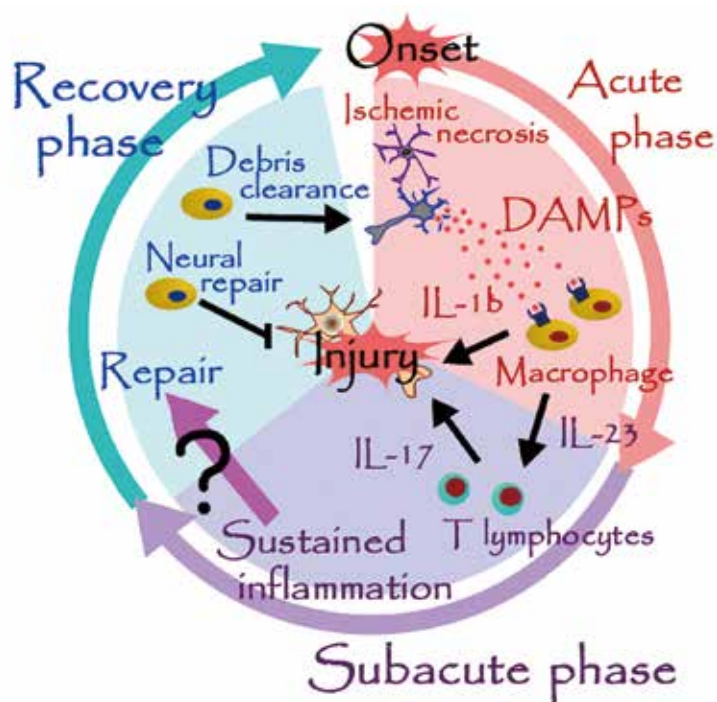




Project Leader **Takashi Shichita** Stroke Renaissance Project

## Sterile Inflammation After Ischemic Stroke



### “What triggers neural repair after stroke?”

Tsuyama J, Nakamura A, Ooboshi H, Yoshimura A, and Shichita T. (2018) “Pivotal role of innate myeloid cells in cerebral post-ischemic sterile inflammation.” *Semin. Immunopathol.*

Shichita T, Ito M, Morita R, Komai K, Noguchi Y, Ooboshi H, Koshida R, Takahashi S, Kodama T, and Yoshimura A. (2017) “Mafb prevents excess inflammation after ischemic stroke by accelerating clearance of danger signals through MSR1.” *Nat. Med.* 23(6): 723-732.

Shichita T, Hasegawa E, Kimura A, Morita R, Sakaguchi R, Takada I, Sekiya T, Ooboshi H, Kitazono T, Yanagawa T, Ishii T, Takahashi H, Mori S, Nishibori M, Kuroda K, Akira S, Miyake K, and Yoshimura A. (2012) “Peroxiredoxin family proteins are key initiators of post-ischemic inflammation in the brain.” *Nat. Med.* 18(6): 911-917.

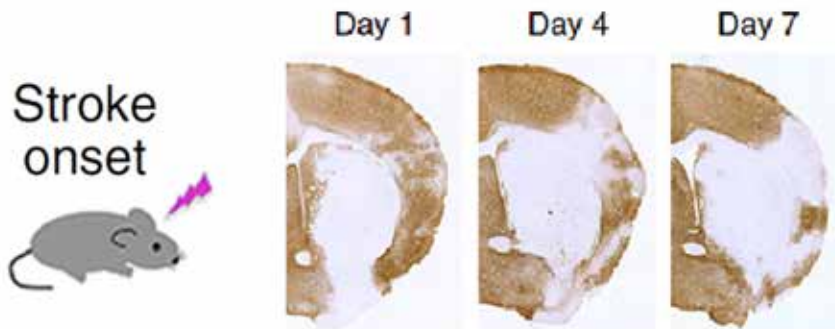
Shichita T, Sugiyama Y, Ooboshi H, Sugimori H, Nakagawa R, Takada I, Iwaki T, Okada Y, Iida M, Cua DJ, Iwakura Y, and Yoshimura A. (2009) “Pivotal role of cerebral interleukin-17-producing gammadelta T cells in the delayed phase of ischemic brain injury.” *Nat. Med.* 15(8):946-950.

