Stanford

# Christina Curtis

Assistant Professor of Medicine (Oncology) and of Genetics

Medicine - Oncology

## Bio

### BIO

Trained in molecular and computational biology and jointly appointed in Medicine and Genetics, Dr. Christina Curtis pursues systems biology and computational approaches to establish a quantitative and mechanistic understanding of cancer progression. Her research is focused on the development and application of innovative experimental and computational approaches to improve the diagnosis, treatment and earlier detection of cancer by leveraging genome-scale data derived from clinical samples coupled with computational modeling and iterative experimentation.

To this end, Dr. Curtis and her team have developed an integrated experimental and computational framework to measure clinically relevant patient-specific parameters and to measure clonal dynamics during tumor progression and through therapy. This led to their description of a Big Bang model of effectively neutral tumor evolution, thereby advancing a quantitative understanding of tumor progression and refining the de facto clonal evolution model. Curtis' research has also redefined the molecular map of breast cancer, revealing 11 subgroups with distinct clinical outcomes and subtype-specific copy number drivers. Her team has gone on to show that these these integrative breast cancer subgroups exhibit distinct spatio-temporal patterns of relapse and have identified four genomically distinct ER+/HER2- subgroups at high-risk of late distant relapse. In ongoing research, she aims to develop a systematic interpretation of genotype/phenotype associations in cancer by leveraging state-of-the-art technologies and robust data integration techniques.

### ACADEMIC APPOINTMENTS

- Assistant Professor, Medicine - Oncology
- Assistant Professor, Genetics
- Member, Bio-X
- Member, Stanford Cancer Institute

### ADMINISTRATIVE APPOINTMENTS

- Co-Director, Molecular Tumor Board, Stanford Cancer Institute, (2014- present)

### HONORS AND AWARDS

- NIH Director's Pioneer Award, NIH (2018)
- Kavli Frontier of Science Fellow, National Academy of Science (USA) (2016)
- AACR Career Development Award, AACR Triple Negative Breast Cancer Foundation - Carol's Crusade for a Cure Foundation (2016)
- Institutional Seed Grant Recipient, American Cancer Society (2013)
- Career Development Award, STOP Cancer (2012)
- V Scholar Award, V Foundation for Cancer Research (2012)

- Scholar-In-Training Award, American Association for Cancer Research (2009)

### BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Editorial Board Member, Cell Systems (2019 - present)
- Annual Meeting Program Committee, American Association for Cancer Research (2018 - present)
- Editorial Board Member, Carcinogenesis: Integrative Cancer Biology (2018 - present)
- Editorial Board Member, Journal of Computational Biology (2017 - present)
- Scientific Advisor, Ontario Institute for Cancer Research, Adaptive Oncology Program (2017 - present)
- Scientific Advisory Board, Cancer Research UK Early Detection Committee (2017 - present)
- Scientific Advisory Board, GRAIL (2017 - present)
- Editorial Board Member, ASCO Journal of Clinical Oncology: Precision Oncology (2016 - present)
- Associate Editor, Breast Cancer Research (2015 - present)

### PROFESSIONAL EDUCATION

- Postdoctoral Fellow, University of Cambridge , Computational Biology (2010)
- PhD, University of Southern California , Molecular and Computational Biology (2007)
- MS, University of Southern California , Bioinformatics and Computational Biology (2005)
- MSc, University of Heidelberg, Germany , Molecular Biology (2003)

### COMMUNITY AND INTERNATIONAL WORK

- The Cancer Genome Atlas, Data Analysis Working Groups

### LINKS

- Curtis Lab for Cancer Computational and Systems Biology: http://med.stanford.edu/curtislab.html

## Research & Scholarship

### CURRENT RESEARCH AND SCHOLARLY INTERESTS

We are particularly interested in elucidating tumor evolutionary dynamics, novel therapeutic targets, and the genotype to phenotype map in cancer. A unifying theme of our research is to exploit ‘omic’ data derived from clinically annotated samples in robust computational frameworks coupled with iterative experimental validation in order to advance our understanding of cancer systems biology. In particular, we employ advanced genomic techniques, computational and mathematical modeling, and powerful model systems in order to:

