

Andrea Sottoriva, PhD, MSc

Professore in Genomica ed Evoluzione Tumorale

Head del Centro di Biologia Computazionale, Human Technopole, Milano

Capogruppo, Centre for Evolution and Cancer, The Institute of Cancer Research, Londra, Regno Unito

Esperienza Professionale

- 2021/06– **Head del Centro di Ricerca in Biologia Computazionale**, Human Technopole, Milano, Italia
- 2020/04– **Direttore del Centre for Evolution and Cancer & Vice-Direttore della Divisione di Patologia Molecolare**, The Institute of Cancer Research, Londra, Regno Unito
- 2018/03– **Vice-Direttore del Centre for Evolution and Cancer**, The Institute of Cancer Research, Londra, Regno Unito
- 2013/10– **Capogruppo**, Centre for Evolution and Cancer, The Institute of Cancer Research, Londra, Regno Unito
- 2011/10– **Postdoc Ricercatore**, University of Southern California, USA
- 2013/09

Formazione Accademica

- 2019/10 **Professore in Genomica ed Evoluzione Tumorale**, The Institute of Cancer Research, Londra, Regno Unito
- 2017/11 **Professore Associato in Dinamiche Evolutive del Cancro**, The Institute of Cancer Research, Londra, Regno Unito
- 2012/08 **Dottorato di Ricerca in Biologia Computazionale**, University of Cambridge, CRUK Research Institute, Cambridge, Regno Unito
- 2008/08 **Master in Biologia Computazionale e Bioinformatica** (cum laude), University of Amsterdam, The Netherlands
- 2006/03 **Laurea in Informatica** (110/110 cum laude), Università di Bologna, Italia

Premi

- 2016/07 **Cancer Research UK Future Leaders in Cancer Research Prize**

Altre Qualificazioni

- Abilitazione Scientifica Nazionale 2018/2020, Fascia 1, 05/E2, Biologia Molecolare
- Abilitazione Scientifica Nazionale 2018/2020, Fascia 1, 06/E2, Patologia Generale e Patologia Clinica

Publications

1. *The co-evolution of the genome and epigenome in colorectal cancer*
Heide T, Househam J, ..., Graham TA*, **Sottoriva A***.
(* joint corresponding authors)
Nature, 2022, <https://doi.org/10.1038/s41586-022-05202-1>.
2. *Phenotypic plasticity and genetic control in colorectal cancer evolution*
Househam J, Heide T, ..., **Sottoriva A***, Graham TA*.
(* joint corresponding authors)
Nature, 2022, <https://doi.org/10.1038/s41586-022-05311-x>.
3. *Germline MBD4-deficiency causes a multi-tumor predisposition syndrome*
Palles C, ..., de Voer RM.
American Journal of Human Genetics, 2022, *in press*.
4. *Circulating tumour DNA sequencing to determine therapeutic response and identify tumour heterogeneity in patients with paediatric solid tumours*
Stankunaite R, ..., **Sottoriva A**, Chesler L, Hubank M.
European Journal of Cancer, 2022, 162:209-220.
5. *Reconstructing single-cell karyotype alterations in colorectal cancer identifies punctuated and gradual diversification patterns*
Bollen Y, Steloo E, ..., Sottoriva A, Graham TA, Snippert H.
Nature Genetics, 2021, 53:1187-1195.

