

# Brain Radiation-Induced Fatigue is Associated with Neuroinflammation and Suppression of Orexin Signaling



OHSU Knight Cancer Institute

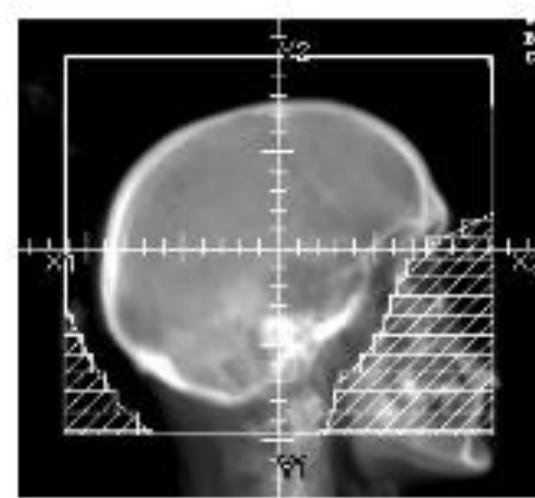
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Department of Radiation Medicine  
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Brenden-Colson Center for Pancreatic Care  
Oregon Health & Science University

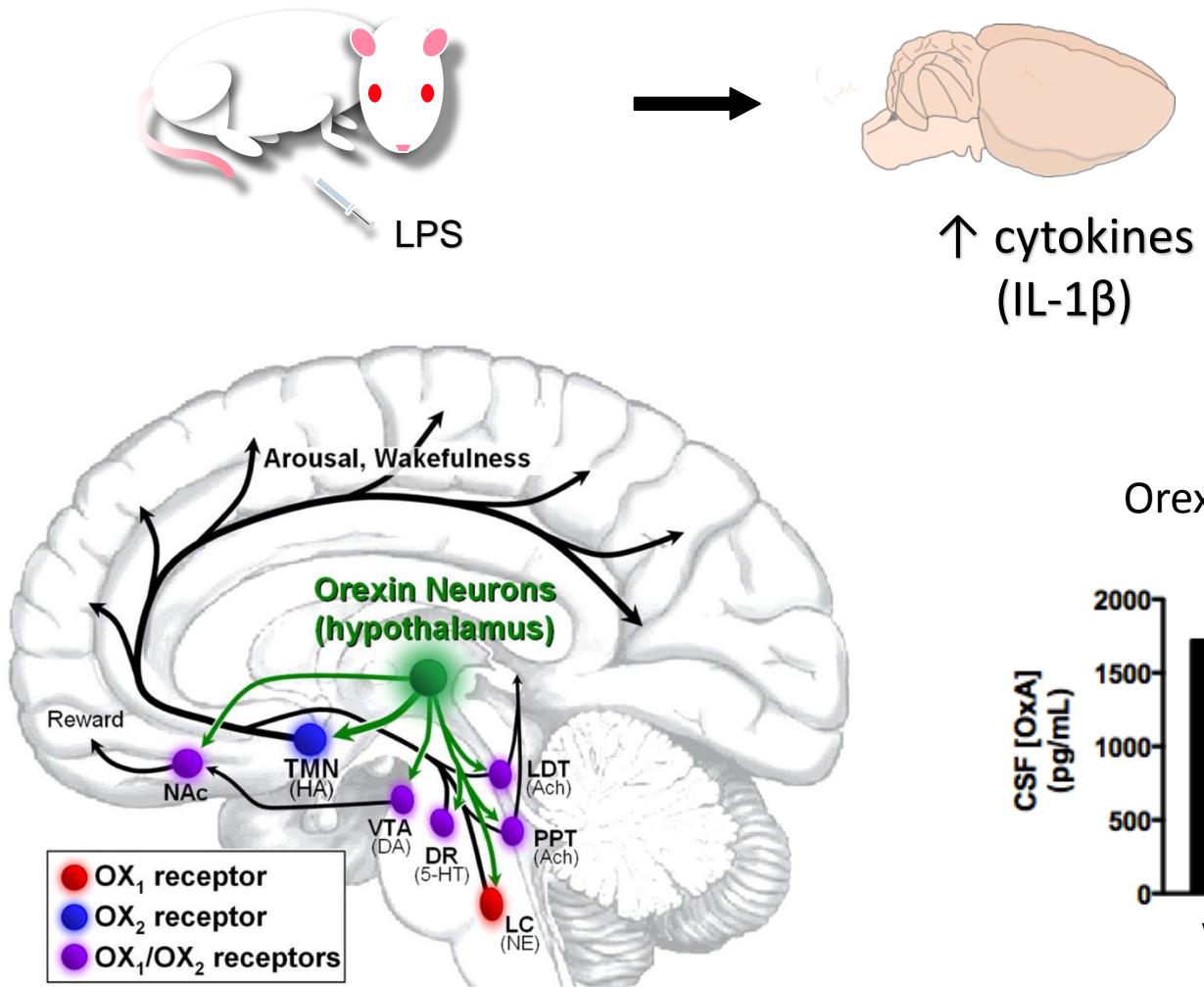
Nothing to disclose

# Brain radiation-induced fatigue

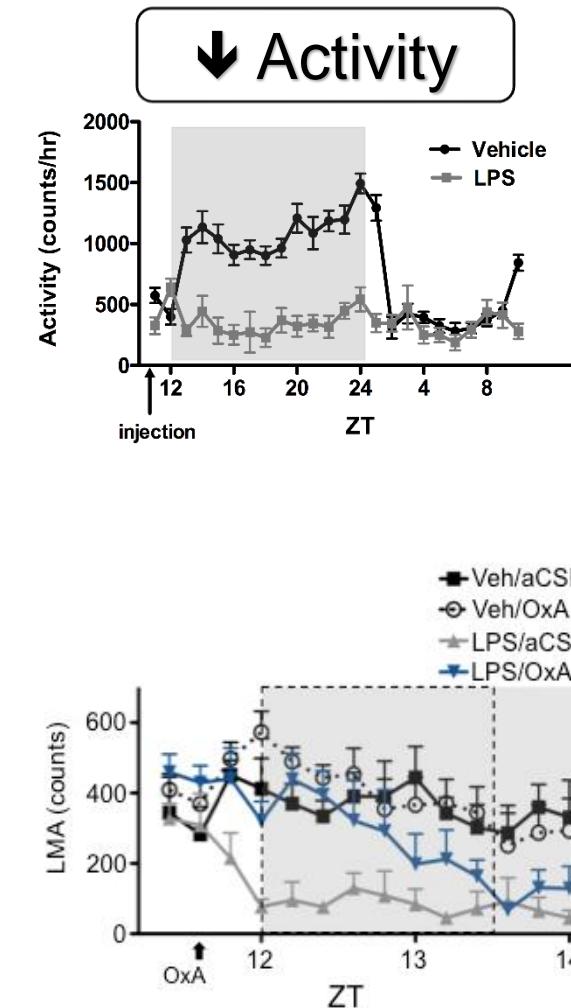
- 200,000 patients/year
  - Brain metastasis
  - Primary intracranial tumor
  - Pediatric brain tumors
- >90% of patients report fatigue
- Cognitive impairment
- Growth Restriction
- Metabolic dysregulation



