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The inflammatory gene - FAT10, Impacts obesity and aging in mammals

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The HLA-F Adjacent Transcript 10 (FAT10) is a non-canonical MHC gene, which consists of two ubiquitin-like (UBL) elements arranged in tandem. Due to this ubiquitin duplication, it is also known as UBD. Early studies implicated FAT10 with the immune system in the context of inflammation. FAT10 expression is highly induced by inflammatory mediators (TNF α and IFN γ) and FAT10 knockout (FAT10ko) mice demonstrate increased susceptibility toward LPS - further implicating FAT10's involvement in inflammatory responses. Surprisingly, we discovered a physiological role for FAT10 in the aging and the obesity of mice. FAT10ko mice demonstrate a significant increase in median and overall lifespan by 20%. Interestingly, these mice have markedly reduced formation of fat tissues under regular chow diet. They are leaner and maintain their lower weight. Leaner body composition was manifested as early as 10 weeks in FAT10ko mice by necropsy and MRI (45% less adipose tissue). FAT10ko mice are metabolically more and insulin and glucose tolerance tests revealed significantly enhanced glucose tolerance and increased insulin sensitivity in these mice. RNA sequencing analysis of MEF cells revealed that the absence of FAT10 expression generates major differences in the expression of genes associated with inflammation, aging and adiposity consistent with the phenotype of the mature animals. This may suggest that the physiological phenotype of FAT10 results from an early stage of development, rather than a late-life somatic effect. Inhibiting FAT10 might be clinically desired due to the impact on adiposity and longevity and the lack of adverse effects associated with FAT10 deficiency.

Biography

Allon Canaan earned his PhD degree from the Weismann Institute of Science (Israel). Subsequently, he moved to the USA for a post-doctorate training at Yale University School of Medicine. Dr. Canaan was the first to demonstrate the engagement of cellular promoters by viral transcription protein (EBNA1) in the infected cell. Recently, Dr. Canaan discovered that the inflammation mediating gene FAT10 plays a role in obesity and aging in mice. Funds for Dr. Canaan work came from the William Prusoff Foundation.

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