1.) Model the evolutionary dynamics of tumor progression and therapeutic resistance and metastasis

2) Elucidate disease etiology and novel molecular targets through integrative analyses of high-throughput omic data

3) Develop techniques for the systems-level interpretation of genotype-phenotype associations in cancer

Our research is funded by the NIH/NCI, NHGRI, Department of Defense, Breast Cancer Research Foundation, American Association for Cancer Research, Susan G. Komen Foundation, Emerson Collective and V Foundation for Cancer Research.

## Teaching

### STANFORD ADVISEES

**Postdoctoral Faculty Sponsor**

Zheng Hu, Kasper Karlsson, Eran Kotler, Hang Xu, Wenting Yang

**Doctoral Dissertation Advisor (AC)**

Joseph Charalel

**Doctoral Dissertation Co-Advisor (AC)**

Susanne Tilk

**Doctoral (Program)**

Susanne Tilk

**Postdoctoral Research Mentor**

Hang Xu, Wenting Yang

### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biomedical Informatics (Phd Program)
- Cancer Biology (Phd Program)
- Genetics (Phd Program)
- Oncology (Fellowship Program)

## Publications

### PUBLICATIONS

- **Dynamics of breast-cancer relapse reveal late-recurring ER-positive genomic subgroups.** *Nature*
  Rueda, O. M., Sammut, S., Seoane, J. A., Chin, S., Caswell-Jin, J. L., Callari, M., Batra, R., Pereira, B., Bruna, A., Ali, H. R., Provenzano, E., Liu, B., Parisien, et al
  2019
- **Clonal replacement and heterogeneity in breast tumors treated with neoadjuvant HER2-targeted therapy.** *Nature communications*
  Caswell-Jin, J. L., McNamara, K., Reiter, J. G., Sun, R., Hu, Z., Ma, Z., Ding, J., Suarez, C. J., Tilk, S., Raghavendra, A., Forte, V., Chin, S. F., Bardwell, et al
  2019; 10 (1): 657
- **Harnessing Tumor Evolution to Circumvent Resistance.** *Trends in genetics : TIG*
  Pogrebniak, K. L., Curtis, C.
  2018
- **Promoter of lncRNA Gene PVT1 Is a Tumor-Suppressor DNA Boundary Element.** *Cell*
  Cho, S. W., Xu, J., Sun, R., Mumbach, M. R., Carter, A. C., Chen, Y. G., Yost, K. E., Kim, J., He, J., Nevins, S. A., Chin, S., Caldas, C., Liu, et al
  2018; 173 (6): 1398
- **Big Bang Tumor Growth and Clonal Evolution.** *Cold Spring Harbor perspectives in medicine*
  Sun, R., Hu, Z., Curtis, C.
  2018; 8 (5)
- **Mapping the in vivo fitness landscape of lung adenocarcinoma tumor suppression in mice** *NATURE GENETICS*
  Rogers, Z. N., McFarland, C. D., Winters, I. P., Seoane, J. A., Brady, J. J., Yoon, S., Curtis, C., Petrov, D. A., Winslow, M. M.
  2018; 50 (4): 483-+
- **The chromatin accessibility landscape of primary human cancers.** *Science (New York, N.Y.)*
  Corces, M. R., Granja, J. M., Shams, S., Louie, B. H., Seoane, J. A., Zhou, W., Silva, T. C., Groeneveld, C., Wong, C. K., Cho, S. W., Satpathy, A. T., Mumbach, M. R., Hoadley, et al
  2018; 362 (6413)
- **Between-region genetic divergence reflects the mode and tempo of tumor evolution.** *Nature genetics*
  Sun, R., Hu, Z., Sottoriva, A., Graham, T. A., Harpak, A., Ma, Z., Fischer, J. M., Shibata, D., Curtis, C.
  2017
- **A population genetics perspective on the determinants of intra-tumor heterogeneity.** *Biochimica et biophysica acta*

