

PROPOSITIONS

TO THE THESIS

Interferon-stimulated Genes and Their Role in Controlling Hepatitis E Virus

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1. Transcription of ISGs is classically thought to be mainly mediated via the Interferon-induced JAK-STAT signaling. This underestimates, however, the importance varieties of non-canonical mechanisms regulating ISG transcription. *(This thesis)*
2. RIG-I, MDA5 and IRF1 are potent anti-HEV ISGs. Activation of RIG-I stimulates cellular innate immunity against HEV without requiring of IFN production, but at least partially necessitating the JAK-STAT signaling. *(This thesis)*
3. IRF1 effectively inhibits HEV replication through the activation of the JAK-STAT pathway, and the subsequent transcription of antiviral ISGs. *(This thesis)*.
4. Convergent transcription of ISG by TNF- α and IFN- α augments their antiviral activity against HCV and HEV. *(This thesis)*
5. The endogenous unphosphorylated ISGF3 complex contains IRF9, unphosphorylated STAT1 and STAT2 and is necessary and sufficient for constitutive ISG transcription and antiviral immunity during homeostasis. *(This Thesis)*
6. The IFN-mediated innate immune response, selected by evolution, is hardwired within genomes and provides a robust first line of defense against invading pathogens. *(W. M. Schneider et al, Annu Rev Immunol. 2014)*
7. Being a dynamic and flexible self-regulatory system, pattern-recognition receptor-dependent innate signaling manages to induce the evolutionary most favorable innate immune responses for the host. *(Xuetao Cao. Nat Rev Immunol. 2016)*
8. Transformative and translational science happens on a foundation of basic research. *(Michael S. Diamond)*. Similarly I hope my studies on non-canonical anti-viral immunity will help shape applied research on combating viral diseases.
9. Weakness and ignorance are not barriers to survival, but arrogance is. *(Remembrance of Earth's Past by Cixin Liu)*. On a same line, I hope that overreliance of limited model systems has not led to make false propositions on the nature of viral defense.
10. Many are stubborn in pursuit of the path they have chosen, few in pursuit of the goal. *(Attributed to Friedrich Nietzsche)*. Analogously, the efforts of setting up an experimental system make us reluctant to change strategy even if that is more appropriate for answering the question at hand.
11. To present problems correctly is the first step towards the innovation. *(Unknown)*