We have identified peroxiredoxin family proteins as DAMPs (damage associated molecular patterns) which trigger the post-ischemic inflammation (*Nat. Med.* 2012). DAMPs induce IL-23 production from infiltrating macrophages and neutrophils, and this sustains the inflammation after ischemic stroke by promoting IL-17 production of gdT lymphocytes (*Nat. Med.* 2009). Cerebral post-ischemic inflammation resolves several days after the stroke onset. The clearance of DAMPs from ischemic brain through MSR1, a scavenger receptor, plays a pivotal role in the resolution of sterile inflammation after ischemic stroke (*Nat. Med.* 2017). Now our question is how the cerebral post-ischemic inflammation switches into the process of neural repair.

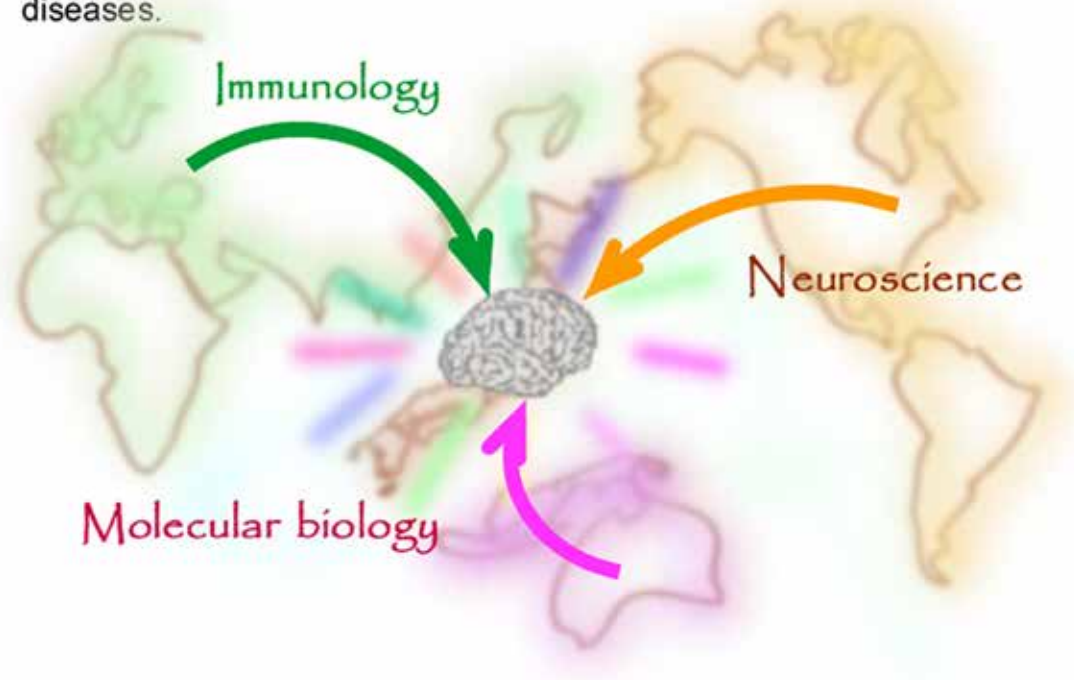


# Stroke Renaissance Project

**Stroke** is a common cause of severe disability and death worldwide; however, few therapeutic agents have been shown to improve the neurological deficits of stroke patients.



In this project, we try to clarify the detailed molecular mechanisms underlying the recovery of brain after stroke. The new research methods and techniques which have been recently developed in the field of immunology or neuroscience will enable us to investigate the precise process of inflammation and regeneration in the injured brain after stroke. The purpose of our project is to develop a new therapeutic method for promoting the recovery of neurological function in patients with cerebrovascular diseases.



# Stroke Renaissance