

THE
Flexner
DISCOVERY
LECTURE SERIES

ROEL NUSSE, PH.D.

WNT SIGNALING STEM CELL CONTROL AND CANCER

APRIL 23, 2015

4:00 P.M.

208 LIGHT HALL

THE
Flexner
DISCOVERY
LECTURE SERIES

Upcoming Discovery Lecture:

ERIC I. KNUDSEN, PH.D.

Stanford University

April 30, 2015

208 Light Hall / 4:00 P.M.

SPONSORED BY:
DEPARTMENT OF CELL AND DEVELOPMENTAL BIOLOGY,
CDB DISTINGUISHED SPEAKER

VANDERBILT  UNIVERSITY
MEDICAL CENTER

WNT SIGNALING STEM CELL CONTROL AND CANCER

Our laboratory is interested in the growth, development and integrity of animal tissues, with a focus on stem cells. Wnt signaling is widely implicated in stem cell control, as a mechanism to regulate the number of stem cells in tissues. Using various cell labeling methods, we have described novel populations of stem cells in various tissues, including in the liver. In that tissue, we found that hepatocytes that reside in the pericentral domain of the liver demonstrate stem cell behavior. Although these cells are functional hepatocytes, they are diploid and thus differ from the mostly polyploid mature hepatocyte population. They are active in homeostatic cell replacement and therefore distinct from oval cells, which require injury for their induction. Adjacent central vein endothelial cells provide the essential source of Wnt signals for the hepatocyte stem cells and thereby constitute the liver stem cell niche. It is noteworthy that liver cancer is often characterized by loss of function mutations in negative components of the Wnt pathway, including Axin and APC. We suggest that pericentral hepatocyte stem cells, normally controlled by a paracrine Wnt signal, are precursors to liver cancer.

We have also asked whether Wnt signals could operate in a directional, oriented manner on stem cells to orchestrate their asymmetric division. We have developed a novel technology that includes immobilized Wnt proteins on small beads and the application of these to single stem cells in culture. By this method, we were able to activate one specific side of the cell by the locally acting Wnt, follow by time-lapse imaging. Our data show that a local source of Wnt proteins sets up the orientation of cell division and the mitotic spindle. The oriented Wnt signal induces asymmetric division of stem cells: the daughter cell in contact with the Wnt source maintains pluripotency, whereas the distal cell differentiates.



ROEL NUSSE, PH.D.

**HOWARD HUGHES MEDICAL INSTITUTE,
DEPARTMENT OF DEVELOPMENTAL BIOLOGY
STANFORD UNIVERSITY, SCHOOL OF MEDICINE**

Dr. Roeland Nusse is a professor in the Department of Developmental Biology at Stanford University School of Medicine, the Virginia and Daniel K. Ludwig Professor of Cancer Research and a Howard Hughes Medical Institute Investigator. Dr. Nusse received his PhD from the Netherlands Cancer Institute at the University of Amsterdam in 1980. He completed postdoctoral studies at the University of California, San Francisco in 1982 working with Dr. Harold Varmus. He joined the Stanford medical faculty in 1990. In 1999 he was appointed as chair of the department. In 2010, he was elected as a member of the National Academy of Sciences. Dr. Nusse is also a fellow of the American Academy of Arts and Sciences and a member of the Royal Dutch Academy of Sciences.

The Cell and Developmental Biology Distinguished Faculty Lecture Series is an annual event in honor of the more than 80 years of excellence in research, teaching and service by the faculty of Vanderbilt University School of Medicine in the Department of Cell and Developmental Biology.

CELL AND DEVELOPMENTAL BIOLOGY PRIMARY FACULTY
(based on faculty census 1985 forward)

