A., **Testa G.**, Thanos D., Theis F. J., Torres-Padilla M. E., Valencia A., Vallot C., Van Oudenaarden A., Vidal M., Voet T. & LifeTime Community	
Basal Progenitor Morphology and Neocortex Evolution	**Kalebic N.**, Huttner W. B.	Trends in Neuroscience
The sociability spectrum: evidence from reciprocal genetic copy number variations	**López-Tobón A.**, Trattaro S., **Testa G.**	Molecular Autism

KMT2B and Neuronal Transdifferentiation: Bridging Basic Chromatin Mechanisms to Disease Actionability	Barbagiovanni G., Gabriele M., **Testa G.**	Neurosci Insights
Copy number variants (CNVs): a powerful tool for iPSC-based modelling of ASD	Drakulic D., Djurovic S., Syed Y. A., Trattaro S., **Caporale N.**, Falk A., Ofir R., Heine V. M., Chawner S. J. R. A., Rodriguez-Moreno A., Van Den Bree M. B. M., **Testa G.**, Petrakis S., Harwood A. J.	Molecular Autism
In Vivo Targeting of Neural Progenitor Cells in Ferret Neocortex by In Utero Electroporation	**Kalebic N.**, Langen B., Helppi J., Kawasaki H., Huttner W. B.	Journal of Visualised Experiments
A small 7q11.23 microduplication involving GTF2I in a family with intellectual disability	Pinelli M., Terrone G., Troglio F., Squeo G. M., Cappuccio G., Imperati F., Pignataro P., Genesio R., Nitch L., Del Giudice E., Merla G., **Testa G.**, Brunetti-Pierri N.	Clinical Genetics
DNA Methylation Signature for EZH2 Functionally Classifies Sequence Variants in Three PRC2 Complex Genes	Choufani S., Gibson W. T., Turinsky A. L., Chung B. H. Y., Wang T., Garg K., Vitriolo A., Cohen A. S. A., Cyrus S., Goodman S., Chater-Diehl E., Brzezinski J., Brudno M., Ming L. H., White S. M., Lynch S. A., Clericuzio C., Temple I. K., Flinter F., McConnell V., Cushing T., Bird L. M., Splitt M.,Kerr B., Scherer S. W., Machado J., Imagawa E., Okamoto N., Matsumoto N., **Testa G.**, Iascone M., Tenconi R., Caluseriu O., Mendoza-Londono R., Chitayat D., Cytrynbaum C., Tatton-Brown K., Weksberg R.	American Journal of Human Genetics
Extracellular matrix-inducing Sox9 promotes both basal progenitor proliferation and gliogenesis in developing neocortex	Güven A., **Kalebic N.**, Long K. R., Florio M., Vaid S., Brandl H., Stenzel D., Huttner W. B.	eLife
		Structural Biology
A micronutrient with major effects on cancer cell viability.	Kapara A., **Vannini A.**, Peck B.	Nature Metabolism
Human Condensin I and II Drive Extensive ATP-Dependent Compaction of Nucleosome-Bound DNA	Kong M., Cutts E. E., Pan D., Beuron F., Kaliyappan T., Xue C., Morris E. P., Musacchio A., **Vannini A.**, Greene E. C.	Molecular Cell
Hybrid Gene Origination Creates Human-Virus Chimeric Proteins during Infection	Ho J. S. Y., Angel M., Ma Y., Sloan E., Wang G., Martinez-Romero C., Alenquer M., Roudko V., Chung L., Zheng S., Chang M., Fstkchyan Y., Clohisey S., Dinan A. M., Gibbs J., Gifford R., Shen R., Gu Q., Irigoyen N., Campisi L., Huang C., Zhao N., Jones J. D., Van Knippenberg I., Zhu Z., Moshkina N., Meyer L., Noel J., Peralta Z., Rezelj V., Kaake R., Rosenberg B., Wang B., Wei J., Paessler S., Wise H. M., Johnson J., **Vannini A.**, Amorim M. J., Baillie J. K., Miraldi E. R., Benner C., Brierley I., Digard P., Łuksza M., Firth A. E., Krogan N., Greenbaum B. D., MacLeod M. K., Van Bakel H., Garcìa-Sastre A., Yewdell J. W., Hutchinson E., Marazzi I.	Cell

DNA origami-based single-molecule force spectroscopy elucidates RNA Polymerase III pre-initiation complex stability	Kramm K., Schröder T., Gouge J., Vera A. M., Gupta K., Heiss F. B., Liedl T., Engel C., Berger I., **Vannini A**., Tinnefeld P., Grohmann D.	Nature Communications
		Computational Biology
Identification of Intrinsic Drug Resistance and Its Biomarkers in High-Throughput Pharmacogenomic and CRISPR Screens	Ayestaran I., Galhoz A., Spiegel E., Sidders B., Dry J. R., Dondelinger F., Bender A., McDermott U., **Iorio F.**, Menden M. P.	Patterns
Analysis of CRISPR-Cas9 screens identify genetic dependencies in melanoma	Christodoulou E., Rashid M., Pacini C., Alastair D., Robertson H., Van Groningen T., Teunisse A. F. A. S., **Iorio F.**, Jochemsen A. G., Adams D. J., Van Doorn R.	Pigment Cell and Melanoma Research
Drug mechanism-of-action discovery through the integration of pharmacological and CRISPR screens	Gonçalves E., Segura-Cabrera A., Pacini C., Picco G., Behan F. M., Jaaks P., Coker E. A., Van Der Meer D., Barthorpe A., Lightfoot H., Mironenko T., Beck A., Richardson L., Yang W., Lleshi E., Hall J., Tolley C., Hall C., Mali I., Thomas F., Morris J., Leach A. R., Lynch J. T., Sidders B., Crafter C., **Iorio F.**, Fawell S., Garnett M. J.	Molecular Systems Biology
CELLector: Genomics-Guided Selection of Cancer In Vitro Models	Najgebauer H., Yang M., Francies H. E., Pacini C., Stronach E. A., Garnett M. J., Saez-Rodriguez J., **Iorio F.**	Cell systems
		Health Data Science
Data mining application to healthcare fraud detection: a two-step unsupervised clustering method for outlier detection with administrative databases	Massi M. C., **Ieva F.**, Lettieri E.	BMC Medical Informatics and Decision Making
Connected from the Outside: The Role of US Regions in Promoting the Integration of the European Research System	**Rabosio E.**, Righetto L., Spelta A., **Pammolli F.**	Quantitative Science Studies
Modelling the Effect of Recurrent Events on Time-to-event Processes by Means of Functional Data	**Ieva F.**, Spreafico M., Burba D.	International Workshop on Functional and Operatorial Statistics
O2S2 for the Geodata Deluge	Menafoglio A., Pigoli D., **Secchi P.**	International Workshop on Functional and Operatorial Statistics
Economic and social consequences of human mobility restrictions under COVID-19	Bonaccorsi G., Pierri F., Cinelli M., Flori A., Galeazzi A., Porcelli F., Schmidt L., Valensise C. M., Scala A., Quattrociocchi W., **Pammolli F.**	Proceedings of the National Academy of Sciences
The Endless Frontier? The Recent Increase of R&D Productivity in Pharmaceuticals	**Pammolli F.**, Righetto L., Abrignani S., Pani L., Pelicci P., **Rabosio E.**	Journal of Translational Medicine

A behavioural approach to instability pathways in financial markets	Spelta A., Flori A., Pecora N., Buldyrev S., **Pammolli F.**	Nature Communications

Publications – 2021

Genomics

Title	Authors	Journal
*Mitochondrial DNA variants modulate N-formylmethionine, proteostasis and risk of late-onset human diseases**	Na Cai, Aurora Gomez-Duran, Ekaterina Yonova-Doing, Kousik Kundu, Annette I. Burgess, Zoe J. Golder, Claudia Calabrese, Marc J. Bonder, Marta Camacho, Rachael A. Lawson, Lixin Li, Caroline H. Williams-Gray, ICICLE-PD Study Group, Emanuele Di Angelantonio, David J. Roberts, Nick A. Watkins, Willem H. Ouwehand, Adam S. Butterworth, Isobel D. Stewart, Maik Pietzner, Nick J. Wareham, Claudia Langenberg, John Danesh, Klaudia Walter, Peter M. Rothwell, Joanna M. M. Howson, Oliver Stegle, Patrick F. Chinnery & **Nicole Soranzo**	Nat Med
Embryonic LTR retrotransposons supply promoter modules to somatic tissues	Kosuke Hashimoto, Eeva-Mari Jouhilai, Virpi Töhönen, **Piero Carninci**, Juha Kere, Shintaro Katayama	Genome Res.
SINEUPs: a novel toolbox for RNA therapeutics	Stefano Espinoza, Carlotta Bon, Paola Valentini, Bianca Pierattini, Abraham Tettey Matey, Devid Damiani, Salvatore Pulcrano, Remo Sanges, Francesca Persichetti, Hazuki Takahashi, **Piero Carninci**, Claudio Santoro, Diego Cotella, Stefano Gustincich	Essays Biochem
A field guide to cultivating computational biology	Gregory P Way, Casey S Greene, **Piero Carninci**, Benilton S Carvalho, Michiel de Hoon, Stacey D Finley, Sara J C Gosline, Kim-Anh Lê Cao, Jerry S H Lee, Luigi Marchionni, Nicolas Robine, Suzanne S Sindi, Fabian J Theis, Jean Y H Yang, Anne E Carpenter, Elana J Fertig	PLoS Biol.
The choice of negative control antisense oligonucleotides dramatically impacts downstream analysis depending on the cellular background	Luca Ducoli, Saumya Agrawal, Chung-Chau Hon, Jordan A Ramilowski, Eliane Sibler, Michihira Tagami, Masayoshi Itoh, Naoto Kondo, Imad Abugessaisa, Akira Hasegawa, Takeya Kasukawa, Harukazu Suzuki, **Piero Carninci**, Jay W Shin, Michiel J L de Hoon, Michael Detmar	BMC Genom Data
Analysis of Enhancer-Promoter Interactions using CAGE and RADICL-Seq Technologies	Alessandro Bonetti, Andrew Tae-Jun Kwon, Erik Arner, **Piero Carninci**	Methods Mol Biol
Low Quantity Single Strand CAGE (LQ-ssCAGE) Maps Regulatory Enhancers and Promoters	Hazuki Takahashi, Hiromi Nishiyori-Sueki, Jordan A Ramilowski, Masayoshi Itoh, **Piero Carninci**	Methods Mol Biol
Antisense RNAs during early vertebrate development are divided in groups with distinct features	Sanjana Pillay, Hazuki Takahashi, **Piero Carninci**, Aditi Kanhere	Genome Res.

Lipid-loaded tumor-associated macrophages sustain tumor growth and invasiveness in prostate cancer	Michela Masetti, Roberta Carriero, Federica Portale, Giulia Marelli, Nicolò Morina, Marta Pandini, Marta Iovino, Bianca Partini, Marco Erreni, Andrea Ponzetta, Elena Magrini, Piergiuseppe Colombo, Grazia Elefante, Federico Simone Colombo, Joke M M den Haan, **Clelia Peano**, Javier Cibella, Alberto Termanini, Paolo Kunderfranco, Jolanda Brummelman, Matthew Wai Heng Chung, Massimo Lazzeri, Rodolfo Hurle, Paolo Casale, Enrico Lugli, Ronald A DePinho, Subhankar Mukhopadhyay, Siamon Gordon, Diletta Di Mitri	J Exp Med
The Helicobacter pylori CagY Protein Drives Gastric Th1 and Th17 Inflammation and B Cell Proliferation in Gastric MALT Lymphoma	Chiara Della Bella, Maria Felicia Soluri, Simone Puccio, Marisa Benagiano, Alessia Grassi, Jacopo Bitetti, Fabio Cianchi, Daniele Sblattero, **Clelia Peano**, Mario Milco D'Elios	Int J Mol Sci
Interplay between Non-Coding RNA Transcription, Stringent/Relaxed Phenotype and Antibiotic Production in Streptomyces ambofaciens	Eva Pinatel, Matteo Calcagnile, Adelfia Talà, Fabrizio Damiano, Luisa Siculella, **Clelia Peano**, Giuseppe Egidio De Benedetto, Antonio Pennetta, Gianluca De Bellis, Pietro Alifano	Antibiotics
		Neurogenomics
Single cell-derived spheroids capture the self-renewing subpopulations of metastatic ovarian cancer	Tania Velletri, Carlo Emanuele Villa, Domenica Cilli, Bianca Barzaghi, Pietro Lo Riso, Michela Lupia, Raffaele Luongo, Alejandro López-Tobón, Marco De Simone, Raoul J P Bonnal, Luca Marelli, Stefano Piccolo, Nicoletta Colombo, Massimiliano Pagani, Ugo Cavallaro, Saverio Minucci, Giuseppe Testa	Cell Death Differ
Novel in vitro Experimental Approaches to Study Myelination and Remyelination in the Central Nervous System	Davide Marangon, **Nicolò Caporale**, Marta Boccazzi, Maria P Abbracchio, **Giuseppe Testa**, Davide Lecca	Front Cell Neurosci
Big Tech Platforms in Health Research: Re-purposing Big Data Governance in Light of the GDPR's Research Exemption	Luca Marelli, **Giuseppe Testa**, Ine Van Hoyweghen	SSRN
Inheritance and flexibility of cell polarity: a clue for understanding human brain development and evolution	**Nereo Kalebic**, Takashi Namba	Development
The Ferret as a Model System for Neocortex Development and Evolution	Carlotta Gilardi, **Nereo Kalebic**	Front Cell Dev Biol
NGN2 induces diverse neuron types from human pluripotency	Hsiu-Chuan Lin, Zhisong He, Sebastian Ebert, Maria Schörnig, Malgorzata Santel, Marina T. Nikolova, Anne Weigert, Wulf Hevers, Nael Nadif Kasri, **ElenaTaverna**, J. Gray Camp, BarbaraTreutlein	Stem Cell Report

MCPH1 inhibits Condensin II during interphase by regulating its SMC2-Kleisin interface	Martin Houlard, Erin E Cutts, Muhammad S Shamim, Jonathan Godwin, David Weisz, Aviva Presser Aiden, Erez Lieberman Aiden, Lothar Schermelleh, Alessandro Vannini, Kim Nasmyth	Elife
Structural basis of Ty3 retrotransposon integration at RNA Polymerase III-transcribed genes	Guillermo Abascal-Palacios, Laura Jochem, Carlos Pla-Prats, Fabienne Beuron, **Alessandro Vannini**	Nat Commun
Linker histone H1.8 inhibits chromatin binding of condensins and DNA topoisomerase II to tune chromosome length and individualization	Pavan Choppakatla, Bastiaan Dekker, Erin E Cutts, **Alessandro Vannini**, Job Dekker, Hironori Funabiki	Elife
A WDR35-dependent coat protein complex transports ciliary membrane cargo vesicles to cilia	Tooba Quidwai, Jiaolong Wang, Emma A Hall, Narcis A Petriman, Weihua Leng, Petra Kiesel, Jonathan N Wells, Laura C Murphy, Margaret A Keighren, Joseph A Marsh, Esben Lorentzen, **Gaia Pigino**, Pleasantine Mill	Elife
In vivo imaging shows continued association of several IFT-A, IFT-B and dynein complexes while IFT trains U-turn at the tip	Jenna L Wingfield, Betlehem Mekonnen, Ilaria Mengoni, Peiwei Liu, Mareike Jordan, Dennis Diener, **Gaia Pigino**, Karl Lechtreck	J Cell Sci
The structural basis of intraflagellar transport at a glance	Mareike A Jordan, **Gaia Pigino**	J Cell Sci
Intraflagellar transport	Gaia Pigino	Curr Biol
Tubulin glycylation controls axonemal dynein activity, flagellar beat, and male fertility	Sudarshan Gadadhar, Gonzalo Alvarez Viar, Jan Niklas Hansen, An Gong, Aleksandr Kostarev, Côme Ialy-Radio, Sophie Leboucher, Marjorie Whitfield, Ahmed Ziyyat, Aminata Touré, Luis Alvarez, **Gaia Pigino**, Carsten Janke	Science (with Cover)
Ccdc113/Ccdc96 complex, a novel regulator of ciliary beating that connects radial spoke 3 to dynein g and the nexin link	Bazan R, Schröfel A, Joachimiak E, Poprzeczko M, **Pigino G**, Wloga D.	PLoS Genet
Thermally Driven Membrane Phase Transitions Enable Content Reshuffling in Primitive Cells	Roger Rubio-Sánchez, Derek K O'Flaherty, Anna Wang, **Francesca Coscia**, Gianluca Petris, Lorenzo Di Michele, Pietro Cicuta, Claudia Bonfio	J Am Chem Soc
Integrated Cryo-Correlative Microscopy for Targeted Structural Investigation In Situ	Marit Smeets, Anna Bieber, Cristina Capitanio, Oda Schioetz, Thomas van der Heijden, Andries Effting, Éric Piel, Éric Piel, Bassim Lazem, **Philipp Erdmann**, Juergen Plitzko	Microscopy Today
Sample Preparation by 3D-Correlative Focused Ion Beam Milling for High-Resolution Cryo-Electron Tomography	Anna Bieber, Cristina Capitanio, Florian Wilfling, Jürgen Plitzko, **Philipp S Erdmann**	J Vis Exp