# Inflammation and activity

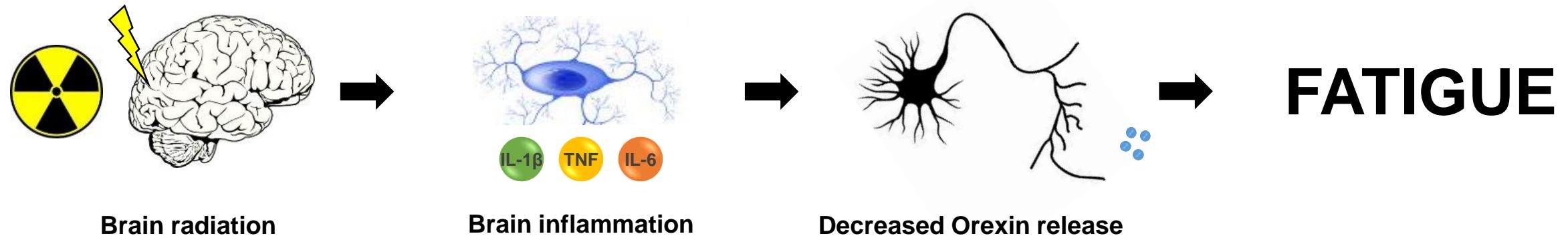


Gotter Pharmacological Rev 2012



Grossberg, Marks J Neurosci 2011

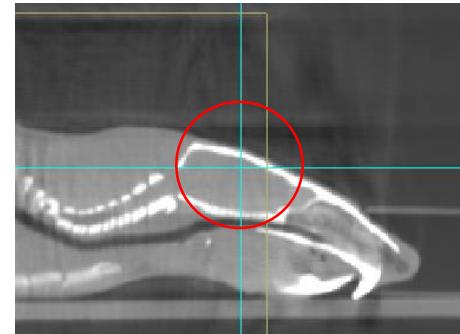
# Hypothesis



# Design

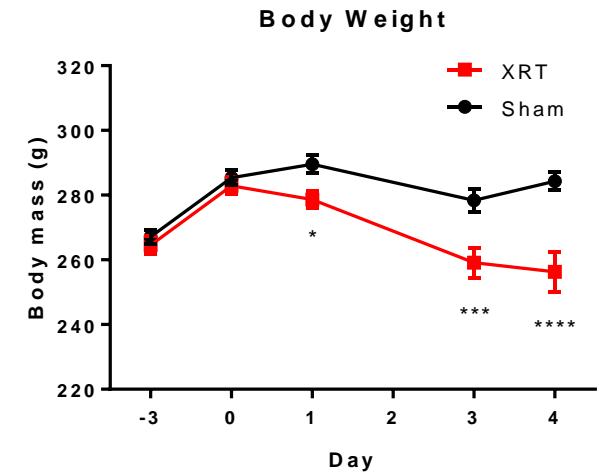
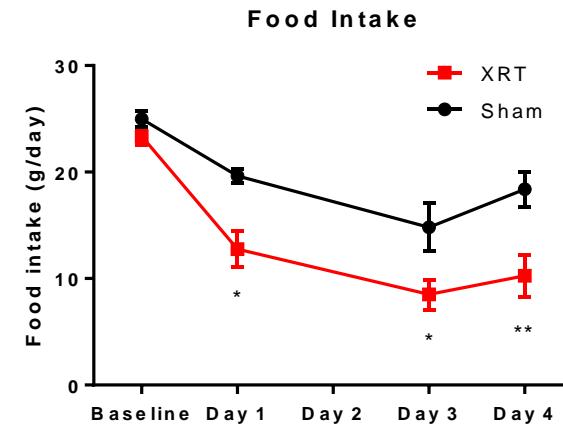
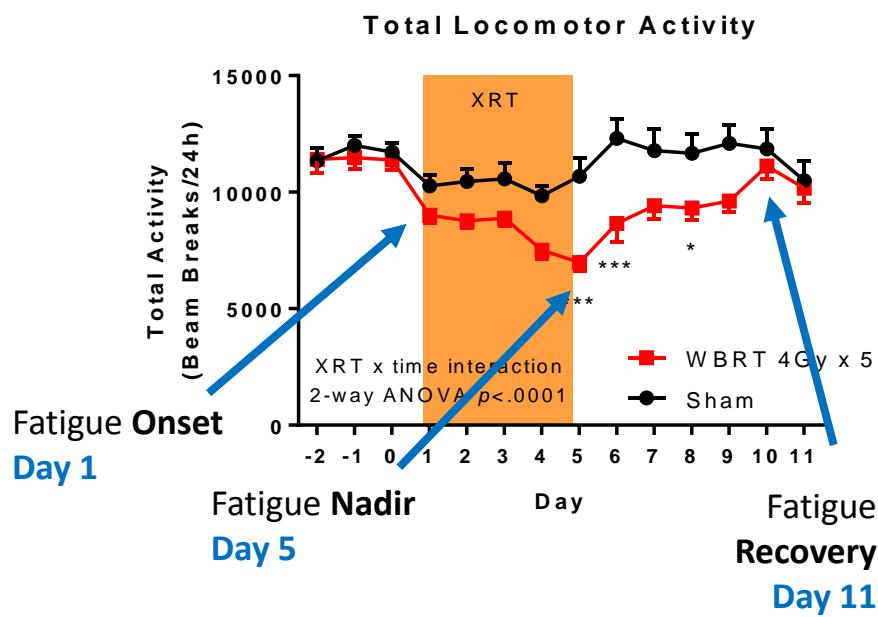