6. *EGFR amplification and outcome in a randomised phase III trial of chemotherapy alone or chemotherapy plus panitumumab for advanced gastro-oesophageal cancers*
Smyth E, Vlachogiannis G, Hedayat S, ..., Sottoriva A, Stange DE, Cunningham D, Valeri N.
Gut, 2021, 70(9):1632-1641.
7. *Subclonal reconstruction of tumors using machine learning and population genetics*
Caravagna G, Heide T, Williams MJ, Zapata L, Nichol D, Chkhaidze K, Cross WH, Cresswell GD, Werner B, Acar A, Louis Chesler, Banes CP, Sanguinetti G, Graham TA, **Sottoriva A**
Nature Genetics, 2020, 52:898-907.
8. *Evolutionary dynamics of neoantigens in growing tumours*
Lakatos E, Williams MJ, Schenck RO, Cross WCH, Househam J, Werner B, Gatenbee C, Robertson-Tessi M, Barnes CP, Anderson ARA, **Sottoriva A***, Graham TA*.
(* joint corresponding authors)
Nature Genetics, 2020, 52:1057-1066.
9. *Exploiting evolutionary steering to control drug resistance in cancer*
Acar A, Nichol D, Fernandez-Mateos J, Cresswell GD, Barozzi I, Hong SP, Trahearn N, Spiteri I, Stubbs M, Burke R, Stewart A, Caravagna G, Werner B, Vlachogiannis G, Maley CC, Magnani L, Valeri N, Banerji U, **Sottoriva A**
Nature Communications, 2020, 11(1):1923.
10. *Measuring the distribution of fitness effects in somatic evolution by combining clonal dynamics and dN/dS ratios*
Williams MJ, Zapata L, Werner B, Barnes CP, **Sottoriva A***, Graham TA*.
(* joint corresponding authors)
eLife, 2020, 9e48714.
11. *Mapping the breast cancer metastatic cascade onto ctDNA using genetic and epigenetic clonal tracking.*
Cresswell GD, Nichol D, Spiteri I, Tari H, Zapata L, Heide T, Maley CC, Magnani L, Schiavon G, Ashworth A, Barry P, **Sottoriva A**
Nature Communications, 2020, 11(1):1446.
12. *Measuring single cell divisions in human cancers from multi-region sequencing data*
Werner B, Case J, Williams MJ, Chkhaidze K, Temko D, Fernandez-Mateos J, Cresswell GD, Nichol D, Cross WH, Spiteri I, Huang W, Tomlinson I, Barnes CP, Graham TA, **Sottoriva A**
Nature Communications, 2020, 11(1):1035.
13. *Prediction of benefit from checkpoint inhibitors in mismatch repair deficient metastatic colorectal cancer: role of tumor infiltrating lymphocytes*
Loupakis F, Depretis I, Biason I, Intini R, Prete AA, Leone F, Lombardi P, Filippi R, Spallanzani A, Cascinu S, Reggiani Bonetti L, Maddalena G, Valeri N, **Sottoriva A**, Zapata L, Salmaso R, Munari G, Rugge M, Dei Tos AP, Golovato J, Sanborn JZ, Nguyen A, Schirripa M, Zagonel V, Lonardi S, Fassan M.
The Oncologist, 2020, 25:1-7.
14. *Resolving genetic heterogeneity in cancers*
Turajlic S, **Sottoriva A**, Graham TA, Swanton C
Nature Reviews Genetics, 2019, 20:404-416.
15. *Analysis of tumour ecological balance reveals resource-dependent adaptive strategies of ovarian cancer*
Nawaz S, Trahearn NA, Heindl A, Banerjee S, Maley CC, **Sottoriva A**, Yuan Y
EBioMedicine, 2019, doi.org/10.1016/j.ebiom.2019.10.001.
16. *Spatially constrained tumour growth affects the patterns of clonal selection and neutral drift in cancer genomic data*
Chkhaidze K, Heide T, Werner B, Williams MJ, Huang W, Caravagna G, Graham TA, **Sottoriva A**
PLoS Computational Biology, 2019, 15(7):e1007243.
17. *Measuring clonal evolution in cancer with genomics.*
Williams MJ, **Sottoriva A**, Graham TA
Annual Review of Genomics and Human Genetics, 2019, 20:309-329.
18. *Evolutionary dynamics of residual disease in human glioblastoma*
Spiteri I, Caravagna G, Cresswell GD, Vatsiou A, Nichol D, Acar A, Ermini L, Chkhaidze C, Werner B, Mair R, Brognaro E, Verhaak R, Sanguinetti G, Piccirillo S, Watts C, **Sottoriva A**
Annals of Oncology, 2019, 30(3):456-463.
19. *Microenvironmental niche divergence shapes BRCA1-dysregulated ovarian cancer morphological plasticity*
Heindl A, Khan AM, Rodrigues DN, Eason K, Sadanandam A, Orbegoso C, Punta M, **Sottoriva A**, Lise S, Banerjee S, Yuan Y
Nature Communications, 2018, 9(1):3917.
20. *Detecting repeated cancer evolution from multi-region tumor sequencing data*
Caravagna G, Giarratano Y, Ramazzotti D, Graham TA, Sanguinetti G, **Sottoriva A**

Nature Methods, 2018, 15:707-714.