In situ cryo-electron tomography reveals gradient organization of ribosome biogenesis in intact nucleoli	**Philipp S Erdmann**, Zhen Hou, Sven Klumpe, Sagar Khavnekar, Florian Beck, Florian Wilfling, Jürgen M Plitzko, Wolfgang Baumeister	Nat Commun
Deposition-free Cryo-FIB Lift-out Transfer for Cryo-Electron Tomography Specimen Preparation	Jürgen Plitzko, **Philipp S Erdman**, Sven Klumpe	Microsc. Microanal.
Epistasis, aneuploidy, and functional mutations underlie evolution of resistance to induced microtubule depolymerization	Mattia Pavani, Paolo Bonaiuti, Elena Chiroli, Fridolin Gross, Federica Natali, Francesca Macaluso, Ádám Póti, **Sebastiano Pasqualato**, Zoltán Farkas, Simone Pompei, Marco Cosentino Lagomarsino, Giulia Rancati, Dávid Szüts, Andrea Ciliberto	EMBO J
		Computational Biology
Functional Impact of Genomic Complexity on the Transcriptome of Multiple Myeloma	Bachisio Ziccheddu, Matteo C Da Vià, Marta Lionetti, Akihiro Maeda, Silvia Morlupi, Matteo Dugo, Katia Todoerti, Stefania Oliva, Mattia D'Agostino, Paolo Corradini, Ola Landgren, Francesco Iorio, Loredana Pettine, Alessandra Pompa, Martina Manzoni, Luca Baldini, Antonino Neri, Francesco Maura, Niccolò Bolli	Clin Cancer Res
Integrated cross-study datasets of genetic dependencies in cancer	Clare Pacini, Joshua M Dempster, Isabella Boyle, Emanuel Gonçalves, Hanna Najgebauer, Emre Karakoc, Dieudonne van der Meer, Andrew Barthorpe, Howard Lightfoot, Patricia Jaaks, James M McFarland, Mathew J Garnett, Aviad Tsherniak, **Francesco Iorio**	Nat Commun
Combinatorial CRISPR screen identifies fitness effects of gene paralogues	Nicola A Thompson, Marco Ranzani, Louise van der Weyden, Vivek Iyer, Victoria Offord, Alastair Droop, Fiona Behan, Emanuel Gonçalves, Anneliese Speak, **Francesco Iorio**, James Hewinson, Victoria Harle, Holly Robertson, Elizabeth Anderson, Beiyuan Fu, Fengtang Yang, Guido Zagnoli-Vieira, Phil Chapman, Martin Del Castillo Velasco-Herrera, Mathew J Garnett, Stephen P Jackson, David J Adams	Nat Commun
Minimal genome-wide human CRISPR-Cas9 library	Emanuel Gonçalves, Mark Thomas, Fiona M Behan, Gabriele Picco, Clare Pacini, Felicity Allen, **Alessandro Vinceti**, Mamta Sharma, David A Jackson, Stacey Price, Charlotte M Beaver, Oliver Dovey, David Parry-Smith, **Francesco Iorio**, Leopold Parts, Kosuke Yusa, Mathew J Garnett	Genome Biol
Project Score database: a resource for investigating cancer cell dependencies and prioritizing therapeutic targets	Lisa Dwane, Fiona M Behan, Emanuel Gonçalves, Howard Lightfoot, Wanjuan Yang, Dieudonne van der Meer, Rebecca Shepherd, Miguel Pignatelli, **Francesco Iorio**, Mathew J Garnett	Nucleic Acids Res

Analysis of CRISPR-Cas9 screens identifies genetic dependencies in melanoma	Eirini Christodoulou, Mamunur Rashid, Clare Pacini, Alastair Droop, Holly Robertson, Tim van Groningen, Amina F A S Teunisse, **Francesco Iorio**, Aart G Jochemsen, David J Adams, Remco van Doorn	Pigment Cell Melanoma Res
CoRe: a robustly benchmarked R package for identifying core-fitness genes in genome-wide pooled CRISPR-Cas9 screens	**Alessandro Vinceti**, Emre Karakoc, Clare Pacini, **Umberto Perron**, **Riccardo Roberto De Lucia**, Mathew J Garnett, **Francesco Iorio**	BMC Genomics
Democratising deep learning for microscopy with ZeroCostDL4Mic	Lucas von Chamier, Romain F Laine, Johanna Jukkala, Christoph Spahn, Daniel Krentzel, Elias Nehme, Martina Lerche, Sara Hernández-Pérez, Pieta K Mattila, Eleni Karinou, Séamus Holden, Ahmet Can Solak, Alexander Krull, Tim-Oliver Buchholz, Martin L Jones, Loïc A Royer, Christophe Leterrier, Yoav Shechtman, **Florian Jug**, Mike Heilemann, Guillaume Jacquemet, Ricardo Henriques	Nat Commun
3D FIB-SEM reconstruction of microtubule-organelle interaction in whole primary mouse β cells	Andreas Müller, Deborah Schmidt, C Shan Xu, Song Pang, Joyson Verner D'Costa, Susanne Kretschmar, Carla Münster, Thomas Kurth, **Florian Jug**, Martin Weigert, Harald F Hess, Michele Solimena	J Cell Biol
Embedding-based Instance Segmentation in Microscopy	Manan Lalit, Pavel Tomancak, **Florian Jug**	Proceedings of Machine Learning Research
The ImageJ ecosystem: Open-source software for image visualization, processing, and analysis	Alexandra B Schroeder, Ellen T A Dobson, Curtis T Rueden, Pavel Tomancak, **Florian Jug**, Kevin W Eliceiri	Protein Sci
		Health Data Science
Integrative analysis of the plasma proteome and polygenic risk of cardiometabolic diseases	Scott C Ritchie, Samuel A Lambert, Matthew Arnold, Shu Mei Teo, Sol Lim, Petar Scepanovic, Jonathan Marten, Sohail Zahid, Mark Chaffin, Yingying Liu, Gad Abraham, Willem H Ouwehand, David J Roberts, Nicholas A Watkins, Brian G Drew, Anna C Calkin, Emanuele Di Angelantonio, Nicole Soranzo, Stephen Burgess, Michael Chapman, Sekar Kathiresan, Amit V Khera, John Danesh, Adam S Butterworth, Michael Inouye	Nat Metab
Novel longitudinal Multiple Overall Toxicity (MOTox) score to quantify adverse events experienced by patients during chemotherapy treatment: a retrospective analysis of the MRC BO06 trial in osteosarcoma	Marta Spreafico, **Francesca Ieva**, Francesca Arlati, Federico Capello, Federico Fatone, Filippo Fedeli, Gianmarco Genalti, Jakob Anninga, Hans Gelderblom, Marta Fiocco	BMJ Open

A Functional Data Analysis Approach to Left Ventricular Remodeling Assessmen	Letizia Clementi, Caterina Gregorio, Laura Savare, **Franceesca Ieva**, Marco D Santambrogio, Laura M Sangalli	EMBC
[18 F]FMCH PET/CT biomarkers and similarity analysis to refine the definition of oligometastatic prostate cancer	Martina Sollini, Francesco Bartoli, Lara Cavinato, **Francesca Ieva**, Alessandra Ragni, Andrea Marciano, Roberta Zanca, Luca Galli, Fabiola Paiar, Francesco Pasqualetti, Paola Anna Erba	EJNMMI Res
Virtual Biopsy for Diagnosis of Chemotherapy-Associated Liver Injuries and Steatohepatitis: A Combined Radiomic and Clinical Model in Patients with Colorectal Liver Metastases	Guido Costa, Lara Cavinato, Chiara Masci, Francesco Fiz, Martina Sollini, Letterio Salvatore Politi, Arturo Chiti, Luca Balzarini, Alessio Aghemo, Luca di Tommaso, **Francesca Ieva**, Guido Torzilli, Luca Viganò	Cancers
Chemotherapy-Associated Liver Injuries: Unmet Needs and New Insights for Surgical Oncologists	Luca Vigano, Martina Sollini, **Francesca Ieva**, Francesco Fiz, Guido Torzilli	Ann Surg Oncol
Development of a method for generating SNP interaction-aware polygenic risk scores for radiotherapy toxicity	Nicola Rares Franco, Michela Carlotta Massi, **Francesca Ieva**, Andrea Manzoni, Anna Maria Paganoni, Paolo Zunino, Liv Veldeman, Piet Ost, Valérie Fonteyne, Christopher J Talbot, Tim Rattay, Adam Webb, Kerstie Johnson , Maarten Lambrecht, Karin Haustermans, Gert De Meerleer, Dirk de Ruysscher, Ben Vanneste, Evert Van Limbergen, Ananya Choudhury, Rebecca M Elliott, Elena Sperk, Marlon R Veldwijk, Carsten Herskind, Barbara Avuzzi, Barbara Noris Chiorda, Riccardo Valdagni, David Azria, Marie-Pierre Farcy-Jacquet, Muriel Brengues, Barry S Rosenstein, Richard G Stock, Ana Vega, Miguel E Aguado-Barrera, Paloma Sosa-Fajardo, Alison M Dunning, Laura Fachal, Sarah L Kerns, Debbie Payne, Jenny Chang-Claude, Petra Seibold, Catharine M L West, Tiziana Rancati, REQUITE Consortium Collaborators	Radiother Oncol
Functional modeling of recurrent events on time-to-event processes	Marta Spreafico, **Francesca Ieva**	Biom J
Dynamic monitoring of the effects of adherence to medication on survival in heart failure patients: A joint modeling approach exploiting time-varying covariates	Marta Spreafico, **Francesca Ieva**	Biom J
Feature Selection for Imbalanced Data with Deep Sparse Autoencoders Ensemble	**Michela Carlotta Massi**,Francesca Gasperoni, **Francesca Ieva, Anna Maria Paganoni**	Statistical Analysis and Data Mining
Learning Signal Representations for EEG Cross-Subject Channel Selection and Trial Classification	**Michela C Massi, Francesca Ieva**	IEEE

4.2 Cohort studies

In 2021, Human Technopole researchers published 8 studies involving groups of people (or cohorts) summarised below.

Title	Authors	Journal
Mitochondrial DNA variants modulate N-formylmethionine, proteostasis and risk of late-onset human diseases*	Na Cai, Aurora Gomez-Duran, Ekaterina Yonova-Doing, Kousik Kundu, Annette I. Burgess, Zoe J. Golder, Claudia Calabrese, Marc J. Bonder, Marta Camacho, Rachael A. Lawson, Lixin Li, Caroline H. Williams-Gray, ICICLE-PD Study Group, Emanuele Di Angelantonio, David J. Roberts, Nick A. Watkins, Willem H. Ouwehand, Adam S. Butterworth, Isobel D. Stewart, Maik Pietzner, Nick J. Wareham, Claudia Langenberg, John Danesh, Klaudia Walter, Peter M. Rothwell, Joanna M. M. Howson, Oliver Stegle, Patrick F. Chinnery & **Nicole Soranzo**	Nature Medicine
Functional Impact of Genomic Complexity on the Transcriptome of Multiple Myeloma	Bachisio Ziccheddu, Matteo C Da Via, Marta Lionetti, Akihiro Maeda, Silvia Morlupi, Matteo Dugo, Katia Todoerti, Stefania Oliva, Mattia D'Agostino, Paolo Corradini, Ola Landgren, **Francesco Iorio**, Loredana Pettine, Alessandra Pompa, Martina Manzoni, Luca Baldini, Antonino Neri, Francesco Maura, Niccolò Bolli	Clin Cancer Res
Integrative analysis of the plasma proteome and polygenic risk of cardiometabolic diseases	Scott C Ritchie, Samuel A Lambert, Matthew Arnold, Shu Mei Teo, Sol Lim, Petar Scepanovic, Jonathan Marten, Sohail Zahid, Mark Chaffin, Yingying Liu, Gad Abraham, Willem H Ouwehand, David J Roberts, Nicholas A Watkins, Brian G Drew, Anna C Calkin, **Emanuele Di Angelantonio**, Nicole Soranzo, Stephen Burgess, Michael Chapman, Sekar Kathiresan, Amit V Khera, John Danesh, Adam S Butterworth, Michael Inouye	Nature Metabolism
Novel longitudinal Multiple Overall Toxicity (MOTox) score to quantify adverse events experienced by patients during chemotherapy treatment: a retrospective analysis of the MRC BO06 trial in osteosarcoma	Marta Spreafico, **Francesca Ieva**, Francesca Arlati, Federico Capello, Federico Fatone, Filippo Fedeli, Gianmarco Genalti, Jakob Anninga, Hans Gelderblom, Marta Fiocco	BMJ Open

[18 F]FMCH PET/CT biomarkers and similarity analysis to refine the definition of oligometastatic prostate cancer	Martina Sollini, Francesco Bartoli, Lara Cavinato, **Francesca Ieva**, Alessandra Ragni, Andrea Marciano, Roberta Zanca, Luca Galli, Fabiola Paiar, Francesco Pasqualetti, Paola Anna Erba	EJNMMI Research
Virtual Biopsy for Diagnosis of Chemotherapy-Associated Liver Injuries and Steatohepatitis: A Combined Radiomic and Clinical Model in Patients with Colorectal Liver Metastases	Guido Costa, Lara Cavinato, Chiara Masci, Francesco Fiz, Martina Sollini, Letterio Salvatore Politi, Arturo Chiti, Luca Balzarini, Alessio Aghemo, Luca di Tommaso, **Francesca Ieva**, Guido Torzilli, Luca Viganò	Cancers
Development of a method for generating SNP interaction-aware polygenic risk scores for radiotherapy toxicity	Nicola Rares Franco, Michela Carlotta Massi, **Francesca Ieva**, Andrea Manzoni, Anna Maria Paganoni, Paolo Zunino, Liv Veldeman, Piet Ost, Valérie Fonteyne, Christopher J Talbot, Tim Rattay, Adam Webb, Kerstie Johnson , Maarten Lambrecht, Karin Haustermans, Gert De Meerleer, Dirk de Ruysscher, Ben Vanneste, Evert Van Limbergen, Ananya Choudhury, Rebecca M Elliott, Elena Sperk, Marlon R Veldwijk, Carsten Herskind, Barbara Avuzzi, Barbara Noris Chiorda, Riccardo Valdagni, David Azria, Marie-Pierre Farcy-Jacquet, Muriel Brengues, Barry S Rosenstein, Richard G Stock, Ana Vega, Miguel E Aguado-Barrera, Paloma Sosa-Fajardo, Alison M Dunning, Laura Fachal, Sarah L Kerns, Debbie Payne, Jenny Chang-Claude, Petra Seibold, Catharine M L West, Tiziana Rancati, REQUITE Consortium Collaborators	Radiother Oncology
Functional modeling of recurrent events on time-to-event processes	Marta Spreafico, **Francesca Ieva**	Biometrical Journal

4.3 Experimental methods and protocols

In 2021, 8 new experimental methods and protocols were developed with the participation of Human Technopole-affiliated researchers.

Below is a brief summary:

Titles	Authors	Description

Minimal genome-wide human CRISPR-Cas9 library	Vinceti, Iorio	Design of an optimised minimal genome-wide library with two sgRNAs per gene (MinLibCas9) that allows for backward compatibility with large resources of CRISPR-Cas9 screens of cancer cell models.
Project Score database: a resource for investigating cancer cell dependencies and prioritizing therapeutic targets	Iorio	Uses genome-wide CRISPR-Cas9 dropout screening data in hundreds of highly annotated cancer cell models to identify genes required for cell fitness and prioritize novel oncology targets.
CoRe: a robustly benchmarked R package for identifying core-fitness genes in genome-wide pooled CRISPR-Cas9 screens	Iorio	Development of an R package implementing existing and novel methods for the identification of core-fitness genes (at two different level of stringency) from joint analyses of multiple CRISPR-Cas9 screens.
Embedding-based Instance Segmentation in Microscopy	Jug	Developing a segmentation method for microscopy image analysis
Democratising deep learning for microscopy with ZeroCostDL4Mic.	Jug	Development of a Deep Learning-based platform for image analysis
Deposition-free Cryo-FIB Lift-out Transfer for Cryo-Electron Tomography Specimen Preparation.	Erdmann	Protocol for Cryo-EM sample preparation
Integrated Cryo-Correlative Microscopy for Targeted Structural Investigation In Situ	Erdmann	Development of a microscopy solution that streamlines the correlative cryo-ET workflow
Sample Preparation by 3D-Correlative Focused Ion Beam Milling for High-Resolution Cryo-Electron Tomography	Erdmann	Protocol for Cryo-EM sample preparation
Single cell-derived spheroids capture the self-renewing subpopulations of metastatic ovarian cancer	Villa	New method to isolate and grow single cells directly from patients' metastatic ascites.
SINEUPs: a novel toolbox for RNA therapeutics	Carninci	Protocol for Cryo-EM sample preparation
Analysis of Enhancer-Promoter Interactions using CAGE and RADICL-Seq Technologies	Carninci	Novel methodology to map genome-wide RNA–chromatin interactions in intact nuclei
Novel longitudinal Multiple Overall Toxicity (MOTox) score to quantify adverse events experienced by patients during	Ieva	Development of a novel longitudinal method that can be applied to any cancer studies with CTCAE-graded toxicity data.

chemotherapy treatment: a retrospective analysis of the MRC BO06 trial in osteosarcoma		
A Functional Data Analysis Approach to Left Ventricular Remodeling Assessment	Ieva	Development of a novel analysis approach based on functional data analysis to evaluate myocardial contractility
Development of a method for generating SNP interaction-aware polygenic risk scores for radiotherapy toxicity	Ieva	Development of a new method for polygenic risk score measurement incorporating SNP-SNP interactions.
Functional modeling of recurrent events on time-to-event processes	Spreafico, Ieva	Novel methodology to model patient survival with relevant dynamic features
Dynamic monitoring of the effects of adherence to medication on survival in heart failure patients: A joint modeling approach exploiting time-varying covariates	Spreafico, Ieva	Define a new personalized monitoring tool exploiting time-varying definition of adherence to medication, within a joint modeling approach
Feature Selection for Imbalanced Data with Deep Sparse Autoencoders Ensemble	Massi, Ieva & Spreafico	Development of a filtering algorithm for the analysis of radiogenomic data
Learning Signal Representations for EEG Cross-Subject Channel Selection and Trial Classification	Massi, Ieva	Development of an algorithm for the analysis of ElectroEncephaloGraphy recording

4.4 Research on Covid-19

The Covid-19 pandemic has represented a momentous challenge prompting a rapid response from the international community. To this situation, the researchers at the Centre for Neurogenomics have provided support from the earliest months of the virus' spread, coordinating the efforts of the LifeTime for Covid-19 initiative, carried out in close collaboration with the other Human Technopole Centres and leading international research institutes, to study the pathogenesis of the virus at the molecular level and at very high resolution.

