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Molecular Biologists Allan Jacobson and Lynne Maquat Share $500,000 Gruber Genetics Prize for Pioneering Work in Nonsense-Mediated mRNA Decay

Allan Jacobson

Lynne Maquat

February 23, 2023, New Haven, CT — The 2023 Gruber Genetics Prize is being awarded to molecular biologists Allan Jacobson, PhD, of the University of Massachusetts Chan Medical School, and Lynne Maquat, PhD, of the University of Rochester School of Medicine and Dentistry, for their contributions in identifying and describing the mechanism of nonsense-mediated mRNA decay (NMD). This complex cellular pathway targets mRNA transcripts containing premature stop codons for degradation, thus preventing the formation of truncated, possibly toxic protein fragments.

As they have also shown, NMD also acts as a mechanism by which a cell can respond to environmental changes. Working independently, these two researchers changed our understanding of the role that mRNA regulation plays in ensuring the proper workings of a cell.

“Through their creativity and dedication to fundamental discovery research, Maquat and Jacobson have elucidated a crucial post-transcriptional regulatory pathway that eliminates transcripts containing a premature stop codon,” says Philip Hieter, Professor in the Michael Smith Laboratories at the University of British Columbia and a member of the Selection Advisory Board to the Prize. “Their discoveries of the molecular components and mechanism of nonsense-mediated mRNA decay have been paradigm shifting, in our understanding of how cells avoid expression of potentially deleterious mRNA transcripts, and in the genetics of human disease.”

The Gruber Genetics Prize, which includes a $500,000 award, will be presented to Jacobson and Maquat at the International Congress of Genetics in Melbourne, Australia, on July 19.

Through his yeast genetic studies, Jacobson identified the core components of the nonsense mediated mRNA decay pathway, demonstrating the role that UPF proteins play in targeting mRNAs with a

premature stop codon for degradation. He was also able to demonstrate the role this pathway plays as a quality control checkpoint for mRNAs with a premature stop codon, whether due to a mutation or gene expression errors.

Through her studies of patients with hemolytic diseases, Maquat demonstrated the importance of nonsense-mediated mRNA decay in humans, by showing that mRNAs with a premature stop codon were more unstable. She went on to elucidate NMD mechanisms in mammalian cells and also showed that NMD acts to eliminate faulty transcripts that are the byproduct of routine errors in human gene expression, and that cells use NMD to adapt to changes in environment, through the fine-tuning of approximately 5-10% of mRNAs.

Already, through the work of Jacobson and Maquat, these discoveries have had implications in treating human diseases such as Duchenne muscular dystrophy and Fragile X syndrome.

“As the best characterized and most highly conserved RNA quality control mechanism, understanding NMD opened scientists' eyes to a new level of genetic regulation that reviews normal as well as mutated mRNAs and provides cells with previously unappreciated resilience and adaptability,” says Allan Spradling, professor at the Carnegie Institution/HHMI and chair of the Selection Advisory Board. “Already, these insights have profound implications in treating human diseases, and the importance of this topic will continue to grow rapidly in the years to come.”

Additional Information

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

The Gruber Foundation proudly presents the 2023 Genetics Prize to Allan Jacobson and Lynne Maquat for their discoveries and pioneering studies on the mRNA surveillance mechanism known as Nonsense Mediated mRNA Decay (NMD). NMD is a complex evolutionarily conserved pathway that plays an important role in genetics and the regulation of gene expression. Jacobson is being recognized for the genetic elucidation and analysis of the NMD pathway and related consequences of premature translation termination. Maquat is being recognized for elucidating the mechanisms and cellular importance of NMD and NMD factors in mammalian cells and human disease.

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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:

- **2022: Ruth Lehmann, James Priess, and Geraldine Seydoux** for embryogenesis discoveries
- **2021: Stuart H. Orkin,** revolutionized our understanding of genetics of inherited blood disorders
- **2020: Bonnie Bassler,** for pioneering discoveries on bacterial communication
- **2019: Bert Vogelstein,** 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,** for establishing 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:

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.

The Gruber Foundation was established in 1993 by the late Peter Gruber and his wife Patricia Gruber. The Foundation began its International Prize Program in 2000, with the inaugural Cosmology Prize.

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For more information on the Gruber Prizes, visit www.gruber.yale.edu, e-mail info@gruber.yale.edu or contact A. Sarah Hreha at +1 (203) 432-6231. By mail: The Gruber Foundation, Yale University, Office of International Affairs, PO Box 208320, New Haven, CT 06520

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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