


Stanford



Michael F. Clarke, M.D.

Karel H. and Avice N. Beekhuis Professor of Cancer Biology
Medicine - Oncology

 Curriculum Vitae available Online

CONTACT INFORMATION

• Administrative Contact

Kristine Hidde - Administrative Associate

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Bio

ACADEMIC APPOINTMENTS

- Professor, Medicine - Oncology
- Member, Bio-X
- Associate Director, Institute for Stem Cell Biology and Regenerative Medicine
- Member, Stanford Cancer Institute
- Member, Wu Tsai Neurosciences Institute

HONORS AND AWARDS

- American Association of Physicians, - (-)
- American Society of Clinical Investigation, - (-)
- Rackham Award, University of Michigan (-)

PROFESSIONAL EDUCATION

- M.D., Indiana University (1977)
- B.A., Indiana University (1973)

LINKS

- Clarke Lab Site: <http://med.stanford.edu/stemcell/institutefaculty/clarke.html>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Dr. Michael F. Clarke is the Karel and Avice Beekhuis Professor in Cancer Biology and Associate Director of the Stanford Institute for Stem Cell and Regenerative Medicine. He is a board certified oncologist with extensive training in molecular biology and stem cell biology. In addition to his clinical duties in the division of Oncology, Dr. Clarke maintains a laboratory focused on two areas of research: i) the control of self-renewal of normal stem cells and their malignant counterparts; and ii) the identification and characterization of cancer stem cells. The main objectives of his laboratory are to pursue how perturbations in the self-renewal machinery contribute to human diseases and to use the findings to aid the development of more effective treatment therapies.

His laboratory has a long history of innovative findings which include: the first to demonstrate that inappropriate expression of a normal gene could cause a tumor; the first to identify a dominant-negative splice variant of an oncogene; the first to identify a molecular regulator of stem cell self-renewal; the first to identify a solid tumor stem cell (in breast cancer) and the first to demonstrate a molecular linkage of a self-renewal program used by normal mammary stem cells and breast cancer cells. Recently, his group described a molecular mechanism that confers resistance to radiation in breast cancer stem cells.

His group was the first to discover that the proto-oncogene Bmi-1 regulates stem cell self-renewal via an epigenetic mechanism. By examining the pathways upstream and downstream of Bmi1, hence the molecular pathways that regulate self-renewal, his laboratory found that USP16, a protein that dampens Bmi1 signals, causes a stem cell defect in various stem cells in Down's syndrome, including neural stem cells.

Since cancers arise as a result of a series of genetic mutations, a better understanding of the consequences of these mutations on the underlying biology of the neoplastic cells will help the development of more effective therapies. Solid tumors such as breast cancers contain heterogeneous populations of neoplastic cells. Through collaboration, his group pioneered and organized a team to use single cell genomics to understand complex tissue hierarchy in normal and malignant cells present in human breast, colon and head and neck cancer tumors. Only a small minority of cancer cells had the capacity to form new tumors in a xenograft model. This tumorigenic cell population could be identified prospectively and consistently had definable and identical phenotype. The tumorigenic cells displayed stem cell-like properties in that they were capable of generating new tumors containing additional stem cells as well as regenerating the phenotypically mixed populations of non-tumorigenic cells present in the original tumor. Effective treatment of cancer will require therapeutic strategies that are able to target and eliminate this tumorigenic subset of cells. His laboratory is pursuing the identification of cancer stem cells in other tumors so that they can be studied. Finally, the laboratory is actively pursuing how cancer stem cells self-renew to maintain themselves and escape the genetic constraints on unlimited self-renewal that regulate normal stem cell numbers. Differences in self-renewal pathways between normal and malignant stem cells could be targeted by new therapeutic agents to eliminate cancer stem cells.