Thanks to the extensive experience of Human Technopole researchers in the fields of single-cell genomics, computational analysis with artificial intelligence algorithms, and the most advanced experimental systems on stem cells, molecular studies were conducted on the immune cells of patients affected by COVID-19, integrating immunogenomic characterisation with clinical and epidemiological analysis conducted by hospital and university collaborators on the large cohorts involved in this study: Prof. Massimo Galli and Agostino Riva from the Luigi Sacco Hospital in Milan, Prof. Antonella Viola from the Città della Speranza Paediatric Research Institute in Padua, and Prof. Domenico Mavilio from the Humanitas Clinical Institute in Milan.

In particular, these studies have revealed how different immune cells react to SARS-CoV-2 infection, how the response differs between patients with varying severities of the disease, and

what the longitudinal dynamics are in the different phases of the disease and the other pandemic waves.

In addition, because of the promising results of these analysis, the study is already expanding to also study with the same approaches the high-resolution longitudinal immune response to Covid-19 vaccination, including the booster dose, to identify the long-term protective characteristics of this crucial public health measure.

Finally, to understand the as-yet-unknown molecular mechanisms underlying the neurological and neuropsychiatric complications of post-Covid, the syndrome characterised by long-term health consequences caused by Coronavirus infection, and which is already beginning to constitute a vast social and health problem given its potentially disastrous long-term effects, researchers at the Centre for Neurogenomics have set up and co-ordinated, together with the German Centre for Neurodegenerative Diseases, a large European research consortium to begin the experimental activities that will enable them to understand how the virus can cause its adverse effects on the central nervous system, through the use of brain organoids.

Still on Covid-19, Human Technopole and the Department of Molecular Medicine, University of Padua, are carrying out the genetic and transcriptomic analysis of the population of Vo' Euganeo and samples collected from Covid patients. The investigations will enable to study evolution and epidemiology of SARS-CoV-2 infection, as well as the identification of potential associations between the illness and the severity of the disease association.

Thanks to an agreement signed with the Lombardy Region, the Health Data Science Centre will be soon investigating the effect of Covid-19 infection on the risk of developing cardiovascular disease to estimate the extent and impact on the regional population and identify those at greater risk through the analysis of health data.

4.5 Scientific partnerships

Human Technopole is committed to improving people's health and well-being through a multidisciplinary and integrated approach to life sciences research, including partnerships and collaborations with other national and international research institutions. From our earliest days of activity, we started a dialogue with universities, research hospitals, and other scientific organisations to explore synergies and promote collaboration initiatives.

Scientific partnerships and collaborations are based on shared scientific interests, common research questions, as well as on complementarity in research capabilities, methods, and competencies.

Interactions with the research community have become more and more intense in the biennium 2020-2021, thanks to the recruitment of the heads of the Research Centres and of the first Group Leaders. Their appointment has indeed triggered numerous initiatives and meetings with several actors of the biomedical scientific community, eager to collaborate with Human Technopole.

Below, a summary.

Scientific Collaboration Agreements

Politecnico di Milano (2018 e 2019)

Agreement to establish a joint research centre – "Centre for Analysis, Decisions and Society (CADS)." From 2019, Human Technopole participates in the PhD programme in Data Analytics and Decision Sciences, funding several fellowships each year for projects of interest to the Joint Centre.

Università Statale di Milano – Scuola Europea di Medicina Molecolare (2019)
From 2019, Human Technopole participates in the PhD programme of the European School of Molecular Medicine (SEMM), funding several fellowships each year for projects of its interest.

Università Statale di Milano (2019)
The agreement provides for synergies in the use of laboratories and facilities for research, the exchange between research staff at all levels, the development of research projects and programmes in areas of common interest, and joint activities in the promotion of public engagement.

Università di Napoli Federico II (2019)
The agreement provides for the exchange between research staff at all levels and the development of collaborative projects in areas of common interest. In addition, the agreement promotes involvement in training activities and the development of joint seminars, symposia and workshops.

Cluster tecnologico nazionale scienze della vita Alisei (Advanced Life Science in Italy) / Cluster Agrifood Nazionale (CL.A.N). (2019)
The agreement aims to identify and bring together relevant companies, organisations and institutions in the national panorama of the life sciences and agri-food sector in order to create an ecosystem capable of enhancing Italian expertise in these fields at European and international level.

Università di Roma Tor Vergata (2020)
The collaboration with the Department of Biology ensures the continued development of the MINT (Molecular Interaction database) and SIGNOR (SIGnalling Network Open Resource) databases.

Università degli Studi di Torino (2020)
The agreement provides for the exchange between research staff at all levels and the development of collaborative projects in areas of common interest. In addition, the agreement promotes involvement in training activities and the development of joint seminars, symposia and workshops.

Fondazione Regionale per la Ricerca Biomedica – FRBB (2021)
The agreement provides for the development of collaborative projects, including the development of proposals for the funding of such research in areas of mutual interest. It also provides for the engagement in joint training activities and programmes of mutual interest and the development and organisation of joint seminars or workshops and other scientific events.

Università di Padova - Dipartimento di Scienze Biomediche (2021)
Already mentioned in the section on Covid-19 studies, the agreement involves the genetic and transcriptomic analysis of the Padua population and the collection of samples from COVID patients. These analysis will make it possible to study the evolution and epidemiology of SARS-CoV-2 infection, as well as to identify possible associations with susceptibility to infection and disease severity.

Istituto Europeo di Oncologia (2021)
The agreement provides for the creation of a Genomics Joint Technology Unit and a Cross Linking and Mass Spectrometry Joint Technology Unit.

Wellcome Sanger Institute (2021)
The agreement involves genome-wide prediction of cancer targets and drug prescriptions in silico using functional genomics and patient data.

IRCCS Neuromed (2021)
The agreement provides for Human Technopole's participation in the Moli-sani project. Specifically, the collaboration involves enhanced genetic studies of medically relevant traits in the Moli-sani study, aligning genomic data with phenotypic and electronic data from existing medical records.

Scuola Internazionale Superiore di Studi Avanzati - SISSA (2021)
The agreement provides for the exchange between research staff at all levels and the development of collaborative projects in areas of common interest. In addition, the agreement promotes involvement in training activities and the development of joint seminars, symposia and workshops.

Eurac Research (2021)

The agreement provides for the exchange between research staff at all levels and the development of collaborative projects in areas of common interest. It also promotes involvement in training activities and the development of joint seminars, symposia and workshops.

IRCCS Oasi Maria Santissima in Sicilia (2021)
The agreement provides for the exchange between research staff at all levels and the development of collaborative projects in areas of common interest. In addition, the agreement promotes involvement in training activities and the development of joint seminars, symposia and workshops.

Participation in consortia and collaborative research activities

As highlighted in the Covid-19 study section, Human Technopole is an associate partner of LifeTime, the pan-European research initiative that aims to revolutionise healthcare by understanding and monitoring human disease at single cell resolution to transform patient care and the sustainability of healthcare systems. The LifeTime consortium brings together more than 120 leading scientists from over 90 European research institutes. The State University of Milan is the official consortium partner, while other Italian associate partners include the European Institute of Oncology, the FIRC Foundation Institute of Molecular Oncology, the Institute of Biomedical Technologies and the Institute of Photonics and Nanotechnology of the National Research Council, as well as several leading Italian universities.

Human Cell Atlas represents a global effort combining expertise in biology, medicine, genomics, technology development and computation with the goal of building a comprehensive collection of reference cell maps, characterising each of the thousands of cell types present in the human body. A systematic study of the molecular mechanisms underlying the production, function and combined activity of different cell types would be an incredibly valuable resource for the global research community.

4.6 Scientific visiting initiatives

Human Technopole is developing the implementation of a Scientific Visitor Programme to encourage mobility and the dissemination of internally developed skills and methods. The aim is to enable external scientists from all over the world and at all career stages to spend time at the Institute to develop research collaborations, learn methods in use at Human Technopole, and use existing facilities.

The Programme started at the end of 2021, with the first scientific visitor in the Research Centre for Structural Biology, and officially began in 2022.

In 2022 (at the time of writing), we counted 16 scientific visitors who have started or are about to begin their experience at Human Technopole.

4.7 Grants and other contributions

Despite its recent establishment, the opening of the first laboratories in April 2021, and the recruiting activities still underway, in 2021, the Foundation has already obtained grants and contributions awarded in the framework of scientific projects and collaboration agreements.

The tables show the list of these resources with evidence of their amount, the project/collaboration, and the grantor. For completeness, data referring to the first months of 2022 are also shown.

RESEARCH CENTRE	INSTITUTE/BODY	PROJECT	EURO
COMPUTATIONAL BIOLOGY	Sanger	Open Targets Consortium	199,365

COMPUTATIONAL BIOLOGY	Google	Google	8,747
POPULATION AND MEDICAL GENOMICS	Impetus Grants	Longevity Impetus Grants	176,062
NEUROGENOMICS	BBRF	BBRF NARSAD Young Investigator Grant 2020	44,000
COMPUTATIONAL BIOLOGY	SVCF	Silicon Valley Community Foundation	17,792
STRUCTURAL BIOLOGY	EMBO	EMBO Postdoctoral Fellowship	133,108
STRUCTURAL BIOLOGY	EU	ERC Consolidator Grant	1,355,538
TOTAL GRANTS FORMALISED 2021			1,934,611*

* Of which 201k/Euros collected as of 12/31/2021

RESEARCH CENTRE	INSTITUTE/BODY	PROJECT	EURO
COMPUTATIONAL BIOLOGY	SVCF	Silicon Valley Community Foundation	17,643
NEUROGENOMICS	WAF	Warren Alpert Distinguished Scholars Fellowship Award	317,811
STRUCTURAL BIOLOGY	EU	ERC Starting Grant	1,498,750
STRUCTURAL BIOLOGY	EMBO	EMBO Postdoctoral Fellowship	130,000
TOTAL GRANTS FORMALISED 2022			1,964,204

RESEARCH CENTRE	INSTITUTE/BODY	PROJECT	EURO
COMPUTATIONAL BIOLOGY	EU	HORIZON-INFRA-2021-SERV-01	767,000
GENOMICS-NEUROGENOMICS	EU	HORIZON-HLTH-2021-DISEASE-04	3,234,940
NEUROGENOMICS	EU	HORIZON-HLTH-2021-STAYHLTH-01	500,000
TOTAL GRANTS AWARDED BUT NOT YET FORMALISED			4,501,940

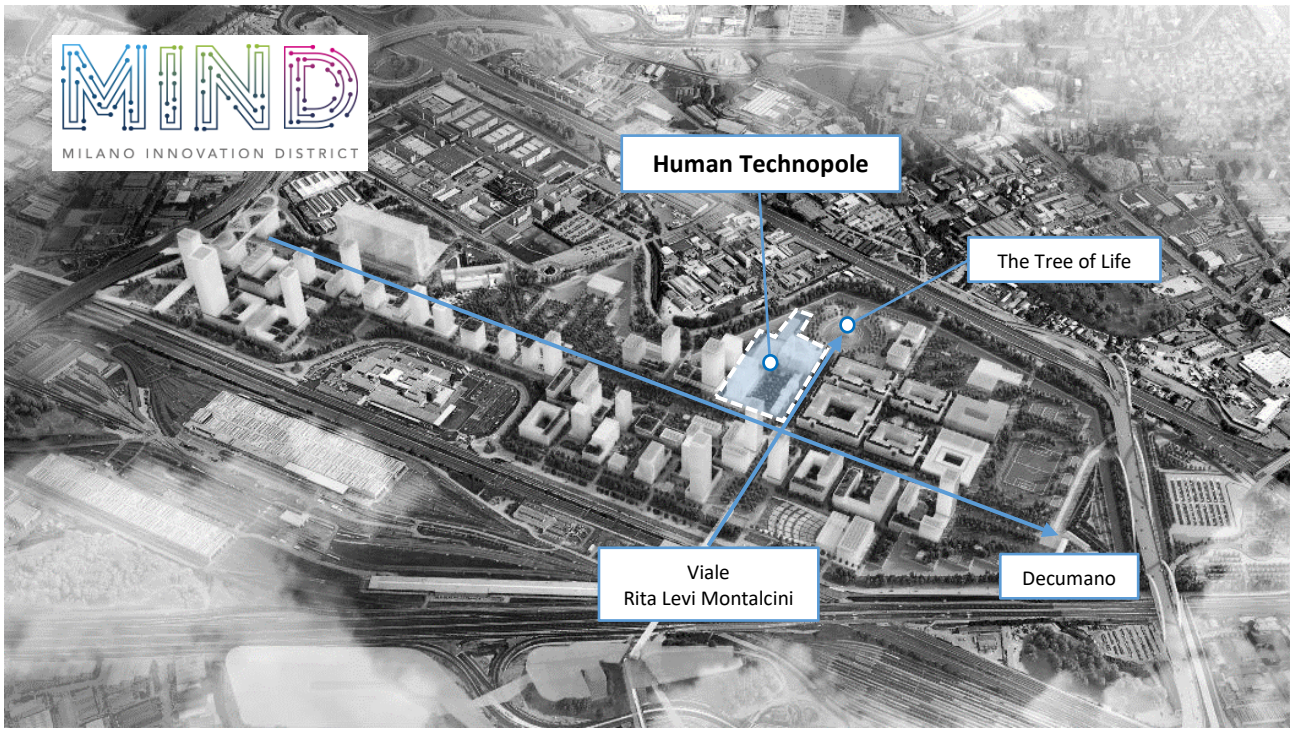
5. THE INFRASTRUCTURAL CAPITAL OF HUMAN TECHNOPOLE

5.1 Our Campus

Our Campus is constantly evolving, and it is built according to criteria of flexibility, innovation, and sustainability, and was conceived and developed in line with the spirit of openness that characterises Human Technopole.

The Human Technopole Campus is located within the new Integrated Intervention Plan (IIP) envisaged to transform the former EXPO 2015 Area, north of Milan, in the MIND – Milano Innovation District – area. The area is characterised by the construction of 3 poles, called "public anchors," consisting of the new IRCCS Galeazzi Hospital-Sant'Ambrogio, the State University of Milan, and, of course, the Research Centre of the Human Technopole Foundation. The development of the district is based on the driven concept of sustainability and experimentation, both from an environmental as well as an economic and social point of view, envisaging the enhancement of eco-compatible mobility, buildings with innovative design, and usable spaces (barrier-free) to ensure synergies between all users and Tenants.

The Human Technopole area develops in the shadow of the Tree of Life, the former symbol of EXPO 2015, together with the Palazzo Italia building, the official headquarters of Human Technopole. The area includes land covering approximately 22,000 sqm from the current Piazzale Expo 2015 to the intersection of the two main roads, Decumano and Viale Rita Levi Montalcini (formerly Cardo Nord).



