Immune system dysfunction as a cause of fatigue

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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)

Han et al., *PNAS* 2013

Saligrama et al., *Nature* 2019
Class I Peptides Immunization Protect The Mice Against MOG induced pathology

Saligrama et al., under review
A new dynamic in autoimmunity:
Some patients with autoimmunity have elevated KIR+ CD8+ cells
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

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.

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