Inflammation and neural repair in ischemic stroke

Department of Neuroinflammation and Repair, Medical Research Institute, Tokyo Medical and Dental University
Takashi Shichita

Stroke is a major cause of disability or death worldwide. The development of therapeutics that improve the functional prognosis of stroke patients remains an unresolved problem. When the brain is injured, inflammation is triggered in the brain tissue and causes tissue swelling, which worsens the patients' functional prognosis. Post-stroke inflammation is resolved within a week after stroke onset, and then patients can regain the lost brain function through rehabilitation and neural repair. We have been clarifying the detailed cellular and molecular mechanisms underlying post-stroke inflammation and neural repair.

Inflammation after organ injuries is triggered by the immune system. Immune cells recognize pathogen-derived molecules to trigger inflammation, whereas the brain is generally considered a sterile organ. We investigated the inflammatogenic molecules within the brain cells and identified peroxiredoxin family proteins that directly activated the immune cells in the post-stroke brain. Macrophages produced various inflammatory molecules, leading to the secondary inflammation exacerbated by lymphocytes. These findings accelerated the development of immunology in the stroke field and therapeutics targeting post-stroke inflammation.

Post-stroke inflammation will resolve around a week after stroke onset. The molecular mechanisms underlying the resolution of post-stroke inflammation were also clarified. Macrophage expressed the scavenger receptors, which were important for clearing peroxiredoxin family proteins from the post-stroke brain and also produced neurotrophic factors that enhanced neural repair and neuronal circuit reorganization. We recently identified the metabolites of di-homo-gamma-linolenic acid as a trigger of reparative functions in neurons around injured brain regions, which were necessary for the neural circuit reorganization to regain the lost brain function after stroke.

Thus, we have been clarifying the cellular and molecular mechanisms underlying inflammation and neural repair after stroke to develop therapeutics that improve the functional prognosis of stroke patients.