Rendering MIND Area Development Project and Location Campus Human Technopole

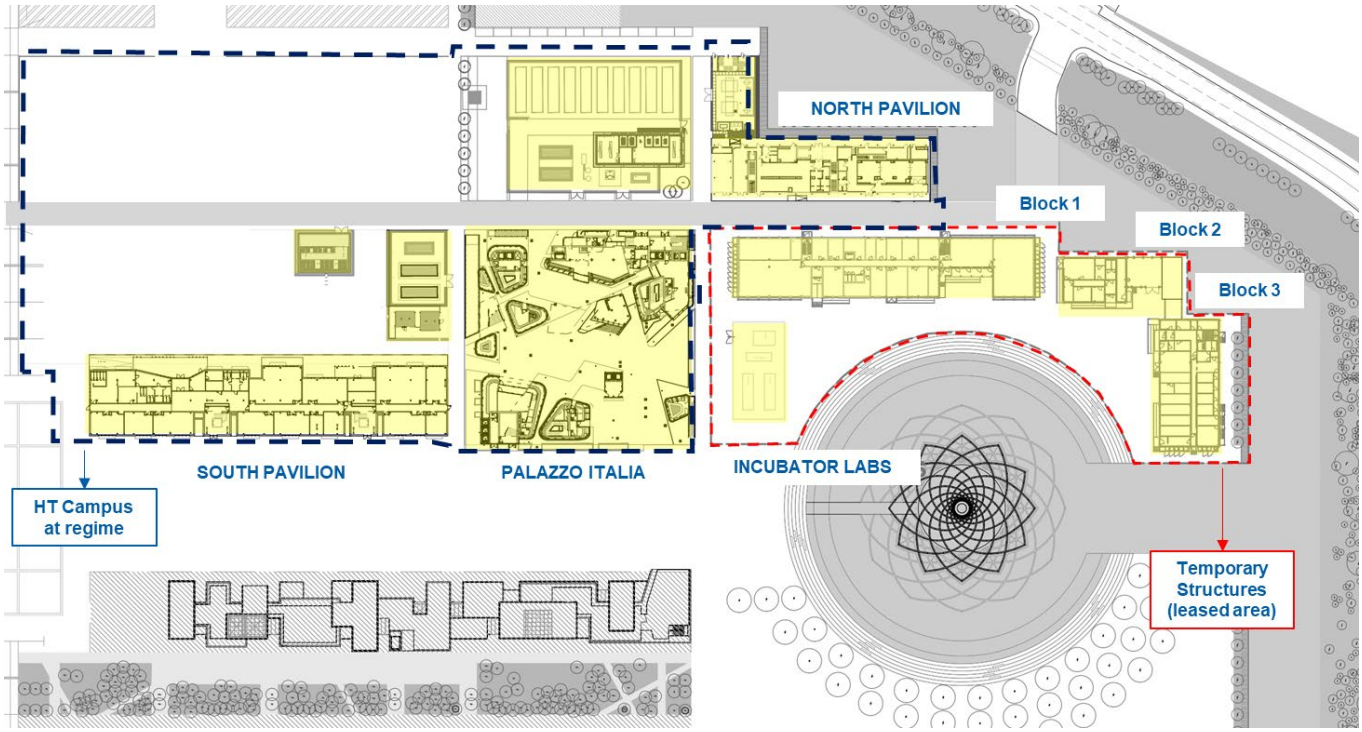
The realisation of the Human Technopole Campus essentially revolves around two main phases:

- The first, to be completed by the end of 2022, regarding the re-functionalisation of some buildings resulting from the 2015 Universal Exhibition (EXPO 2015) and the construction of some temporary structures
- The second, regarding the construction of new buildings and the completion of the National Platforms for the Italian scientific community and research infrastructures envisaged in the 2020-2024 Strategic Plan

Phase 1

In the current phase, the Campus has already operational:

- the areas related to the so-called Manufatti di Primo (18,300sqm of total surface area) resulting from Expo 2015. These buildings, including the external technical regions around them, were purchased by Human Technopole in the 2020-2021 period following the first round of refurbishment work and transformed for the new purposes of Human Technopole
- the areas relating to the so-called Temporary Facilities or Incubators Labs, which extend for about 5,000sqm around the western part of the Tree of Life square. This area, acquired through a long-term lease from Arexpo S.p.A., includes three blocks with annexed technical areas covering approximately 3,300sqm, built directly by Fondazione Human Technopole with the support of Arexpo S.p.A.



Campus HUMAN TECHNOPOLE: Phase 1 – First Settlement Manufactures and Incubators Labs

Buildings owned by Human Technopole

Leased area for Temporary Structures

HUMAN TECHNOPOLE Campus in full swing

Palazzo Italia

The iconic Italian pavilion during EXPO 2015, and at present institutional headquarters of the Foundation, following a significant refurbishment; it now houses offices, open spaces, meeting rooms, an auditorium, a restaurant, several panoramic terraces, and event spaces. The building has also a basement and an external technical area where the Campus node cabin and a prefabricated Data Centre (shelter) are located.

Palazzo Italia was purchased by Human Technopole on July 31, 2020, following an initial period of use of the building on a free loan basis to enable the initial settlement of staff.

To support its settlement programme, in 2021 Human Technopole commissioned the design of some redesigns of the interior spaces of Palazzo Italia, including the creation of new offices, better acoustic mitigation of the most sensitive areas, and the renovation of the former restaurant to create a staff canteen. In addition, a logistics centre was built in the basement, including the data centre, a warehouse, and a depot for storing biological changes in liquid nitrogen. The contract envisaged a phased construction to allow for the Foundation's normal operations, and the full completion of all works, still in progress, is scheduled for March 2023. Palazzo Italia is also undergoing a complete refurbishment in interior design, signage and landscaping, and common areas.

When all work is completed, the building will come to house over 300 people, including employees and collaborators of Human Technopole.

North Pavilion

The former Ferrarini Pavilion underwent a refurbishment to make it suitable for imaging facilities with cryo-electron microscopes (Cryo-EM) and optical microscopes (Light Microscopy Imaging) that are sensitive to noise, vibration, and fluctuations in temperature and air humidity.

It is equipped with support spaces for sample preparation and offices for the managers of the two facilities. The first-floor houses approximately fifteen workstations for the staff of the Image Analysis Facility, as well as support workstations for users of the two facilities.

Purchased by Human Technopole on September 28, 2021, the building now houses more than 10 high-tech and recently manufactured microscopes, with a total value of more than EUR 20 million.

South Pavilion (former Cardo Nord-Ovest)

The building underwent a refurbishment to make it suitable for housing primary and secondary laboratories and was subsequently purchased by Human Technopole on September 28, 2021, and partially fitted out. The building currently houses the staff of several research groups. To further expand its functionality, Human Technopole commissioned the design of some plant upgrades for the creation of a new Bio-Security Level 3 (BSL3) area and the construction of an automation platform. Following the tender procedure, the works were awarded in July 2022, and completion is estimated for early 2023.

The building will permanently house around 65 researchers and support workstations for collaborators and users of the Genomics and Neurogenomics facilities in support of the other buildings, the laboratory kitchen, cold rooms, and an additional storage room.

Incubator labs

Human Technopole built these temporary facilities in the area adjacent to Palazzo Italia to support several scientific functions in the first phase of the Foundation's development before being permanently relocated to the new building, now in the final design phase, known as the South Building, in 2027.

They consist of three blocks, two of which, on two levels, are mainly dedicated to laboratories, and a third, on one level, which houses the support structure for the electron cryo-microscopy facility with two microscopes, a sample preparation room, and a microscope control room. It houses around 150 "wet" workstations, i.e., individual counters for experimental researchers, support desks, support laboratories, instrument rooms, cell cultures, environmental chambers, sequencers, core services (glassware washing, kitchen, warehouse, etc.), and some offices.

Two additional technical areas and the technical gas storage areas completed the temporary facilities section.

To date, the temporary facilities are fully functional – except the Animal Research facility in Block 3, for which the ministerial authorisation procedure is in progress – and already house approximately 100 researchers and Ph.D. students.

Other Campus Infrastructure

At the Campus level, we would like to highlight the further project for the construction of the main tanks and liquid nitrogen distribution lines to improve the operating conditions of the cryo-microscopy in the North Pavilion and to serve the cold storage of biological samples. The same project also includes:

- the supply of containers,
- the set-up of cold storage in the basement of Palazzo Italia, and
- the collection of technical gases.

In 2021, the organisational design of the works was completed, and the tender was launched in February 2022. The results are expected to be completed by 2022.

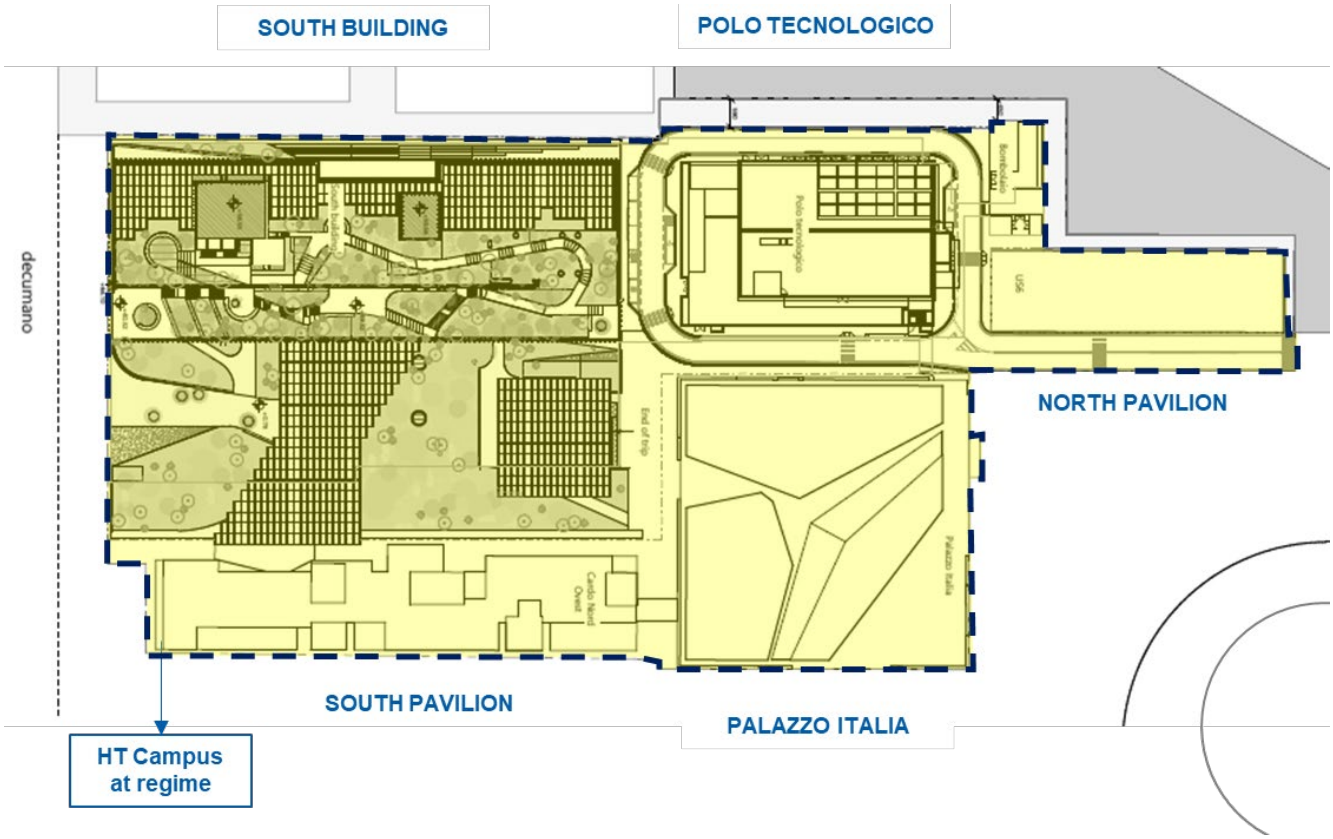
Phase 2

The Campus, in its future configuration, will include the following:

- the areas related to Palazzo Italia, the North and South Pavilion, including the external technical regions as described above
- the areas related to the new buildings being planned (South Building and Polo Tecnologico)
- the areas related to the road network connecting the buildings

Overall, when fully operational, the Human Technopole Campus will occupy an area of approximately 22,000sqm and have a total surface area of roughly 46,000sqm, divided between five primary and permanent buildings, including new buildings of 27,500sqm.

To reach this goal, the land is currently being purchased from Arexpo S.p.A. for an additional 11,000sqm of land to allow for the new buildings, which will also house the National Platforms, starting from 2023.



Phase 2 – First Settlement, Technology Pole and South Building

Buildings/Owned areas of Human Technopole

Human Technopole Campus at full capacity

South Building and Technological Pole

May 2019 saw the publication of the international design competition for the South Building, the main building of the Human Technopole Campus, which, once completed, will house laboratories for 800 permanent scientists, as well as management offices and training and events spaces, with a total capacity of 2,000 users.

The Project of Technical-Economic Feasibility (PFTE), realised by the winning designer of the competition, also envisages a rationalisation of the location of the technical areas of the Campus, learned in successive phases, and the construction of a single Technopole, thus acquiring free surface area for greenery and spaces for interaction.

The Final Project, delivered at the end of May 2022 and in the process of being approved, envisages housing in the new buildings not only the research groups and instrumentation currently housed in the temporary structures of the Incubator Labs, but also the systems of all the existing technical areas (multi-purpose units and generators), together with the new Data Centre, with an installable power of about 500kW.

A space of approximately 8,000sqm on three levels will house the National Platforms, as per Law 160/2019.

There are also plans to build a 450-cover canteen and a sloping green roof, with a high architectural value, entirely practicable. In addition, the Technological Pole will house 90 parking spaces in the basement and a network of new underground connections between the buildings.

The Foundation's goal is to finish construction of the new facilities by mid-2027 to start the transfer of what is currently housed in the Incubator Labs immediately afterwards.

The HUMAN TECHNOPOLE Facilities

The facilities hosted by our Campus have been conceived to be accessible to internal and external users to best meet the needs of the scientific community.

The first facilities that are already operational are the Data Centre (first phase), the Genomics Facility, the Cryo-Electron Microscopy Facility, the Optical Microscopy Imaging Facility, the Image Analysis Facility, and the Automated Stem Cell and Organoid Facility.

In addition, other technology platforms are under development, including the Fluorescence Activated Cell Sorting (FACS) Facility, Protein Expression and Purification, Crystallisation and Biophysics, Proteomics, Metabolomics, Animal Research Facility, and Transgenic Facility.

The high-technological impact facilities, best known as National Platforms, are also in the process of being approved, following the outcome of the consultations carried out by Human Technopole in accordance with the Convention, introduced by Article 1, paragraph 275, of Law No. 160/2019, between Human Technopole and the founding Italian Ministries.

Below is a detailed description of the first six facilities implemented.

5.2 The Data Centre

Research activity requires considerable storage capacity to manage and analyse massive amounts of clinical information, biological data, images, etc. For this reason, our Campus has been equipped with a Data Centre facility to enable Human Technopole researchers to process data in the shortest possible time.

Pending the completion of the South Building and the Technopole, the Institute was equipped with a "UPS" room with static uninterruptible power supplies with 2N-type redundancy and a "Library" room.

In addition, the electrical supply networks, the fire-fighting network, and the air-conditioning units for thermal load reduction were upgraded and reinforced. A Faraday cage was also built inside the "Library" room to protect the magnetic fields.

The configuration adopted allows the HPC (High-Performance Computing) servers and data backup systems to be adequately housed, leaving room for additional services for further expansion.

Dr. Alessandra Poggiani (Director of Administration) and Mr. Carlos Fernandez (ICT Manager) manage the Facility in coordination with the steering committee composed of the Foundation's Director, Prof. Iain Mattaj, and the Head of Computational Biology, Dr. Andrea Sottoriva.

5.3 The Cryo-Microscopy Facility

The Human Technopole Cryo-Microscopy Facility is designed to study in detail the structure of single macromolecules and entire cellular compartments, combining single-particle analysis (SPA), electron tomography (ET) and correlative light-electron microscopy (CLEM) workflows.

The Cryo-Electron Microscopy Facility will make a decisive contribution in supporting the scientific needs of Human Technopole's five interdisciplinary research centres: using SPA, it is indeed possible to obtain the high-resolution 3D structure of proteins, enzymes, and other macromolecules. In addition, ET is used within the Cryo-Electron Microscopy Facility to explore the internal architecture of cells, tissues, and organoids. Using focused ion beam scanning electron microscopy (FIB-SEM) technology, the Facility can open a window to look inside vitrified samples. In addition, the Facility supports the preparation of samples (e.g., high-pressure freezing, freeze substitution, heavy metal staining, immersion freezing, micro-patterning) and their analysis (e.g., sample screening by negative staining and Cryo-Electron Microscopy, correlative microscopy).

The facility benefits from state-of-the-art equipment, including:	A Thermo Scientific Titan Krios G4i 300kV TEM electron microscope equipped with a Thermo Scientific Falcon 4 detector, a Thermo Scientific Selectris X energy filter, a Thermo Scientific CETA 16M camera and a Volta phase-plate
	A Thermo Scientific Spectra 300kV STEM electron microscope equipped with a Thermo Scientific CETA 16M camera with speed enhancement package for tomographic analysis
	A Thermo Scientific Glacios 200kV TEM electron microscope equipped with a Thermo Scientific Falcon 4 detector, a CETA 16M camera and a Volta phase-plate
	A Thermo Scientific Talos L120C 120kV TEM electron microscope equipped with a Thermo Scientific CETA 16M camera for analysis at both ambient and cryogenic temperatures (via Gatan ELSA cryo-holder)
	A Thermo Scientific Aquilos 2 dual-beam electron microscope for preparing lamellae at cryogenic temperatures.

Ancillary equipment includes a fluorescence microscope with a cryo-stage for CLEM applications, immersion freezing devices, glow discharge units, plasma cleaners, carbon coating system and other sample preparation tools for high-pressure freezing, freeze replacement and ultra-microtomy of embedded and vitrified resin samples.

The Facility is managed by Dr. Paolo Swuec, Head of CryoElectron Microscopy.

Paolo Swuec, Head of CryoElectron Microscopy Facility
Paolo Swuec is a biochemist. After obtaining a PhD in Structural Biology from the Francis Crick Institute (UK), he moved to the University of Milan to set up and run the country's first cryo-electron microscopy laboratory. During his career, he has made important contributions to the understanding of the protein machinery involved in several key biological processes such as DNA repair and replication, viral integration and gene editing.

5.4 The Imaging Facility for Optical Microscopy

Optical microscopy is a technique that allows samples to be observed using light and enables high-resolution images of models to be obtained without disturbing their development and growth. It is an irreplaceable tool for studying the dynamic processes that take place inside cells

and living organisms. The Facility focuses on 3D imaging in response to the growing demand to study highly dynamic and ever-changing processes.

