

## Neuropsychiatric Lupus: the Neuroinflammatory Model

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Neuropsychiatric systemic lupus erythematosus (NPSLE) is a severe complication that can occur in patients with SLE. The disease negatively impacts the overall SLE outcome (tenfold increase in mortality rates<sup>1</sup>) and the quality of life of up to 75% of lupus patients<sup>2</sup>. Clinically and biologically NPSLE remains poorly understood and there is no accurate marker allowing its diagnosis and/or prognosis. It can affect both the central and peripheral nervous systems. In our ongoing studies, we are trying to understand the mechanisms of central manifestations, such as psychosis, depression and memory loss.

Currently, we are investigating the disease progression in a spontaneous lupus murine model, the MRL/lpr strain<sup>3</sup>. As the disease is yet to be thoroughly investigated, our experimental scope is large: it ranges from behavioural to molecular pathway studies. To date, we have performed various behavioural tests<sup>3</sup> showing that the diseased mice are suffering from cognitive deficits. These observations led us to look into the anatomical structures of their brains using magnetic resonance imaging, which unveiled a degenerative state of the structure. We also investigated the possible peripheral immune cell infiltration of the brain by flow cytometry, and we observed elevated numbers of various lymphocytic cells in the central nervous system of our mice. In conclusion, our current evidence is pointing to a neuroinflammatory development of the disease.

In the future, we would like to look in greater detail on how does the disease progress in the brain of these mice and relate our discoveries to human disease. We would like to explore the complement pathway, as proposed by Bialas and colleagues<sup>4</sup>. Another possible target that interests us is the NLRP3 inflammasome<sup>5</sup>. Current approaches involve confocal microscopy on mice brains and cell culture experiments on human cell lines, the latter could help us explore molecular pathways of neuroinflammation in a genetically human background.

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