Hu, Z., Sun, R., Curtis, C.
2017; 1867 (2): 109-126

- **A Big Bang model of human colorectal tumor growth.** *Nature genetics*
  Sottoriva, A., Kang, H., Ma, Z., Graham, T. A., Salomon, M. P., Zhao, J., Marjoram, P., Siegmund, K., Press, M. F., Shibata, D., Curtis, C.
  2015
- **The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups** *NATURE*
  Curtis, C., Shah, S. P., Chin, S., Turashvili, G., Rueda, O. M., Dunning, M. J., Speed, D., Lynch, A. G., Samarajiwa, S., Yuan, Y., Graef, S., Ha, G., Haffari, et al
  2012; 486 (7403): 346-352
- **Assessment of ERBB2/HER2 Status in HER2-Equivocal Breast Cancers by FISH and 2013/2014 ASCO-CAP Guidelines.** *JAMA oncology*
  Press, M. F., Seoane, J. A., Curtis, C., Quinaux, E., Guzman, R., Sauter, G., Eiermann, W., Mackey, J. R., Robert, N., Pienkowski, T., Crown, J., Martin, M., Valero, et al
  2018
- **Quantification of subclonal selection in cancer from bulk sequencing data (vol 50, pg 895, 2018)** *NATURE GENETICS*
  Williams, M. J., Werner, B., Heide, T., Curtis, C., Barnes, C. P., Sottoriva, A., Graham, T. A.
  2018; 50 (9): 1342
- **Quantification of subclonal selection in cancer from bulk sequencing data** *NATURE GENETICS*
  Williams, M. J., Werner, B., Heide, T., Curtis, C., Barnes, C. P., Sottoriva, A., Graham, T. A.
  2018; 50 (6): 895-+
- **AGBT meeting report** *GENOME BIOLOGY*
  Bhatt, A. S., Curtis, C.
  2018; 19: 60
- **Organoids reveal cancer dynamics** *NATURE*
  Kuo, C. J., Curtis, C.
  2018; 556 (7702): 441–42
- **Higher Absolute Lymphocyte Counts Predict Lower Mortality from Early-Stage Triple-Negative Breast Cancer.** *Clinical cancer research : an official journal of the American Association for Cancer Research*
  Afghahi, A., Purington, N., Han, S. S., Desai, M., Pierson, E., Mathur, M. B., Seto, T., Thompson, C. A., Rigdon, J., Telli, M. L., Badve, S. S., Curtis, C., West, et al
  2018
- **Bayesian Network Inference Modeling Identifies TRIB1 as a Novel Regulator of Cell-Cycle Progression and Survival in Cancer Cells** *CANCER RESEARCH*
  Gendelman, R., Xing, H., Mirzoeva, O. K., Sarde, P., Curtis, C., Feiler, H. S., McDonagh, P., Gray, J. W., Khalil, I., Korn, W. M.
  2017; 77 (7): 1575-1585
- **Integrated genomic characterization of oesophageal carcinoma** *NATURE*
  Kim, J., Bowlby, R., Mungall, A. J., Robertson, A. G., Odze, R. D., Cherniack, A. D., Shih, J., Pedamallu, C. S., Cibulskis, C., Dunford, A., Meier, S. R., Kim, J., Raphael, et al
  2017; 541 (7636): 169-?
- **Early mutation bursts in colorectal tumors.** *PloS one*
  Zhao, J., Salomon, M. P., Shibata, D., Curtis, C., Siegmund, K., Marjoram, P.
  2017; 12 (3)
- **Intestinal Enteroendocrine Lineage Cells Possess Homeostatic and Injury-Inducible Stem Cell Activity** *Cell Stem Cell*
  Yan, K., Gevaert, O., Zheng, G., Anchang, B., Probert, C., et al
  2017; 21 (1): 78 - 90.e6
- **Intestinal Enteroendocrine Lineage Cells Possess Homeostatic and Injury-Inducible Stem Cell Activity.** *Cell stem cell*
  Yan, K. S., Gevaert, O., Zheng, G. X., Anchang, B., Probert, C. S., Larkin, K. A., Davies, P. S., Cheng, Z. F., Kaddis, J. S., Han, A., Roelf, K., Calderon, R. I., Cynn, et al
  2017; 21 (1): 78–90.e6