The Facility is equipped with state-of-the-art fluorescence microscopy systems, including:

- A confocal with multi-channel laser excitation and super-resolution
- A confocal with multiphoton excitation and super-resolution
- A structured illumination system
- A spinning disk system with simultaneous multi-chamber acquisition
- Several wide-field microscopes

The microscopes are equipped with incubators and CO2 pressure control to enable uninterrupted image and film acquisition using live tissues and cells over extended periods.

A fundamental point of the Facility's activities is the synergy with the other existing facilities at Human Technopole, in particular with the Facility for Cryo-Electron-Microscopy and the Automated for Stem Cells and Organoids, to streamline work procedures and facilitate sample analysis through a holistic and structured approach of experimental data acquisition and processing.

The Facility is managed by Dr. Nicola Maghelli, Senior Manager Light Microscopy Facility.

Nicola Maghelli, Senior Manager Light Microscopy Facility
After graduating in physics from the University of Pisa, he received his PhD from the Institute of Experimental Physics at the University of Ulm. His career then continued as a Postdoc and staff scientist at the Max Planck Institute and the CSBD in Dresden, where he founded and directed the Advanced Imaging Facility. During his scientific career, he designed and built multiple advanced microscopy systems, which were successfully employed in the study of biological processes.

5.5 The Image Analysis Facility

Modern imaging techniques in optical and electron microscopy and computational approaches are changing the way biomedical research is conducted. Solutions for image restoration, downstream (semi-) automated processing, intelligent microscopy or real-time image analysis, and the management and visualisation of big data are crucial for the success of image- and imaging-centred research. Human Technopole's Image Analysis Facility provides many of these skills. Users can focus on research and benefit from the central state-of-the-art methods, tools, and services.

The core mission of the Image Analysis Facility is to act as a knowledge incubator, helping to preserve knowledge about Human Technopole's complex bio-image analysis workflows.

In addition to this essential technical support, the Image Analysis Facility offers training opportunities for scientific personnel with different backgrounds and career paths. This activity is vital to keep the community educated and informed, including the use of new knowledge-exchange models. The key to our mission is to build bridges between all Human Technopole research centres and research communities in Italy and elsewhere. The Facility is meant to be a place where scientists can meet, exchange ideas and experiences, and, of course, a place to be supported by the Facility's staff.

Florian Jug, Research Group Leader and Head of Image Analysis Facility
Florian Jug holds a PhD in computational neuroscience from the Institute of Theoretical Computer Science at the ETH Zurich. His research aims to push the boundaries of what artificial intelligence and machine learning can do to better analyse and quantify biological data. His team makes a strong contribution to the Fiji software (around 100,000 active users) and collaboratively develops methods such as CARE, Noise2Void, PN2V, DivNoising etc. It organises scientific conferences (e.g., the I2K conference), workshops (e.g., the BIC workshops at high-level computer vision conferences) and various practical training courses on machine learning for bio-image analysis (e.g., DL@MBL at Woods Hole) or microscopy (e.g., Quantitative Imaging at Cold Spring Harboe).

5.6 The Genomics Facility

The Genomics Facility is a strategic infrastructure for implementing Human Technopole's mission and projects. Thanks to a team of specialised and highly qualified professionals with proven technical and scientific experience in the application of sequencing technologies in different fields of investigation, the Facility can provide innovative and cutting-edge services in other lines of genomic, transcriptomic, epigenomic, and metagenomic research.

The Genomics Facility has state-of-the-art tools at its disposal, including:	NovaSeq 600 Illumina, the most powerful sequencer manufactured by Illumina
	Chronium Controller e Chronium X10x Genomics
	CellenONE f1.4 ScienION
	Chromium Connect 10x Genomics
	BD Rhapsody Single-Cell Analysis System BD Bioscience
	MiSeq Illumina
	TapeStation 4200 Agilent
	Fragment Analyzer Agilent
	FEMTO Pulse Agilenti
	Bravo NGS Workstation Agilent
	Covaris E220 Focused ultrasonicator
	QIACube HUMAN TECHNOPOLE QIAGEN
	Glomax Discover Microplate Reader Promega

The Genomics Facility collaborates with the Human Technopole research centres on research projects whose objectives include:

- Genomic studies of large patient cohorts aimed at identifying genetic markers associated with disease predisposition and onset
- Functional genomic studies aimed at understanding the molecular mechanisms underlying transcriptional and epigenetic regulation
- Neurogenomics studies to analyse the differentiation of neuronal cells and tissues from pluripotent stem cells to brain organoids
- Single-cell sequencing studies to obtain immune profiles in Covid19 patients, to study the immune infiltrate in tumours, or to determine the immunological mechanisms underlying the onset of diseases of the immune system

Dr. Clelia Peano, Senior Manager of the High-Throughput Sequencing Operations, manages the Facility.

Clelia Peano, Senior Manager of High-Throughput Sequencing Operations
She holds a degree in Biology from the University of Parma and a PhD in Biotechnology from the same University. She was head of the Genomics Unit at the Istituto Clinico Humanitas, where she was responsible for both NGS and single-cell sequencing platforms, staff working in the Facility and programming sequencing projects for about 40 basic and clinical research groups. She is also a researcher at the National Research Council where she set up an independent research group at the Institute of Genetic and Biomedical Research.

5.7 The Automated Facility for Stem Cells and Organoids (in progress)

The Facility for the Generation of Stem Cells and Organoids is an innovative technological infrastructure that aims to create the first national core facility for the generation, maintenance, differentiation, and genome engineering of pluripotent stem cells.

Through the design and realisation of a state-of-the-art robotic platform, the Facility translates the processes of:

- Reprogramming of somatic cells into pluripotent stem cells
- Generation and long-term maintenance of organoids
- Genome engineering of stem cells and cell lines

The primary mission is to simplify and rationalise the processes required for the genesis of biological models to study disease. Highly qualified staff and the latest technologies for laboratory automation allow the Facility to offer a highly diversified portfolio of services, which also includes resources for training and organising workshops on the latest innovations in automation and stem cells.

The Facility is in progress under the leadership of Dr. Giovanni Fagà, Head of Automation of Automated Stem Cell and Organoid Facility.

Giovanni Fagà, Head of Automation – Automated Stem Cell and Organoid Facility
After his Master's degree in Biological Sciences at the University of Milan, he completed his PhD in Molecular Biology at the European Institute of Oncology in Milan, where he worked since 2009 coordinating the validation, development and pilot screening activities of high throughput biological and biochemical assays. From 2016 to 2020, he joined the IFOM Institute (Molecular Oncology Foundation) as Senior Automation Scientist.

6. THE IMPLEMENTATION OF NATIONAL RESEARCH PLATFORMS

6.1 The regulatory framework

Paragraph 276, Article 1, of Law No. 160/2019 provided for the signing, by 31 December 2020, of an Agreement between the Human Technopole Foundation and the founding Ministries, to define the modalities for the implementation of the following activities to be carried out by the Institute:

- Regular identification of infrastructure facilities with a high technological impact through open consultations with the national scientific community

- Implementation and expansion of the infrastructure facilities with the majority use of the financial resources allocated to the Foundation
- Promotion of discussion with the national research system to maximise the compatibility and integration of the Foundation's facilities with those present in the national research system
- Launching and coordinating the annual competitive procedures for the evaluation and selection of projects submitted for access to the infrastructure facilities by researchers or groups of researchers belonging to universities, Scientific Hospitalisation and Treatment Institutes (IRCCS), and public research entities, to which the predominant use of the Foundation's infrastructure facilities is guaranteed.

6.2 The Conclusion of the Convention

On December 30, 2020, the Ministry of Economy and Finance, the Ministry of Health, the Ministry of University and Research, and the Human Technopole Foundation entered into the Convention governing the identification of National Platforms with high technological impact in the field of health, genomics, nutrition and data, and decision science to be implemented at the Foundation.

Specifically, National Platforms (NPs) of/for <<specific macro technological area of investment>> with high technological impact, are defined as facilities, expertise, resources and related services used by the scientific community to conduct high quality research in their respective fields, unconstrained by institutional or national affiliation. NPs meet the definition of research introduced by the European Strategy Forum for Research Infrastructure (ESFRI).

These platforms will be accessible to the national and international scientific community for the conduct of high-quality research in their respective fields, unconstrained by institutional affiliation.

The Convention states that those platforms will have to be identified by public consultations open to the scientific community.

6.3 The Technical Committee

The Convention also provides for the establishment of a Technical Committee (TC), appointed by Interministerial Decree No. 207 of January 26, 2021, by the Directorate General for Research of the Ministries of University and Research and Health.

Below is the composition of the TC:

- Prof. Iain Mattaj, Director of the Human Technopole Foundation, acting as President
- Dott. Vincenzo De Felice, (then) Director General for the Coordination, Promotion and Development of Research of the Ministry of Universities and Research (replaced by Interministerial Decree of October 6, 2021, by Dr. Gianluca Consoli, Director General for Internationalisation and Communication), as Vice President
- Dott. Giovanni Leonardi, (then) Director General of Research and Innovation in Healthcare of the Ministry of Health (replaced by Interministerial Decree of October 6, 2021, by Dr Giuseppe Ippolito, Director General of Research and Innovation in Healthcare)

- Dr. Gelsomina Pappalardo, Italian Representative in the European Strategy Forum for Research Infrastructures (ESFRI)
- Prof. Walter Ricciardi, Coordinator of the Human Technopole Scientific Committee

The tasks of the TC:

- Survey the major research infrastructures already present in the country and in the EU and their state of operation and openness to the national scientific community
- Define the procedure for acquiring proposals on possible NPs
- Organise and conduct first-level public consultations
- Organise and conduct second-level public consultations
- Draw up the final report on the outcome of the consultations

6.4 First-level consultation

The Convention envisages the launch of public consultations in order to identify the NPs that the national scientific community is most interested in.

The first-level consultation involves collective stakeholders of particular relevance to life sciences research and is aimed at gathering reflections and indications that will make it possible to draw up an initial list of possible NPs to be implemented at the Human Technopole Foundation site.

The first-level consultation took place between July 23 and September 30, 2021 and was attended by 167 stakeholders selected by the TC on the basis of the provisions of the Convention.

A total of 29 facilities were proposed and assessed by the TC with the support of international experts.

Through the first-level consultation, the TC identified three areas with high demand for research infrastructure:

- OMICS – including genomics, single-cell multiomics, genome engineering, proteomics, metabolomics (nutrition)
- IMAGING – which will span multiple scales to include molecular and cellular imaging and structural biology
- DATA HANDLING AND ANALYSIS CORE – which will support the above two domains

6.5 Second-level consultation

It takes place through the publication of the results of the first-level Consultation and is addressed at the entire scientific community, invited to express its opinion on the outcome of the first-level Consultation and to propose any justified additions and/or deletions.

The second-level consultation took place between April 19 and May 31, 2022. Although it falls outside the period covered by this Report, for the sake of completeness, it should be noted that it involved 1,625 stakeholders from the national scientific community, whose input was collected through questionnaires.

6.6 The Final Report

It summarises the results of the two levels of consultation and identifies the NPs that the national scientific community is most interested in. It is addressed to Human Technopole and the Ministries. Although outside the period covered by this Report, for the sake of completeness, it should be noted that the TC accomplished the final report and sent a copy to the Human Technopole Foundation and the founding Ministries on September 16, 2022.

1. **INITIATION OF ACTIVITIES PREPARATORY TO CONSULTATIONS:**
   a) Reconnaissance of existing research infrastructures
   b) Preparation of the consultation form
2. **FIRST-LEVEL CONSULTATION**
   aimed at representative stakeholders of the national research system
3. **SECOND-LEVEL CONSULTATION**
   aimed at the whole scientific community
4. **IDENTIFICATION, IMPLEMENTATION AND ACCESS TO PNs**

7. HUMAN TECHNOPOLE AT THE SERVICE OF THE NATIONAL AND INTERNATIONAL SCIENTIFIC COMMUNITY

7.1 The first months of Human Technopole and listening to the national scientific community

From the earliest months, Human Technopole has met with many representatives of the biomedical research community throughout Italy to present the institute, identify potential areas of cooperation, and foster synergies. These meetings have primarily served to present Human Technopole and its plans for development, as well as to learn about the research, training, and clinical activities carried out within the national biomedical scientific community.

Given its strong focus on human biology and health, Human Technopole paid particular attention to interactions with IRCCS – Istituti di Ricovero e Cura a Carattere Scientifico (Scientific Hospitalisation and Treatment Institutes) and other potential clinical partners to collaborate to enable the rapid translation of research results to patients and to ensure that Human Technopole's research, expertise, and infrastructure could be effectively channelled to strengthen Italy's clinical research and healthcare capabilities.

At the same time, Human Technopole participated in international scientific conferences and events and began to stimulate and build links with European and global initiatives, networks, and infrastructures in the areas most relevant to Human Technopole's purpose. In this context, Human Technopole has stimulated productive discussions with selected biomedical research infrastructures from the ESFRI (European Strategy Forum on Research Infrastructures) roadmap, extensive European and international research consortia, and individual potential research partners on a global level.

7.2 Training programmes

Human Technopole supports researchers in their scientific and professional development through training initiatives on cutting-edge biomedical and life sciences research topics, as well as training activities that strengthen their career path.

Human Technopole offers training opportunities to scientists working at the institute (internal training) as well as scientists working at other research centres in Italy and abroad (external training). Human Technopole's multidisciplinary and international environment provides the ideal environment for the development of talented young scientists.

7.2.1 PhD Programmes

Human Technopole is committed to providing high-quality, international training for young researchers through participation in doctoral programmes in collaboration with national and international academic institutions.

Currently, Human Technopole is a partner in the following PhD programmes:

Joint PhD in Data Analytics and Decision Sciences (DADS) with Politecnico di Milano
Since 2018, the Foundation has been part of the joint PhD programme in Data Analytics and Decision Sciences (DADS) with the Politecnico di Milano, a Human Technopole/PoliMi collaboration involving three departments – Electronics, Information and Bioengineering (DEIB), Management, Economics and Industrial Engineering (DIG) and Mathematics (DMAT) – and the Analysis, Decisions and Society Centre (now the Health Data Science Centre). The part of this three-year programme involving the Health Data Science Centre is aimed at training highly qualified data analysts and data managers capable of carrying out research relevant to the health system and health care at universities, clinical research centres, hospitals, health authorities, international institutes, financial institutions, technology companies, regulatory bodies and other public bodies. Human Technopole funded the scholarships of three DADS PhD students in 2018, four in 2019 and four in 2020.

PhD in Systems Medicine of the European School of Molecular Medicine (SEMM)
In 2019, Human Technopole joined the four-year PhD programme in Systems Medicine of the European School of Molecular Medicine (SEMM), as host institution. Born from the collaboration between several Italian life sciences research institutes, the Università Statale di Milano and the Federico II University of Naples, SEMM is a private foundation that promotes training and integrates basic, translational, and clinical research in the emerging fields of biomedicine. In this context, SEMM's PhD in Systems Medicine offers doctoral programmes in Molecular Oncology, Human Genetics, Computational Biology and Medical Humanities, as well as comprehensive training courses, mainly taught by professors from SEMM's host institutions, in areas relevant to and focused on these fields of biomedicine. Human Technopole has funded the scholarships of two SEMM PhD students in 2019, three in 2020 and eighteen in 2021. Each of these students is currently engaged in a research project under the supervision of a Human Technopole Group Leader. Human Technopole has participated in the development of SEMM's PhD in Systems Medicine through the design and development of training activities open to all PhD students from other institutions as well.

PhD in Artificial Intelligence coordinated by the National Research Council CNR
In 2021, Human Technopole was admitted as the host institute of the national PhD programme in Artificial Intelligence, which is coordinated by the National Research Council (CNR) and consists of five PhD courses involving 61 universities and research institutes. Human Technopole has joined as host institute the AI & Health and Life Sciences PhD Course, whose lead university is the Campus Bio-Medico University in Rome. Human Technopole's participation is of great strategic value, both in terms of attracting excellent young computational scientists and in terms of contributing expertise to shape activities in the field of AI at a national level. Despite not hosting any PhD students in Artificial Intelligence in 2021, Human Technopole has given its full availability for the organisation of training activities, such as lectures, seminars and courses, open to all PhD students.

7.2.2 Curricular traineeships

Human Technopole supports and promotes internships as a training opportunity for students and graduates who want to experience what they have learnt during their studies in a working context. The internship represents an example of collaboration with universities in terms of training.

In 2021, Human Technopole activated five curricular internships, giving as many students regularly enrolled in the graduate course in Bioinformatics for computational genomics at the University of Milan the opportunity to train for a period of twelve months in its laboratories under the supervision of expert researchers.

7.2.3 Internal training programmes

One of the most critical aspects for Human Technopole is improving the skills of its scientists. Through training programmes and initiatives, Human Technopole supports researchers in their scientific and career development, providing training on cutting-edge topics and technologies in biomedical and life sciences research and actively promoting scientists' career development at all stages of their professional lives. In-house training activities indirectly provide input to the national and international scientific community that will welcome Human Technopole researchers in the future or establish scientific collaborations with them.

In parallel with the establishment of a critical mass of scientists suitable for the organisation of internal training activities (which took place in 2020-2021), Human Technopole organised an in-house science training course and collaborated on a series of seminars with other institutes.

