Body size shapes immune defenses across species

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Differences in host competence—the ability of a host to encounter and transmit a disease agent to another host or a vector—are a key factor influencing disease dynamics within host communities. The immune system, in particular, plays a critical role in determining host competence because it contributes to defenses determining a host's susceptibility and suitability to a pathogen. Allometries—how a trait changes with body size—provides a promising framework for making interspecific predictions about immune defenses and disease dynamics. The Safety Factor Hypothesis posits that large animals should have disproportionately stronger immune defenses because of their disproportionate risk of exposure to infectious organisms and disproportionately slower ability to keep pace with pathogen replication. Data on granulocyte concentrations in hundreds of bird and mammal species demonstrate hypermetric scaling, supporting the safety factor hypothesis. In contrast, data on the functional antibacterial capacity of complement in scores of bird and mammal species indicate that large and small hosts have proportional protection. Our team also queried the effects of body size of nine species of primates on the regulatory architecture of innate immune responses of blood by inducing simulated bacterial infections with lipopolysaccharide (LPS) in whole-blood samples *ex vivo* and quantifying gene transcription. Novel comparative transcriptomic approaches revealed that transcriptional response to infection was more dramatic in larger species, with large primates disproportionately prioritizing innate immune gene expression over non-immune genes during infection relative to small primates. After an LPS challenge, large species disproportionally upregulated gene expression of genes with disproportionately lesser constitutive expression, indicating compensatory changes. These transcriptomics results support the Safety Factor Hypothesis. Overall, results indicate that body size impacts the regulation of immune responses to bacterial infections. By extension, body size has consequences on host competence and disease dynamics, and integrating allometries of immune defenses into allometric models of competence and epidemiological models will enhance predicting subsequent implications for disease dynamics.