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Controlling obesity by targeting adipose tissue cell populations

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Changes in the relative abundance of thermogenic beige adipocytes and lipid-storing white adipocytes in adipose tissue underlie the progression of obesity and metabolic disease. We have discovered that mouse and human adipose tissue contains distinct beige and white adipocyte progenitor populations marked by PDGFR α or PDGFR β expression, respectively. Our recent report [1] suggests that adipocyte lineage specification and metabolism can be modulated through PDGFR signaling. We have also developed 'hunter-killer' peptides, composed of a cell surface receptor-binding domain and a proapoptotic domain, for targeted ablation of cells in adipose tissue. A hunter-killer peptide D-WAT, targeting PDGFR β + white adipocyte progenitors, suppresses high fat dietinduced obesity development and enabled maintenance of active metabolism [2-5]. Another compound, Adipotide, targeting endothelial cells and adipocytes in white fat, reverses obesity in several animal models [6] and has shown promise in a clinical trial. In unpublished studies, we have developed a hunter-killer compound D-BAT, based on a peptide that targets brown fat tissue [7], which may relieve hypermetabolic conditions. New experimental approaches to fat tissue composition and function control will be discussed.

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