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## Ronald Evans and Robert Lefkowitz Honored with Albany Medical Center Prize

Howard Hughes Medical Institute investigators Ronald M. Evans and Robert J. Lefkowitz, together with Johns Hopkins School of Medicine professor Solomon H. Snyder, have been awarded the Albany Medical Center's 2007 Prize in Medicine and Biomedical Research.

The annual Albany Prize recognizes extraordinary and sustained contributions to improving health care and promoting biomedical research with translational benefits applied to improved patient care. This year's awardees are recognized for groundbreaking discoveries revealing how cells use receptor molecules to communicate with their environment.

The work of Evans, Lefkowitz, and Snyder has illuminated how different types of receptors enable cells to respond to the information conveyed by hormones, neurotransmitters, growth factors, and drugs. Understanding how receptors transmit signals to trigger action within the cell has helped give rise to a new and rapid phase of drug development. Lefkowitz, whose lab is at Duke University Medical Center, and Evans, who is at the Salk Institute for Biological Studies, have each focused their research on large families of receptor molecules with distinct mechanisms of triggering cellular activity.

Lefkowitz's work with G protein-coupled receptors, the largest and most pervasive family of cell receptors, began in 1982 with the identification of the gene for the  $\beta$ -adrenergic receptor, which helps regulate the body's fight-or-flight response by reacting to epinephrine. Shortly thereafter, he discovered another seven adrenergic receptors. These receptors--and all G-protein receptors--share a basic structure, in which the molecule weaves its way back and forth seven times across a cell's membrane. When the portion of the molecule that lies outside the cell connects with the receptor's favored signaling molecule, the internal portions of the molecule can trigger the appropriate cellular response.

About a thousand G protein-coupled receptors are now known to contribute to physiological processes including pain tolerance, glucose metabolism, and the regulation of heart rate and blood pressure. Understanding the similarities

that shape how these receptors function has helped pharmaceutical researchers target these molecules in the body. Lefkowitz has also discovered two new families of proteins that desensitize G protein-coupled receptors, a finding that has helped scientists understand how receptors become tolerant of certain drugs.

Evans has focused on a family of receptors that relay signals that have already worked their way into cells directly to the nucleus, where they can control gene activity. Early in his career, Evans isolated the growth hormone gene, and set out to identify the switches that turn it on. In rapid succession, he and his colleagues discovered several receptors capable of regulating that and other genes. All these receptors work by binding to an activating molecule—a hormone or vitamin—and then heading for the nucleus to tweak the activity of a target gene.

To date Evans has turned up nearly 50 receptors that are part of this nuclear receptor superfamily. Among these are two that play key roles in regulating the storage and burning of fat, PPAR $\gamma$  and PPAR $\delta$ . Malfunction of nuclear receptors can lead to high blood pressure, obesity, diabetes, and cancer, and these molecules are among the most widely investigated pharmaceutical targets in the world.

The Albany Medical Center Prize is the largest prize in medicine in the United States. Lefkowitz, Evans, and Snyder will share the \$500,000 award.