CLINICAL TRIALS

- Biopsy of Human Tumors for Cancer Stem Cell Characterization: a Feasibility Study, Not Recruiting

Teaching

STANFORD ADVISEES

Postdoctoral Faculty Sponsor

Sabra Djomehri

Postdoctoral Research Mentor

Sabra Djomehri

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)
- Stem Cell Biology and Regenerative Medicine (Phd Program)

Publications

PUBLICATIONS

- **Inhibiting USP16 rescues stem cell aging and memory in an Alzheimer's model.** *eLife*
Reintz, F., Chen, E. Y., Nicolis di Robilant, B., Chuluun, B., Antony, J., Jones, R. C., Gubbi, N., Lee, K., Ho, W. H., Kolluru, S. S., Qian, D., Adorno, M., Piltti, et al
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- **LEFTY1 Is a Dual-SMAD Inhibitor that Promotes Mammary Progenitor Growth and Tumorigenesis.** *Cell stem cell*
Zabala, M., Lobo, N. A., Antony, J., Heitink, L. S., Gulati, G. S., Lam, J., Parashurama, N., Sanchez, K., Adorno, M., Sikandar, S. S., Kuo, A. H., Qian, D., Kalisky, et al
2020
- **Clinical and Therapeutic Implications of Cancer Stem Cells.** *The New England journal of medicine*
Clarke, M. F.
2019; 380 (23): 2237–45
- **Clinical and Therapeutic Implications of Cancer Stem Cells. Reply.** *The New England journal of medicine*
Clarke, M. F.
2019; 381 (10): e19
- **Bcl11b maintains the long-term mammary stem cell and is crucial for drug resistance in breast cancer.**
Cai, S., Kalisky, T., Dalerba, P., Clarke, M., Stanford Univ
AMER ASSOC CANCER RESEARCH.2018: 23
- **Single-cell transcriptomics of 20 mouse organs creates a Tabula Muris.** *Nature*
2018; 562 (7727): 367–72
- **Stromal Gli2 activity coordinates a niche signaling program for mammary epithelial stem cells** *SCIENCE*
Zhao, C., Cai, S., Shin, K., Lim, A., Kalisky, T., Lu, W., Clarke, M. F., Beachy, P. A.
2017; 356 (6335): 284-?
- **A Quiescent Bcl11b High Stem Cell Population Is Required for Maintenance of the Mammary Gland.** *Cell stem cell*
Cai, S., Kalisky, T., Sahoo, D., Dalerba, P., Feng, W., Lin, Y., Qian, D., Kong, A., Yu, J., Wang, F., Chen, E. Y., Scheeren, F. A., Kuo, et al
2017; 20 (2): 247-260 e5
- **Targeted chromatin ligation, a robust epigenetic profiling technique for small cell numbers.** *Nucleic acids research*
Zarnegar, M. A., Reinitz, F. n., Newman, A. M., Clarke, M. F.
2017; 45 (17): e153
- **CDX2 as a Prognostic Biomarker in Colon Cancer.** *New England journal of medicine*
Dalerba, P., Sahoo, D., Clarke, M. F.
2016; 374 (22): 2184-?
- **CDX2 as a Prognostic Biomarker in Stage II and Stage III Colon Cancer** *NEW ENGLAND JOURNAL OF MEDICINE*
Dalerba, P., Sahoo, D., Paik, S., Guo, X., Yothers, G., Song, N., Wilcox-Fogel, N., Forgo, E., Rajendran, P. S., Miranda, S. P., Hisamori, S., Hutchison, J., Kalisky, et al
2016; 374 (3): 211-222
- **CDX2 as a Prognostic Biomarker in Stage II and Stage III Colon Cancer.** *The New England journal of medicine*
Dalerba, P., Sahoo, D., Paik, S., Guo, X., Yothers, G., Song, N., Wilcox-Fogel, N., Forgo, E., Rajendran, P. S., Miranda, S. P., Hisamori, S., Hutchison, J., Kalisky, et al
2016; 374 (3): 211-22
- **A cell-intrinsic role for TLR2-MYD88 in intestinal and breast epithelia and oncogenesis.** *Nature cell biology*
Scheeren, F. A., Kuo, A. H., van Weele, L. J., Cai, S., Glykofridis, I., Sikandar, S. S., Zabala, M., Qian, D., Lam, J. S., Johnston, D., Volkmer, J. P., Sahoo, D., van de Rijn, et al
2014; 16 (12): 1238-1248
- **A cell-intrinsic role for TLR2 MYD88 in intestinal and breast epithelia and oncogenesis** *NATURE CELL BIOLOGY*
Scheeren, F. A., Kuo, A. H., van Weele, L. J., Cai, S., Glykofridis, I., Sikandar, S. S., Zabala, M., Qian, D., Lam, J. S., Johnston, D., Volkmer, J. P., Sahoo, D., van de Rijn, et al
2014; 16 (12): 1238-U245
- **Usp16 contributes to somatic stem-cell defects in Down's syndrome.** *Nature*
Adorno, M., Sikandar, S., Mitra, S. S., Kuo, A., Nicolis Di Robilant, B., Haro-Acosta, V., Ouadah, Y., Quarta, M., Rodriguez, J., Qian, D., Reddy, V. M., Cheshier, S., Garner, et al
2013; 501 (7467): 380-384