WBRT 4Gy x 5



Home Cage Locomotor Activity

# Brain radiation-induced fatigue

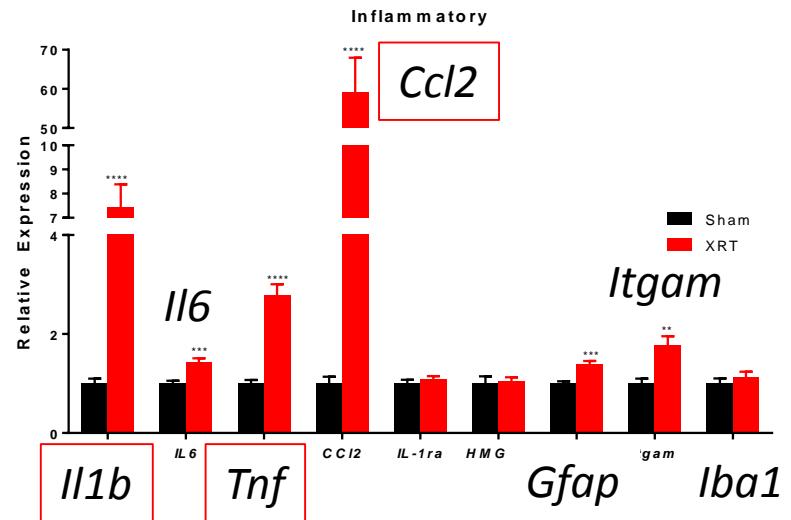


# Inflammatory Gene expression

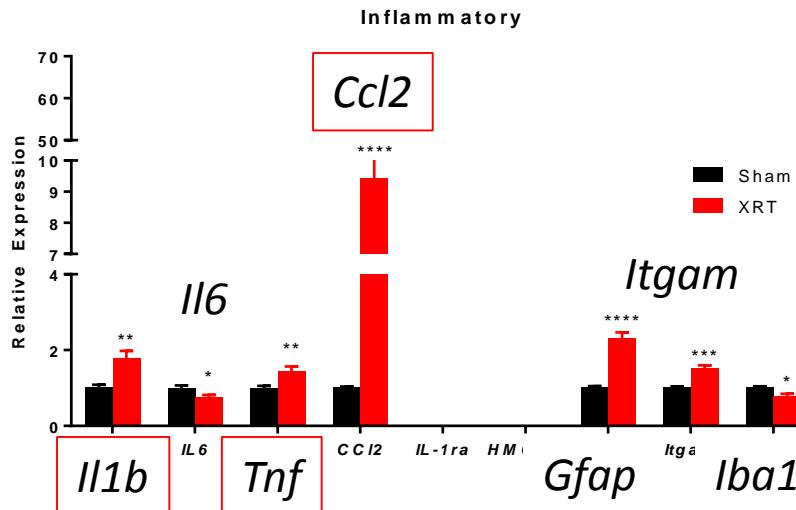