| | |
|---|--------------|
| James W. Ward, M.D., Professor Emeritus# | 1958-1993 |
| Jack Davies, M.D., Professor Emeritus# | 1963-1991 |
| G. Rodman Davenport, Ph.D., Associate Professor# | 1963-1993 |
| Alvin M. Burt, Ph.D., Professor Emeritus | 1966-2000 |
| Loren H. Hoffman, Ph.D., Professor# | 1969-1999 |
| John A. Freeman, M.D., Ph.D., Professor | 1971-1994 |
| Vivien A. Casagrande, Ph.D., Professor | 1975-present |
| James A. McKanna, Ph.D., Associate Professor Emeritus | 1976-2002 |
| Gary E. Olson, Ph.D., Professor Emeritus | 1977-2008 |
| Alfred G. Kasselberg, M.D., J.D., Assistant Professor | 1978-2001 |
| Jeanette J. Norden, Ph.D., Professor Emeritus | 1978-2013 |
| Paula C. Hoos, Ph.D., Associate Professor | 1982-1997 |
| Harold L. Moses, M.D., Professor | 1985-2000** |
| W. Jackson Pledger, Ph.D., Professor | 1985-1994 |
| Edward B. Leof, Ph.D., Associate Professor | 1985-1992 |
| Lynn M. Matrisian, Ph.D., Professor | 1986-2000 |
| Stephen R. Hann, Ph.D., Professor | 1986-present |
| Jeffrey T. Holt, M.D., Professor | 1987-2002 |
| Brigid L.M. Hogan, Ph.D., FRS, Professor | 1988-2002 |
| J. Ann Richmond, Ph.D., Professor | 1989-2000+ |
| Christopher V.E. Wright, D.Phil., Professor | 1990-present |
| Bruce W. Ennis, Ph.D., Assistant Professor | 1990-1993 |
| Steven K. Hanks, Ph.D., Professor Emeritus | 1990-2011 |
| Susan R. Fox, Ph.D., Assistant Professor | 1990-1993 |
| Kathleen L. Gould, Ph.D., Professor | 1991-present |
| Claude M. Nagamine, Ph.D., Assistant Professor | 1991-2000 |
| Mary Ann Arildsen, M.D., Ph.D., Assistant Professor | 1991-1998* |
| David M. Miller, Ph.D., Professor | 1994-present |
| David I. Greenstein, Ph.D., Associate Professor | 1994-2006 |
| Peng Liang, Ph.D., Associate Professor | 1995-2000 |
| Peter A. Kolodziej, Ph.D., Assistant Professor# | 1995-2005 |
| Albert B. Reynolds, Ph.D., Professor | 1996-2000+ |
| David W. Threadgill, Ph.D., Assistant Professor | 1996-2000 |
| Chin Chiang, Ph.D., Professor | 1997-present |
| Arthur F. Dalley, Ph.D., Professor | 1998-present |
| Christopher F.J. Hardy, Ph.D., Associate Professor | 2002-2009 |
| Susan R. Wentz, Ph.D., Professor** | 2002-present |
| Daniela Drummond-Barbosa, Ph.D., Assistant Professor | 2002-2009 |
| Guoqiang Gu, Ph.D., Associate Professor | 2002-present |
| Ethan Lee, M.D., Ph.D., Associate Professor | 2003-present |
| Laura A. Lee, M.D., Ph.D., Associate Professor | 2003-2104 |
| Matthew J. Tyska, Ph.D., Associate Professor | 2004-present |
| Irina N. Kaverina, Ph.D., Associate Professor | 2005-present |
| Byeong J. Cha, Ph.D., Assistant Professor | 2005-2009 |
| Stacey S. Huppert, Ph.D., Assistant Professor | 2005-2012 |
| Patricia A. Labosky, Ph.D., Associate Professor | 2006-2012 |
| Ryoma Ohi, Ph.D., Associate Professor | 2007-present |
| Melanie Ohi, Ph.D., Associate Professor | 2007-present |
| William Tansey, Ph.D., Professor | 2009-present |
| Andrea Page-McCaw, Ph.D., Associate Professor | 2010-present |
| Ian G. Macara, Ph.D., Professor and Chair | 2012-present |
| Ken Lau, Ph.D., Assistant Professor | 2013-present |
| Jason MacGurn, Ph.D., Assistant Professor | 2013-present |
| Dylan Burnette, Ph.D. Assistant Professor | 2014-present |
| Marija Zanic, Ph.D. Assistant Professor | 2014-present |

* Chair of Cell Biology (1985-2000), Emeritus Director, Vanderbilt-Ingram Cancer Center

** Chair of Cell Biology (2002-2012), Vanderbilt University Provost and Vice Chancellor for Academic Affairs

+ Department of Cancer Biology, Vanderbilt University School of Medicine

^ Department of Pathology, Microbiology and Immunology, Vanderbilt University School of Medicine

Deceased

