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Increased mobility of inflammatory macrophages in the very early stage of obesity-induced chronic inflammation in adipose tissues

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Abstract

Low-grade chronic inflammation of adipose tissue has been fully demonstrated to be critical in obesity and its related pathological phenomenon. Immune cells, such as macrophages, T/B lymphocytes, neutrophils and eosinophils, have all been shown to play respective roles in the exacerbating processes, although the initial events triggering the chronic inflammatory cascades have still been elusive. We have recently established intravital imaging system to visualize the inflammatory processes of obese adipose tissues, and analyzed the immune cell dynamics in the very early stage of obesity (just five days after starting high-fat and high-sucrose feeding). In this condition, neither the total number of accumulated macrophages nor the average sizes of adipocytes were unchanged, although the mobility (i.e. the cell tracking velocity) of macrophages infiltrating in adipose tissues was increased significantly, meaning that some factors stimulating immune reactions were produced and secreted from adipocytes in this initial stages. By means of the expressional analyses with mature adipocyte fractions from this stage, we identified a crucial molecule that was up-regulated in the early phase of obesity and may trigger the chronic inflammation courses. We found that macrophages exhibit a positive chemotaxis toward this molecule, and this also promoted inflammatory responses in 3T3-L1 adipocytes. These results suggest that the newly identified factor induced in the very early event of obesity would be a critical component that regulates the initial step of inflammatory cascade in obese adipose tissue.