21. *Longitudinal liquid biopsy and mathematical modelling of clonal evolution forecast waiting time to treatment failure in a phase II colorectal cancer clinical trial*
Khan K, Cunningham D, Werner B, Vlachogiannis G, Spiteri I, Heide T, Fernandez-Mateos J, Vatsiou A, Lampis A, Damavandi MD, Lote H, Huntingford IS, Hedayat S, Chau I, Tunariu N, Mentrasti G, Trevisani F, Rao S, Anandappa G, Watkins D, Starling N, Thomas J, Peckitt C, Khan N, Rugge M, Begum R, Hezelova B, Bryant A, Jones T, Proszek P, Fassan M, Hahne JC, Hubank M, Braconi C, **Sottoriva A**, Valeri N*
(* joint corresponding authors)
Cancer Discovery, 2018, 8(10):1-16.
22. *Quantification of subclonal selection in cancer from bulk sequencing data*
Williams MJ, Werner B, Heide T, Curtis C, Barnes CP, **Sottoriva A**, Graham TA*
(* joint corresponding authors)
Nature Genetics, 2018, 50(6):895-903.
23. *Patient-derived organoids model treatment response of metastatic gastrointestinal cancers*
Vlachogiannis G, Hedayat S, Vatsiou A, Jamin Y, Fernandez-Mateos J, Khan K, Lampis A, Eason K, Huntingford I, Burke R, Rata M, Koh D, Tunariu N, Collins D, Hulkki-Wilson S, Regulan C, Spiteri I, Moorcraft SY, Chau I, Rao S, Watkins D, Fotiadis N, Bali M, Darvish-Damavandi M, Lote H, Eltahir Z, Smyth EC, Begum R, Clarke PA, Hahne JC, Dowsett M, de Bono J, Workman P, Sadanandam A, Fassan M, Sansom OJ, Eccles S, Starling N, Braconi C, **Sottoriva A**, Robinson SP, Cunningham D, Valeri N
Science, 2018, 359(6378): 920-926.

The spatiotemporal evolution of lymph node spread in early breast cancer
Barry P, Vatsiou A, Spiteri I, Nichol D, Cresswell GD, Acar A, Trahearn N, Hrebien S, Garcia-Murillas I, Chkhaidze K, Ermini L, Huntingford IS, Cottom H, Zabaglio L, Koeble K, Khalique S, Rusby J, Muscara F, Dowsett M, Maley CC, Natrajan R, Yuan Y, Schiavon G, Turner N, **Sottoriva A**
Clinical Cancer Research, 2018, 24(19):4763-4770.
24. *The evolutionary landscape of colorectal tumorigenesis*
Cross W, Kovac M, Mustonen V, Temko D, Davis H, Baker A, Biswas S, Arnold R, Chegwiddden L, Gatenbee G, Anderson AR, Koelzer VH, Martinez P, Jiang X, Domingo E, Woodcock D, Feng Y, Kovacova M, Jansen M, Rodriguez-Justo M, Ashraf S, Guy R, Cunningham C, East JE, Wedge DC, Wang LM, Palles C, Heinimann K, **Sottoriva A**, Leedham SJ, Graham TA, Tomlinson IPM
Nature Ecology and Evolution, 2018, 34:1-6.
25. *Variation of mutational burden in healthy human tissues suggests non-random strand segregation and allows measuring somatic mutation rates*
Werner B, **Sottoriva A**
PLoS Computational Biology, 2018, 16(4):e1006233.
26. *Reply to 'Neutral tumor evolution?'*
Heide T, Zapata L, Williams MJ, Werner B, Barnes CP, Graham TA, **Sottoriva A**
Nature Genetics, 2018, 50(12):1633-1637.
27. *Reply to 'Currently available bulk sequencing data do not necessarily support a model of neutral tumor evolution'*
Werner B, Williams MJ, Barnes CP, Graham TA, **Sottoriva A**
Nature Genetics, 2018, 50(12):1624-1626.
28. *Reply to: 'Revisiting signatures of neutral tumor evolution in the light of complexity of cancer genomic data'*
Williams MJ, Werner B, Heide T, Barnes CP, Graham TA, **Sottoriva A**
Nature Genetics, 2018, 50(12): 1628-1630.
29. *Reply: Is the evolution of tumors Darwinian or non-Darwinian?*
Williams MJ, Werner B, Barnes CP, Graham TA, **Sottoriva A**
National Science Review, 2018, 0:1-3, doi: 10.1093/nsr/nwx131.
30. *Robust RNA-based in situ mutation detection delineates colorectal cancer subclonal evolution*
Baker A, Huang W, Wang XM, Jansen M, Ma X, Kim J, Anderson C, Wu X, Pan L, Su N, Luo Y, Domingo E, Heide T, **Sottoriva A**, Lewis A, Beggs A, Wright N, Rodriguez-Justo M, Park E, Tomlinson I, Graham TA
Nature Communications, 2017, 8(1998) doi:10.1038/s41467-017-02295-5.
31. *Reply: Uncertainties in tumor allele frequencies limit power to infer evolutionary pressures*
Williams MJ, Werner B, Barnes CP, Graham TA, **Sottoriva A**
Nature Genetics, 2017, 49:1289-1291.
32. *Classifying the evolutionary and ecological features of neoplasms*
Maley C, Aktipis A, Graham T, **Sottoriva A**, et al.
Nature Reviews Cancer, 2017, 17(10):605-619.
33. *Between-region genetic diversity reflects the mode and tempo of tumour evolution*
Sun R, Hu Z, **Sottoriva A**, Graham TA, Harpak A, Ma Z, Fischer JM, Shibata D, Curtis C

