In vivo molecular imaging revealed obese adipose tissue remodeling and malfunction in metabolic syndrome

Satoshi Nishimura, Mika Nagasaki, Ichiro Manabe, Takashi Kadowaki, Seiryo Sugiura, and Ryozo Nagai,
Department of Cardiovascular Medicine, The University of Tokyo
Hongo 7-3-1, Bunkyo-ku, Tokyo 113-0033, Japan
E-mail: snishi-tky@umin.ac.jp

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Metabolic syndrome is a major cause of cardiovascular disease, and obese visceral adipose tissue remodeling and malfunction based on chronic inflammation plays a central role. Adipose tissue contains multiple cell types including stromal cells: adipocytes, macrophages, and endothelial cells, and their interaction is important in obese adipose tissue remodeling including angiogenesis, and adipogenesis [1], but little is known about the detailed mechanisms of these cell-cell interactions, because much of the structural and functional integrity of the tissue is lost when it is fixed, processed and sectioned. A visualization technique, based on laser confocal microscopy was therefore developed that made it possible to precisely evaluate the three-dimensional structures in living tissue, and the cell dynamics in vivo with a high time and spatial resolution [2].

We found close spatial and temporal interrelationships between angiogenesis and adipogenesis, and both were augmented in obesity [1]. VEGF-antibody inhibited not only angiogenesis but also the formation of adipogenesis in obesity. In obesity, close interactions of activated platelets, leukocytes, and endothelial cells in the vessel walls of adipose tissue was also observed in the microcirculation of visceral obese fat pads, which were indicative of activation of the leukocyte adhesion cascade, a hallmark of inflammation [2]. Local platelet activation in obese adipose tissue was observed, and upregulated expression of adhesion molecules on macrophages and endothelial cells suggests their interactions contribute to local activation of inflammatory processes within obese visceral adipose tissue. Interestingly, the heightened leukocyte-endothelial interactions were not observed in subcutaneous fat in the same mice, and administration of anti-ICAM1 antibody normalized the cell dynamics seen in visceral fat. Using our new imaging technique to analyze the complex cellular interplay within obese adipose tissue, we have been able to show that visceral adipose tissue obesity is an inflammatory disease and to evaluate potential therapeutic interventions against it.