

Research Project Proposal
Academic year 2017-2018

Project Nº 31	
Title: Cell cycle and metabolism: who regulates whom?: Role of Cdk2 in adipose tissue (ADIPOCLYN)	
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<p>Summary</p> <p>The machinery that controls cell cycle progression is well-established as a determinant for cancer initiation. In addition, few studies have described roles for Cdks in metabolism, suggesting connections between obesity and cancer. Adipose proliferation, differentiation and metabolism are partially regulated by Cdks. In contrast, the roles of Cdk2 have not been studied in mature adipocytes. In addition, AKT is a major regulator of the adipose biology and in the context of proliferation Cdk2 regulates AKT and vice versa. Preliminary results from our lab have revealed expression of Cdk2 in mature adipocytes, overexpressed in obesity, and also Cdk2 is modulating insulin sensitivity and glucose-induced transport suggesting a novel cell cycle-independent role.</p> <p>Taken together, we hypothesize that Cdk2 functions in adipose tissue go beyond than just controlling adipocyte differentiation and these new functions may play a role in obesity. Therefore, we aim to develop a strategy to comprehensively map the roles of Cdk2 as regulators of adipose metabolism and their functional connections. In a combined effort, we will determine the metabolic role of Cdk2 using cellular and animal models including adipose tissue specific knockout mice. We believe that our investigations are essential for the optimal design of clinical approaches to cell cycle deregulations, obesity, and the associated co-morbidities.</p> <p>References</p> <ol style="list-style-type: none"> 1. Kim SY, Lee JH, Merrins MJ, Gavrilova O, Bisteau X, Kaldis P, et al. (2017) Loss of cyclin dependent kinase 2 in the pancreas links primary β-cell dysfunction to progressive depletion of β-cell mass and diabetes. J. Biol. Chem. 292, 3841-53. 2. Miettinen TP, Pessa, HK, Caldez MJ, Fuhrer T, Diril MK, Sauer U, Kaldis P. (2014) Identification of transcriptional and metabolic programs related to mammalian cell size. Curr. Biol., 24, 598-608. 3. Lagarrigue S, Lopez-Mejia IC, Denechaud PD, Escoté X, et al. (2016) CDK4 is an essential insulin effector in adipocytes. J Clin Invest.;126(1):335-48. 	