## Hypothalamus



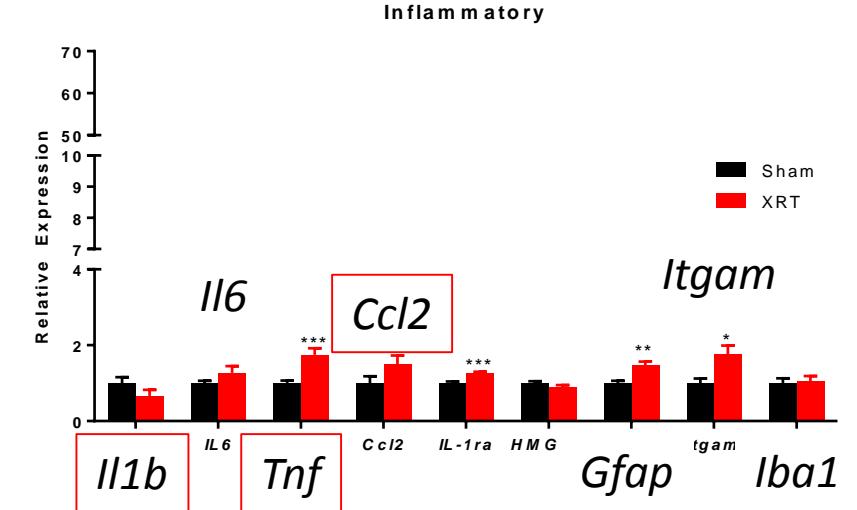
**Onset**  
**Day 1**



**Nadir**  
**Day 5**

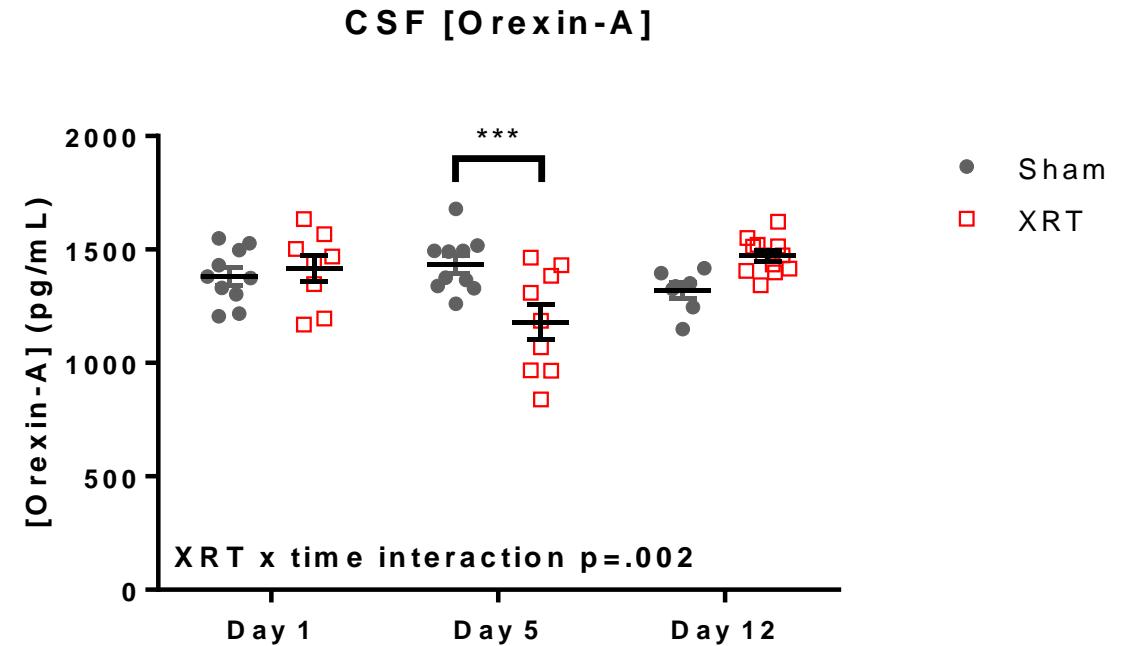
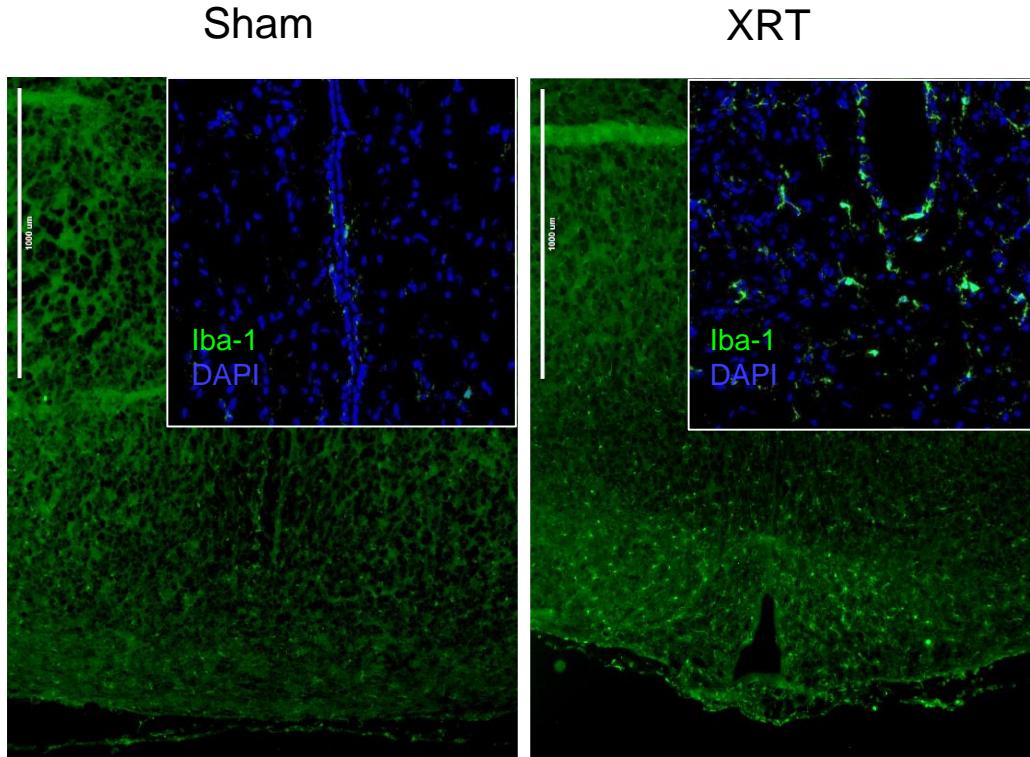


