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UT Southwestern scientist shares 2011 Nobel Prize in Physiology or Medicine

DALLAS – Oct. 4, 2011 – Dr. Bruce A. Beutler, the new director of the Center for the Genetics of Host Defense at UT Southwestern Medical Center, shared the Nobel Prize in Physiology or Medicine with two other scientists for their discoveries in how the immune system works. The announcement was made Monday.

Dr. Beutler and Dr. Jules A. Hoffmann of Strasbourg University's Institut de Biologie Moléculaire et Cellulaire in France shared half the prize for their discovery of receptor proteins that recognize disease-causing agents and activate innate immunity, the first step in the body's immune response. The other half went to the late Dr. Ralph M. Steinman of Rockefeller University in New York for his discovery of the dendritic cell and its role in adaptive immunity.

UT Southwestern faculty members now have won five Nobel Prizes since 1985. Dr. Michael Brown and Dr. Joseph Goldstein (1985), Dr. Johann Deisenhofer (1988), Dr. Alfred Gilman (1994) and Dr. Beutler (2011) have been honored by the Nobel Assembly at Karolinska Institutet in Sweden.

Dr. Beutler, who returned on Sept. 1 to UT Southwestern, where he made his seminal discoveries, was searching for a receptor able to bind the bacterial product, lipopolysaccharide (LPS), which can cause life-threatening septic shock, which involves overstimulation of the immune system.

"It's a happy day. I'm absolutely delighted. It reaffirms that the time we spent cloning the LPS receptor gene at UT Southwestern in the 1990s was time well spent," Dr. Beutler said.

Dr. Beutler's original studies at UT Southwestern, where he was a faculty member and Howard Hughes Medical Institute Investigator from 1986 to 2000, built upon the identification of tumor necrosis factor (TNF) as a key mediation of inflammation and to the identification of Toll-like receptors as sensors that act like sentinels to alert the host immune system when infection is present.

In 1998, Beutler and his UT Southwestern colleagues discovered that mice resistant to LPS had a mutation in a gene that was quite similar to the Toll gene of the fruit fly. This Toll-like receptor (TLR) turned out to be the elusive LPS receptor. When it binds LPS, signals are activated that cause inflammation and, when LPS doses are excessive, results in septic shock. These findings showed that mammals and fruit flies use similar molecules to activate innate immunity when encountering pathogenic microorganisms. Dr. Beutler's laboratory had discovered the sensors of innate immunity.

The discoveries of Drs. Beutler and Hoffmann triggered an explosion of research in innate immunity. About a dozen different TLRs have now been identified in humans and mice.

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UT Southwestern President Dr. Daniel Podolsky hailed the impact of Dr. Beutler's work on many disease processes.

"His discoveries have led to recognition of a new dimension of immune response, with profound implications for understanding our ability to respond to both infectious diseases and cancer. They are already leading to development of new therapeutic agents that represent new paradigms for treatment," Dr. Podolsky said.

"Undoubtedly the powerful genetic approaches that he used in making these discoveries will continue to yield profound new insights into mechanisms of molecular function and disease. We are especially delighted by his return to where he did his initial groundbreaking work and know that he will continue in his path of important discovery for many years to come," Dr. Podolsky added.

Dr. Greg Fitz, executive vice president for academic affairs, provost and dean of UT Southwestern Medical School, said, "Dr. Beutler's scientific contributions to understanding innate immunity are profound, and already have opened new vistas into how we respond to bacteria and well beyond. We are just delighted by this news. He has an incredibly sophisticated approach, and all of his work from discovery of the LPS receptor gene onward is at the very highest level. He is now leading a new Center for the Genetics of Host Defense, and I am convinced that the best may be yet to come."

Dr. Beutler received the Shaw Prize in Sept. 28 award ceremonies in Hong Kong, sharing that honor with two other scientists. In 2008, he was elected to the National Academy of Sciences, and was also named to the Institute of Medicine.

Prior to his return to UT Southwestern, Dr. Beutler was chairman of the Department of Genetics at Scripps Research Institute in La Jolla, Calif.

The medical center's Nobel history began when Dr. Brown and Dr. Goldstein received the 1985 Nobel Prize in physiology or medicine for their discovery of the basic mechanisms of cholesterol metabolism. Their findings led to the development of the cholesterol-lowering statin drugs.

Dr. Deisenhofer received the Nobel Prize in chemistry in 1988 for using X-ray crystallography to describe the 3-D structure of a protein molecule. This structure helped explain the process of photosynthesis.

In 1994 Dr. Gilman received the Nobel Prize in physiology or medicine for his discovery of G proteins, research that has led to a more complete understanding of how cells receive signals and respond to external stimuli.

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