Clarification of the molecular machinery to form and regulate the microenvironment specific for triggering the rupture of intracranial aneurysms through the spatial transcriptomics

Tomohiro Aoki, M.D., Ph.D.
Department of Pharmacology
The Jikei University School of Medicine

Subarachnoid hemorrhage due to rupture of intracranial aneurysm has the poor prognosis, i.e. the mortality rate up to 50 %, in spite of the modern technical advancement in medical treatment and care. Because many intracranial aneurysms can be found out before rupture during brain check or imaging diagnosis, there is a chance to prevent the rupture of these incidentally found lesions. There is not, however, any treatment intervention other than invasive surgical procedures like micro-neurosurgical clipping or endovascular therapy to such an incidentally found lesion. The development of a novel method to stratify rupture-prone so-called dangerous lesions among many intracranial aneurysms or of a less-invasive medical therapy to prevent rupture is socially demanded.

We have clarified the molecular machineries to trigger the formation of and to mediate the progression of intracranial aneurysms by using originally-established animal models of this disease. Nowadays, through our studies and studies from other research groups, intracranial aneurysm has defined as the non-physiological hemodynamic force-triggered macrophage-mediated chronic inflammatory disease affecting intracranial arteries. We have further revealed the formation of the specific microenvironment including neovessels and neutrophil accumulation at the prospect site of rupture and the rupture point. The transition of the microenvironment in the process leading to rupture might therefore be required. However, the details mechanisms regulating the transition of the microenvironment remains to be elucidated.

Based on the above background, in this research proposal, we aim to clarify the specific microenvironment regulating the rupture of intracranial aneurysm and also a subtype of cells and factors responsible for the formation of this microenvironment by combining the spatial transcriptomics, histopathological studies using human specimens with experimental studies using animal models of intracranial aneurysms. Furthermore, we will expand studies to develop novel therapeutic drugs, drug-eluting endovascular devices to prevent the rupture or a diagnostic method to stratify rupture-prone lesions.