**Recovery**  
**Day 12**



# Brain radiation-induced fatigue

## Biology



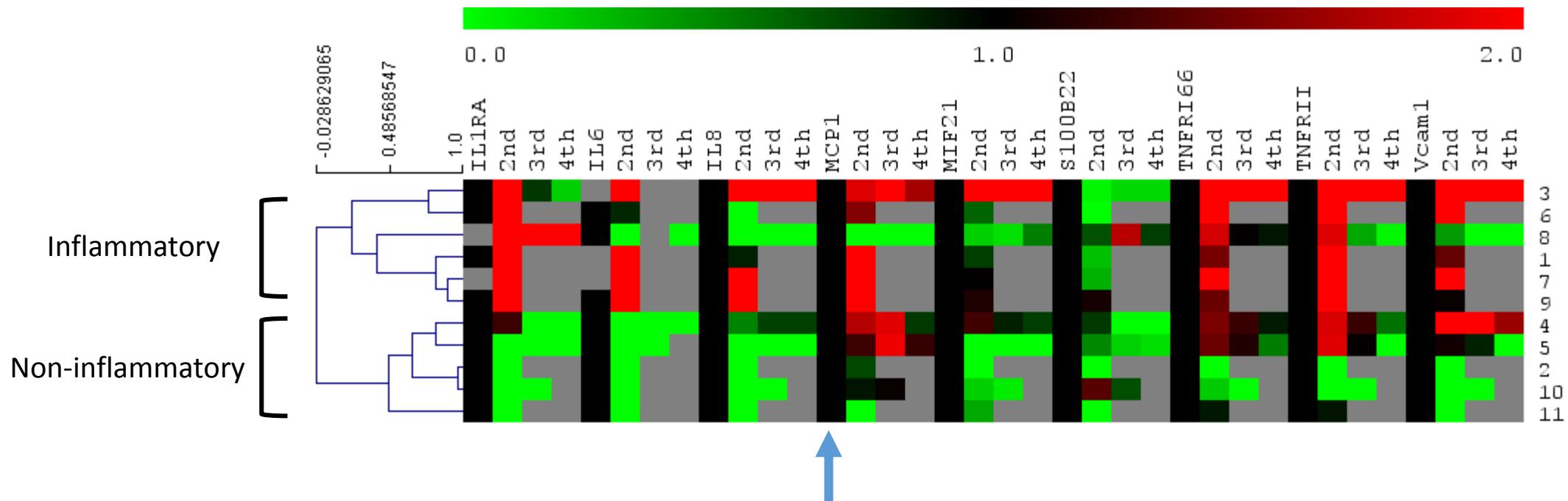
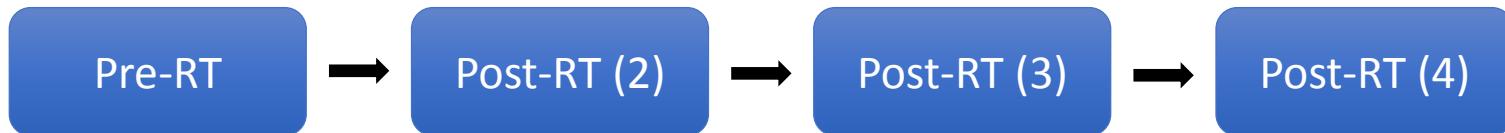
Grossberg, Dantzer, Grosshans *unpublished*

# Brain radiation-induced fatigue

## *Clinical*



## 11 pediatric patients with brain tumors treated with RT



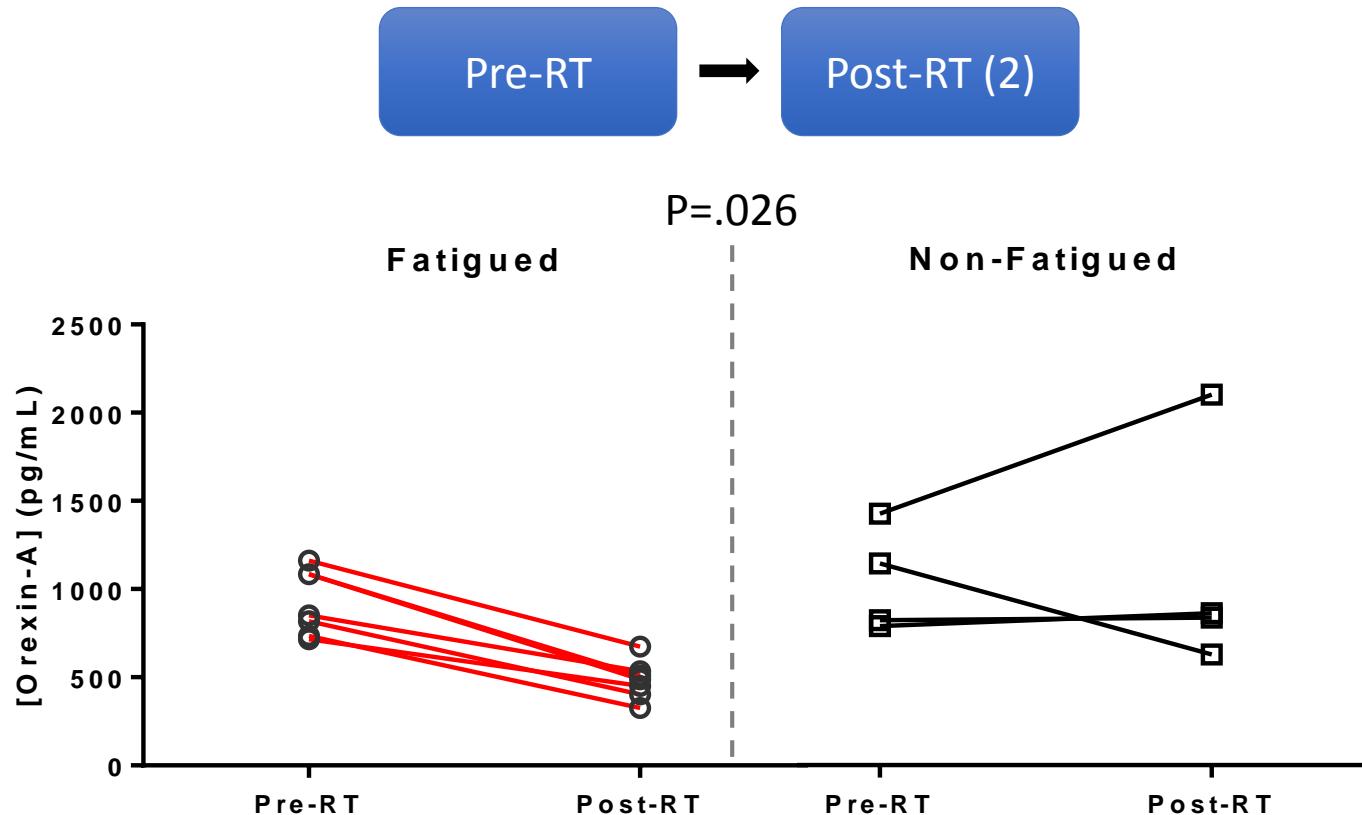
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# Brain radiation-induced fatigue

