Department of Pharmacology

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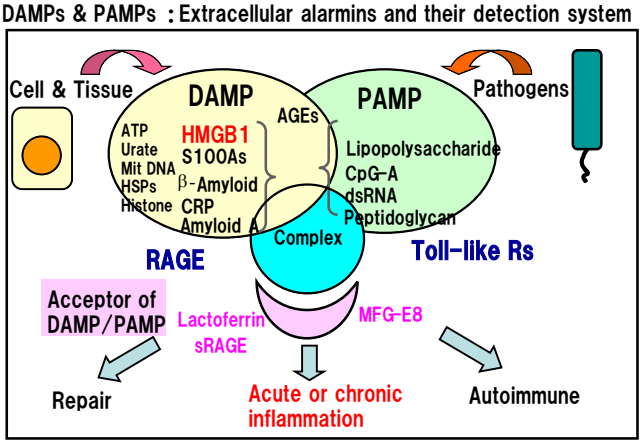
Inflammatory processes are involved in pathogenesis of many diseases, including atherosclerosis, brain infarction, traumatic brain damage, diabetic complications and Alzheimer's disease. We have been trying to find a cutting edge of inflammatory responses, especially focused on the initiation of inflammation by damage-associated molecular patterns (DAMPs). We hypothesized that there might be intermediate acceptor systems for DAMPs and PAMPs. An increasing evidence suggests that these factors may form a diverse range of complexes in combination and play functional roles as signaling molecules in extracellular space. The recognition of complexes by plasma membrane receptors is not clear at present, however, the signaling processes may provide a therapeutic strategy for the treatment of inflammatory diseases. We are interested in the identification of novel DAMPs and their recognition by inflammatory cells. The following research projects are in progress in our laboratory now.

DAMPs & PAMPs : Extracellular alarmins and their detection system



＊＊＊Main themes in Pharmacology＊＊＊

1. Anti-HMGB1 monoclonal antibody therapy for the treatment of brain infarction, traumatic brain injury, vasospasm, and neuropathic pain.
2. Analysis of the interaction between RAGE and its ligands and development of drugs interfering with the interaction.
3. Mechanism for blood-brain barrier disruption by brain inflammation and development of its prevention method.
4. Regulation of neutrophil activity and its application for inflammatory diseases including sepsis.
5. Searching for novel DAMPs and their acceptors as the therapeutic targets.

＊＊＊References＊＊＊

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•Wake H et al., EBioMedicine, 2016.
•Nakamura et al., PLos ONE, 2013.
•Okuma et al., Ann Neurol., 2012.
•Shichita et al., Nature Med., 2012.
•Zhang et al., Stroke, 2011.
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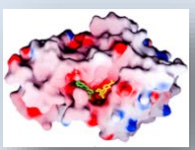
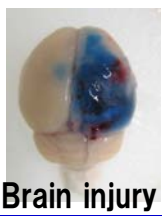
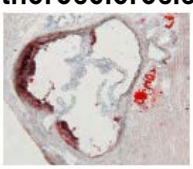


Brain infarction



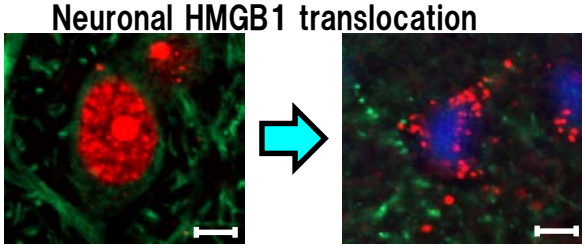
Brain injury

Atherosclerosis

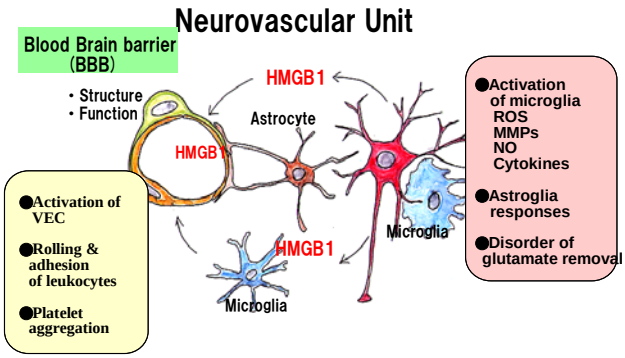


HMGB1 mediates the disruption of neurovascular unit

Neuronal HMGB1 translocation



Neurovascular Unit



Plasma histidine-rich glycoprotein protects against septic lethality