- **A p53 Super-tumor Suppressor Reveals a Tumor Suppressive p53-Ptpn14-Yap Axis in Pancreatic Cancer.** *Cancer cell*
  Mello, S. S., Valente, L. J., Raj, N., Seoane, J. A., Flowers, B. M., McClendon, J., Bieging-Rolett, K. T., Lee, J., Ivanochko, D., Kozak, M. M., Chang, D. T., Longacre, T. A., Koong, et al
  2017; 32 (4): 460–73.e6

- **Inferring Tumor Phylogenies from Multi-region Sequencing.** *Cell systems*
  Hu, Z., Curtis, C.
  2016; 3 (1): 12-14

- **Genome co-amplification upregulates a mitotic gene network activity that predicts outcome and response to mitotic protein inhibitors in breast cancer** *BREAST CANCER RESEARCH*
  Hu, Z., Mao, J., Curtis, C., Huang, G., Gu, S., Heiser, L., Lenburg, M. E., Korkola, J. E., Bayani, N., Samarajiwa, S., Seoane, J. A., Dane, M. A., Esch, et al
  2016; 18

- **Genome co-amplification upregulates a mitotic gene network activity that predicts outcome and response to mitotic protein inhibitors in breast cancer.** *Breast cancer research*
  Hu, Z., Mao, J., Curtis, C., Huang, G., Gu, S., Heiser, L., Lenburg, M. E., Korkola, J. E., Bayani, N., Samarajiwa, S., Seoane, J. A., A Dane, M., Esch, et al
  2016; 18 (1): 70-?

- **Many private mutations originate from the first few divisions of a human colorectal adenoma** *JOURNAL OF PATHOLOGY*
  Kang, H., Salomon, M. P., Sottoriva, A., Zhao, J., Toy, M., Press, M. F., Curtis, C., Marjoram, P., Siegmund, K., Shibata, D.
  2015; 237 (3): 355-362

- **Genomic profiling of breast cancers.** *Current opinion in obstetrics & gynecology*
  Curtis, C.
  2015; 27 (1): 34-39

- **Contributions to Drug Resistance in Glioblastoma Derived from Malignant Cells in the Sub-Ependymal Zone** *CANCER RESEARCH*
  Piccirillo, S. G., Spiteri, I., Sottoriva, A., Touloumis, A., Ber, S., Price, S. J., Heywood, R., Francis, N., Howarth, K. D., Collins, V. P., Venkitaraman, A. R., Curtis, C., Marioni, et al
  2015; 75 (1): 194-202

- **Comprehensive molecular characterization of gastric adenocarcinoma** *NATURE*
  Bass, A. J., Thorsson, V., Shmulevich, I., Reynolds, S. M., Miller, M., Bernard, B., Hinoue, T., Laird, P. W., Curtis, C., Shen, H., Weisenberger, D. J., Schultz, N., Shen, et al
  2014; 513 (7517): 202-209

- **The Breast Cancer Oncogene EMSY Represses Transcription of Antimetastatic microRNA miR-31 (vol 53, pg 806, 2014)** *MOLECULAR CELL*
  Vire, E., Curtis, C., Davalos, V., Git, A., Robson, S., Villanueva, A., Vidal, A., Barbieri, I., Aparicio, S., Esteller, M., Caldas, C., Kouzarides, T.
  2014; 54 (1): 203-203

- **Genome-driven integrated classification of breast cancer validated in over 7,500 samples** *Genome Biology*
  Ali, R., Rueda, O. M., Chin, S., Curtis, C., Dunning, M. J., Aparicio, S., Caldas, C.
  2014; 15 (8): 431