## Clinical



11 pediatric patients with brain tumors treated with RT



**Fatigue correlated with post-RT**  
- sTNFR1  
- sTNFR2

# Brain radiation-induced fatigue

## Clinical



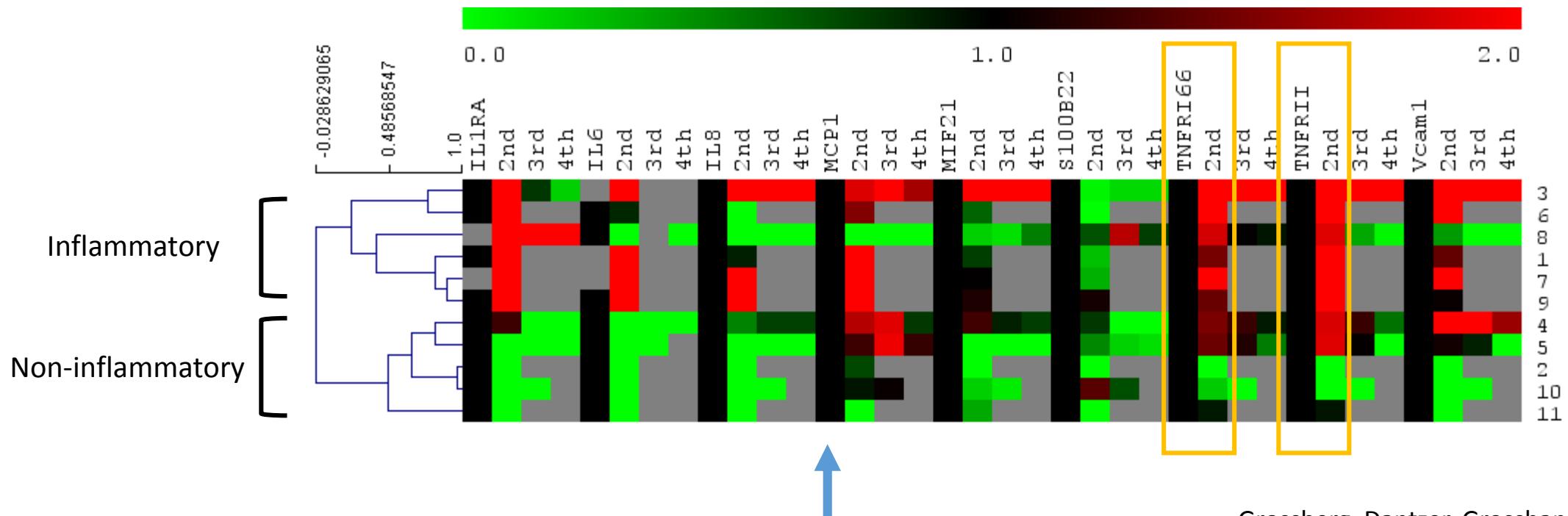
11 pediatric patients with brain tumors treated with RT

