

Immune system dysfunction as a cause of fatigue

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Disclaimer and Disclosures

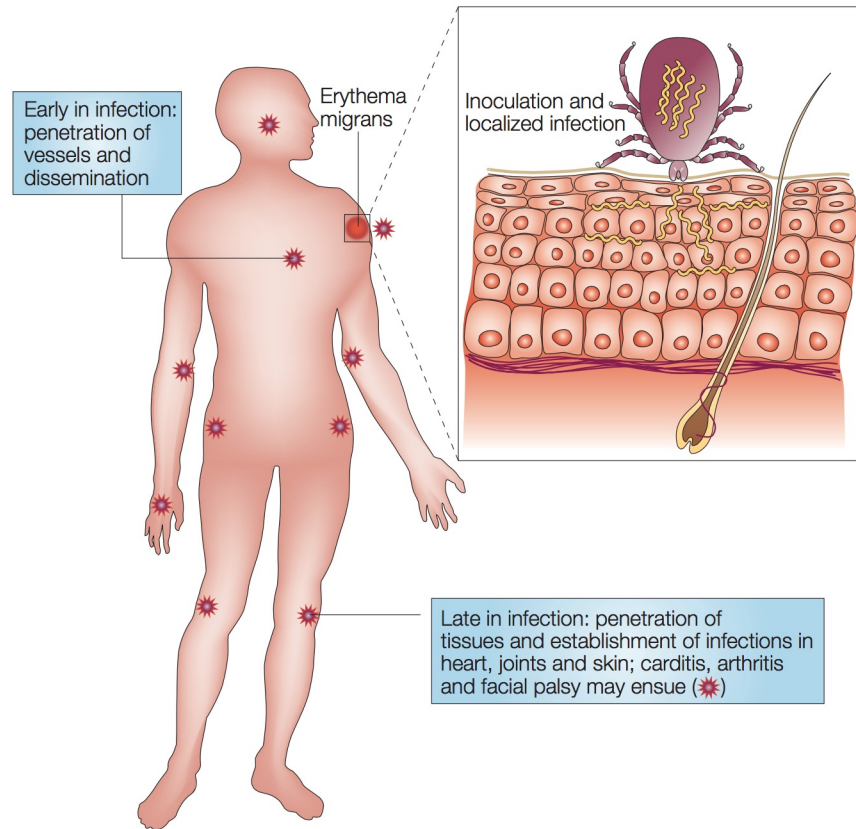
Disclaimer

This certifies that the views expressed in this presentation are those of the author and do not reflect the official policy of the NIH.

Disclosure

I am a co-founder of an early stage company, Mozart Therapeutics Inc., that seeks to develop treatments for autoimmune diseases, including those described here, using the T cell circuitry we have discovered.

Lyme disease



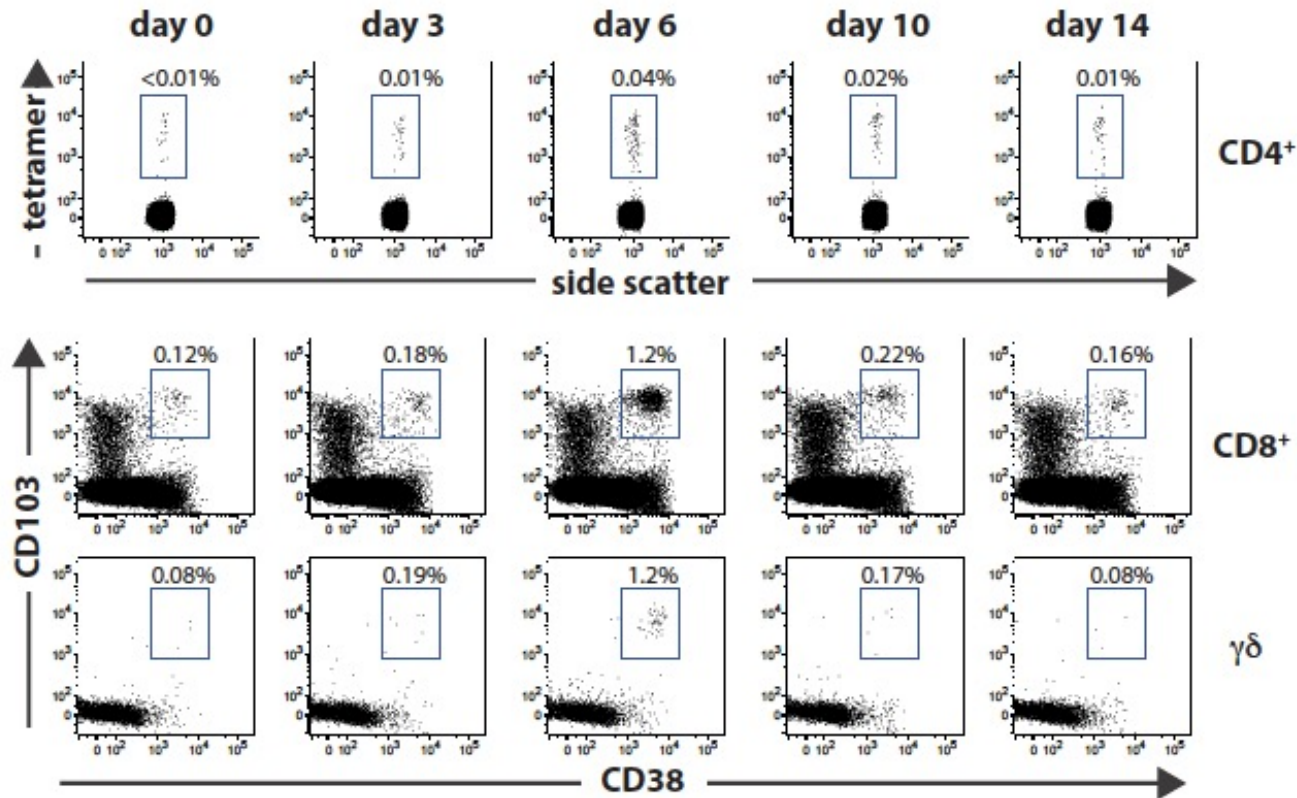
Stage I: Early-localized Lyme disease: A painless transient inflammatory skin rash.

