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CEE review 09-004

DOES REDUCED MHC DIVERSITY DECREASE VIABILITY OF VERTEBRATE POPULATIONS?

Systematic Review Protocol

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1. BACKGROUND

Pathogens are considered as one of the major extinction factors (Wilcove et al., 1998). It has been argued that the depletion of genetic diversity within populations may make them more vulnerable to pathogen assault (Altizer et al., 2003; de Castro and Bolker, 2005; O'Brien and Evermann, 1988). Firstly, inbreeding depression associated with population bottlenecks (Keller and Waller, 2002) may limit the ability of individuals to mount an effective immune response. Indeed, inbreeding has been demonstrated to increase susceptibility to infections (Acevedo-Whitehouse et al., 2003; 2005; Coltman et al., 1999; Ilmonen et al., 2008; Reid et al., 2007; Ross-Gillespie et al., 2007; Spielman et al., 2004). Secondly, the loss of variation at genes responsible for resistance to parasites may render populations more susceptible to infection. This argument applies to highly polymorphic vertebrate Major Histocompatibility Complex (MHC) genes, which code for proteins presenting pathogen-derived antigens to T-cells, thus initiating the adaptive immune response (Janeway et al., 2004). Hughes (1991) suggested that retention of variation in these genes is an essential element of effective conservation programmes, but this argument remains controversial: selective breeding aimed at retention of MHC diversity may lead to a decrease in genome-wide heterozygosity and inbreeding depression (Hedrick, 2001). Apart from MHC, other polymorphic genes can influence the effectiveness of defenses against pathogens (Acevedo-Whitehouse and Cunningham, 2006). Here however we concentrate on MHC genes only, as they are the most polymorphic genes known in vertebrates, and their function and evolution is better understood than that of other genes involved in the immune response.

2. OBJECTIVE OF THE REVIEW

2.1 Primary question IS MHC VARIATION IMPORTANT FOR CONSERVATION OF VERTEBRATE POPULATIONS? can be split into three secondary questions:

2.2 Secondary question

(1) CAN DRIFT RENDER MHC LOCI EFFECTIVELY NEUTRAL AND THUS REDUCE THEIR DIVERSITY IN POPULATIONS? (2) CAN REDUCED VARIATION AT MHC INCREASE POPULATION-LEVEL PARASITE LOAD OR PREVALENCE OF DISEASE? (3) DOES REDUCED VARIATION AT MHC INCREASE PROBABILITY OF POPULATION EXTINCTION?

3. METHODS

3.1 Search strategy

Published studies will be identified through searching the ISI Web of Knowledge and Scopus (1996-2008) database and by examining lists of references cited in these studies. The search strategies will use a combination of MHC AND drift for the first question, MHC diversity (or variation) AND infection (or disease, parasite(s), pathogen(s)) for the second question; MHC AND extinction (or population survival or population viability) for the third question. The relevance of a study will be first assessed by reading the title and abstract, and

then by reading full texts of the papers considered relevant. Two reviewers must reach consensus regarding which studies should be included. .

3.2 Study inclusion criteria

- **Relevant subject(s):** populations of any vertebrate species
- **Types of intervention:** Decreased MHC diversity (e.g. through bottleneck)
- **Types of comparator:** No decrease in MHC diversity
- **Types of outcome:** extinction (actual recorded extinction under natural or experimental conditions); assessment of population-level pathogen infection load.
- **Types of study**: the extracted data should include tests of neutrality of MHC genes in populations which have undergone a decrease in population size as well as data on variation at multiple putatively neutral loci; parasite/pathogen loads or disease prevalence in populations differing in the level of MHC variation; recorded extinctions of populations with different levels of MHC variation;
- **Potential reasons for heterogeneity:** variation in methodologies used to test for selection; pathogen type; host life history; host ecology.

3.3 Study quality assessment

The following criteria were used to assess the quality of studies:

- Number of populations
- Sample size per population
- Tests of neutrality of MHC variation
- Tests for signatures of historical balancing selection
- MHC sequence data

3.4 Data extraction strategy

The quantity, quality and type of information available to address the components of this review are currently unknown. Methods for extraction and synthesis are therefore imprecise and will be the subject of protocol amendment prior to commencing this phase of the work.

3.5 Data synthesis

Depending on the number of studies considered relevant: a meta-analysis or qualitative synthesis (tabulation) will be considered.

4. POTENTIAL CONFLICTS OF INTEREST AND SOURCES OF SUPPORT

Funded by Polish Academy of Sciences. We are not aware of any conflicts of interests.

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