Pre-RT

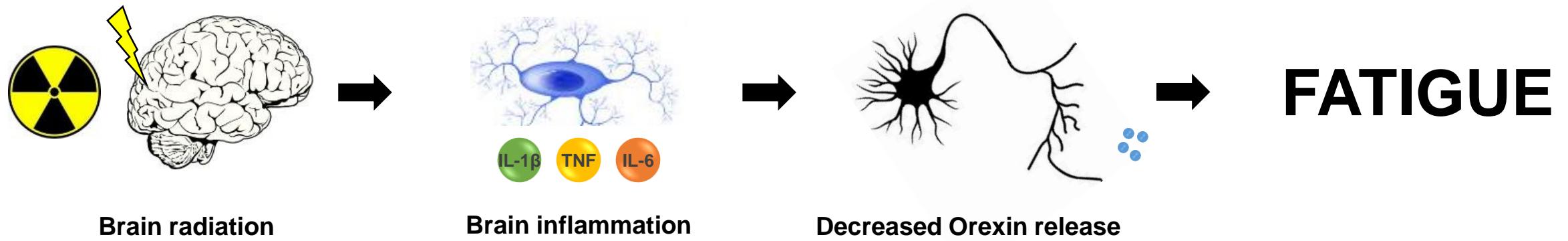
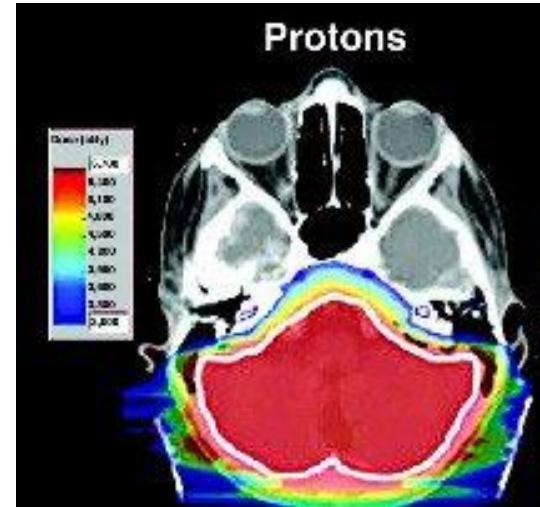
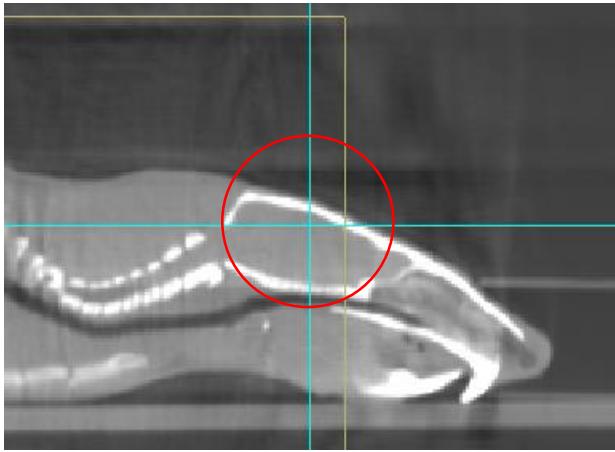
Post-RT (2)

Post-RT (3)

Post-RT (4)



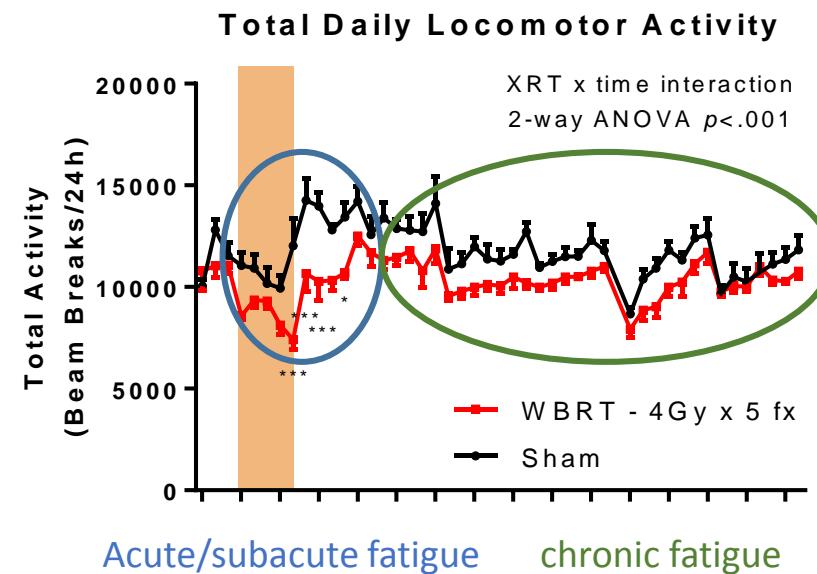
# Brain radiation-induced fatigue



# Brain radiation-induced fatigue

## Questions

- Can we demonstrate *causation*?
- Is fatigue *reversible*? Is fatigue *preventable*?
- What are the drivers of *chronic fatigue* after WBRT?



# Acknowledgements

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## Brain Radiation and Fatigue



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- Phillip Gross



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