In vivo multi-photon molecular imaging technique reveals inflammatory cell cross-talks in adult common diseases

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To elucidate the underlying mechanisms of adult common diseases based on chronic inflammation, it is vital to examine the multi-cellular kinetics in living animals. Therefore, we developed in vivo imaging technique based on single- and multi-photon microscopy, and we assessed dynamic cellular interplay in diseased conditions. Metabolic syndrome is a major risk factor of cardiovascular events, and adipose tissue obesity based on chronic inflammation play a central role. Our imaging revealed close spatial and temporal interrelationships between angiogenesis and adipogenesis in obese adipose (Fig a, Ref 1). In addition, increased leukocyte-platelet-endothelial cell interactions in the microcirculation of obese adipose were observed, a hallmark of inflammation (Ref 2). We also found that large numbers of CD8+ effector T cells infiltrated into obese adipose, and these cells were essential for the initiation and development of adipose inflammation (Ref 3).

By our in vivo imaging technique, multiple cell-types were specifically visualized (Fig b). Thrombus formation can be induced by laser irradiation which cause ROS production inside the blood vessel (Fig c, Ref 4). ROS signal was amplified and maintained by inflammatory cytokines, and integrin signaling. Using this technique, we revealed how discoid platelet aggregations occurred onto intact endothelium in single platelet level. We also elucidated that Lnk (adapter protein) regulates integrin signaling leading to stabilization of developing thrombus in vivo (Ref 5). In addition, we established human iPS-derived platelets, and we confirmed artificial platelets can circulate, and contribute to the thrombus formation in vivo, indicating the clinical usefulness considering the cell therapy for future (Ref 6).

We also examine the bone marrow reconstructive process after transplantation, and elucidated that T cell proliferations have pivotal roles in this process (Fig d).

Our results clearly demonstrated the power of our imaging technique to analyze complex cellular interplays in inflammatory diseases, especially parenchymal and stromal cell cross talks, and to evaluate new therapeutic interventions against them.

References

(a) Adipose tissue remodeling in obesity including adipogenesis and angiogenesis (b) Multi-cellular kinetics visualized by novel in vivo imaging technique (c) Thrombus formation and single platelet kinetics revealed by in vivo imaging (d) T cell proliferations in bone marrows after transplantation