

## NIEHS grantee kicks off high-profile lecture series at NIH

By Eddy Ball

NIEHS grantee Andrew Feinberg, M.D., was the featured speaker Sept. 3 at the opening talk in the 2014-2015 Wednesday Afternoon Lecture Series at the National Institutes of Health (NIH) in Bethesda, Maryland. He reported on developments in his NIEHS-supported research on “The Epigenetic Basis of Common Human Disease.”

### Linked Video

[Watch as Feinberg describes his interdisciplinary approach to epigenetic research \(59:41\)](#)

#### Feinberg

(<http://epigenetics.jhu.edu/?section=personnelPages&personID=2>)

is the recipient of grants from several NIH institutes, but his lecture focused primarily on his NIEHS-administered funding for developing “A General Stochastic Epigenetic Model for Evolution, Development, and Disease,”

([http://projectreporter.nih.gov/project\\_info\\_description.cfm?aid=8708093&icde=21653416&ddparam=&ddvalue=&ddsub=&cr=4&csb=default&cs=ASC](http://projectreporter.nih.gov/project_info_description.cfm?aid=8708093&icde=21653416&ddparam=&ddvalue=&ddsub=&cr=4&csb=default&cs=ASC))

The grant is managed by health scientist administrator Lisa Chadwick, Ph.D.

In his introduction of Feinberg, NIH Director Francis Collins, M.D., Ph.D., commented on the speaker’s long list of honors, including his distinguished professorships, membership in the Institute of Medicine, and selection as a 2011 NIH Director’s Pioneer Award recipient.

Reflecting on his long relationship with Feinberg, dating back to their tenures as faculty members at the University of Michigan, Collins said, “I don’t know exactly what Andy’s going to put in front of you today, but I’m sure you’ll find it to be interesting and provocative.”

The first part of Feinberg’s lecture echoed what he presented at the February 2013 meeting of the NIEHS of the National Advisory Environmental Health Sciences Council (see [story](#)), of which he is now a member. The second half reported on



*“He is, in fact, a remarkably creative scientist,” Collins, above, said of Feinberg, who has synthesized insights from the fields of quantum physics, astronomy, and mathematics, as well as the humanities, with his biomedical training and research. (Photo courtesy of NIH)*



*“You have to look at genetics and epigenetics together,” Feinberg explained, through a series of examples of new insight achieved through integrated methodologies. (Photo courtesy of NIH)*

subsequent work that points to newly discovered targets for possible therapeutic interventions.

## Forging an integrated theory

Feinberg opened his talk with the question that drives his research — what shapes the observable characteristics of health and disease in individuals, or their phenotypes, resulting from the interaction of genes with the environment.

Referring to studies finding that genetics alone could explain no more than 20 percent of all disease, Feinberg looked beyond genetics to changes in gene expression that don't change DNA, but profoundly influence health and disease. "Our environment shapes, in a remarkable way, our phenotype, but not through the genes themselves, but through influencing how the epigenome might take place," he explained.

Around the turn of the century, Feinberg expanded his research beyond epigenetics and cancer, a connection well established by that time. "I became very interested in whether or not one could begin to explore the epigenetic basis of common disease, generally," he said, "particularly where environmental exposure might be important."

Exploring what he calls variably methylated regions, which are present in up to half of the genome, Feinberg has steadily refined a general stochastic, or random element, epigenetic model.

The model both explains how the degree of plasticity in defined regions can influence tissue-specific differences that are separate from DNA, which is consistent across tissues, a sort of inner organism process of selection, and natural selection on a species level consistent with a Darwinian model. He presented recent data on aging, rheumatoid arthritis, and diabetes-related obesity in support of the model.

Just as his model integrates evolution, development, and disease, Feinberg's group has combined methodologies and models, specifically comparative human and mouse tissue studies, for new insights.

"The integration of epigenetic information with genetic sequence could reveal patterns related to human disease that we wouldn't know otherwise," he said. He pointed to newly discovered cases of distant regulation of the genome, identified by epigenetic analysis, by single nucleotide polymorphisms, which were revealed through genome-wide association studies.

Significantly, some of these patterns could lead to potential interventions. "I think that this might be a way to uncover new targets that are, if not the primary generators of these phenotypes, certainly mediators, and they're drugable. That is, we might be able to come up with compounds that can modify the phenotype," he concluded.



With his Johns Hopkins mentor, *Bert Vogelstein, M.D.* ([http://www.hopkinsmedicine.org/kimmel\\_center\\_center/experts/Laboratory\\_Scientists/detail/6424146D144F331F200D784A751851DB/Bert\\_Vogelstein](http://www.hopkinsmedicine.org/kimmel_center_center/experts/Laboratory_Scientists/detail/6424146D144F331F200D784A751851DB/Bert_Vogelstein)) , Feinberg, left, reported the identification of DNA hypomethylation as a signature of cancer, in a landmark 1983 *paper* (<http://www.ncbi.nlm.nih.gov/pubmed/6185846>) in *Nature*. In the course of three decades, his research has expanded dramatically in range and volume from that insight about cancer. (Photo courtesy of NIH)

## More about the Pioneer Award and the Wednesday Afternoon Lecture Series

The NIH Director's Pioneer Award (<http://commonfund.nih.gov/pioneer/index>) program provides grants from the NIH Common Fund for highly innovative approaches that have the potential to produce an unusually high impact on a broad area of biomedical or behavioral research. It complements traditional, researcher-initiated NIH grant programs, by supporting individual scientists of exceptional creativity.

Each year the *Wednesday Afternoon Lecture Series* (<http://wals.od.nih.gov/>) features some of the biggest names in biomedical and behavioral research, nominated by the NIH community. This academic year's lineup includes 34 scientists from across the spectrum of biomedical research.

The Environmental Factor is produced monthly by the [National Institute of Environmental Health Sciences \(NIEHS\)](http://www.niehs.nih.gov/) (<http://www.niehs.nih.gov/>)

, Office of Communications and Public Liaison. The content is not copyrighted, and it can be reprinted without permission. If you use parts of Environmental Factor in your publication, we ask that you provide us with a copy for our records. We welcome your [comments and suggestions](#). ([bruskec@niehs.nih.gov](mailto:bruskec@niehs.nih.gov))

This page URL: NIEHS website: <http://www.niehs.nih.gov/>  
Email the Web Manager at [webmanager@niehs.nih.gov](mailto:webmanager@niehs.nih.gov)