Evolutionary genetic dissection of the genus Homo and its immune response

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Abstract

Over the last decade, population genetic studies have clearly indicated that immunity and host defense functions are among the functions most frequently subject to natural selection, whether purifying, positive or balancing. These studies, combined with functional genomic approaches, such as the mapping of expression quantitative trait loci (eQTLs), have helped to identify genes, functions, and mechanisms of prime importance for host survival and involved in phenotypic variation and differences in disease risk, in particular infectious, autoimmune and inflammatory disorders. I will present different cases of how immune response genes, and the pathways they trigger, have been targeted by natural selection, in its different forms and intensities, helping to delineate genes that fulfil essential functions in host defence, with respect to those exhibiting higher immunological redundancy. Furthermore, our population genetic analyses show that the contemporary diversity of immunity genes results from different demographic and selective events, including positive selection at some genes in specific human populations occurring mostly during the Neolithic transition. I will also discuss how population-specific genetic variation can profoundly impact immune-related molecular phenotypes, such mRNA expression upon infection (response eQTLs), and how the identification of advantageous regulatory variants helps to uncover evolutionarily beneficial mechanisms, such as attenuated inflammation, in specific human populations. Finally, I will present data showing that population adaptation to pathogen pressures can be facilitated by the acquisition, via admixture, of advantageous alleles from locally "adapted" populations. These events involve, for example, archaic introgression from Neanderthals, who introduced variants affecting immune responses to viral challenges into European genomes, or post-admixture selection among African Bantu-speaking populations, who acquired adaptive alleles related to immune responses or food metabolism from local populations of rainforest hunter-gatherers or pastoralists. This presentation will provide a glimpse into how population and functional genomic approaches increase our understanding of whether and how populations can adapt to environmental changes, including those related to pathogen pressures, over different time scales.

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