- **Identification of a cKit(+) Colonic Crypt Base Secretory Cell That Supports Lgr5(+) Stem Cells in Mice** *GASTROENTEROLOGY*
Rothenberg, M. E., Nusse, Y., Kalisky, T., Lee, J. J., Dalerba, P., Scheeren, F., Lobo, N., Kulkarni, S., Sim, S., Qian, D., Beachy, P. A., Pasricha, P. J., Quake, et al
2012; 142 (5): 1195-?
- **Single-cell dissection of transcriptional heterogeneity in human colon tumors** *NATURE BIOTECHNOLOGY*
Dalerba, P., Kalisky, T., Sahoo, D., Rajendran, P. S., Rothenberg, M. E., Leyrat, A. A., Sim, S., Okamoto, J., Johnston, D. M., Qian, D., Zabala, M., Bueno, J., Neff, et al
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- **Downregulation of miRNA-200c Links Breast Cancer Stem Cells with Normal Stem Cells** *CELL*
Shimono, Y., Zabala, M., Cho, R. W., Lobo, N., Dalerba, P., Qian, D., Diehn, M., Liu, H., Panula, S. P., Chiao, E., Dirbas, F. M., Somlo, G., Pera, et al
2009; 138 (3): 592-603
- **Association of reactive oxygen species levels and radioresistance in cancer stem cells** *NATURE*
Diehn, M., Cho, R. W., Lobo, N. A., Kalisky, T., Dorie, M. J., Kulp, A. N., Qian, D., Lam, J. S., Ailles, L. E., Wong, M., Joshua, B., Kaplan, M. J., Wapnir, et al
2009; 458 (7239): 780-U123
- **Long-term haematopoietic reconstitution by Trp53(-/-)p16(Ink4a(-/-))p19(Arf(-/-)) multipotent progenitors** *NATURE*
Akala, O. O., Park, I., Qian, D., Pihalja, M., Becker, M. W., Clarke, M. F.
2008; 453 (7192): 228-U12
- **A gene signature in breast cancer - Reply** *NEW ENGLAND JOURNAL OF MEDICINE*
Clarke, M. F., Liu, R., Wang, X.
2007; 356 (18): 1888
- **The prognostic role of a gene signature from tumorigenic breast-cancer cells.** *NEW ENGLAND JOURNAL OF MEDICINE*
Liu, R., Wang, X., Chen, G. Y., Dalerba, P., Gurney, A., Hoey, T., Sherlock, G., Lewicki, J., Shedden, K., Clarke, M. F.
2007; 356 (3): 217-226
- **Bmi-1 dependence distinguishes neural stem cell self-renewal from progenitor proliferation** *NATURE*
Molofsky, A. V., Pardal, R., Iwashita, T., Park, I. K., Clarke, M. F., Morrison, S. J.
2003; 425 (6961): 962-967
- **Bmi-1 is required for maintenance of adult self-renewing hematopoietic stem cells** *32nd Annual Meeting of the International-Society-for-Experimental-Hematology*
Park, I., Qian, D., Kiel, M., Becker, M., Prohaska, S., Weissman, I., Morrison, S., Clarke, M.
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- **Bmi-1 is required for maintenance of adult self-renewing haematopoietic stem cells** *NATURE*
Park, I. K., Qian, D. L., Kiel, M., Becker, M. W., Pihalja, M., Weissman, I. L., Morrison, S. J., Clarke, M. F.
2003; 423 (6937): 302-305
- **Prospective identification of tumorigenic breast cancer cells** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Al-Hajj, M., Wicha, M. S., Benito-Hernandez, A., Morrison, S. J., Clarke, M. F.
2003; 100 (7): 3983-3988
- **Mesenchymal tumor cells drive adaptive resistance of Trp53(-/-) breast tumor cells to inactivated mutant Kras.** *Molecular oncology*
van Weele, L. J., Djomehri, S. I., Cai, S., Antony, J., Sikandar, S. S., Qian, D., Ho, W. H., West, R., Scheeren, F. A., Clarke, M. F.
2022
- **Publisher Correction: Cell types of origin of the cell-free transcriptome.** *Nature biotechnology*