- **A tumor DNA complex aberration index is an independent predictor of survival in breast and ovarian cancer.** *Molecular oncology*
  Vollan, H. K., Rueda, O. M., Chin, S. F., Curtis, C., Turashvili, G., Shah, S., Lingjærde, O. C., Yuan, Y., Ng, C. K., Dunning, M. J., Dicks, E., Provenzano, E., Sammut, et al
  2014

- **Precise inference of copy number alterations in tumor samples from SNP arrays** *BIOINFORMATICS*
  Chen, G. K., Chang, X., Curtis, C., Wang, K.
  2013; 29 (23): 2964-2970

- **The shaping and functional consequences of the microRNA landscape in breast cancer** *NATURE*
  Dvinge, H., Git, A., Graef, S., Salmon-Divon, M., Curtis, C., Sottoriva, A., Zhao, Y., Hirst, M., Armisen, J., Miska, E. A., Chin, S., Provenzano, E., Turashvili, et al
  2013; 497 (7449): 378-382

- **Improving Breast Cancer Survival Analysis through Competition-Based Multidimensional Modeling** *PLOS COMPUTATIONAL BIOLOGY*
  Bilal, E., Dutkowski, J., Guinney, J., Jang, I. S., Logsdon, B. A., Pandey, G., Sauerwine, B. A., Shimoni, Y., Vollan, H. K., Mecham, B. H., Rueda, O. M., Tost, J., Curtis, et al

2013; 9 (5)

- **Systematic Analysis of Challenge-Driven Improvements in Molecular Prognostic Models for Breast Cancer** *SCIENCE TRANSLATIONAL MEDICINE*
  Margolin, A. A., Bilal, E., Huang, E., Norman, T. C., Ottestad, L., Mecham, B. H., Sauerwine, B., Kellen, M. R., Mangravite, L. M., Furia, M. D., Vollan, H. K., Rueda, O. M., Guinney, et al
  2013; 5 (181)

- **Intratumor heterogeneity in human glioblastoma reflects cancer evolutionary dynamics** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Sottoriva, A., Spiteri, I., Piccirillo, S. G., Touloumis, A., Collins, V. P., Marioni, J. C., Curtis, C., Watts, C., Tavare, S.
  2013; 110 (10): 4009-4014

- **Single-Molecule Genomic Data Delineate Patient-Specific Tumor Profiles and Cancer Stem Cell Organization** *CANCER RESEARCH*
  Sottoriva, A., Spiteri, I., Shibata, D., Curtis, C., Tavare, S.
  2013; 73 (1): 41-49

- **Quantitative Image Analysis of Cellular Heterogeneity in Breast Tumors Complements Genomic Profiling (vol 4, 161er6, 2012)** *SCIENCE TRANSLATIONAL MEDICINE*
  Yuan, Y., Failmezger, H., Rueda, O. M., Ali, H. R., Graef, S., Chin, S., SCHWARZ, R. F., Curtis, C., DUNNING, M. J., Bardwell, H., Johnson, N., Doyle, S., Turashvili, et al
  2012; 4 (161)

- **Calling Sample Mix-Ups in Cancer Population Studies** *PLOS ONE*
  Lynch, A. G., Chin, S., Dunning, M. J., Caldas, C., Tavare, S., Curtis, C.
  2012; 7 (8)

- **A Sparse Regulatory Network of Copy-Number Driven Gene Expression Reveals Putative Breast Cancer Oncogenes** *IEEE-ACM TRANSACTIONS ON COMPUTATIONAL BIOLOGY AND BIOINFORMATICS*
  Yuan, Y., Curtis, C., Caldas, C., Markowetz, F.
  2012; 9 (4): 947-954

- **The clonal and mutational evolution spectrum of primary triple-negative breast cancers** *NATURE*
  Shah, S. P., Roth, A., Goya, R., Oloumi, A., Ha, G., Zhao, Y., Turashvili, G., Ding, J., Tse, K., Haffari, G., Bashashati, A., Prentice, L. M., Khattra, et al
  2012; 486 (7403): 395-399

