

Selection Committee

Darryl C. De Vivo, M.D.
Sidney Carter Professor of Neurology
and Professor of Pediatrics

Salvatore DiMauro, M.D.
Lucy G. Moses Professor of Neurology

John M. Driscoll, Jr., M.D.
Reuben S. Carpentier Professor of
Pediatrics

James H. Garvin, M.D., Ph.D.
Professor of Clinical Pediatrics

Marc C. Patterson, M.D., FRACP
Professor of Clinical Neurology
and Clinical Pediatrics

Timothy A. Pedley, M.D.
Henry & Lucy Moses Professor of
Neurology

Lewis P. Rowland, M.D.
Professor of Neurology

I. Bernard Weinstein, M.D.
Frode Jensen Professor of Medicine

Previous Gibling Lectures

1997: Huda Y. Zoghbi, M.D.
“The Rise of Repeats and the Fall of Neurons:
Implications for Pathogenesis”

1998: Hugo W. Moser, M.D.
“Genetics, Pathogenesis and Therapy of
Adrenoleuko-dystrophy and Other Peroxisomal
Disorders”

1999: Judah Folkman, M.D.
“Angiogenic Research: Experimental & Clinical
Studies”

2000: Christopher A. Walsh, M.D., Ph.D.
“Scrambling, Doubling, and Disabling the Human
Brain:
Genes Required for Cerebral Cortical
Development”

2001: Joseph J. Volpe, M.D.
“Brain Injury in the Premature Infant – From
Pathogenesis to Prevention”

2002: Elizabeth H. Blackburn, Ph.D.
“Telomerase, Cell Proliferation and Cell Death”

2003: Gideon Dreyfuss, Ph.D.
“The Survival of Motor Neurons Complex: An
Assembly Machine for Ribonucleoprotein
Particles”

2004: Scott L. Pomeroy, M.D. Ph.D.
“Using Genomics to Identify Molecular Therapeutic
Targets in Central Nervous System Embryonal
Tumors”

2005: Kevin P. Campbell, Ph.D.
“Molecular Pathogenesis of Muscular Dystrophy
with Brain Malformations”

The Division of Pediatric Neurology
The Department of Neurology
The Department of Pediatrics
The M.D-Ph.D. Program
College of Physicians & Surgeons of Columbia
University
New York Presbyterian Hospital

Present

The Twenty-First
Annual
Colleen Gibling
Memorial Lecture



**Pediatric Brain Tumors:
Promise & Problems Targeting
the Sonic Hedgehog Pathway**

Tom Curran, Ph.D.

Member, St. Jude Faculty
Chair, Developmental Neurobiology
Co-Leader,
Neurobiology & Brain Tumor Program
St. Jude Children's Research Hospital
Memphis, TN



Tuesday, April 11, 2006 at 4:30 PM

**Neurological Institute
Alumni Auditorium, 1st Floor**
710 West 168th Street, New York, NY 10032

The Colleen Giblin

Memorial Lecture

This lecture series honors the memory of Colleen, a young child who died on January 4, 1985 of a recurrent brain tumor. Colleen's parents, Mr. and Mrs. Paul J. Giblin, established this lecture series one year later to bring distinguished scientists who are committed to finding cures for brain tumors and other devastating neurological disorders of childhood to the Columbia University Medical Center to share information and to exchange ideas. In 1990 following his Giblin Lecture, Professor J. Michael Bishop applauded the members of the Giblin Foundation for their noble work and admonished them that the road to a cure will be long and there is no clear end in sight. These sentiments also have been expressed recently by our 2006 Giblin Lecturer in a special article entitled: *Lost in Translation: The Future of Cancer Research?* that appeared one year ago in *Clinical Cancer Research*. It is the continuing hope and expectation of the Giblin Family and the Colleen Giblin Charitable Foundation for Pediatric Neurology Research that this collaborative interaction between scientists and clinicians will catalyze the investigative enterprise and accelerate the transfer of ground-breaking laboratory advances to the clinical arena.



Tom Curran, Ph.D.

