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Editorial

# Embryonic and Fetal Adipogenesis

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Adipogenesis is the process by which undifferentiated precursor cells (preadipocytes) get differentiated into mature adipocytes. Adipose tissue originates in the embryonic mesoderm that contains a variety of cells: mesenchymal cells, preadipocytes, fibroblasts and adipocytes. In human embryo and fetuses adipose tissue progressively develops from the 14$^{th}$ to the 24$^{th}$ weeks of gestation strongly associated with the formation of blood vessels, and fat lobules are the earliest identified structures before typical vacuolated fat cells appear [1]. White adipocytes are the primary cell type in mammals for the energy storage and mobilization in the form of tricylglycerides and have paracrine and endocrine functions through the synthesis and secretion of adipokines and growth factors whereas brown adipocytes have abundance of mitochondria and actively contribute to energy expenditure by the expression of the mitochondrial uncoupling protein [2]. It was generally assumed that brown and white adipocytes were derived from a common adipogenic precursor, although by using a primary cell model from mice it was concluded that brown preadipocytes have a distinct origin that white adipose tissue [3]. However, although the process of adipogenesis is still minimally characterized, by studying human fetal mesenchymal stem cells differentiation it has been concluded that brown adipocytes are indeed derived from the mesenchymal linage, along with white adipocytes [4].

Adipogenesis is a tightly regulated cellular differentiation process that requires the sequential activation of several transcription factors. The process of adipogenesis requires highly organized and controlled expression of a cascade of transcription factors in the preadipocytes, which are regulated by hormones, nutrients and epigenetic factors. Embryonic and fetal adipose tissue precursors and regulatory mechanisms appear distinct from adults. The principal regulator of adipocyte differentiation is the nuclear hormone receptor PPARγ, which induction and maintenance in adults is facilitated by other transcription factor such as C/EBPα [5], which is the founding member of the CCAAT enhancer-binding protein family. The coordination of PPARγ with C/EBPα maintains adipocyte gene expression in adults [6]. However, in mice it has been shown that the precursor cells giving rise to mature adipocytes during embryogenesis is fully C/EBPα independent [7]. As recently reviewed [8], from studies in mice, embryonic and fetal adipogenesis requires Zfp423 which is a multi zinc-finger transcription factor that is expressed in preadipocytes and mature adipocytes and has been found to be essential for terminal differentiation of adipocytes during fetal adipose tissue development [9]. These transcription factors participate in a single pathway of fat cell development with PPARγ being the proximal effector of adipogenesis [10]. The activity of PPARγ is modulated by a gene regulation cascade of selected corepressors and coactivators like steroid receptor coactivator 1 (SRC1), nuclear receptor corepressor (NCoR), the silencing mediator for retinoid and thyroid hormone receptor (SMRT) and an $NAD^+$-dependent histone deacetylase and chromatin-silencing factor (SIRT1) which have been proposed to control adipogenesis [11,12].

By studying transgenic mice it has been shown that embryonic preadipocytes that proliferate during the prenatal period expressed perilipin and adiponectin [13], which is at odds with the previous believe that these markers are exclusively expressed in fully differentiated adipocytes in adults [14,15].

Finally, it must be recognized that the origin and development of adipose tissues during intrauterine life is still poorly understood. Moreover, although most of what we know about adipogenesis comes from studies of rodents either in vivo or in cell culture there are examples of adipose tissue function that do not translate from rodents to the human. Therefore, careful interpretation of the findings from experimental animal models should be taken into account for their extrapolation to the human fetal adipogenesis. During pregnancy, maternal health conditions and nutrition state are known to influence the developmental patterning of adipose tissue with lifelong impli-

cations and given the endocrine function of adipose tissue and that alterations of adipocyte development promote metabolic disease state in adults future studies in the area of embryonic and fetal adipogenesis is warranted.

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