In 2021, Human Technopole gradually planned internal training activities. Examples are the seminars held by the institute's Group Leaders and the seminars, courses, and conferences held by international speakers organised in-house or at other research institutes. This activity finally took shape in 2022 with 12 events and involved around 200 scientists with more than 100 hours of training and professional development.

Internal training events 2020-2021
In 2021, the first internal training course took place, focusing on the introduction of the High-Performance Computing (HPC) Cluster at Human Technopole, with a special focus on the architecture, available resources, and use. The course trainers were experts from the Human Technopole's Information Technology department, setting an example of how, even internally at Human Technopole, interdisciplinarity is essential to give scientists a biological background access to cutting-edge technologies.

Seminars and conferences 2020-2021
In 2021, Human Technopole participated with two events in the SEMM Technological Roundtables series open to all scientists from SEMM-affiliated institutes. The SEMM Technological Roundtables aim to create new opportunities for exchange and communication on science and technology topics across all SEMM-affiliated institutes, with the aim of guiding research in new directions, establishing new collaborative interactions and gaining access to technologies that may not be routinely used in the various institutes.

The two seminars organised by Human Technopole were:

- *"Towards a Mechanistic Understanding of Molecular and Cellular Processes by cryoEM", held on November 12, 2021, organised by our Group Leaders Gaia Pigino and Alessandro Vannini.*
- *"Structural and Conformational Proteomics", held on December 3, 2021, co-organised by Alessandro Vannini and Tiziana Bonaldi from the European Institute of Oncology (IEO).*

7.2.4 External training programmes

The inspiring theme of Human Technopole's external training activities is to create a centre of excellence and reference at the international level for the training of promising researchers in the biomedical sciences through access to Human Technopole's skills, methods, and resources.

Training events for external scientists include conferences, symposia, workshops, and theoretical and practical courses relating to scientific and technological development in areas/technologies related to Human Technopole's research fields and at the forefront of modern biomedical research.

All external training activities involve Human Technopole scientists and internationally renowned scientists sharing their knowledge and recent discoveries. This activity allows participants not only to expand their expertise, but also to create possible future synergies on joint research projects and thus foster not only the sharing of knowledge but also that of discovery.

In 2020 and 2021, due to the pandemic and the impossibility of realising in-person courses, the first two external training courses were virtual, and the planning of external training events for 2022 was started.

External training events 2020-2021
In 2021, Florian Jug, Group Leader of the Research Centre for Computational Biology and Head of the Image Analysis Facility, organised two training courses for external scientists on computational methods for improving the images obtained from microscopy. These training activities involved around 60 scientists including participants, speakers and instructors from institutes of excellence around the world.

The expansion of the Human Technopole team and the start of research at the Campus laboratories have given a great boost to the training activities offered by the institute to the national and international scientific community. These activities will range from technology transfer to the computational analysis of omics data in the field of neurogenomics, passing through courses with theoretical and practical sessions in areas such as genomics and structural biology, and will be summarised in the next Report, dedicated to the 2022-2023 biennium.

7.3 The Early Career Fellowship Programme

Human Technopole has set up the Early Career Fellowship Programme (ECF), an initiative aimed at supporting the professional development of talented researchers, helping them start their own independent research activities in Italy.

The first call, published in October 2020, saw five young scientists receive a grant of EUR 1 million over five years to develop innovative research projects in Human Technopole's research areas. The winners, selected by experts with an international profile, are all from abroad and have set up their own research labs in institutions across Italy: Scuola Internazionale Superiore di Studi Avanzati (SISSA) in Trieste, IRCCS Humanitas in Milan, University of Milano-Bicocca, TIGEM in Naples, and Istituto Italiano di Tecnologia (IIT) in Genoa.

Selections for the ECF 2021 edition were opened in October 2021 and the names of the new winners will be known by the end of 2022.

Veronica Krenn

She comes from the Institute for Molecular Biotechnology in Vienna and will develop her project "Human neuroimmunobiology" at the Università degli Studi Milano-Bicocca

Gabriele Micali

He comes from the ETH in Zurich and will develop his project "Individual behaviors matter: understanding colonisation resistance in the human gut from a bacterial single-cell perspective" at the IRCCS Humanitas in Milan.

Carmen Falcone

She comes from the University of California and will develop her project "The role of interlaminar astrocytes in the primate brain" at the International School for Advanced Studies (SISSA) in Trieste.

Mirko Cortese

He comes from the University of Heidelberg and will develop his project "Unravelling the molecular and structural determinants of SARS-CoV-2-induced cellular remodelling and cytopathogenesis" at TIGEM in Naples.

Dafne Campigli Di Giammartino

She comes from the Weill Cornell Medical School of New York and will develop her "Epitranscriptomic modulation of chromatin architecture" project at the IIT in Genoa.

7.4 Participation and organisation of conferences and seminars

Human Technopole researchers participated in and contributed to the organisation of conferences and seminars. The following are examples of conferences in which the Head of Research Centres were involved.

Nicole Soranzo
EMBO Course in Population Genomics (March 2021)
Gordon Research Conference on the Cell Biology of Megakaryocytes and Platelets, Lucca, Italy (April 2021)
Cell Symposia "20 Years of the Human Genome: From Sequence to Substance" San Diego, USA (Academic Organiser & Speaker) (April 2021)
The Italian Genetics Association (AGI) and The Italian Society of Agricultural Genetics (SIGA) Seminar Series 2021 (virtual) (July 2021)

Giuseppe Testa
Society for Neuroscience (SFN), Global Connectome 2021 (Talk and Poster)
European Academy for Biomedica Science (ENABLE) - Talk
Welcome Connecting Science, Genomics of Brain Disorders 2021 (Poster)
Mario Negri Gynecologic Oncology, MaNGOMeeting 2021 - Talk
World Wide Neuro Lecture 2021 - Lecture
Master of Neurosciences of the Université de Paris, Brain Organoid Course 2021 - Talk
Società Italiana di Biologia dello Sviluppo e della Cellula, 66°Convegno GEI-SIBSC 2021 - Talk
Institut Curie, 16th International Curie Course on Epigenetics 2021 - Lecture
Cluster for Excellence MBexC, Excellence Cluster Seminar Series Epigenetic Regulation of Gene Transcription
Maastricht University, TERMIS 6th World Congress 2021 _talk
Lake Como School of Advanced Studies, School of Neuroscience 2021 – Organiser

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Piero Carninci
School of BABS Online Seminar, Virtual/Video, Australia
PhD Colloquia 2021, Virtual/Video, Italy
Joint AGI-SIGA Seminar Series 2021, Virtual/Video

Long non-coding RNAs: from interactome to function, Noncoding RNA World: From Mechanism to Therapy, Virtual/Video, Switzerland
SCIENCE & LAW International Law Answers to Scientists' Current Challenges, Virtual/Video, Italy
NEUMOTRIESTE 2021, Virtual/Video, Italy
Computational biology and artificial intelligence for personalized medicine, Virtual/Video, Russia
Weekly Centre of Excellence Roundtable, Virtual/Video, Australia
The 59th Annual Meeting of the Biophysical Society of Japan, Virtual/Video, Japan
IRCN Salon, Virtual/Video, Japan
The WINGS-LST Plenary Lecture @The U of Tokyo, Virtual/Video, Japan
The 44th Annual Meeting of the Molecular Biology Society of Japan (MBSJ), Yokohama, Japan

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Gaia Pigino
Invited Seminar @ The Joint Division of Biology/Cellular and Molecular Medicine Seminar Series, UC San Diego.
Invited Seminar @ Center for Membrane and Cell Physiology, University of Virginia.
Invited Seminar @ PRBB/CRG Session (Barcelona)
Invited Talk @ Como Lake School of Advanced Studies -Cryo-EM workshop (remote)
Invited Talk @ Dynamic Cell IV - Online Conference
Invited Talk @ BSCB GenSoc UK Cilia Network e-Symposium
Invited Seminar @ Cell Biology Seminars Series, Johns Hopkins University (remote)
Keynote Speaker @ XXV SIBPA 2020-2021 Conference (Società Italiana di Biofisica Pura ed Applicata) (remote)
Keynote Speaker @French Microscopy Society Meeting 2021 (Remote)
Session Chair @ 19th International Conference on the Cell and Molecular Biology of Chlamydomonas (France)
Co-organizer @ Dynein 2021 Meeting (Remote)
Invited Talk @ EMBO/EMBL Symposium Seeing is Believing - Imaging the Molecular Processes of Life (remote)
Keynote Speaker @ Cilia Summer School (France)
Invited Seminar @ ThermoFisher - Electron Microscopy Webinars (online)
Invited Lecture @ TU Dresden (remote)
Invited Talk @ CELL BIO virtual 2021- ASCB/EMBO Meeting - Cytoskeletal Dynamics in Health and Disease.
Invited Talk @ Asia-Pacific Cryo-EM Symposium (remote)

Alessandro Vannini
Università Roma Tre Understanding RNA Polymerase III Transcription in Health and Disease
YaYa foundation USA - Seminar: Understanding RNA Polymerase III Transcription in Health and Disease
GBMC-FMI Virtual Graduate Student Symposium 2021
Annual Meeting SFFR Belgrade – Lecture for SFFR Award 2021
OddPols meeting – UC Denver – USA
Lubjana FEBS congress - Molecular Machines
UNiTrento Understanding RNA Polymerase III Transcription in Health and Disease
Organiser of SEMM Technological table "Structural and Conformational Proteomics and their Impact in Life Science" – Milan
Vienna Biocentre Understanding RNA Polymerase III Transcription in Health and Disease

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Andrea Sottoriva
EACR Biannual Congress, Turin, Italy talk

Emanuele Di Angelantonio
European Society of Cardiology 2021 Congress
European Preventive Cardiology 2021 Congress

Francesca Ieva
TEDxParma - Infinito Futuro, Parma (IT) - talk
NBMDS - New Bridges between Mathematics and Data Science, Valladolid (Spain) - talk
ISCB 2021, (virtual) 42nd annual conference of the International Society of Clinical Biostatistics - Poster
IWFOS 2021 (virtual) 5th International Workshop on Functional and Operatorial Statistics - Poster
SIS 2021 (virtual), 50th edition of the Scientific Meeting of the Italian Statistical Society. Florence (IT) - talk
Artificial Intelligence in Cancer Medicine (virtual), Milan (Italy) - Talk
ESTRO 2021, Optimal Radiotherapy for all, Madrid (E) – Poster

8. TECHNOLOGY TRANSFER

In July 2021, following the provisions of Article 49-bis of Decree-Law No. 34 of May 19, 2020, converted with amendments by Law No. 77 of July 17, 2020, Human Technopole set up a new structure called the "Centre for Innovation and Technology Transfer in the Life Sciences" (CITT). The Centre has the task of fostering innovative processes in the field of life sciences through:

- The promotion of collaboration between private players in the innovation system and national and European research institutes
- The dissemination of research results and knowledge transfer
- The support of patenting activities and the valorisation of intellectual property
- The promotion and funding of highly innovative research projects carried out in collaboration with companies and start-ups for the development of biotechnologies, artificial intelligence technologies for genetic, proteomic, and metabolomic analysis, technologies for diagnostics, active surveillance, the protection of fragile individuals, the improvement of quality of life and active aging.

A further function that the centre intends to perform is the organisation of specific training courses to encourage an entrepreneurial mindset in the academic world and help fill the general shortage of technology transfer professionals in the life sciences sector.

In addition to training courses, CITT is involved in organising initiatives concerning the exploitation of research results. Through its numerous contacts with key players in the Italian life sciences sector, CITT is exploring the national technology transfer landscape to identify further ways to benefit the wider national scientific community.

CITT's activities, in addition to those already present in Human Technopole, identify models of collaboration with corporate partners operating in genomics, data analysis, biomedical imaging, and many other areas. Potential partnerships with companies include, for example, the implementation of joint post-doctoral projects or programmes, collaborative training initiatives, and R&D collaborations for the co-development of new tools (e.g., algorithms and software) and applications.

9. OUTREACH E STAKEHOLDER ENGAGEMENT

9.1 Integrated reporting 2020-2021

In September 2020, although not one of the entities required under Legislative Decree 254/2016, Human Technopole started an integrated reporting activity to monitor how the Foundation creates sustainable value in the short and long term.

Through the integrated reporting, Human Technopole intends to analyse and assess the resources used to achieve its strategic objectives and facilitate the coordination of internal departments in collecting and organizing valuable information for decision-making.

Furthermore, the document makes explicit how economic, social and environmental sustainability are put in place in decision-making processes, strategy and governance, including through the ways in which it interacts and engages with stakeholders, both direct as well as indirect ones.

Finally, the integrated reporting responds to the need of making transparent the Foundation's path of responsible and sustainable growth in terms of organisational behaviour, practices and activities.

The first version of Human Technopole's integrated reporting, covering the 2020 financial year, was published in September 2021 as a "pilot" project. At the same time, the second edition is currently being finalised.

Regarding Human Technopole's strategic objectives, the Integrated Reporting explores the following aspects:

- On the stakeholders' side, the relative importance of each strategic objective in their perception and the "direction" of their expectations (in terms of greater or lesser commitment by Human Technopole to the specific purpose)
- On the part of Human Technopole, the evaluation of the strategic objectives in terms of current and future commitment and the relative impact on the Foundation's activities

The importance of the strategic objectives for stakeholders is photographed by analysing the results of the listening, involvement, and dialogue initiatives that Human Technopole undertakes using interviews, surveys, institutional relations at the national and local levels, and media monitoring.

In the 2021 financial year, it was deemed appropriate to carry out an update of the materiality matrix drawn up in 2020, conducting a series of additional interviews and analysis aimed at refining the "engagement" process and confirming the priorities expressed by stakeholders in the previous year.

9.2 MIND and the innovation ecosystem

Human Technopole is in the heart of MIND (Milano Innovation District), a new city district extending over one million square meters above the former Expo 2015 area and located northwest of Milan. Today, MIND represents one of the most significant urban regeneration projects at a national level and is also increasingly attractive to international investors.

The location of Human Technopole in the MIND district represents an opportunity for the development of relations, collaborations, and partnerships with organisations and institutions of absolute importance in the field of scientific research and technology transfer, as well as an essential public presence for the redevelopment of the new Milan area.

Human Technopole's footprint in the district also includes aspects linked to the community: the Foundation, for example, has promoted an action to change the district's toponymy – approved and currently being implemented by the Municipalities of Milan and Rho – to name streets after women and men of science, innovators, and leading figures in the life sciences, with a proposal that, for the first time in Italy, sees a fair gender breakdown. The first street, to be renamed in May 2021, was the one on which Palazzo Italia opens, named at our request after Nobel Prize winner for Medicine Rita Levi-Montalcini.

9.3 Outreach activity

Human Technopole plays an active role in communicating science effectively. We started our outreach activities, while the construction of the laboratories was still in progress, with the **#RememberMyName** campaign to tell the story of the discoveries and revolutionary ideas of lesser-known scientists.

Thanks to the development of our scientific activity, we could tell the story of Human Technopole's work through communication campaigns, events, initiatives and awareness-raising activities aimed at a wide and varied audience: children, young people, students, teachers and citizens of all nationalities and backgrounds. Below are some examples of the activities carried out in the two-year period 2020/2021.

HT Presents

In 2021, Human Technopole launched the "HT Presents" programme, a series of online meetings to explore and discuss science, innovation and society, with the message that science is everyone's business. The "HT Presents" events were held throughout the year, taking as their starting point the publication of a non-scientific essay, to be read through the lens of science, to fuel a debate between the author, Human Technopole and representatives of academia, science and industry.

Collaboration agreements with non-scientific bodies and institutions

The Foundation's reporting activities also include the construction of a network of agreements with relevant partners for dissemination activities: in this framework, in the two-year period 2020/21, Human Technopole joined the Alliance for Sustainable Development (ASviS) and contributed to the production of a video on the excellence of the Italian Life Sciences supply chain together with the Ministry of Foreign Affairs and International Cooperation. Human Technopole has also signed an agreement with Associazione Civita to jointly promote initiatives for the dissemination of scientific culture.

G20

Human Technopole contributed to the work of the Italian G20, participating in the drafting of the paper "Culture and sciences for life: towards a global health literacy alliance for a sustainable future" as part of the T20 activities on 'Global Health and Covid-19'.

Other outreach activities

Human Technopole has partnered with Fondazione Feltrinelli to organise events, workshops and seminars to discuss how science can improve our quality of life and the importance of promoting a knowledge-based society and culture.

The Foundation is a scientific partner of the Festival delle Scienze, an annual science festival organised in collaboration with National Geographic. Representatives of Human Technopole's scientific leadership spoke at the international conference for the Italian Research Day in the World.

Human Technopole participated in the annual event with the Fondazione Musica per Roma with three public workshops and three educational events for high school students.

Human Technopole and Associazione Civita have organised:

- A moment of discussion and debate between representatives from the world of research, culture, politics and industry to reflect on the potential of science and culture for the relaunch of the country's economy, in view of the presentation of the National Recovery and Resilience Plan. The event saw the participation, among others, of the Undersecretary of the Ministry for Economic Development Anna Ascani ("The role of culture and science in relaunching the country's economy" – April 2021).
- An event with representatives from the worlds of research, culture and politics to discuss popularisation of science, as part of a broader reflection on how to rebuild trust in competence ("Science and culture in balance between content and entertainment" – November 2021)

10. THE HUMAN TECHNOPOLE STRUCTURE: GOVERNANCE AND HUMAN RESOURCES

10.1 Governance

Human Technopole's Articles of Association and Rules and Regulations provide for a governance system structured according to a dual model. The Supervisory Board, chaired by the Foundation's Chairman, is the body responsible for the general direction and control of the Foundation's activities, while the Management Committee, chaired by the Foundation's Director, is the administrative body responsible for carrying out the activities necessary to ensure the ordinary progress and achievement of the Foundation's purpose.