Nature Genetics, 2017, 49(7):1015-1024.

34. *Carbon dating cancer: defining the chronology of metastatic progression in colorectal cancer*
Lote H, Spiteri I, Ermini L, Vatsiou A, Roy A, McDonald A, Maka N, Balsitis M, Bose N, Simbolo M, Mafficini A, Lampis A, Hahne JC, Trevisani F, Eltahir Z, Mentrasti G, Findlay C, Kalkman EAJ, Punta M, Werner B, Lise S, Aktipis A, Maley C, Greaves M, Braconi C, White J, Fassan M, Scarpa A, **Sottoriva A***, Valeri N*
(* joint corresponding authors)
Annals of Oncology, 2017, 28(6):1243-1249.
35. *Detecting truly clonal alterations from multi-region profiling of tumours*
Werner B, Traulsen A, **Sottoriva A***, Dingli A*
(* joint corresponding authors)
Scientific Reports, 2017, 7:44991, doi:10.1038/srep44991.
36. *EGFRvIII mutations can emerge as late and heterogeneous events in glioblastoma development and promote angiogenesis through Src activation*
Eskilsson E, Rosland GV, Talasila KM, Knappskog S, Keunen O, **Sottoriva A**, et al.
Neuro Oncology, 2016, 18(12):1644-1655
37. *Catch my drift? Making sense of genomic intra-tumour heterogeneity*
Sottoriva A, Barnes CP, Graham TA
BBA - Reviews on Cancer, 2017, doi:10.1016/j.bbcan.2016.12.003.
38. *Measuring cancer evolution from the genome*
Graham TA, **Sottoriva A**
Journal of Pathology, 2016, 241(2):183-191.
39. *Functional versus non-functional intratumor heterogeneity in cancer*
Williams MJ, Werner B, Graham TA, **Sottoriva A**
Molecular & Cellular Oncology (commentary), 2016, 3(4):e1162897.
40. *The cancer stem cell fraction in hierarchically organized tumors can be estimated using mathematical modeling and patient-specific treatment trajectories*
Werner B, Scott JG, **Sottoriva A**, Anderson AR, Traulsen A, Altrock PM
Cancer Research, 2016, 76(7):1705-1713.
41. *Identification of neutral tumor evolution across cancer types*
Williams MJ, Werner B, Barnes CP, Graham TA, **Sottoriva A**
Nature Genetics, 2016, 48:238-244.
42. *Cancer evolution and the limits of predictability in precision cancer medicine*
Lipinski KA, Barber LJ, Davies MN, Ashenden M, **Sottoriva A**, Gerlinger M
Trends in Cancer, 2016, 2(1):49-63.
43. *Many private mutations originate from the first few divisions of a human colorectal adenoma*
Kang H, Salomon M, **Sottoriva A**, Zhao J, Toy M, Press MF, Curtis C, Marjoram P, Siegmund K, Shibata D
Journal of Pathology, 2015, 237(3):355-362.
44. *A Big Bang model of human colorectal tumor growth*
Sottoriva A, Kang H, Ma Z, Graham TA, Salomon M, Zhao J, Marjoram P, Siegmund K, Press MF, Shibata D, Curtis C
Nature Genetics, 2015, 47(3):209-216.
45. *The epigenetic profile of human adventitial progenitor cells correlates with therapeutic outcomes in a mouse model of limb ischemia*
Gubernator M, Slater SC, Spencer HL, Spiteri I, **Sottoriva A**, Riu F, Rowlinson J, Avolio E, Katare R, Mangialardi G, Oikawa A, Reni C, Campagnolo P, Spinetti G, Touloumis A, Tavaré S, Prandi F, Pesce M, Hofner M, Klemens V, Emanuelli C, Angelini G, Madeddu P
ATVB, 2015, 35(3):675-688.
46. *The role of the sub-ventricular zone in gliomagenesis*
Piccirillo SGM, **Sottoriva A**, Colin W
Aging, 2015, 10(7):738-739.
47. *Current challenges in glioblastoma intratumor heterogeneity, residual disease, and models to predict disease recurrence*
Ellis HP, Greenslade M, Powell B, Spiteri I, **Sottoriva A**, Kurian KM
Frontiers in Oncology, 2015, 5:251.
48. *Contributions to drug resistance in glioblastoma derived from malignant cells in the sub-ependymal zone*
Piccirillo SGM, Spiteri I, **Sottoriva A**, Touloumis A, Ber S, PriceSJ, HeywoodR, Francis NJ, Collins VP, Venkitaraman AR, Curtis C, Marioni JC, Tavaré S, Watts C
Cancer Research, 2015, 75(1):194-202.
49. *Defining stem cell dynamics in models of intestinal tumor initiation*

