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## Signal Pathway Controls Creation of Fat Cells

According to Ronald M. Evans, body fat is not the inert, butter-like substance you think it is. Instead, fat plays an active role in the body, releasing and responding to hormones. What's more, Evans's research suggests scientists may one day be able to control fat development in the body.

In a paper published in the December 1, 1995, issue of *Cell*, Evans, an HHMI investigator and director of the Gene Expression Laboratory at The Salk Institute for Biological Studies, and colleagues reported the discovery of a previously unknown hormone that determines the number of fat cells in the body. This hormone serves as the "trigger" for signaling precursor cells (fibroblasts) to differentiate into fat cells (adipocytes).

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Fibroblasts, Evans explained, have the potential to become fat, muscle, or certain skin cells. The signals that cause fibroblasts to follow one fate rather than another have long intrigued scientists.

Evans and colleagues introduced the newly discovered fat-triggering hormone called 15d-PGJ2 to fibroblasts in culture. Then, using a technique developed by collaborator Bruce M. Spiegelman at Harvard Medical School, they tracked the cells' differentiation. Put simply, Evans said, "The fibroblasts became adipocytes."

Because altered levels of 15d-PGJ2 play a role in the development of obesity, a potential drug might block the hormone's action, thus preventing fat cells from forming.

That's good news for the estimated 30 percent of Americans who are obese—those whose body weights exceed recommended levels by 20 percent. Obese individuals are susceptible to a range of complications, including:

non-insulin dependent diabetes, hypertension, stroke, arthritis, gout, heart disease, atherosclerosis, and certain types of cancer.

Evans explained that most of a body's fat cells are created during embryogenesis and the first 10 years of life. So an antagonist to block the action of 15d-PGJ2 won't melt fat from adults. But therapies for those predisposed to obesity or for young people who are becoming morbidly obese could one day be based on the signal pathway elucidated in the 15d-PGJ2/PPAR interaction.

Genetically-based therapeutics may one day offer the best solution to obesity-related health problems, Evans said. "(Obesity is a) complex problem with a real genetic aspect. Not many people are forceful enough to change their habits as required to fight it."