博士論文(要約)

Pathological cell profiling by whole-body imaging with single cell resolution

(一細胞解像度全身イメージングによる
病理学的解析技術の開発)

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Mammalian bodies are composed of more than a billion of cells per cubic centimeter, which makes whole-body cell profiling of an organism one of the most ultimate challenges in biology and medicine. The events initiating even from a single cell may disrupt homeostatic balance and lead to a fatal disease such as cancer. To achieve the systems-level elucidation of cellular mechanisms underlying the diseases, one of the technical challenges is the development of the 3D analytical platform. In this study, I focus on establishing a comprehensive cellular analysis in the whole body by the combination of technologies of tissue clearing, optical imaging, and image informatics. First, I find that an aminoalcohol decolorizes blood by eluting the heme chromophore from hemoglobin. Direct transcardial perfusion of an aminoalcohol-containing reagent decolorizes nearly transparent almost all organs and the entire body of adult mice. Next, I optimize refractive-indices of clearing reagent to comprehensively detect the distribution of the pathological cells in the entire body of adult mice. I validate that this method can be applicable to 14 cancer model mice induced by 10 cell lines. This method succeeds in visualizing the overview of multistep metastatic processes, in which metastatic cells are generated from the primary tumor, perpetuate in a perivascular position, escape from immune surveillance, and reject by the immune system. This CUBIC-based cancer analysis is also applicable to the pharmacological profiling.