Stage II: Early-disseminated Lyme disease: Joint or muscle pain, inflammation.

Stage III: Late-persistent Lyme disease: Fatigue, fever, malaise, chronic arthritis

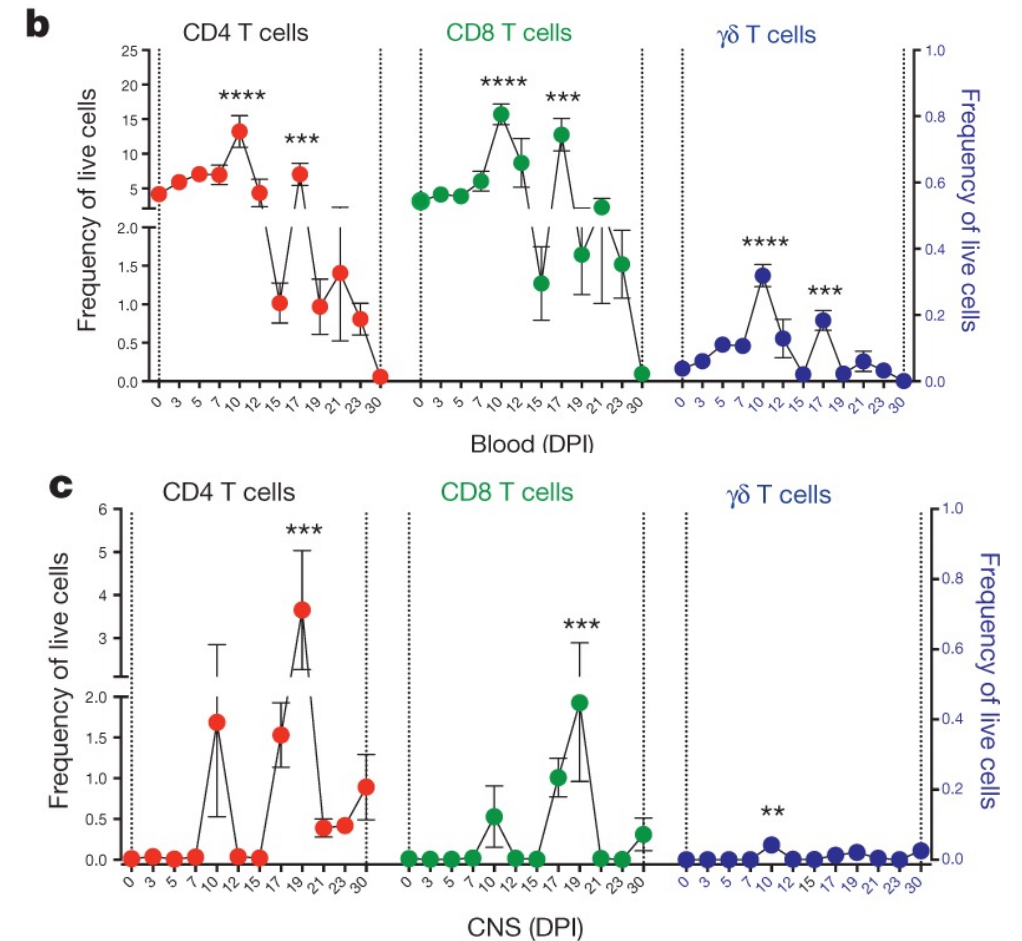
Waves of T cell activity in Celiac patients after gluten challenge and in a mouse model of autoimmunity (EAE)

