

THE
Flexner
DISCOVERY
LECTURE SERIES

PAUL D. LAMSON LECTURESHIP

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JONATHAN G. SEIDMAN, PH.D.

NEXT GENERATION SEQUENCING HAS
REVOLUTIONIZED CARDIOVASCULAR GENETICS

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MARCH 14, 2013
4:00 P.M.
208 LIGHT HALL

Upcoming Discovery Lecture:

JEFFREY A. WHITSETT, M.D.
Cincinnati Children's Hospital

March 28, 2013
208 Light Hall / 4:00 P.M.

VANDERBILT  UNIVERSITY
MEDICAL CENTER

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The ultimate opportunity presented by discovering the genetic basis of human heart disease is accurate prediction and prevention of disease. For these genetic discoveries to change medicine requires the ability to identify at-risk individuals prior to overt disease manifestations and developing novel therapies which delay or prevent clinical expression. The cardiomyopathies, many of which are inherited as Mendelian traits, provide a paradigm for fulfilling these opportunities. Using traditional human genetic methodologies, we learned that HCM is caused by mutations in genes encoding cardiac myosin heavy chain, α tropomyosin, cardiac troponin T and cardiac myosin binding protein-C, therein establishing an “idiopathic” condition as a disease of the sarcomere. Parallel analyses of DCM revealed a diverse range of genetic etiologies, including mutations in sarcomere protein genes, calcium regulating genes, and molecules with unknown functions in myocyte biology, thus indicating a multiplicity of mechanisms that predispose the heart to fail. Based on the discovery of HCM and DCM disease genes and the advent of next generation sequencing technologies this research has been translated into clinical gene-based diagnosis, providing the opportunity for early and accurate identification of individuals at risk for developing cardiomyopathies. Application of advanced sequencing strategies for characterization of the consequences of human cardiomyopathy mutations on myocyte biology has also provided unexpected insights into the molecular pathways that are activated by gene mutations. Selective targeting of key molecules in these pathways has enabled novel pre-emptive strategies that show promise for attenuating the development and progression of cardiomyopathies in human patients.



JONATHAN G. SEIDMAN, PH.D.

**HENRIETTA B. AND FREDERICK H. BUGHER FOUNDATION
PROFESSOR OF GENETICS HARVARD MEDICAL SCHOOL**

Dr. Jonathan Seidman is the Henrietta B. and Frederick H. Bugher Foundation Professor of Genetics at Harvard Medical School. He received his undergraduate degree from Harvard University ('72) and his Ph.D. degree from the University of Wisconsin-Madison. His postdoctoral studies were carried out in Dr. Philip Leder's laboratory at the National Institute of Child Health and Human Development. He has been a member of the Genetics Department, Harvard Medical School since 1981.

The Seidman Laboratory, which Jonathan co-runs with his wife Christine Seidman, M.D., studies the genetic basis for human disease. Heart disease is the laboratory's principle focus, but efforts are also devoted to hearing loss, vascular malformations and metabolic abnormalities. Investigations range from the discovery of genetic variants in rare and common cardiovascular phenotypes to elucidation of how genetic variations alter signaling mechanisms in model organisms, information that has been translated into novel therapeutic interventions in human patients. To advance these efforts, the laboratory also applies high-throughput genomic sequencing for basic investigations and for clinical application.

Dr. Seidman is a member of The Genetics Society of America and the American Society of Human Genetics. He has received several awards including the Gill Heart Institute Award for Outstanding Contributions to Cardiovascular Research (2000), the 12th Annual Bristol-Myers Squibb Award for Distinguished Achievement in Cardiovascular Research (2002) jointly with Christine Seidman, M.D., the Lefoulon-Delalande Foundation, Grand Prix for Science (2007) joint recipient with Christine Seidman, M.D., and the Katz Prize for Cardiovascular Research awarded by Columbia University School of Medicine (2008) jointly with Christine Seidman, M.D. He is also a member of the National Academy of Science (2007) and the Institutes of Medicine (2007).
