Toxic milk

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In the August 1 issue of G&D, Dr. Ronald Evans (Salk Institute) and colleagues report on their discovery that mutations in the mouse gene encoding PPARã adversely affect lactation milk quality, and have serious health consequences for nursing pups.

“By examining PPARã functions in vivo, our work reveals an unexpected link between diet, inflammation and the quality of mothers milk, “ explained Dr. Evans.

PPARã (peroxisome proliferator-activator receptor gamma) is a nuclear receptor that is known to regulate metabolism and inflammation in various organisms. In fact, human PPARã is the main target of the drug class of thiazolidinediones (TZDs), which is used to manage diabetes.

Dr. Evans and colleagues sought to determine the role of PPARã in the lactating mammary gland. They generated a strain of mice that, as adults, lacked PPARã only in hematopoietic and endothelial cells. When these PPARã-deficient animals became mothers, they appeared normal, but the milk they produced most certainly was not.

"We were delighted and surprised by the discovery because it directly explores one of life's most common events - breast feeding. These findings will enhance the understanding of why milk is healthful and the molecular pathways that create the bodies own quality control pipe line," says Dr. Evans.

The researchers noticed that pups of the PPARã-deficient females – who

were, themselves, genetically normal - were displaying a number of abnormalities, most noticeably marked hair loss across their trunks and growth retardation. The scientists determined that these abnormalities were due to their ingestion of “toxic milk” from their PPARã-deficient mothers: Either fostering by PPARã-normal mothers or weaning to solid food effectively cured these small and balding pups.

Through a variety of experimental approaches, Dr. Evans and colleagues determined that PPARã loss results in increased levels of pro-inflammatory lipids being released into the mothers’ milk. Ingestion of this “toxic milk” sets off an inflammatory response in the skin of nursing pups, which ultimately disrupts the hair growth cycle and renders them largely bald. In fact, treatment with the common anti-inflammatory aspirin completely rescues hair loss in these pups.

Source: Cold Spring Harbor Laboratory