



**Dept of Cellular and Physiological Sciences
Centre for Brain Health
LSI Neuroscience Research Group
Centre for Blood Research**



Maria-Grazia De Simoni, PhD

**Head of the Laboratory of Inflammation and
Nervous System Diseases**

**Pharmacological Research Institute Mario Negri,
Milano, Italy**

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Hosted by Dr. Christian Naus

The lectin complement pathway in ischemic stroke

Clinical and experimental evidence implicates the lectin pathway (LP) of complement activation in brain ischemic injury. Its rapid activation in response to danger signals expressed early after injury and its ability to control and co-ordinate multiple pathogenic cascades make it a hub in acute brain injury (1). In ischemic mice, mannose-binding lectin (MBL), one of the activator molecules of LP, is deposited on the brain ischemic endothelium and drives vascular dysfunction contributing to brain injury. Its functional inhibition by gene deletion or pharmacological targeting is protective (2,3,4). Available evidence suggests that MBL induces vascular dysfunction through multiple actions, triggering the activation of a pro-coagulant and pro-inflammatory state and a direct endothelial damage after its cellular deposition. In human stroke LP activation is associated with unfavorable outcome, with a few studies highlighting a role for LP activation molecules, such as MBL, ficolin-1 and ficolin-3 as independent predictors of outcome. LP also plays a role in chronic conditions such as atherosclerosis a major risk factor for stroke. LP initiator molecules are present within atherosclerotic plaques and their plasma levels change in patients with rupture-prone plaques, indicating their potential use as markers for cardiovascular risk assessment in atherosclerotic patients (5). The multiple lines of evidence documenting the LP's contribution to brain injury, its role as a hub in several pathogenic vascular events, and the proof of its druggability make it an attractive target for the development of therapeutic tools for acute brain conditions and for the control of risk factors.

1) Fumagalli et al., Stroke, 2016; 2) Longhi et al., CCM, 2014; 3) Orsini et al., Circulation, 2012; 4) De Blasio et al., JCBFM, 2017; 5) Fumagalli et al., Front Immunol, 2017