MHC diversity and pathogen resistance – a meta-analysis

Supervised by: Dr Hannah Dugdale

Pathogen-mediated selection is hypothesised to maintain diversity in the major histocompatibility complex (MHC). One of the three mechanisms underlying pathogen-mediated selection of MHC diversity is the heterozygote advantage. MHC heterozygous individuals are theorized to be able to recognize and bind more antigens than homozygous individuals, and therefore trigger immune responses more effectively against pathogens. There has been mixed support for the heterozygote advantage, however, so this project will conduct a phylogenetic meta-analysis to quantify any overall heterozygote advantage effect.

Several factors could affect detection of a heterozygote advantage, and these will be considered in the analysis. Studies vary in the type of MHC genes measured, in terms of whether they analysed class I and/or class II MHC genes, which have different functions. Class I MHC molecules are involved in intracellular antigen binding, whereas class II molecules are mainly involved in extra-cellular immune defence. Similarly the type and quantity of pathogens considered can vary, in terms of whether pathogen intensity or prevalence was measured, whether single or co-infection were analysed, or whether pathogens were primarily intra- or extra-cellular. It is also important that taxonomic grouping and field versus laboratory study differences are accounted for. Finally, the project will test whether a publication bias exists in the literature, both in terms of whether studies with non-significant or small effect sizes are under-published and whether there is a publication year bias in effect sizes.

The student should be familiar with or interested in learning R, and have an interest in Bayesian statistics and immune gene evolution. This project offers a unique opportunity to learn how to conduct systematic reviews and meta-analyses and collaborate with international experts in these methods (Kamiya & Nakagawa). The student will be trained to extract effect sizes from publications and to use the R package MCMCGLMM

Suggested reading

Kamiya T, O'Dwyer K, Westerdahl H, Senior A & Nakagawa S. A quantitative review of MHC-based mating preference: the role of diversity and dissimilarity. Mol Ecol 23, 5151–5163 (2014).

Nakagawa S & Poulin R. Meta-analytic insights into evolutionary ecology: an introduction and synthesis. Evol Ecol 26, 1085–1099 (2012).

Sin YW, Annavi G, Dugdale HL, Newman C, Burke T & Macdonald DW. Pathogen burden, co-infection and major histocompatibility complex variability in the European badger (*Meles meles*). Mol Ecol 23, 5072–5088 (2014).

Spurgin LG & Richardson DS. How pathogens drive genetic diversity: MHC, mechanisms and misunderstandings. Proc R Soc B 277, 979–988 (2010).