Immune responses in neurodegenerative diseases: Protection or progression?

https://www.neurodegenerationresearch.eu/survey/immune-responses-in-neurodegenerative-diseases-protection-or-progression/

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Contact information of fellow
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Immune responses in neurodegenerative diseases: Protection or progression?

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Alzheimer's disease & other dementias

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Research Abstract
Many neurodegenerative diseases, including Alzheimer's and Parkinson's disease, are progressive and incurable. Much attention has been paid to understand the insults likely to kill neurons, such as reactive oxygen species and protein aggregation. In addition, it is clear that

immune and inflammatory responses are involved in these diseases, but in general it is unclear whether they are protective or promote the disease process.

Here I propose to gain insight in basic mechanisms and control of immune maintenance in response to neurodegeneration in vivo. Hereto, I will use unique features of the zebrafish (Danio rerio) model system to study immune cell responses to neuronal degeneration with high spatiotemporal precision in vivo. Recently, I developed a reporter in zebrafish, which labels dying cells, allowing visualization of engulfment of these cells by macrophages [van Ham et al., 2010; van Ham et al., Curr. Biol., accepted]. In the proposed research, I will investigate in vivo responses to neurodegeneration. I will use this reporter in conjunction with genetically targeted neuronal cell ablation and with disease models related to protein aggregation. By using live imaging I aim to dissect beneficial and damaging immune responses initiated by neurodegeneration. In combination with transgenic markers for different immune cells and genetic and chemical perturbation, we will clarify and determine which immune cells respond when, and to what extend to neurodegeneration. Second, we will define whether immune pathways increase disease progression or are protective. Last, as a complementary approach, I will use small molecule screening to identify drugs that modify these immune responses.

In all, this project aims to unravel basic in vivo mechanisms involved in neurodegenerative diseases. By discovering small molecules affecting interactions controlling these mechanisms, my project will identify research tools and drugs for possible therapeutic interventions.

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