Tom Curran, Ph.D. was born in Addiewell, a tiny Scottish village that was the first site where oil shale was mined commercially. His chemistry project as a High School Senior involved the study of the extraction procedure involved in the release of gas and oil from the shale that was mined commercially in that area. This was his first real exposure to science and influenced his academic choices as he enrolled in the University of Edinburgh to study biological sciences. After receiving his Bachelor of Science Degree in 1978 he entered Graduate Studies at the Imperial Cancer Research Fund Laboratories and University College London, receiving his Ph.D. Degree in 1982. He then completed post-doctoral studies at the Salk Institute, San Diego and later joined Hoffman-La Roche in Nutley, New Jersey where he rose to the position of Associate Director of the Roche Institute of Molecular Biology while maintaining an Adjunct Professorship at Columbia University. In 1995 he moved to Memphis, TN to Chair the Department of Developmental Neurobiology at St. Jude Children's Research Hospital. Before moving from an academic and industrial environment to a research hospital, Professor Curran had focused on basic scientific issues and derived great pleasure and sense of accomplishment in witnessing the growth of post-doctoral research fellows and graduate students into mature, independent scientists. At St. Jude Children's Research Hospital the goal was to launch a new department focused on Developmental Neurobiology and to interface closely with the clinical brain tumor service to improve the diagnosis and treatment of children with this dreaded condition. In his words: ***basic research allowed you to ask fundamental questions and any answer, particularly if it is unexpected, is useful. Translational research differs from basic research to the extent that you know the results you want and you have to find a way to deliver.***

Professor Curran spent a week in the Neuro-Oncology Clinic shortly after arriving at St. Jude Children's Research Hospital and for the first time met children with brain tumors. This experience had a profound effect on his research program and launched him into a new project on medulloblastoma.

Professor Curran is an accomplished investigator with more than two hundred and fifty publications. His research spans the fields of cancer, signal transduction and neurobiology. While a graduate student in London, he discovered the *fos* oncogene and demonstrated that the protein product forms a leucine zipper dimer with Jun to function as the mammalian transcription factor AP-1. Also, he has shown that *c-fos* expression is induced by a variety of extracellular stimuli associated with cell proliferation, differentiation, apoptosis and neuronal activation. The Curran Laboratory has also demonstrated that the *ras* gene functions as an upstream activator of *c-fos* expression, and these observations support the emerging view that many oncogenes participate in a common signaling pathway. In this model, *Fos* is viewed as the archetype of a set of transcription factors that function by coupling short-term signals, elicited by cell surface stimuli, to long-term changes in cellular phenotype by regulating expression of specific target genes. More recently, the Curran Laboratory has identified DNA methyl transferase-1, a target gene that is both necessary and sufficient for the induction of the morphological transformation by *fos*. This finding indicates that *Fos* causes transformation by enhancing the level of DNA methylation which in turn results in the repression of specific target genes, thus introducing a possible link between *fos* function and the organization of chromatin.

The neurobiological contributions of the Curran Laboratory has expanded in recent years to include the control of cell migration in brain development.

Two genes have been discovered that are responsible for cell migration during early brain development. The reeler gene, *reelin*, encodes a large extracellular protein, Reelin, which directs the migration of neuronal populations throughout the brain. Reelin, for example, is secreted by the Cajal Retzius cells and directs the positioning of underlying cortical plate neurons in the cerebral cortex. Reelin functions through a signaling pathway that involves the *Disabled-1* protein which is present in the target cells of Reelin. Mutations in the *reelin* gene produce a neurological phenotype in the mouse with tremors, dystonia and ataxia resulting from the disturbance of migration of postmitotic neurons in the developing nervous system. The Curran Laboratory have shown that reelin and mouse disabled-1 are expressed in complementary patterns during brain development and possibly function in the same signaling pathway that control cell migration in the developing brain.

These seminal contributions in molecular oncology and in neurobiology have focused international attention on the Curran Laboratory. Professor Curran has won numerous awards including the Passano Foundation Young Scientist Award in 1992, the Golgi Award from the Camillo Golgi Foundation and the Italian Academy of Neuroscience in 1994, the Javitz Neuroscience Investigator Award, NINDS in 2001, the LIMA International Award for Excellence in Pediatric Brain Tumor Research in 2004 and Election to the Royal Society, London in 2005. He is Past President of the American Association for Cancer Research and a Member of the National Cancer Institute Board of Scientific Advisors. Currently he continues as a Member and Chairman, Department of Developmental Neurobiology, St. Jude Children's Research Hospital and Professor, Department of Anatomy and Neurobiology at the University of Tennessee College of Medicine. On the occasion of the 21st Annual Colleen Giblin Memorial Lecture, it is a great pleasure and honor to welcome Professor Tom Curran to the Columbia University Medical Center.