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Why leveraging sex differences in immune tradeoffs may illuminate the evolution of senescence

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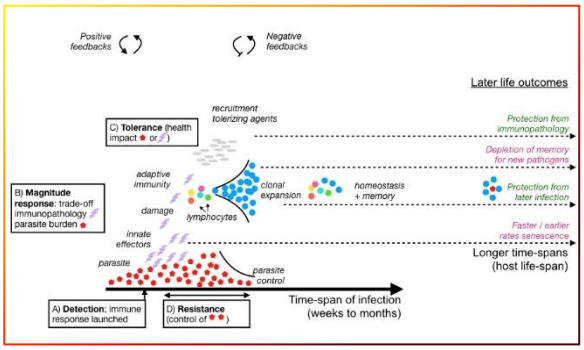
How might immune function shape *aging*, the increases in mortality and declines in fertility experienced at late ages by organisms across the tree of life? Classic evolutionary theory tells us that features that increase early life survival (or fertility) at the expense of later survival (or fertility) should spread within populations: such features will increase fitness simply as a result of the rarity of older individuals. But placing immune function within this framework is challenging. The immune system must balance being extremely reactive to threats ranging from infections to cancer, yet also amenable to being rapidly shut down, since many aspects of immune function, from inflammation to auto-immunity, are dangerous to the host. The interdependent, highly responsive immune system that has evolved to meet these challenges makes it hard to identify or interpret the associated trade-offs governing outcomes in early vs. late life. Indeed, for some phenomena associated with immunity, the exact opposite pattern to the expected "increased early survival at the expense of late survival" is observed. For example, early pathogen exposure (with concomitant risk of early mortality) could shape the immune system's ability to learn to 'curb' itself (thus reducing the risk of late life mortality).

Sex differences in immune function provide a potentially powerful probe of



how trade-offs affecting immune function play out across the life course, and thus affect aging. Differences in 'competing' and 'caring' between the sexes have evolved repeatedly. A range of theoretical models of how this should affect immune function have been developed. Each of these framings, from quantitative predictions (with males typically the 'weaker' sex) to qualitative predictions (with females more tolerant, or with greater abilities of pathogen discrimination) have implications for the evolution of aging. Outcomes may be further modulated by host specific features of biology, from transfer of immune protection across generations (via parental antibodies) to the unique challenges faced by mammalian hosts during pregnancy. Empirical data, and particularly longitudinal measurements of immune function in both sexes, in tandem with careful theoretical framing of expectations of evolutionary outcomes, have the potential to allow us to break new ground in this important area.