Celiac patients



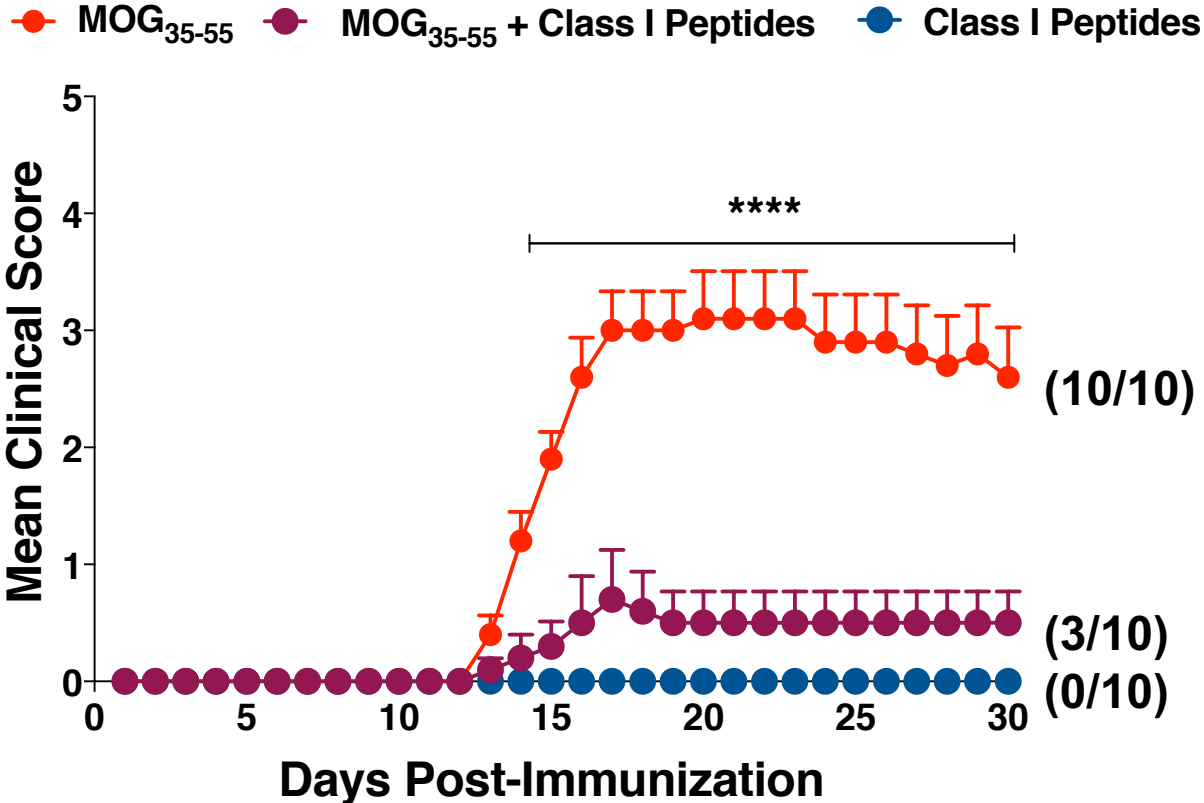
Han et al., *PNAS* 2013

EAE



Saligrama et al., *Nature* 2019

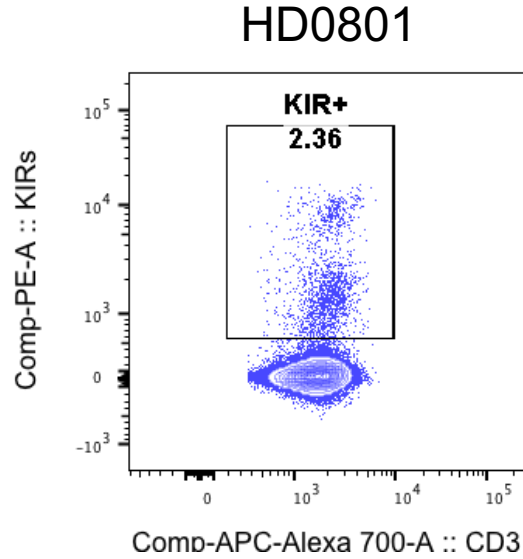
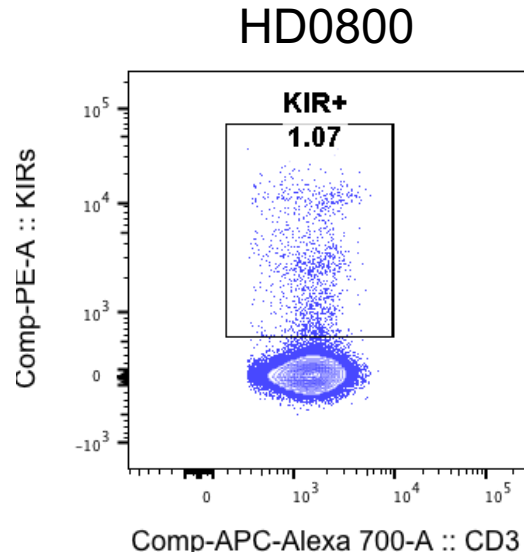
Class I Peptides Immunization Protect The Mice Against MOG induced pathology