Vermeulen L, Morrissey E, van der Heijden M, Nicholson AM, **Sottoriva A**, Buczacki S, Kemp R, Tavaré S, Winton DJ
Science, 2013, 342:995-998.

50. *The shaping and functional consequence of the miRNA landscape in breast cancer*
 Dvinge H, Git A, Graf S, Salmon-Divon M, Curtis C, **Sottoriva A**, Zhao Y, Hirst M, Armisen J, Miska EA, Chin SF, Provenzano E, Turashvili G, Green A, Aparicio S, Caldas C
Nature, 2013, 497:378-382.
51. *Intra-tumor heterogeneity in human glioblastoma reflects cancer evolutionary dynamics*
Sottoriva A, Spiteri I, Piccirillo SGM, Touloumis A, Collins PV, Marioni JC, Curtis C, Watts C, Tavaré S
PNAS, 2013, 110(10):4009-4014.
52. *Single-molecule genomic data delineate patient-specific tumor profiles and cancer stem cell organization*
Sottoriva A, Spiteri I, Shibata D, Curtis C, Tavaré S
Cancer Research, 2013, 73(1):41-49.
53. *Modeling evolutionary dynamics of epigenetic mutations in hierarchically organized tumors*
Sottoriva A, Vermeulen L, Tavaré S
PLoS Computational Biology, 2011, 7(5).
54. *ANTARES: The first undersea neutrino telescope*
 ANTARES collaboration
Nuclear Instruments and Methods in Physics Research A, 2011, 656: 11-38.
55. *Integrating approximate Bayesian computation with complex agent-based models for cancer research*
Sottoriva A, Tavaré S
COMPSTAT 2010, Physica Verlag. pp. 57-66, 2010.
56. *Exploring cancer stem cell niche directed tumor growth*
Sottoriva A, Slood PM, Medema JP, Vermeulen L
Cell Cycle, 2010, 9(8): 1472-1479.
57. *Cancer stem cell tumor model reveals invasive morphology and increased phenotypical heterogeneity*
Sottoriva A, Verhoeff JJ, Borovski T, McWeeney SK, Naumov L, Medema JP, Slood PM, Vermeulen L
Cancer Research, 2010, 70: 46-56.
58. *A multiphysics and multiscale software environment for modeling astrophysical systems*
 Portegies Zwart S, et al.
New Astronomy, 2009, 14:369-378.