- **Effects of BRCA2 cis-regulation in normal breast and cancer risk amongst BRCA2 mutation carriers** *BREAST CANCER RESEARCH*
  Maia, A., Antoniou, A. C., O'Reilly, M., Samarajiwa, S., Dunning, M., Kartsonaki, C., Chin, S., Curtis, C. N., McGuffog, L., Domchek, S. M., Easton, D. F., Peock, S., Frost, et al
  2012; 14 (2)

- **Penalized regression elucidates aberration hotspots mediating subtype-specific transcriptional responses in breast cancer** *BIOINFORMATICS*
  Yuan, Y., Rueda, O. M., Curtis, C., Markowetz, F.
  2011; 27 (19): 2679-2685

- **ZNF703 is a common Luminal B breast cancer oncogene that differentially regulates luminal and basal progenitors in human mammary epithelium** *EMBO MOLECULAR MEDICINE*
  Holland, D. G., Burleigh, A., Git, A., Goldgraben, M. A., Perez-Mancera, P. A., Chin, S., Hurtado, A., Bruna, A., Ali, H. R., Greenwood, W., Dunning, M. J., Samarajiwa, S., Menon, et al
  2011; 3 (3): 167-180

- **The importance of platform annotation in interpreting microarray data** *LANCET ONCOLOGY*
  Dunning, M. J., Curtis, C., Barbosa-Morais, N. L., Caldas, C., Tavare, S., Lynch, A. G.
  2010; 11 (8): 717-717

- **The pitfalls of platform comparison: DNA copy number array technologies assessed** *BMC GENOMICS*
  Curtis, C., Lynch, A. G., Dunning, M. J., Spiteri, I., Marioni, J. C., Hadfield, J., Chin, S., Brenton, J. D., Tavare, S., Caldas, C.
  2009; 10

- **Drosophila melanogaster p53 has developmental stage-specific and sex-specific effects on adult life span indicative of sexual antagonistic pleiotropy** *AGING-US*
  Waskar, M., Landis, G. N., Shen, J., Curtis, C., Tozer, K., Abdueva, D., Skvortsov, D., Tavare, S., Tower, J.

2009; 1 (11): 903-936

- **Swift: primary data analysis for the Illumina Solexa sequencing platform** *BIOINFORMATICS*
  Whiteford, N., Skelly, T., Curtis, C., Ritchie, M. E., Loehr, A., Zaranek, A. W., Abnizova, I., Brown, C.
  2009; 25 (17): 2194-2199

- **Product Length, Dye Choice, and Detection Chemistry in the Bead-Emulsion Amplification of Millions of Single DNA Molecules in Parallel** *ANALYTICAL CHEMISTRY*
  Tiemann-Boege, I., Curtis, C., Shinde, D. N., Goodman, D. B., Tavare, S., Arnheim, N.
  2009; 81 (14): 5770-5776

- **A screen of apoptosis and senescence regulatory genes for life span effects when over-expressed in Drosophila** *AGING-US*
  Shen, J., Curtis, C., Tavare, S., Tower, J.
  2009; 1 (2): 191-211

- **Explaining differences in saturation levels for Affymetrix GeneChip (R) arrays** *NUCLEIC ACIDS RESEARCH*
  Skvortsov, D., Abdueva, D., Curtis, C., Schaub, B., Tavare, S.
  2007; 35 (12): 4154-4163

- **Transcriptional profiling of MnSOD-mediated lifespan extension in Drosophila reveals a species-general network of aging and metabolic genes** *GENOME BIOLOGY*
  Curtis, C., Landis, G. N., Folk, D., Wehr, N. B., Hoe, N., Waskar, M., Abdueva, D., Skvortsov, D., Ford, D., Luu, A., Badrinath, A., Levine, R. L., Bradley, et al
  2007; 8 (12)

- **Scambio, a novel guanine nucleotide exchange factor for Rho** *MOLECULAR CANCER*
  Curtis, C., Hemmeryckx, B., Haataja, L., Senadheera, D., Groffen, J., Heisterkamp, N.
  2004; 3