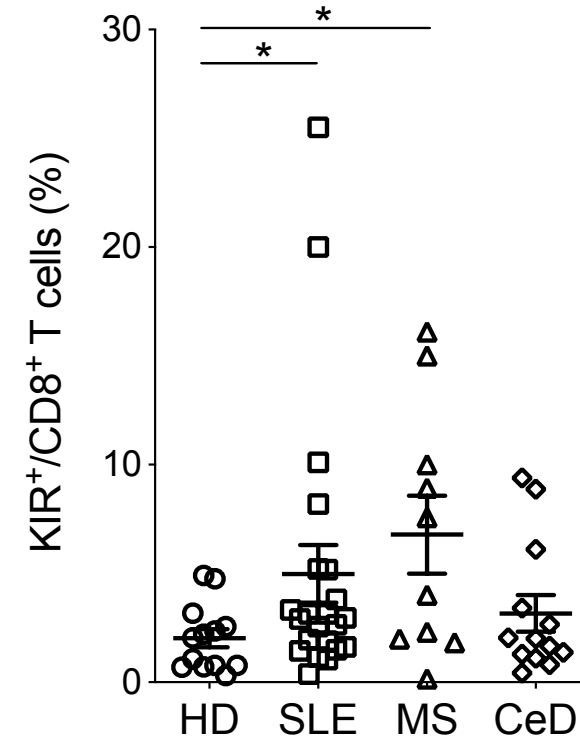
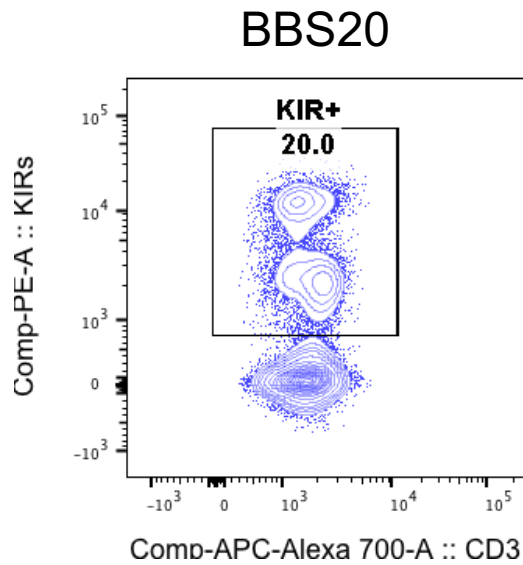
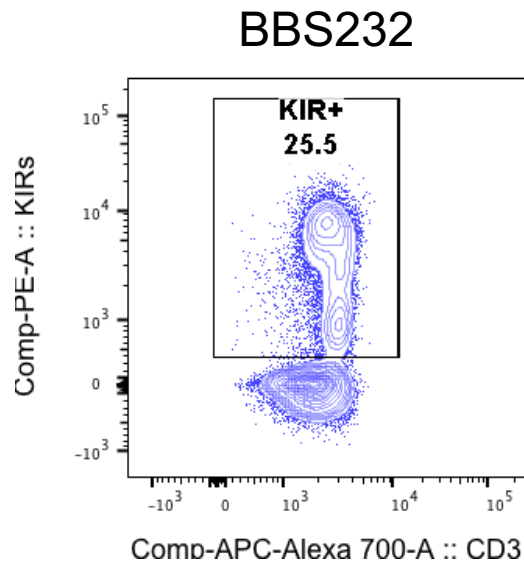
A new dynamic in autoimmunity:

Some patients with autoimmunity have elevated KIR+ CD8+ cells

Healthy Donors



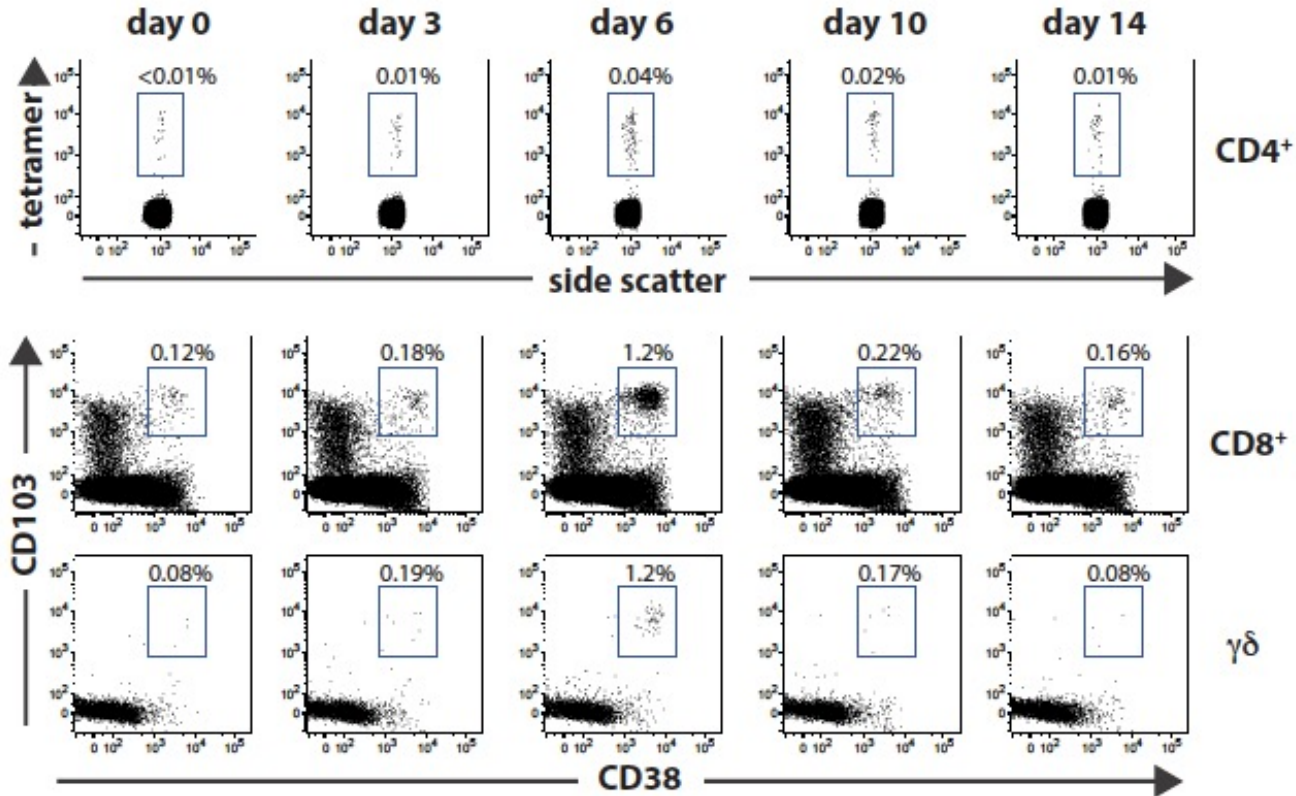
Lupus patients



Jing Li

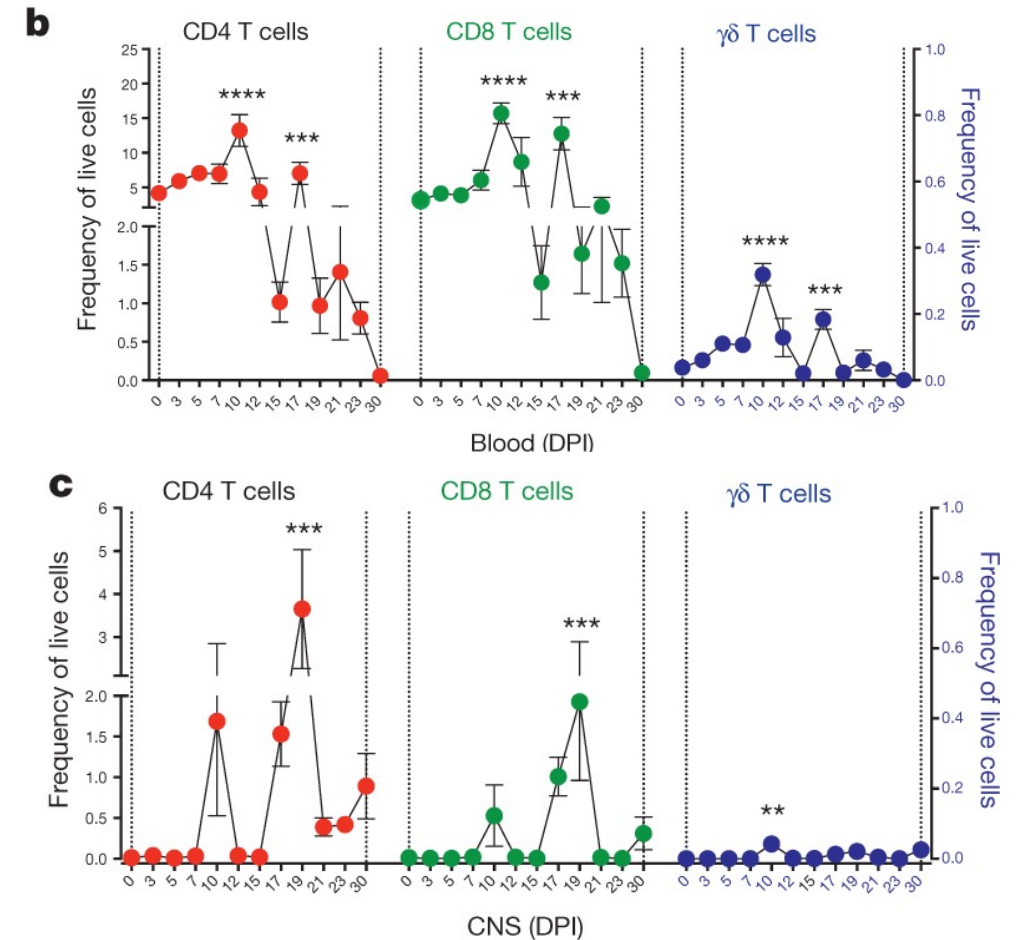
Waves of T cell activity in Celiac patients after gluten challenge and in a mouse model of autoimmunity (EAE)

