Stanford

Michael F. Clarke, M.D.

Karel H. and Avice N. Beekhuis Professor in Cancer Biology

Medicine - Oncology

CONTACT INFORMATION

- **Administrative Contact**

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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

HONORS AND AWARDS

- American Association of Physicians, - (-)

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PROFESSIONAL EDUCATION

- M.D., Indiana University (1977)

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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

Vinnie Alford, Jane Antony, Zhen Qi, Andre St Amant

1 OF 2

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)

1 OF 2

Publications

PUBLICATIONS

- **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

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