Vorperian, S. K., Moufarrej, M. N., Tabula Sapiens Consortium, Quake, S. R., Jones, R. C., Karkania, J., Krasnow, M., Pisco, A. O., Quake, S. R., Salzman, J., Yosef, N., Bulthaupt, B., Brown, P., et al
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- **Molecular hallmarks of heterochronic parabiosis at single-cell resolution.** *Nature*
Palovics, R., Keller, A., Schaum, N., Tan, W., Fehlmann, T., Borja, M., Kern, F., Bonanno, L., Calcuttawala, K., Webber, J., McGeever, A., Tabula Muris Consortium, Luo, J., et al
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- **Cell types of origin of the cell-free transcriptome.** *Nature biotechnology*
Vorperian, S. K., Moufarrej, M. N., Tabula Sapiens Consortium, Quake, S. R., Jones, R. C., Karkanas, J., Krasnow, M., Pisco, A. O., Quake, S. R., Salzman, J., Yosef, N., Bulthaupt, B., Brown, P., et al
2022
- **RNA splicing programs define tissue compartments and cell types at single-cell resolution** *ELIFE*
Olivieri, J., Dehghannasiri, R., Wang, P. L., Jang, S., de Morree, A., Tan, S. Y., Ming, J., Wu, A., Consortium, T., Quake, S. R., Krasnow, M. A., Salzman, J.
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- **TACH101, a first-in-class pan inhibitor of KDM4 histone lysine demethylases.**
Yoo, S., Chandhasin, C., Del Rosario, J. R., Chen, Y. K., Stafford, J., Quake, S., Perabo, F., Clarke, M. F.
AMER ASSOC CANCER RESEARCH.2021
- **Inhibition of histone lysine demethylases with TACH101, a first-in-class pan-inhibitor of KDM4.**
Chandhasin, C., Yoo, S., Del Rosario, J., Chen, Y. K., Stafford, J., Perabo, F., Clarke, M. F.
LIPPINCOTT WILLIAMS & WILKINS.2021
- **Pharmacologic characterization of TACH101, a first-in-class KDM4 inhibitor for development as a cancer therapeutic.**
Yoo, S., Chandhasin, C., Del Rosario, J., Chen, Y. K., Stafford, J., Perabo, F., Clarke, M. F.
LIPPINCOTT WILLIAMS & WILKINS.2021
- **Depletion of Trp53 and Cdkn2a Does Not Promote Self-Renewal in the Mammary Gland but Amplifies Proliferation Induced by TNF-#.** *Stem cell reports*
van Weele, L. J., Scheeren, F. A., Cai, S. n., Kuo, A. H., Qian, D. n., Ho, W. H., Clarke, M. F.
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- **Single-cell transcriptional diversity is a hallmark of developmental potential.** *Science (New York, N.Y.)*
Gulati, G. S., Sikandar, S. S., Wesche, D. J., Manjunath, A. n., Bharadwaj, A. n., Berger, M. J., Ilagan, F. n., Kuo, A. H., Hsieh, R. W., Cai, S. n., Zabala, M. n., Scheeren, F. A., Lobo, et al
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- **Ageing hallmarks exhibit organ-specific temporal signatures.** *Nature*
Schau, N. n., Lehallier, B. n., Hahn, O. n., Pálovics, R. n., Hosseinzadeh, S. n., Lee, S. E., Sit, R. n., Lee, D. P., Losada, P. M., Zardeneta, M. E., Fehlmann, T. n., Webber, J. T., McGeever, et al
2020
- **Northstar enables automatic classification of known and novel cell types from tumor samples.** *Scientific reports*
Zanini, F. n., Berghuis, B. A., Jones, R. C., Nicolis di Robilant, B. n., Nong, R. Y., Norton, J. A., Clarke, M. F., Quake, S. R.
2020; 10 (1): 15251
- **A single-cell transcriptomic atlas characterizes ageing tissues in the mouse.** *Nature*
2020
- **Clinical and Therapeutic Implications of Cancer Stem Cells Reply** *NEW ENGLAND JOURNAL OF MEDICINE*
Clarke, M. F.
2019; 381 (10): E19–+
- **Solid tumor cancer stem cells: From bench to bedside**
