

Broad Institute of MIT and Harvard, the Whitehead Institute at MIT, and the Gallo Foundation at the University of California, San Francisco. He has received the highest scientific awards of the American Society of Nephrology, the Council for High Blood Pressure Research, the American Society of Hypertension, the American Heart Association, the International Society of Hypertension, and the International Society of Nephrology. He received the Wiley Prize for Biomedical Sciences in 2008. He was elected to American Academy of Arts & Sciences in 2012. He received the 2014 Breakthrough Prize in Life Sciences in 2013.



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RICHARD LIFTON, M.D., Ph.D.

DISCOVERY OF DISEASE GENES AND PATHWAYS BY
NEXT GENERATION DNA SEQUENCING



MARCH 6, 2014
4:00 P.M.
208 LIGHT HALL

Upcoming Discovery Lecture:

BLAKE S. WILSON, DSc
Duke University

March 13, 2014
208 Light Hall / 4:00 P.M.

VANDERBILT  UNIVERSITY
MEDICAL CENTER

DISCOVERY OF DISEASE GENES AND PATHWAYS BY NEXT GENERATION DNA SEQUENCING

The cost of DNA sequencing has dropped one million-fold over the last 15 years, drastically changing the questions that can be posed and answered. In particular, this technology provides opportunity to identify rare mutations with large impact on disease risk beyond the constraints of classical Mendelian genetics. To take advantage of these opportunities, we developed methods for selective sequencing of the ~21,000 protein-coding genes in the genome and drove the cost to < \$500 per sample, allowing substantial experimental exploration. We have used this technology to identify disease-related genes in several distinct settings including somatic mutations in neoplasia; de novo mutations in autism, congenital heart disease and other diseases in which clinical features suggested a role for mutation with large effect and impaired reproductive fitness; rare diseases arising in the setting of consanguineous union. We are also using this technology in the clinic to identify known or new disease genes in hospitalized patients in whom traditional approaches have not yielded a diagnosis. We expect these approaches will allow annotation of the consequence of mutation of all 21,000 protein-coding genes and compendia of specific allelic associations. The continuing reductions in cost of DNA sequencing suggest the coming of routine and inexpensive sequencing of whole genomes, and raise questions about the both the utility and pitfalls of routine genome-level sequencing in large populations.



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Richard Lifton is Chair of the Department of Genetics, Sterling Professor of Genetics and Internal Medicine, Executive Director of the Yale Center for Genome Analysis and Investigator of the Howard Hughes Medical Institute at Yale University School of Medicine. He graduated summa cum laude from Dartmouth College, then received M.D. and Ph.D. degrees (in Biochemistry) from Stanford University. He completed clinical training in Internal Medicine at Brigham and Women's Hospital, served as Chief Medical Resident there and continued on the faculty at Harvard Medical School before being recruited to Yale in 1993. He has used human genetics and genomics to identify more than 35 human disease genes that identify key pathways underlying common diseases including hypertension, myocardial infarction, osteoporosis, cerebral hemorrhage, congenital heart disease and neoplasia. In the particular case of hypertension, which affects more than a billion people worldwide, these studies have led to new therapeutic approaches to the treatment and prevention strategies for the general population. His group recently developed a method for rapidly and inexpensively sequencing all the genes in the genome that is being widely used for disease gene discovery and clinical diagnosis. He is an elected member of the National Academy of Sciences, and the Institute of Medicine. He serves as Chair of the Scientific Advisory Board and advisor to the President of Merck Pharmaceuticals and is a member of the Governing Councils of the Institute of Medicine, the Association of American Physicians, and the Coalition for the Life Sciences, as well as the Scientific Advisory Boards of the Massachusetts General Hospital, the
