

Introduction

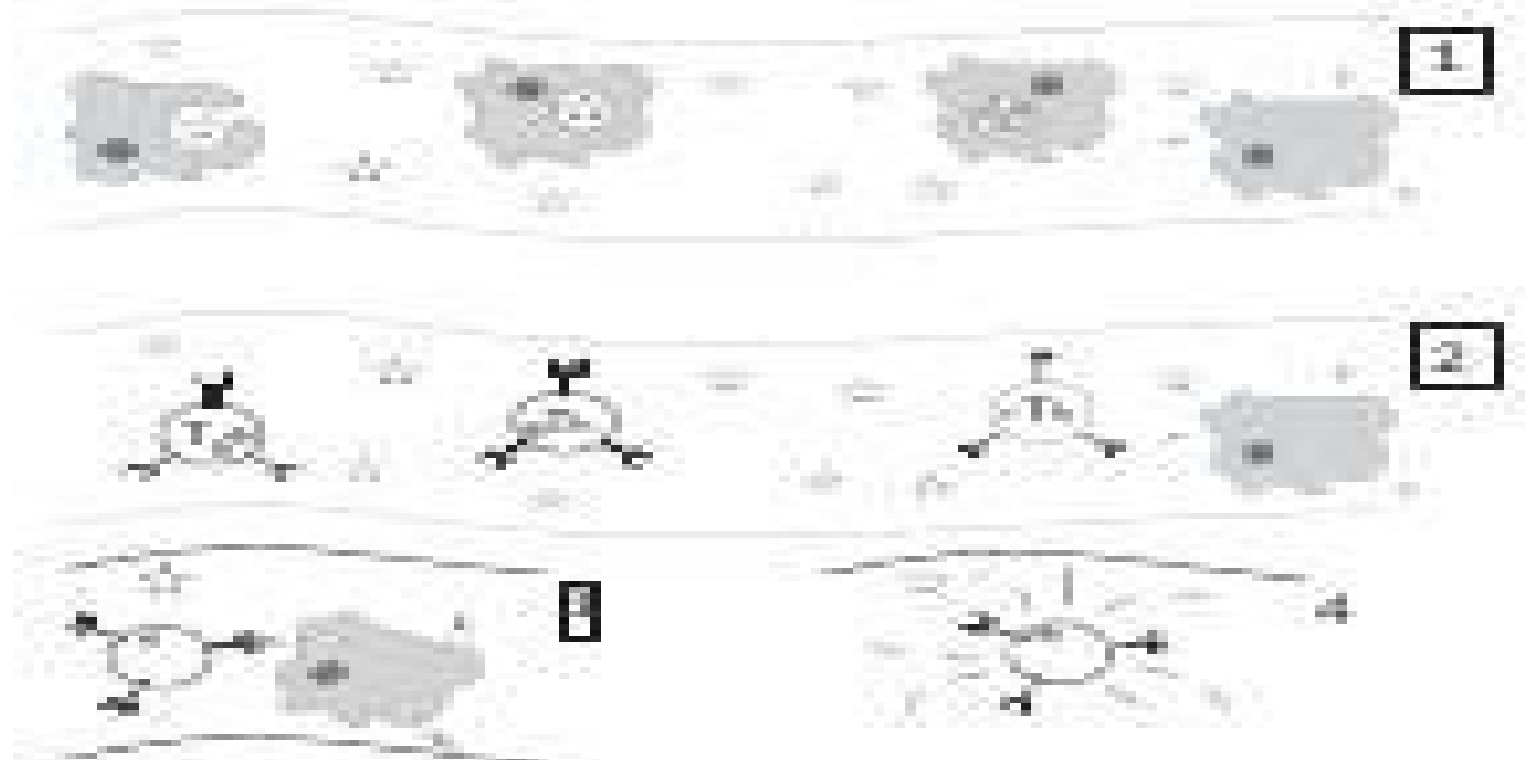
What does our immune system protect us from, and how?

Why?

2

Our body is under constant potential attack by invading foreign cells and pathogens. Our genes are well suited to this. These cells pathogens are absorbed and eliminated, unless sometimes we are prevented to body can work this function. Some keeping the organism healthy. Cells of the immune system are body.

Block 1 - Cell Mediated Response



Pogil Immune In Model1 A Pathogen

Jiming Sheng



Pogil Immune In Model1 A Pathogen:

Evolution of Immune System Against Diverse Antigens Jiming Sheng, 2021 The immune system evolves across the host's lifetime to protect against the wide array of threats in nature. While the immune system is capable of evolving and adapting to a single antigen Ag, it becomes a challenging task to defend against diverse antigenic targets including mutants of the same pathogen or a wide spectrum of pathogen species. First, the rapid intra-host diversification of highly mutable pathogens such as human immunodeficiency virus (HIV) or hepatitis C virus (HCV) creates a coevolutionary arms race with the immune system. As a result, viruses persist into a chronic infection in most subjects and are only cleared in rare cases. In addition, the vaccination trials so far to elicit broadly neutralizing antibodies (bnAbs) against highly mutable viruses have met with failure. Second, the immune system has to allocate its finite amount of adaptive immune cells against the wide spectrum of pathogens in the environment. As memory cells accumulate from each pathogen encounter, the host's immune repertoire gradually becomes skewed: more adaptive immune cells are dedicated to the frequent pathogens while fewer are reserved for the rare pathogens. The skewed repertoire in the elderly has been correlated with immune risk phenotype and a chronic inflammatory response even in the absence of pathogens, but whether there is a mechanistic connection remains unknown. My dissertation aims to address the following questions regarding the evolution of the immune system against diverse antigenic targets:

1. What are the mechanisms and deciding factors behind the distinct coevolutionary outcomes observed in different subjects?
2. What makes a viable vaccine design strategy to guide immune system evolution towards bnAbs?
3. What are the side effects of a skewed immune repertoire as a result of adapting to different pathogens encountered during host's lifetime? Also, how can human intervention alleviate these side effects?

My dissertation shows that:

1. Different coevolutionary outcomes are decided by the timing and efficacy of successive narrow and broad antibody (Ab) responses, which in turn are determined by the conservation level and initial diversity of Ag.
2. A viable vaccine strategy to elicit bnAbs should balance suppression of strain-specific B cells and preserving cross-reactive B cells. The corresponding optimal selection strength should increase in time as driven by the evolution of B cell cross-reactivity.
3. Mediated by adaptive innate feedback, repeated pathogen encounters during host lifetime and resulting memory inflation may trigger a fragility in which any encounter with a novel pathogen will cause the system to irreversibly switch from health to chronic inflammation (CI). In addition, the onset of CI strongly depends on the history of encountered pathogens; the timing of onset can be delayed drastically when the same set of infections is encountered in a specific order.

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