Clarke, M. F.
AMER ASSOC CANCER RESEARCH.2019
- **ASXL1 regulates cellular differentiation and initiates tumorigenesis in colon**
Isobe, T., Zarnegar, M. A., Matsubara, J., Abdel-Wahab, O., Clarke, M. F.
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- **Usp16 modulates Wnt signaling in primary tissues through Cdkn2a regulation.** *Scientific reports*
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- **Usp16 modulates Wnt signaling in primary tissues through Cdkn2a regulation** *SCIENTIFIC REPORTS*
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- **Serially transplantable mammary epithelial cells express the Thy-1 antigen.** *Breast cancer research : BCR*
Lobo, N. A., Zabala, M., Qian, D., Clarke, M. F.
2018; 20 (1): 121
- **Serially transplantable mammary epithelial cells express the Thy-1 antigen** *BREAST CANCER RESEARCH*
Lobo, N., Zabala, M., Qian, D., Clarke, M. F.
2018; 20
- **The DLK1-DIO3 imprinted region regulates long-term proliferation in normal and malignant breast epithelium**
Zabala, M., Lobo, N. A., Seoane, J. A., Stelzer, Y., Luong, A. V., Isobe, T., Zarnegar, M. A., Watanabe, N., Antonana, S., Lam, J., Qian, D., Sikandar, S. S., Kuo, et al
AMER ASSOC CANCER RESEARCH.2018: 95
- **Characterizing the role of the nuclear coactivator AIB1 in triple-negative breast cancer.**
Cai, S., Kalisky, T., Dalerba, P., Clarke, M., Stanford Univ
AMER ASSOC CANCER RESEARCH.2018: 42–43
- **Effect of ASXL1 on the stemness of colorectal cancer initiating cells.**
Isobe, T., Zarnegar, M. A., Abdel-Wahab, O., Clarke, M. F.
AMER SOC CLINICAL ONCOLOGY.2018
- **A CD47-associated super-enhancer links pro-inflammatory signalling to CD47 upregulation in breast cancer** *NATURE COMMUNICATIONS*
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- **Role of epithelial to mesenchymal transition associated genes in mammary gland regeneration and breast tumorigenesis.** *Nature communications*
Sikandar, S. S., Kuo, A. H., Kalisky, T. n., Cai, S. n., Zabala, M. n., Hsieh, R. W., Lobo, N. A., Scheeren, F. A., Sim, S. n., Qian, D. n., Dirbas, F. M., Somlo, G. n., Quake, et al
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2016
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Chen, E. C., Karl, T. A., Kalisky, T., Gupta, S. K., O'Brien, C. A., Longacre, T. A., van de Rijn, M., Quake, S. R., Clarke, M. F., Rothenberg, M. E.
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- **Quantitative assessment of single-cell RNA-sequencing methods.** *Nature methods*

- Wu, A. R., Neff, N. F., Kalisky, T., Dalerba, P., Treutlein, B., Rothenberg, M. E., Mburu, F. M., Mantalas, G. L., Sim, S., Clarke, M. F., Quake, S. R.
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2014; 11 (1): 41-46
 - **Usp16 contributes to somatic stem-cell defects in Down's syndrome.** *Nature*
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Dalerba, P., Clarke, M. F.
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 - **Identifying the metastatic seeds of breast cancer.** *Nature biotechnology*
Kuo, A. H., Clarke, M. F.
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Sen, A., Rothenberg, M. E., Mukherjee, G., Feng, N., Kalisky, T., Nair, N., Johnstone, I. M., Clarke, M. F., Greenberg, H. B.
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