The Role of Interleukin-10 in Regulating Neuroinflammation Relevant to Tauopathies

Lea L. Weston
Shanya Jiang
Devon Chisholm
Kiran Bhaskar

Follow this and additional works at: https://digitalrepository.unm.edu/hsc-bbhrd
The role of interleukin-10 in regulating neuroinflammation relevant to tauopathies
Lea L Weston, Shanya Jiang, Devon Chisholm, and Kiran Bhaskar
University of New Mexico Health Sciences Center, Albuquerque, NM

Background

**Tauopathies** are neurodegenerative diseases, including Alzheimer’s disease, that are associated with pathological accumulation of the microtubule associated protein tau (MAPT, or tau) (Lee et al., 2001). Abnormal **hyperphosphorylated tau** (pTau) strongly correlate with cognitive impairment (Nelson et al., 2012).

**Neuroinflammation** is also associated with tauopathies (Gerhard et al., 2006b; Edison et al., 2008) and is implicated in driving tau pathology (Yoshiyama et al., 2007, Maphis et al., 2015b). Therefore, it is compelling to understand the role of anti-inflammatory cytokines in limiting neuroinflammation and tau pathology. **Interleukin-10 (IL-10)** is a well-established anti-inflammatory cytokine with roles in limiting inflammation in the central nervous system (CNS) (Strie et al., 2003; Lobo- Silva et al., 2016; Burmeister and Marriott, 2018).

Here, we determine if IL-10 regulates inflammatory-induced tau pathology by examining the role of IL-10 on tau phosphorylation during an acute inflammatory challenge. We also examined IL-10 in the context of slow progression of neuroinflammation and pTau progression in a human tau expressing (hTau) mouse model.

Our findings suggest a distinct importance of IL-10 in limiting tau hyperphosphorylation after an acute inflammatory challenge, however, its role in limiting early expression and/or chronic progression of cytokines and tau phosphorylation remains unclear.

**Hypothesis**

The anti-inflammatory effects of IL-10 regulate tau phosphorylation in tauopathies.

**Support and Acknowledgements**

**IDP T32**

**BHII Mini-Grant**

**Project ID:** BHII 2017-2001
**BHII RFA:** 2017-2018

The Stephanie Ruby Predoctoral Travel Award Molecular Genetics Microbiology Dept.

Thanks to Dr. Erin Milligan for #10 mice; Dr. Lauren Turgeon for MIG training; Dr. Russ Morten for Behavior Training; and Jeff Thompson for fMRI assistance and other lab support.

**Induce tau pathology with LPS**

**IL10** vs. non-Tg (WT) (3 mg/kg i.p) 24 hours

**Neuroinflammation and Tau Pathology?**

**IL10** enhances LPS-induced cytokine levels and microglia activation

**IL10** increases LPS-induced levels of activated p38 MAPK*

**IL10** enhances LPS-induced tau phosphorylation

**Human tau (hTau) transgenic mouse model experiments**

**IL10** mice have increased IL-1β, IL-6, & IL-12 but low levels of IL-10. Further deletion of IL-10 does not enhance cytokine levels.

Deletion of IL-10 in hTau mice does not significantly alter tau phosphorylation or total tau levels by 6 months of age.

**Summary**

- IL-10 deficiency in increased inflammatory markers, microglia activation and tau pathology in an acute model of inflammation.
- IL-10 deficiency did not alter inflammatory cytokines, microglia activation, or tau phosphorylation in this human tau (hTau) mouse model at 6 months of age.
- This suggests that the low-level cytokine expression in 6-month hTau mice is not dependent on IL-10 regulation. It’s not clear if IL10 affects inflammation and pTau with increased aging.