

## Research of Note



Timothy C. Wang '83

JORG MEYER

**Clues to Source of Esophageal Cancer.** Esophageal adenocarcinoma is the fastest-rising solid tumor in this country. Now, P&S scientists have identified the earliest cellular and molecular changes that lead to this deadly cancer, using a new genetically engineered mouse model of esophagitis, the inflammatory disorder involved in the development of Barrett's esophagus, an asymptomatic precancerous condition. For decades, it was believed that the physiological changes associated with Barrett's esophagus originate in the lower esophagus. "However, our study shows that Barrett's esophagus actually arises in the gastric cardia, a small region between the lower part of the esophagus and the upper, acid-secreting portion of the stomach," says lead investigator Timothy C. Wang, M.D. "The bile acid and inflammatory cytokines activate stem cells at this transition zone, and they begin migrating up toward the esophagus." Dr. Wang's research also suggests a possible therapeutic pathway for high-risk patients with Barrett's esophagus: the notch cell signaling system, which when inhibited blocked the proliferation and survival of premalignant cells.

### Non-Hereditary Cases of Schizophrenia.

More than half the cases of non-hereditary, or sporadic, schizophrenia are caused by "new" protein-altering gene mutations, according to research at P&S supported by funding from the Lieber Foundation. In work published in the journal *Nature Genetics*, Maria Karayiorgou, M.D., and Joseph A. Gogos, M.D., Ph.D., examined the genomes of genetically isolated Afrikaner families of European descent in South Africa. The participants included patients with schizophrenia, their families, and healthy people in control groups. The researchers identified 40 mutations, all in different genes and most of them protein-altering, that were associated with sporadic schizophrenia. The findings could point the way to finding more mutations, perhaps hundreds, that contribute to schizophrenia. "The fact that the mutations are all from different genes is particularly fascinating," says Dr. Karayiorgou. "It suggests that many more mutations than we suspected may contribute to schizophrenia."

## Research Initiative: Translational Neuroscience

The principal goal of the new Columbia Translational Neuroscience Initiative is to enhance translational neuroscience research and therapeutics development by coordinating existing strengths in neuroscience, neurology, neurological surgery, psychiatry, and pathology. The Initiative will provide an overarching programmatic vision to better understand and treat brain disease and trauma by connecting the clinical neuroscience departments and translational centers at the medical center with each other and with faculty on the Manhattanville and Morningside campuses.

Different diseases and injuries that affect the nervous system target a specific set of brain regions and functions, and many successful translational centers and programs at Columbia have studied each condition as an individual set of scientific and therapeutic challenges. Recognizing that many pathological processes and disease mechanisms – from protein misfolding to axonal degeneration to inflammation – are common to many neurodegenerative, neurodevelopmental, and neuropsychiatric disorders suggests that studying these processes across different disease areas may generate new synergies and enhance integration.

The Translational Neuroscience Initiative will encourage scientific and clinical collaboration, oversee joint recruitment efforts, and create new shared facilities. Initial plans call for inclusion of any faculty member or translational research group whose work relates to neurological, neurodevelopmental, and neuropsychiatric disorders, from basic mechanistic and biochemical studies to novel animal and cell models to systems biology approaches to preclinical research. Full members will be faculty with significant publications and/or grants relevant to the areas of neuroscience, neuropsychiatry, neurology, and neurotrauma. Members will be drawn from departments (Neurology, Neurological Surgery, Pathology, Psychiatry, Biochemistry, and Rehabilitation & Regenerative Medicine), from centers and institutes (the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, the Gertrude H. Sergievsky Center, the Motor Neuron Center, the Lieber Center for Schizophrenia Research, and the Sackler Institute for Developmental Psychobiology), and from divisions and initiatives (movement disorders and systems biology).

The move of the Department of Neuroscience to Manhattanville in 2016 emphasizes the need for intercampus collaboration among faculty and research groups dedicated to the brain. The Initiative will facilitate coordination, recruitment, training opportunities for clinicians and basic scientists, and bench-to-bedside translation of findings through clinical populations.

The historical leadership of P&S in neuroscience, neurology, neurological surgery, psychiatry, pathology, and biochemistry has provided for important contributions by individuals in basic and translational neuroscience. Combining vision, resources, and strategies through the Translational Neuroscience Initiative will strengthen the potential of the large and diverse neuroscience community at P&S to contribute in even greater ways toward understanding the mysteries of the mind and brain.

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Three leaders of the new translational neuroscience initiative are, from left, Richard Mayeux, M.D., the Gertrude H. Sergievsky Professor of Neurology, Psychiatry, and Epidemiology and chair of neurology; Christopher Henderson, Ph.D., the Gurewitsch/Vidda Professor of Rehabilitation and Regenerative Medicine and chief of regenerative medicine; and Michael L. Shelanski, M.D., Ph.D., the Delafield Professor and Chair of Pathology & Cell Biology. [Not pictured: Robert Solomon, M.D., the Byron Stookey Professor of Neurological Surgery and chair of neurological surgery, and Jeffrey Lieberman, M.D., the Lieber Professor of Psychiatry, Lawrence C. Kolb Professor and Chair of Psychiatry, and director of the New York State Psychiatric Institute.]

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