Celiac patient



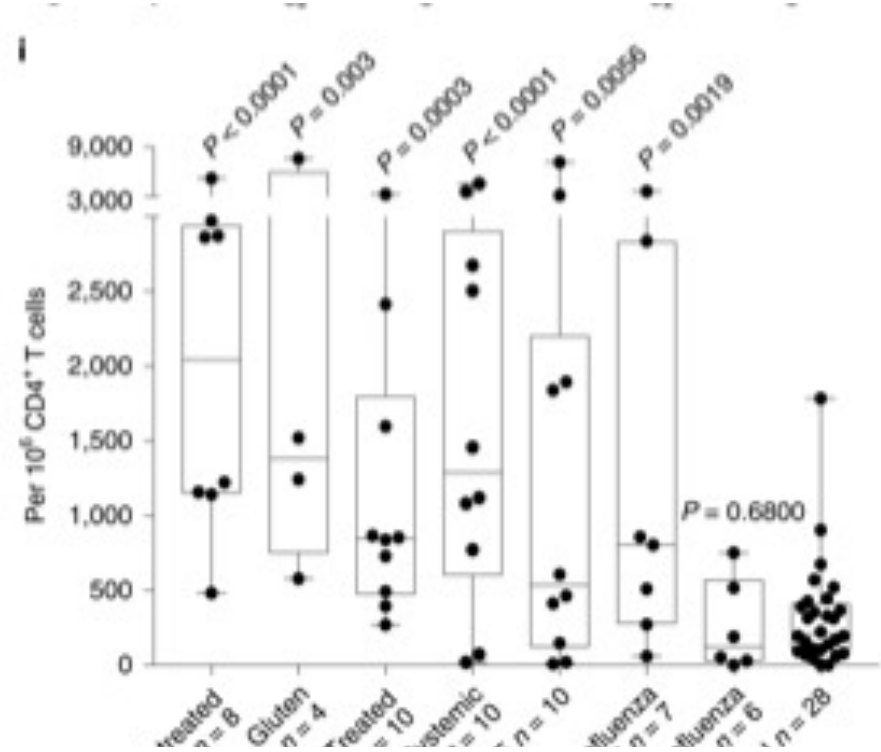
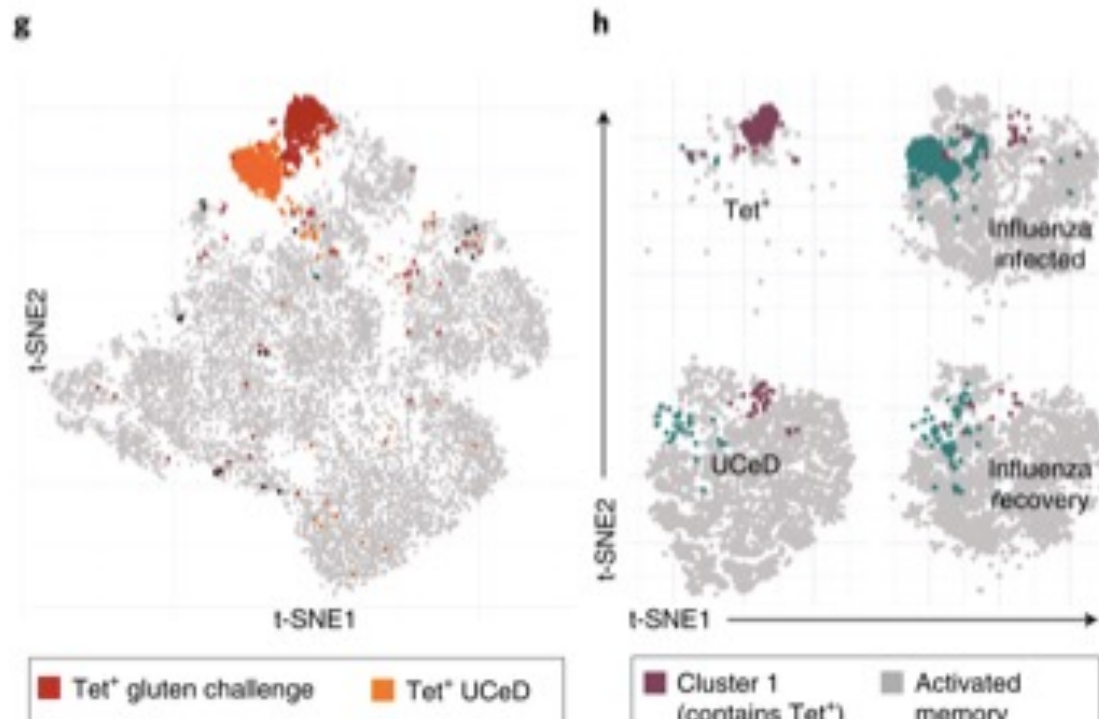
Han et al., *PNAS* 2013

