Dynamic Flow Biomimetic Vascularized Fat-on-a-Chip Model to Study Early Stages of Obesity
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Obesity is a metabolic disorder affecting about 650 million adults and 124 million children worldwide. In the US, 93.3 million adults are affected by obesity. The first line of treatment comprises of lifestyle and diet changes; however, these approaches are often ineffective once the disease has progressed. Alternatively, invasive surgical procedures for fat elimination performed at later stages have often proven to be insufficient. While treatments exist for obesity, there is a limited understanding of the underlying biological mechanisms in the initial stages, when the condition can be potentially reversed. Early stages of obesity arise due to dysregulated expansion of adipose tissue and lack of proportional increase in the vasculature. To investigate obesity, 2D cell studies and in vivo models have been used. However, they lack endothelial-adipocyte interactions, essential for fat tissue dynamics. Likewise, the mice models are time consuming, expensive, and often have different responses to drug testing studies. To address these limitations, the concept of organ-on-a-chip using microfluidics was introduced. The few currently existing fat-on-a-chip models have shorter lifespans, low cell density, and uni-channel design, preventing adipocyte-endothelial interaction and nutrient gradient. However, our sophisticated multi-channel design becomes more physiologically relevant to human fat tissue microenvironment since it is tested under dynamic flow conditions and also supports higher cell concentration, continuous perfusion, and growth factor gradient. This enhances the endothelial-adipocyte interface, cell differentiation and successfully enables testing of the role of angiogenesis-and-adipogenesis-promoting factors like YAP/TAZ. Understanding the pathophysiology of early obesity can further the discovery of novel drugs targeting fat metabolism. This fat-on-a-chip can also assess the interaction of fat with other organs-on-a-chip, leading to new therapeutics for obesity related diseases of diabetes and cardiovascular disorders.