Abstract Template

Abstract Title: Lipid Droplets Can "Talk" to the Cell Nucleus and Regulate Leptin Expression.

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Leptin represents a central metabolic regulator that controls food intake, energy expenditure, lipid metabolism, and several other important physiological functions of the mammalian organism. Production of leptin by adipocytes is acutely controlled by nutrient uptake. In addition, it has been long known that larger adipocytes with significant triglyceride stores secret more leptin, than smaller cells, although the regulation of leptin expression has not been understood mechanistically. We have shown that insulin and nutrients dramatically increase the expression of the transcription factor Egr1 *via* the mTORC1-mediated pathway. Egr1 directly binds to the leptin promoter and stimulates leptin expression. Unexpectedly, the lipid droplet (LD) protein FSP27 (a.k.a. CideC) may act a novel regulator of the transcriptional activity of Egr1. To this end, we have found that FSP27 is localized not only on the surface of LDs, but also in the cell nucleus. Furthermore, FSP27 binds to Egr1 and blocks its effect on the activity of the leptin promoter. Expression of endogenous FSP27 is induced in differentiating 3T3-L1 adipocytes between days 2 and 3 when LDs are beginning to form. When we ectopically express FSP27 in undifferentiated pre-adipocytes, it is localized predominantly in the cell nucleus and is then distributed to the LD upon cell differentiation so that in differentiated adipocytes, over 80% of total FSP27 is associated with LDs in the cytosol. We suggest that increasing size of LDs may "pull" FSP27 out of the nucleus which should lead to the activation of leptin expression *via* Egr1. Thus, FSP27 may link the size of LDs (i.e. intracellular triglyceride reserves) to the expression of leptin.

Keywords—*Egr1, FSP27, Leptin, Lipid Droplets*

Professional Biography (100-150 words)

My research career started in the former Soviet Union where I worked on RNA-binding proteins and translational control. This work brought me position of a "senior scientist" in the USSR Academy of Sciences and a National Prize for the Young Scientists in 1987. In 1991, when the State support for science largely deteriorated, I moved to the US, where I took a temporal job as a visiting lecturer at Harvard Medical School with late Dr. Bert L. Vallee. Since 1992, my professional career was associated with Boston University School of Medicine where I rose through the ranks to full professor in 2003. In the meanwhile, my research interests have largely changed from regulation of protein synthesis to nutritional biochemistry, insulin action, and metabolic disease.



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Any Comments: none