EAE

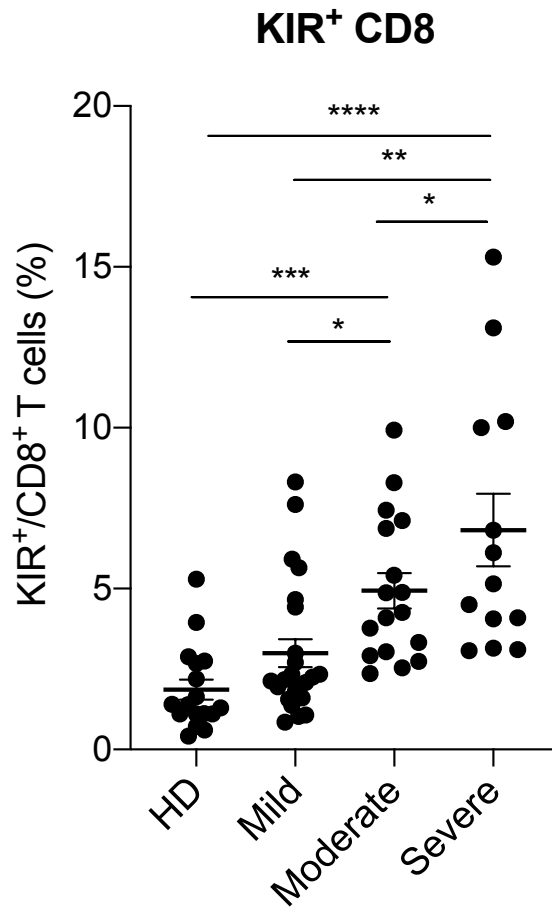


Saligrama et al., *Nature* 2019

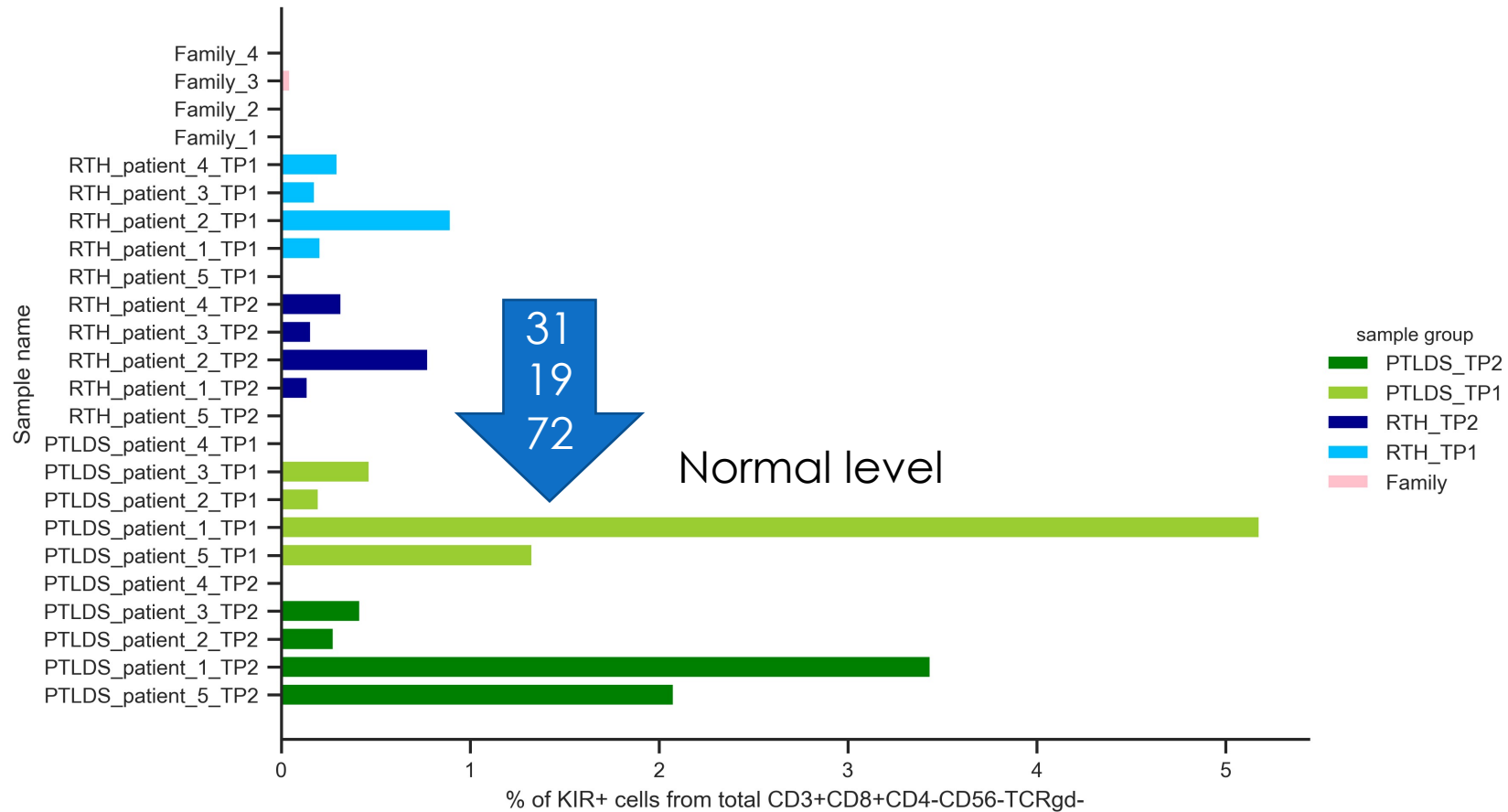
Labeling gluten-specific T cells in Celiac patients showed that this was a small subset of CD4+ T cells and this subset was elevated in various autoimmune diseases such as Lupus, Scleroderma and MS (not shown). Christophersen et al., Nat. Med. 2019.



