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## HHMI Investigators Joan Steitz and Ronald Evans Honored with Gairdner International Award

HHMI investigators Joan A. Steitz and Ronald M. Evans were among five scientists honored today with the prestigious Gairdner International Award in recognition of their contributions to medical science.

Presented to medical scientists worldwide whose work is expected to significantly improve the quality of life, the Gairdner Award is one of the most esteemed awards in medical research. In addition to Steitz and Evans, 23 current HHMI investigators are recipients of the Gairdner Award. Of the 279 scientists who have received the Gairdner in the past 47 years, 65 have gone on to win the Nobel Prize.

The Gairdner Foundation honored Evans for his pioneering work on nuclear hormone receptors, which play important roles in physiology, nutrition, and disease, including diabetes, heart disease, and cancer. Steitz received the award for her studies identifying and revealing the function of small nuclear ribonucleoproteins (snRNPs), cellular complexes that play a key role in the splicing of pre-messenger RNA, an early step in the conversion of gene to protein.

Evans, whose lab is at the Salk Institute for Biological Studies, studies a family of proteins that regulate gene activity to govern a broad range of physiological processes, from maintaining cholesterol balance to disposing of toxic chemicals. These molecules, known as nuclear receptors, work by binding to an activating molecule--a hormone or vitamin--then migrating to the cell's nucleus, where they tweak the activity of target genes. Evans has identified nearly 50 receptors that are part of this nuclear receptor superfamily, and helped revealed surprising similarities in how these molecules function. The molecules are good targets for disease treatment, and drugs acting on nuclear receptors are used to treat conditions ranging from diabetes to leukemia.

Today, Evans focuses on a family of nuclear receptors that regulate fat metabolism. Known as peroxisome-proliferator-activated receptors, these molecules trigger genes involved in either storing or burning fat. By exploring the function of these key regulatory genes, Evans hopes to further understanding of the molecular basis of obesity-related diseases such as diabetes and syndrome X, a disorder characterized by high blood pressure, heart disease, and insulin resistance.

Steitz, an investigator at Yale University and a long-time leader in RNA research, is best known for her discovery and characterization of small nuclear ribonucleoproteins (snRNPs) - short strands of RNA complexed with small proteins that, in all but the simplest organisms, play a critical role in the conversion of genes to protein. Scientists discovered in the seventies that eukaryotic genes (those belonging to organisms whose cells contain a nucleus) are interrupted by large segments of DNA--sometimes known as "junk DNA"--that do not encode any protein. All this "junk" is copied into RNA along with the desired genetic information, and must be removed before protein production proceeds. Steitz demonstrated that snRNPs are responsible for excising the non-coding regions and splicing together the resulting segments--a process that is essential for healthy cell function, as demonstrated by current estimates that 10 to 15 percent of human genetic diseases can be attributed to splicing errors.

Today Steitz continues to investigate how a variety of snRNPs contribute to RNA processing, not only during gene expression but also as a critical step in the production of the type of RNA that makes up ribosomes, the protein-making factories of the cell. Her research may yield new insights into the diagnosis and treatment of lupus, an autoimmune disease that develops when patients make antibodies against their own DNA, snRNPs, or ribosomes.