The President

The President is the legal representative of the Foundation and the guarantor of the strategic direction. He manages institutional and public relations and promotes training and dissemination activities related to the social and economic impact of scientific research and the Foundation's public engagement.

Marco Simoni was the first President of the Foundation, from 2018 to 2022. On July 7, 2022, Prime Minister Draghi appointed Gianmario Verona as the Foundation's new President.

Marco Simoni is a political economist with experience in government and academia. He graduated in Political Science from La Sapienza University in Rome and holds a PhD in Political Economy from the London School of Economics. He is an adjunct professor at the Luiss University of Rome, where he teaches European and international political economy. From 2007 to 2016, he was a faculty member at the London School of Economics, where he also taught and did research in the same field, until he became associate professor. He interrupted his academic activity to serve, between 2014 and 2018, as Advisor to the Italian Prime Minister - first Matteo Renzi and then Paolo Gentiloni – on international economic relations and industrial policy.

Gianmario Verona is Professor of Management at Bocconi University, of which he was Rector from 2016 to 2022. He holds a degree in Business Administration and a PhD in Business Administration from Bocconi University. His research, teaching and consulting activities focus on strategic and organisational management of technology and innovation. Between 2007-2013, he was Winter Term Visiting Professor at Tuck School of Business, Dartmouth College. Between 1997 and 1998, Visiting Scholar at the Massachusetts Institute of Technology (MIT). He is currently an independent member of the board of directors of the Italian Institute of Technology, the Romeo and Enrica Invernizzi Foundation and the Silvio Tronchetti Provera Foundation. Between 2016 and 2020, he was an independent member of the board of directors of Manuli Rubber Industries Corporation.

The Supervisory Board

The Supervisory Board ensures the excellence of the Foundation and compliance with the rules for the appointment of its bodies, verifies the use of resources, supervises the general coordination of internal control functions, manages the process of scientific evaluation of the Foundation's activities and carries out general guidance and control activities.

According to the Articles of Association, the Supervisory Board consists of thirteen members, including the Chairman, appointed as follows:

- seven by decree of the President of the Council of Ministers, of which two are designated by the Minister of Economy and Finance, one by the Minister of Health and one by the Minister of Education, University and Research.
- the remaining ones by decree of the President of the Council of Ministers, having heard the Ministers of Economy and Finance, Health, and Education, University and Research, designated as follows
    - one, by agreement between the Municipality of Milan and the Lombardy Region
    - one, by agreement between the participants, provided that, also in association with each other, they pay at least three per cent of the annual contribution granted by the State
    - one, by the Conference of Italian University Rectors – CRUI
    - one, by the Council of Presidents of Public Research Organisations
    - two, by the Supervisory Board from among scientists in disciplines related to the Human Technopole project and among international public health experts, who mainly carry out their activities abroad.

The first Supervisory Board of Human Technopole, in office during the two-year period covered by this paper, consisted of the following members:

- Prof. Marco Simoni, President of the Foundation, Adjunct Professor of European and International Political Economy at Luiss University, Rome
- Prof. Giovanna Iannantuoni, Rector of the Milano Bicocca University
- Prof. Massimo Inguscio, Professor emeritus of Physics of Matter at the University Campus Bio-Medico, Rome
- Prof. Marco Mancini, Pro-Rector for Organisational Autonomy, Administrative Innovation and Resource Planning and Professor of "Glottology and Linguistics", Department of Modern Letters and Cultures, University "La Sapienza", Rome
- Prof. Mauro Marè, Full Professor of Financial Science, Luiss University, Rome
- Dr. Biagio Mazzotta, State Accountant General (from September 30, 2021, replacing Dr. Daniele Franco, Director General of the Bank of Italy)
- Avv. Marcella Panucci, Chief of Staff at the Ministry for Public Administration
- Prof. Maria Grazia Roncarolo, Director of the Centre for Definitive and Curative Medicine and Professor of Paediatrics and Medicine at Stanford University
- Prof.ssa Donatella Sciuto, Pro-rector of the Politecnico di Milano
- Prof. Roberta Siliquini, Professor Department of Public Health and Paediatric Sciences, Turin, Italy

- Prof. Gianluca Vago, President of the National Centre for Oncological Hadrontherapy Foundation (CNAO), Pavia
- Prof. Alessandro Vespignani, Professor of Physics at Northeastern University and Founding Director of the Northeastern Network Science Institute, Boston

For the sake of completeness of information, the current composition of the Supervisory Board, following the Prime Ministerial Decree of July 7, 2022, is also shown below:

- Prof. Gianmario Verona, President Human Technopole and Rector of Bocconi University, Milan
- Dr. Maura Francese, Chief Secretary to the Minister of Economy and Finance
- Prof. Giovanna Iannantuoni, Rector of Milan Bicocca University
- Prof. Massimo Inguscio, Professor Emeritus of Physics of Matter at the University Campus Bio-Medico, Rome
- Dr. Giuseppe Ippolito, Director General for Research and Innovation in Health, Ministry of Health
- Dr. Biagio Mazzotta, State Accountant General
- Avv. Marcella Panucci, Chief of Staff at the Ministry for Public Administration
- Dr. Francesca Pasinelli, Director General Telethon
- Prof. Maria Grazia Roncarolo, Director of the Centre for Definitive and Curative Medicine and Professor of Paediatrics and Medicine at Stanford University
- Prof. Serena Sileoni, Professor of Constitutional Law at the Suor Orsola Benincasa University of Naples and Advisor to the Prime Minister in the Draghi Government
- Prof. Gianluca Vago, President of the National Centre for Oncology Hadrontherapy Foundation (CNAO), Pavia
- Prof. Alessandro Vespignani, Professor of Physics at Northeastern University and Founding Director of the Northeastern Network Science Institute, Boston

The Director

The Director of the Foundation is responsible for the implementation of the multi-year strategic plan and chairs the Management Committee. Iain Mattaj is the first Director of the Foundation, appointed in 2018 following an international competition.

Iain Mattaj is an internationally renowned scientist whose research over the years has made significant contributions to the field of ribonucleoprotein particles (RNPs) that function in the processing of messenger RNA precursors. From 2005 to 2018, he was Director-General of the European Molecular Biology Laboratory (EMBL, Heidelberg), Europe's flagship laboratory for life sciences, world-renowned for its outstanding research in molecular biology and for hosting a significant number of Nobel Prizes over the past twenty years, including the 2017 Nobel Prize in Chemistry for cryo-EM.

Due to age limits, Prof. Mattaj will end his term of office on December 31, 2022. For completeness of information, we would like to point out that the call for the search for a new Foundation Director closed on July 7, 2022.

The Management Committee

The Management Committee carries out the administrative work necessary to ensure the ordinary progress and activities of the Foundation. The Committee consists of five members, including the Director who chairs it. Each member of the Management Committee remains in office for four years and until new members are appointed. Each member can only be confirmed once. The members of the Management Committee are appointed by the Supervisory Board.

The Management Committee is currently composed of:

- Iain Mattaj, Director
- Prof. Irene Bozzoni, Professor of Molecular Biology at "La Sapienza" University, Rome
- Dr. Nando Minnella, Director General of the National Institute of Nuclear Physics, Rome
- Prof. Stefano Piccolo, Full Professor of Molecular Biology at the University of Padua, Italy

- Dr. Fabio Terragni, Managing Director of Alchema Srl, Milan

The Scientific Committee

In order to ensure the efficiency, effectiveness and cost-effectiveness of the Foundation's actions, the Supervisory Board has decided to proceed in 2019 with the establishment of a Scientific Advisory Board that, during the phase of setting up the laboratories and completion of the recruitment of scientific staff, would provide through its own activities, on a temporary basis and, in any case, no later than January 1, 2022, to perform the functions and attributions statutorily provided for under the Scientific Committee, whose high operating costs would not be consistent with the concrete activity that the same would be called upon to carry out in the initial phase. This Body, during 2020, carried out an advisory and evaluation activity for the benefit of the Supervisory Board and the Management Committee regarding the Programmatic plan of the 2020-2024 Multi-year Scientific Activity Plan, the appointment of committees for the selection of scientific staff and the purchase of scientific equipment.

Below is the composition of the Scientific Advisory Board:

- Walter Ricciardi (Coordinator), Professor of Hygiene and Preventive Medicine Università Cattolica del Sacro Cuore, Rome
- Geneviève Almouzni, Director Centre National de la Recherche Scientifique, France
- Margaret McMahon, Global Head Data Science Roche, Switzerland
- Gennaro Melino, Director Tor Vergata Oncoscience Research Centre, Italy
- Giulio Superti-Furga, Scientific Director Research Center for Molecular Medicine, Austria

In January 2022, the Supervisory Board appointed the 14 members of the Scientific Committee from some of the most important scientific institutions in Italy, Europe and the United States. These experts, among whom are eminent scientists from outside the Institute, including the 5 members of the previous Scientific Advisory Board, are given an important advisory role by the Foundation's Statute: indeed, they oversee and assess the protocols of the scientific activities both in terms of quality and consistency with the Human Technopole's multi-year plans.

For the sake of completeness, the overall composition of the Scientific Committee is given below:

- Geneviève Almouzni, Institut Curie, France
- Andrea Ballabio, Telethon Institute of Genetics and Medicine (TIGEM), Italy
- Pietro De Camilli, Yale School of Medicine, USA
- Kristian Helin, The Institute of Cancer Research, UK
- Alberto Mantovani, Istituto Clinico Humanitas, Italy
- Margaret McMahon, Roche Information Solutions Data & Analytics, Switzerland
- Gennaro Melino, Tor Vergata University, Italy
- Luca Pani, University of Miami (USA) e Università di Modena e Reggio Emilia, Italy
- Alfio Quarteroni, Politecnico di Milano, Italy
- Walter Ricciardi, Università Cattolica del Sacro Cuore in Rome, Italy
- Nadia Rosenthal, The Jackson Laboratory, USA
- Michael Snyder, Stanford University School of Medicine, USA
- Giulio Superti-Furga, Research Center for Molecular Medicine (CeMM), Austria
- Fiona Watt, European Molecular Biology Organization, Germany

The Board of Auditors

The Board of Auditors consists of three full members and three alternate members. They are appointed from among those included in the register of statutory auditors by Decree of the President of the Council, upon the proposal of the Ministry of Economy and Finance and after

designation by the Founding Ministries. The Board of Auditors monitors the administration and accounts of the Foundation, carries out cash audits, prepares reports on the final accounts, which it submits to the Supervisory Board.

- Fabrizio Valenza, Chairman
- Claudia Mezzabotta, Full Member
- Martino Vincenti, Full Member

The Supervisory Board

Acknowledging the dictates of Decree 231/2001, the Foundation set up a Supervisory Board (SB), endowed with autonomous powers of initiative and control. The Foundation's Supervisory Board has approved the "Supervisory Board Charter," which regulates matters of primary interest to it. Human Technopole has opted for a Supervisory Board consisting of three members.

- Vito Branca, President
- Salvatore Scuto, Full Member
- Andrea Callea, Full Member

10.2 Human Capital

10.2.1 Organisational Regulations, Functions and Organisation Chart

The implementation of Human Technopole's scientific activities goes hand in hand with the expansion and consolidation of work teams and administrative activities, aimed at providing efficient and flexible services and creating an optimal working environment for scientists.

On March 25, 2021, the Supervisory Board, at the proposal of the Management Committee, approved the Human Technopole "Organisational Model," which codifies the organisational structure as well as the distribution of tasks and responsibilities within the organisation. The Organisational Regulation defines Human Technopole's organisational structure in its macro-structure, illustrates the activities and responsibilities of the various organisational units, and defines the hierarchical and functional relations between them. The organisational structure is instrumental to the pursuit of Human Technopole's institutional and statutory purposes and meets the criteria of good management performance, transparency, effectiveness and efficiency. The organisational structure of Human Technopole consists of the following departments/areas:

Office of the President: this area, in addition to managing and supporting the activities of the Foundation's Chairman, coordinates the activities of the Supervisory Board. Liaising with the managers involved for the issues of its competence, it takes care of the preparation of the documentation supporting the meetings of the Board, draws up the agenda and the minutes. In addition, it oversees official correspondence with the supervising Ministries, the Court of Auditors and the Supervisory Board, also coordinating with the Foundation's other governance bodies such as the Management Committee, the Scientific Committee and the Board of Auditors.

Office of the Director: this area, in addition to managing and supporting the Director of the Foundation, acts as a point of contact for the members of the Management Committee, for whose meetings it draws up the agenda and minutes, and coordinates any managers involved for issues within its remit. It manages interactions between the Director and internal functions, as well as

external stakeholders. The Document Management and Protocol Service also reports to the area, which is responsible for the registration, filing and sorting of incoming, outgoing and internal documents.

Administrative Management: in 2021, as part of organisational development, the Administrative Management was established, headed by the Administrative Director and including all functions supporting the operation of the entity. Within it, the figure of the Manager in charge of keeping accounts and corporate records was also established, in accordance with the provisions of the circulars of the Ministry of Economy and Finance for the application of Article 154-bis of the TUF to investee companies. Within the Administrative Department operate the Areas:

- **Campus Development & Facility Management**: responsible for the strategic planning, development, and management of the Human Technopole Campus, including land, buildings, technical areas and temporary infrastructure with a total area of 27,579sqm and a built-up area of 50,582sqm.
- **Finance**: supports the economic management and oversees the financial sustainability of the Foundation. The principles guiding the department's activities are transparency and "internal customer" orientation. Transparency is crucial, especially since Human Technopole benefits primarily from public funds. The reporting of costs incurred is therefore geared towards gaining credibility and acceptance. The Finance Department supports this process by ensuring full accountability and strict internal controls also by developing policies and rules to prevent fraud and minimise operational risks.
- **Human Resources (HR)**: ensures the administrative management of the Foundation's staff and supervises the process of recruitment and conversion of staff contracts. In addition, it defines, in line with the Foundation's strategic plan and objectives, human resources guidelines and policies.
  During the first months of 2022, the Foundation, adhering to the values of equal opportunities, inclusion and equality, decided to adopt a Gender Equality Plan (GEP), responding to the guidelines of the European Institute for Gender Equality (EIGE), with the aim of further strengthening and formalising the ongoing commitment to provide support to all staff members, regardless of gender, nationality, religion, disability, age, cultural background or gender identity.
- **Health, Safety & Environment (HSE)**: takes care of the updating and application of legal prescriptions of environmental, health and safety interest in the workplace, oversees the monitoring of the deadlines of the consequent fulfilments and relations with the competent Authorities and with the Supervisory Body ex. Legislative Decree 231/01.
- **ICT & Digitalisation:** develops and supports the IT ecosystem with a service-oriented mentality, ensuring high quality support for users. The area manages the entire IT infrastructure of Human Technopole and implements IT standards and processes in accordance with the regulations applied by the relevant authorities.
- **Procurement & Supply chain**: guides and manages the procurement and acquisition activities of works, services and supplies in compliance with the provisions of Legislative Decree No. 50 of April 18, 2016, as amended, and the applicable procurement and public contracts regulations.

The structure of the Institute also includes the following additional departments:

Communication: develops and leads the implementation of the Institute's communication strategy and provides strategic advice by guiding communication leadership. It drafts and

distributes content for internal and external communication, supports the organisation of events and the dissemination of Human Technopole science. The area also handles relations with the press and media.

Compliance and Internal Audit: In order to ensure the correctness, effectiveness and efficiency of its activities, the Foundation, in addition to guaranteeing the first-level controls formalised in the operational procedures, decided to implement an Internal Control System structured around several activities, namely Compliance and Internal Audit. During the year 2021, the department codified, and subsequently implemented, the definition of internal regulatory documents. The process of drafting and sharing them internally has also been defined and implemented, in order to ensure that the various Areas/Departments are supervised. The function also manages the Register of Conflicts of Interest, fed by the declarations of new entrants, and the preliminary investigation of cases such as agreements/collaborations of the Foundation. The function works transversally to spread awareness within the Foundation of the public nature of the funds that finance it and, therefore, of the care and rigour required in their spending/use.

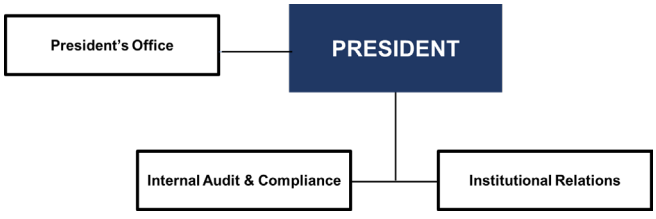
With reference to Internal Audit activities, the annual Internal Audit Plan, based on risk analysis, has been developed since 2020.

Legal: The Legal Department has the task of overseeing all the Foundation's activities with independent judgement for aspects of legal nature. The Head of the Department ("General Counsel") is a registered lawyer, qualified to plead before higher courts, who represents Human Technopole for this purpose through specific powers of attorney.

