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Treatment of Vascular Diseases with Antibody Therapeutics and Platform Formation for Developing New Drugs

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The development of antibody therapeutics for the treatment of rheumatic arthritis, malignant lymphoma and mammary cancer has brought the evolution in clinical practice. The technology of producing chimera, humanized and complete human monoclonal antibodies solved the problem of the host response to xenogenic monoclonal antibody. The antibody drugs targeting for different molecules are increasing in number now, and some of them are in clinical trials.

In this lecture, I will talk about the possible therapeutic availability of anti-high mobility group box-1 (HMGB1) monoclonal antibody for diverse diseases including brain infarction, vasospasm after subarachinoidal hemorrhage, atherosclerosis and colon cancer. At the beginning of my talk, I will review the history of “Re-discovery of HMGB1” as a damage (danger)-associated molecular pattern (DAMP). In 1999, Tracey’s group in New York found a candidate protein in the supernatant of LPS-stimulated RAW 264.7 cell, a mouse macrophage cell line, as a late mediator of septic shock. They performed protein sequence and identified the candidate as HMGB1, that was originally characterized as architectural non-histone nuclear protein. It was also reported that polyclonal antibody against HMGB1 protected mice from LPS-induced lethality. Their studies promoted the investigation for the involvement of this novel cytokine-like factor in different types of inflammatory diseases such as acute lung injury, arthritis, ischemic liver injury and acute pancreatitis.

I will present the characterization of monoclonal antibodies against HMGB1, its strong protective effects on blood-brain barrier after ischemic insult in rat leading to amelioration of brain infarction, the suppression of atherosclerotic plaque formation in mouse, and the inhibition of colon cancer growth using tumor-bearing mouse model. At the end, I will show you the *in vitro* assay method for searching low molecular weight compounds displacing anti-HMGB1 monoclonal antibody.