Conference

1. 2022/09/12, *Bertinoro Computational Biology Meeting*, Bertinoro, Italy
2. 2022/06/27, *Systems Genetics of Cancer*, Cambridge, UK
3. 2021/06/11, *EACR Biannual Congress*, Turin, Italy
4. 2020/10/09, *ESMO Molecular Analysis for Precision Oncology (MAP) congress*, Amsterdam, Netherlands (cancelled for COVID)
5. 2020/06/18, *EACR Biannual Congress*, Turin, Italy (cancelled for COVID)
6. 2020/03/19, *SEMM PhD students Bioinformatics Advanced Course (IEO/IFOM)*, Milan, Italy (cancelled for COVID)
7. 2020/03/13, *AACR Evolutionary Dynamics in Carcinogenesis and Response to Therapy*, Denver, USA (cancelled for COVID)
8. 2020/01/20, *Keystone Symposium in Cancer Evolution and Combinatorial Therapies*, Banff, Canada
9. 2019/09/23, *Heterogeneity and Evolution in Cancer*, CNIO, Madrid, Spain
10. 2019/07/22, *Society for Molecular Biology and Evolution, Cancer Evolution Symposium*, Manchester, UK
11. 2019/06/13, *Systems Genetics of Cancer*, Berlin, Germany
12. 2019/03/26, *CRUK International Symposium Oesophageal Cancer*, London, UK
13. 2019/03/14, *Biomedical Data Science School*, Edinburgh, UK
14. 2019/03/05, *Genetic and epigenetic evolution*, Turin, Italy
15. 2019/02/14, *Statistical Physics Approaches to Systems Biology*, Havana, Cuba
16. 2018/07/01, *EACR Biannual Congress*, Amsterdam, Netherlands
17. 2017/06/05, *Evolutionary Biology and Ecology of Cancer Sanger Summer School*, Cambridge, UK
18. 2018/03/22, *First International Workshop on Tumor Evolution and Heterogeneity*, Rome, Italy
19. 2017/11/06, *National Cancer Research Institute – Chair of the Cancer Evolution Session*, Liverpool, UK
20. 2017/06/30, *International Symposium on Genomic Medicine*, Seoul, South Korea
21. 2017/06/15, *Advanced Seminar on Cancer Cell Heterogeneity*, Lund, Sweden
22. 2017/06/14, *Karolinska Institutet Cancer Genomics Summer School*, Stockholm, Sweden
23. 2017/05/24, *Cancer Development and Complexity Workshop and School*, Como, Italy
24. 2017/05/11, *CRUK Marshall Symposium in Cancer Evolution*, UK
25. 2017/03/06, *ICREA-FIJC on ITH and Cancer Evolution*, Barcelona, Spain
26. 2016/11/14, *CANCEROMATICS III*, Madrid, Spain

27. 2016/10/06, *Evolution and Medicine Conference*, Barcelona, Spain
28. 2016/09/20, *Seminar at San Raffaele Scientific Institute*, Milan, Italy
29. 2016/09/19, *Seminar at Candiolo Cancer Institute*, Candiolo, Italy
30. 2016/09/12, *Systems Genetics of Cancer Workshop*, Cambridge, UK
31. 2016/07/14, *Evolutionary Biology and Ecology of Cancer Sanger Summer School*, Cambridge, UK
32. 2016/07/10, *EACR Biannual Congress*, Manchester, UK
33. 2016/06/29, *Nottingham Pathology*, Nottingham, UK
34. 2016/05/25, *Cancer Development and Complexity Workshop and School*, Como, Italy
35. 2016/05/10, *Seminar at Cancer Research UK Manchester Research Institute*, Manchester, UK
36. 2016/04/16, *AACR Annual Meeting*, New Orleans, USA
37. 2015/05/12, *Phylogeny Meets Genomics*, Munich, Germany
38. 2015/02/20, *Mathematical Biology and Ecology Seminar Series*, Oxford, UK
39. 2015/02/04, *MBI Heterogeneity and the Microenvironment*, Columbus, USA
40. 2014/11/04, *National Cancer Research Institute Conference*, Liverpool, UK
41. 2013/04/08, *AACR Annual Meeting*, Washington, USA