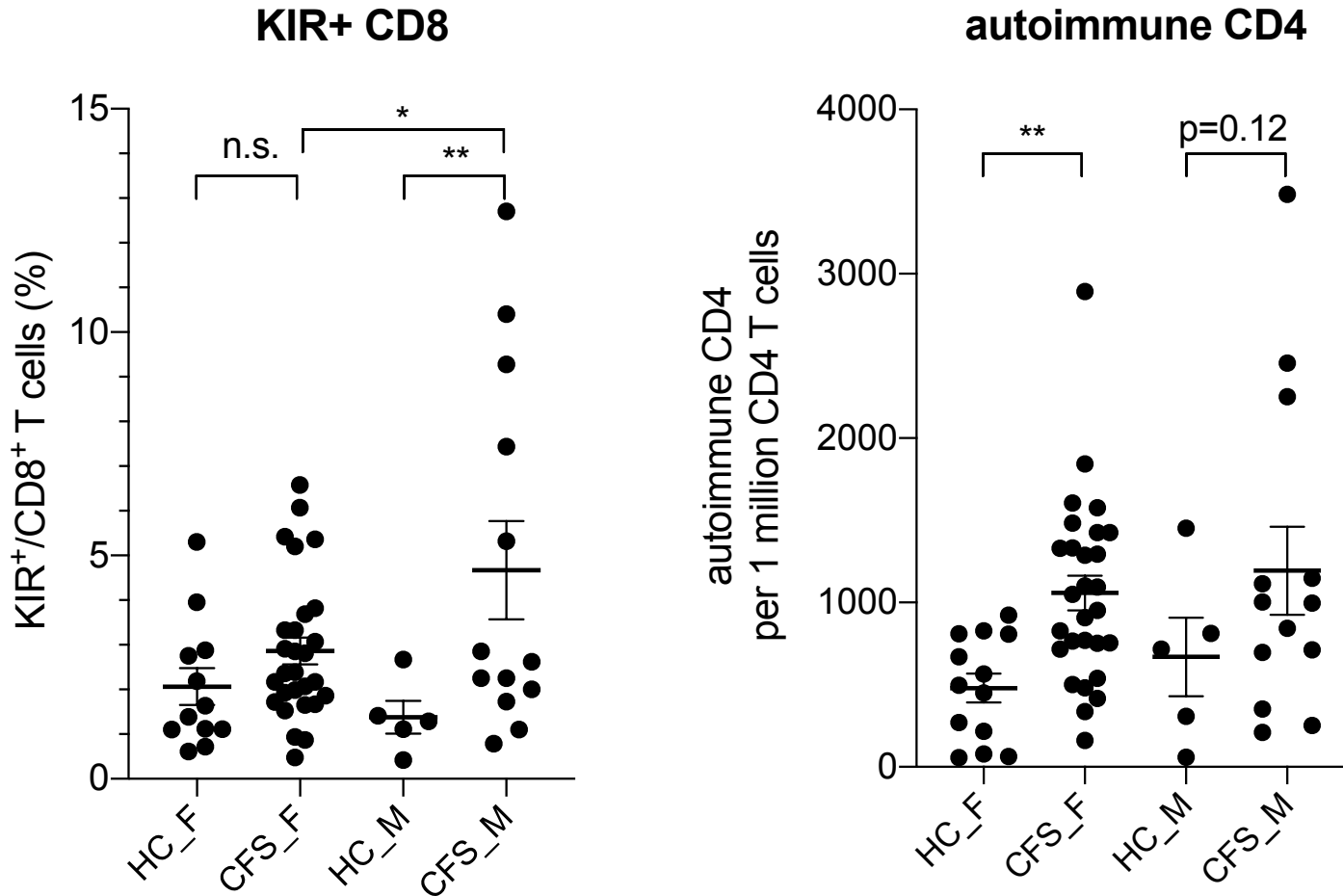
Increased frequency of KIR⁺ CD8 in COVID-19 patients, especially those with moderate or severe disease (Jing Li et al.)



We also see elevated Kir⁺ CD8⁺ T cells in the peripheral blood of some Lyme patients



Chronic Fatigue/ME patients show increased KIR⁺CD8⁺ T cells in males and females show increased autoimmune CD4⁺ T cells (Jing Li, J. Wilhelmy)



Conclusions

1. These data suggest some types of fatigue are caused by autoimmunity triggered by an infectious disease.
2. The T cell circuitry described here normally suppresses autoreactive immune cells that arise during an infection, but can fail, for unknown reasons.

Credits

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Ana Jimena Pavlovitch-Bezyk
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Ron Davis
Nielsen Fernandez-Becker

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