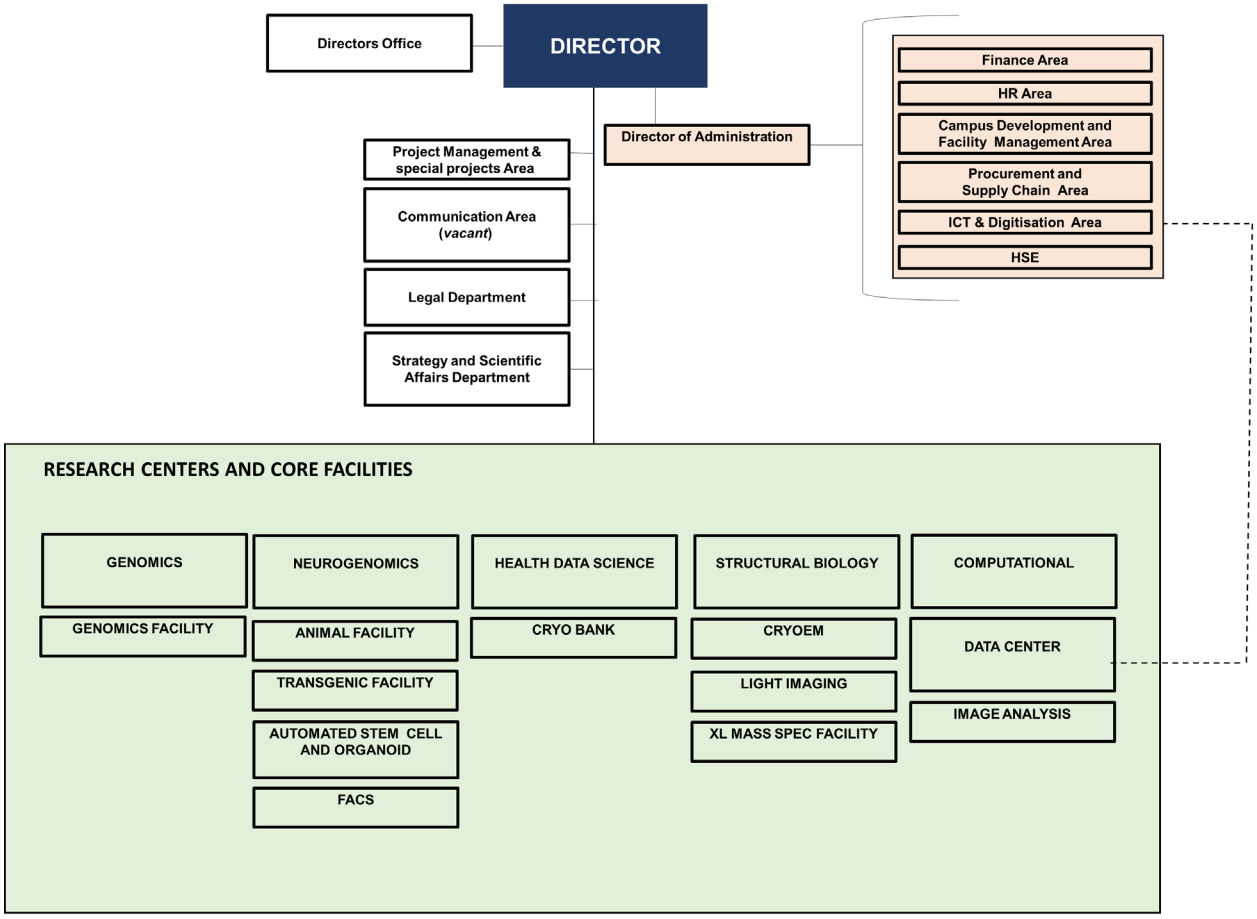
Institutional Relations: the area oversees and develops institutional relations with national and local governmental institutions, European and international organisations, trade associations and companies. The area supports the Foundation's external relations and communication, expanding its network of contacts and promoting appropriate stakeholder engagement actions with relevant interlocutors. In addition, the Institutional Relations area supports the realisation of events, initiatives and strategic information campaigns and represents Human Technopole at public events.

Strategy and Scientific Affairs: The department's main task is to support Human Technopole in developing its institutional and scientific strategy by coordinating the updating of the scientific programme and strategic plan. Furthermore, in addition to ensuring that knowledge of potentially relevant external activities and initiatives is constantly updated, it contributes to the development of regulations, procedures and guidelines concerning the training, supervision and mentorship of scientists. The department works closely with Human Technopole scientists to gather needs, identify optimal solutions for research facilities, guide decision-making processes and assist in budget planning.

ORGANISATIONAL CHART:



DIRECTORATE- SUMMARY TABLE



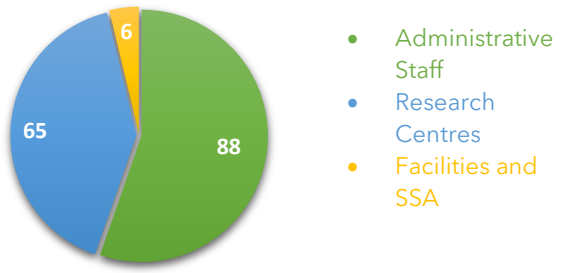
10.2.2 Human Technopole in numbers

Below is an overview of the Human Technopole workforce as of December 31, 2021, compared with the previous year:

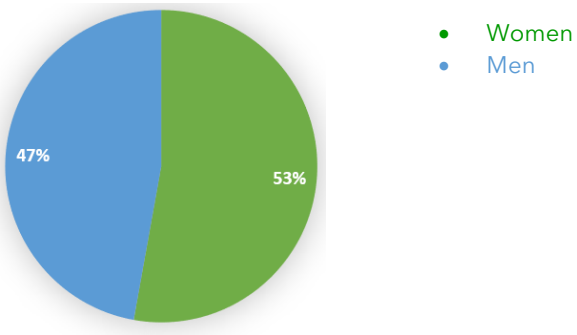
70 Employees (December 2020)		159 Employees (December 2021)	
	32		75
	38		84

The following tables show the Human Technopole population as of December 31, 2021, divided by area of work, gender, age, and nationality:

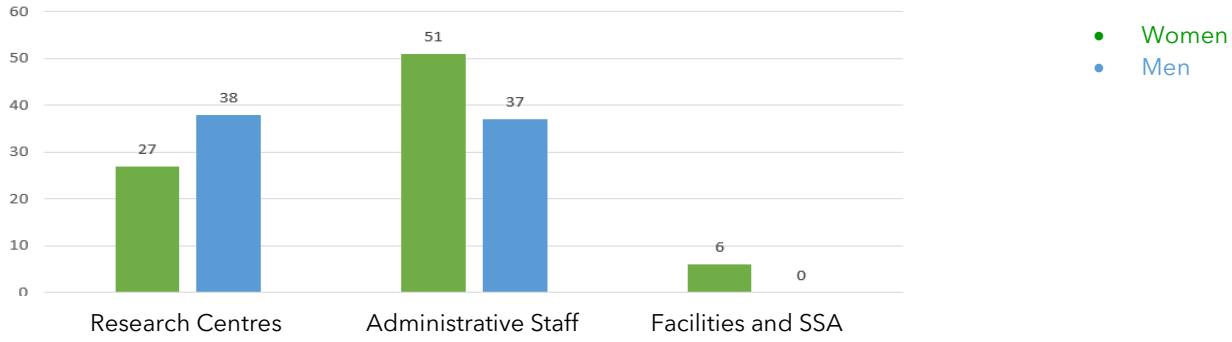
HUMAN TECHNOPOLE EMPLOYEES BY AREA



HUMAN TECHNOPOLE OVERALL GENDER DIVERSITY RATIO

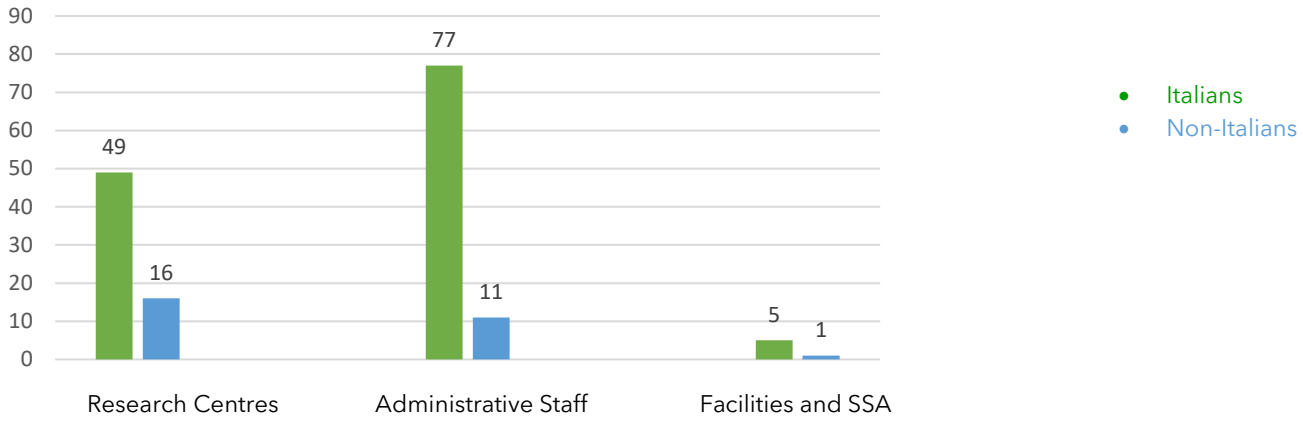


HT GENDER DISTRIBUTION AMONG AREAS – 2021

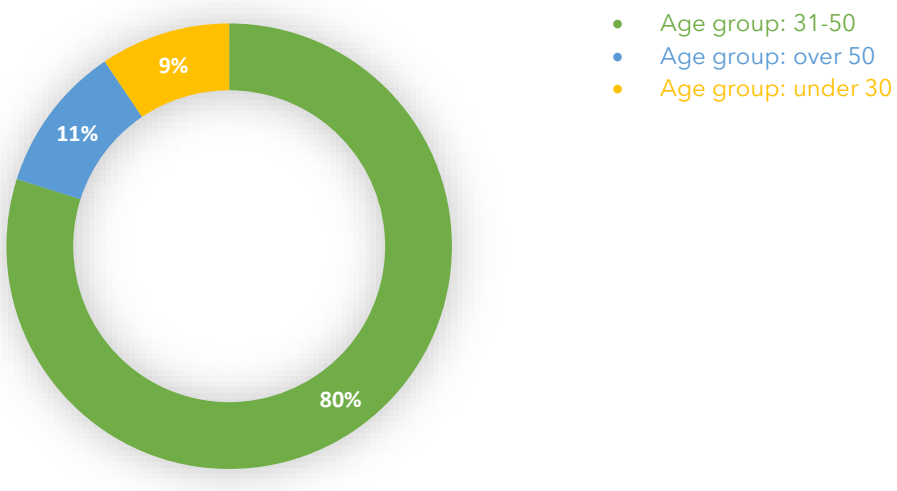


HT NON-ITALIANS/ITALIANS RATIO

HT NON-ITALIANS/ITALIANS DISTRIBUTION



HUMAN TECHNOPOLE DISTRIBUTION BY AGE GROUP



11. THE HUMAN TECHNOPOLE OF TOMORROW

HUMAN TECHNOPOLE will continue to grow not only by recruiting talents from around the world and building state-of-the-art infrastructures and laboratories, but also by creating collaborations with players in the life sciences chain.

At the time of writing, the Foundation's Supervisory Board is – as prescribed by the Convention signed with the founding Ministries on December 30, 2020 – defining the National Platforms implementation, based on the results reported in the Final Report on the public consultation conducted to identify the priorities perceived by the national scientific community.

In 2023, we will begin to work on the implementation of the National Platforms, thus becoming an innovative and crucial infrastructure hub for the national and international life sciences scientific community.

We will also continue to carry out research activities, and among the projects that will bear fruit in the near future is that of our Genomics Centre with the Istituto Neurologico Mediterraneo - Neuromed IRCCS in Isernia for the analysis of the DNA of the over 24,000 citizens who have been participating in the large epidemiological study "Moli-sani" since 2005. Through the complete analysis of the DNA of the project participants, Human Technopole will investigate how the expression of individual genes varies in the subjects, highlighting recurring characteristics that can be associated with the likelihood of developing certain diseases. In this way, we will help identify tools for prevention and early diagnosis of these diseases.

Another project that will open new scenarios for scientific research – in this case in the field of the autism spectrum and intellectual disability – is that of the Neurogenomics Centre in collaboration with the Irccs Associazione Oasi Maria Santissima di Troina. Thanks to the data collected by the Sicilian institute, our neuroscience experts will sequence the biological samples of 1,500 people with autism, to understand the genetic and epigenetic mechanisms activated during brain development.

By the end of 2022, the names of the winners of the second edition of the Early Career Fellowship Programme will be known, and through them we will have further exchanges with the best scientific realities in our country.

Great impetus will be given to this mission by the new Human Technopole governance. In 2022, in addition to the renewal of the Supervisory Board and its President, there will also be the renewal of the Management Committee, which will be headed in 2023 by the new Director of the Institute, an internationally renowned scientist currently being selected by an international search committee.

The new Director will ensure full continuity, further expanding the successes achieved with the necessary scientific leadership and guidance.

We will strengthen our ties with the business system and promote innovation through the new Technology Transfer Centre, which has already launched the first training initiatives dedicated to the national scientific community.

Finally, we will continue to go public about Human Technopole: a constantly evolving project. Heritage of all, as the science it produces.

12. MAIN ACTIVITIES TIMELINE 2020 AND 2021

2020

GOVERNANCE ACTIVITIES

- Consolidation of the Supervisory Board
- New Convention with Ministries
- Organisational model as per Legislative Decree 231/2001
- Establishment of the Compliance, Internal Audit, HSE functions

SCIENTIFIC ACTIVITIES

- Partnership with the University of Turin and Naples
- Early Career Fellowship Programme
- COVID: project with University of Padua, IEO, Sacco (LifeTime FET and COVID-19 Host Genetic)
- PhD agreements with SEMM and Politecnico di Milano
- Further activities and relations with the national and international scientific community

PROCUREMENT ACTIVITIES

- Conclusion of European Calls for Tenders for Data Storage, High performance compuing and laboratory furniture
- Consolidation in the use of the Sintel platform provided by Aria Spa
- Use, where possible, of the Consip Convention

MANAGEMENT ACTIVITIES & OPERATIONS

- Strategic Plan of Scientific Activity 2020-2024
- Completion of selection procedures for directors of research centres and consolidation of Management Operations
- Development of the ERP system
- Launch of a preliminary reporting system for monitoring and management of HT activities and ongoing operational results
- Launch of commercial activities
- Launch and management of the CITT (Center for Innovation and Technology Transfer)
- Creation of a new corporate identity (brand identity) and revamping of the website
- Recruitment of new people for the scientific and non-scientific area

CAMPUS ACTIVITIES

- Purchase of Palazzo Italia
- Signing of the urban planning agreement with Galeazzi Hospital, Università Statale di Milano, Arexpo, Lendlease and the municipalities of Rho and Milan
- Presentation of the project for the new HT building
- Lease agreement for the areas where the Incubator Labs are built
- Construction work on the Incubator Labs
- Renovation of the North and South Pavillion
- Installation of the GARR network

2021

GOVERNANCE ACTIVITIES

- Procedure for identifying the members of the Scientific Committee
- Adoption of new organisational regulations
- Adoption of regulations for the definition, drafting and approval of regulations and procedures
- Adoption of the new purchasing and campus management regulations
- Adoption of the new regulation of incentives for technical functions

SCIENTIFIC ACTIVITIES

- Completion of the scientific leadership structure
- Initiation of research and scientific service activities in laboratories on the HT Campus
- Numerous publications in prestigious journals, including Science, Nature, and Nature Communications
- Awarding by scientists of their first research grants
- Formal scientific collaborative partnerships, for example, with IRCCS Oasi Maria SS., the "International School for Advanced Studies" (SISSA), EURAC Research and the Regional Foundation for Biomedical Research (FRBB)
- Covid 19: Continued studies of the epidemiology and dynamics of the disease
- Started advanced scientific training activities and events aimed at both internal and external HT scientists
- Identification of the top 5 deserving scientists for grants from the first call "ECF programme" and launch of the second call

ADMINISTRATIVE AND INSTITUTIONAL ACTIVITIES

- ERP development and initiation of projects to integrate new softwares (Warehouse, Assets, Concur, Siope, E-catalogues, Success factor)
- Initiation of Cyber Security, Data and IT governance, Network access control projects
- Initiating the set up and configuration of Data Centres
- Process mapping and HSE risk management
- Development and consolidation of the preliminary reporting system and starting up of the accounting risk management project
- Initiation of PMO and PPM projects
- Initiation of the functional acts for carrying out the activities of the CITT
- Intense hiring activities in both scientific and administrative areas
- Consolidation in the use of the Sintel platform and use, where possible, of Consip agreements
- Initiation of administrative activities consequent to the inclusion of the Foundation in the ISTAT list
- Promotion of meetings and institutional initiatives with key stakeholders and building of a network of agreements with relevant partners
- Outreach activities with Mind partners and launch of the HTpresents Project
- Initiation of internal audit operational activities

CAMPUS ACTIVITIES

- Acquisition and continuation of the North and South Pavilion re-functionalisation activities
- Completion of the feasibility project of the South building
- Completion of construction work and delivery of the Incubator Labs
- PITA refunctionalisation and continuation of work on liquid nitrogen distribution line
- Initiation of BMS integration project