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Hematologist-Oncologist Stuart Orkin Receives $500,000 Gruber Genetics Prize for His Groundbreaking Research on the Genetics of Inherited Blood Disorders

Stuart H. Orkin

March 2, 2021, New Haven, CT – The 2021 Gruber Genetics Prize recognizes hematologist-oncologist and geneticist Stuart H. Orkin, M.D., for his pioneering discoveries of the genetic underpinnings of blood disorders. His remarkable body of work has not only revolutionized our understanding of how these illnesses occur but has also led to promising new gene-based therapies for thalassemia and sickle cell disease, two inherited blood disorders that affect millions of people around the world. Dr. Orkin is the David G. Nathan Distinguished Professor of Pediatrics at Harvard Medical School and the Dana-Farber/Boston Children's Cancer and Blood Disorders Center, and an Investigator of the Howard Hughes Medical Institute.

The prize, which includes a $500,000 award, will be presented to Orkin at the annual meeting of the American Society of Human Genetics in October.

"Dr. Orkin has led the field of hematology for more than 40 years," says Eric Olson, professor at UT Southwestern and member of the Selection Advisory Board. "His work has been deeply mechanistic, groundbreaking and impactful. Through a series of seminal discoveries, he has helped to unravel key molecular mysteries behind how blood cells develop—and how inherited blood disorders occur."

Early in his career, Orkin identified many genetic mutations behind the various types of thalassemia, an inherited blood disorder characterized by inadequate production of the protein beta-globin, one of two chains of hemoglobin, the oxygen-carrying component of red cells. This ambitious undertaking led to the creation of the first comprehensive genetic "catalogue" of a human molecular disease. Orkin also identified the gene that causes another inherited blood disorder, chronic granulomatous disease. This discovery marked the first time a laboratory technique known as "positional cloning" was used to identify a gene responsible for a human disease.

Orkin then went on to isolate and characterize GATA1, a master regulator of all genes in developing red cells and the founding member of a family of GATA proteins directing differentiation of cells in many tissues. More recently, Orkin's laboratory identified the gene—BCL11A—that controls the switch between fetal and adult hemoglobin that occurs around the time of birth, thus solving a hematologic enigma that had long evaded scientists. Orkin and his team demonstrated that turning off BCL11A interferes with the silencing of fetal hemoglobin. Inactivating BCL11A in adult, genetically engineered mice reactivates expression of fetal hemoglobin and eliminates the signs of sickle cell disease. These stunning findings have led to the development of exciting new gene-based therapies for beta-thalassemia and sickle cell disease—therapies that have already shown clinical promise.

"Thanks to Dr. Orkin's insights, elegant experiments, and tenacity, we are on the cusp of making major therapeutic breakthroughs for several inherited hematologic disorders," says Aravinda Chakravarti, professor at New York University School of Medicine and member of the Selection Advisory Board. "It's a great honor to be awarding the Gruber Genetics Prize to such an extraordinary scientist."

Additional Information

In addition to the cash award, the recipient will receive a gold laureate pin and a citation that reads:

The Gruber Foundation proudly presents the 2021 Genetics Prize to Stuart Orkin for his pioneering discoveries of the genetic and molecular basis of common blood diseases and the gene regulatory mechanisms that govern blood cell development. He elucidated the mechanism of regulation of the switch from fetal to adult hemoglobin, and reduced to practice the reactivation of fetal hemoglobin as a therapeutic strategy for sickle cell disease and the thalassemias. Stuart Orkin's science has beautifully illustrated the successful progression from fundamental genetics to mechanistic biology to therapeutic development and intervention, which can transform the lives of millions of patients in need.

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The Genetics Prize is presented to a leading scientist, or up to three, in recognition of groundbreaking contributions to any realm of genetics research.

Laureates of the Gruber Genetics Prize:

- **2020: Bonnie Bassler,** for pioneering discoveries on bacterial communication
- **2019: Bert Vogelstein,** for discoveries of new genetic pathways and processes contributing to cancer
- **2018: Joanne Chory and Elliot Meyerowitz,** for helping revolutionize plant molecular biology, with implications for global agriculture, the environment, and human health and disease
- **2017: Stephen Elledge,** for discovering and characterizing the molecular mechanisms of the DNA damage response pathway in eukaryotic cells

- **2016: Michael Grunstein and David Allis,** for the discovery of the role of histone proteins and their covalent modification in the regulation of eukaryotic gene expression
- **2015: Emmanuelle Charpentier and Jennifer Doudna**, for establishing a framework for universal genome editing
- **2014: Victor Ambros, David Baulcombe, and Gary Ruvkun**, for pioneering the study of small non-coding RNA's, molecules that are recognized as playing a critical role in regulating gene expression
- **2013: Svante Pääbo,** for pioneering the analysis of ancient DNA
- **2012: Douglas C. Wallace,** for his groundbreaking contributions to mitochondrial genetics
- **2011: Ronald Davis,** for pioneering development and application of recombinant-DNA techniques
- **2010: Gerald Fink**, whose work in yeast genetics advanced the field of molecular genetics
- **2009: Janet Davison Rowley,** for her seminal discoveries in molecular oncology
- **2008: Allan C. Spradling,** for his work on fly genomics
- **2007: Maynard V. Olson,** for his contributions to genome science
- **2006: Elizabeth H. Blackburn,** for studies of telomeres and telomerase, and her science advocacy
- **2005: Robert H. Waterston,** for his pivotal role in the Human Genome Project
- **2004: Mary-Claire King,** for three major findings in modern genetics: the similarity of the human and chimpanzee genomes, finding a gene that predisposes to breast cancer, and forensic genetics.
- **2003: David Botstein,** a driving force in modern genetics who established the ground rules for human genetic mapping
- **2002: H. Robert Horvitz,** who defined genetic pathways responsible for programmed cell death
- **2001: Rudolf Jaenisch,** who created the first transgenic mouse to study human disease

The Prize recipients are chosen by the Genetics Selection Advisory Board. Its members are:

Marlene Belfort, University at Albany, SUNY; **Aravinda Chakravarti**, New York University, School of Medicine; **Philip Hieter,** Michael Smith Laboratories at the University of British Columbia; **Jeannie T. Lee**, Harvard Medical School; **James Lupski**, Baylor College of Medicine; **Eric N. Olson**, The University of Texas Southwestern Medical Center; **Allan Spradling**, Carnegie Institution for Science (Chair).

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The Gruber International Prize Program honors individuals in the fields of Cosmology, Genetics and Neuroscience, whose groundbreaking work provides new models that inspire and enable fundamental shifts in knowledge and culture. The Selection Advisory Boards choose individuals whose contributions in their respective fields advance our knowledge and potentially have a profound impact on our lives. The Genetics Society of America partners with the Foundation on the Genetics Prize, and nominates the members of the Genetics Selection Advisory Board.

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For more information on the Gruber Prizes, visit www.gruber.yale.edu,
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Media materials and additional background information on the Gruber Prizes are in our online newsroom: www.gruber.yale.edu/news-media

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