FIRST WORKSHOP

"DYNAMICAL SYSTEMS APPLIED TO BIOLOGY AND NATURAL SCIENCES "

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ABSTRACT | Mario Recker

Title

"Competing evolutionary pressures shape the pattern of antigenic switching in malaria"

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Abstract

Many vector or sexually transmitted pathogens prolong infection by continually evading host immune responses in a process of programmed antigenic variation. For the malaria parasite /Plasmodium falciparum/ this entails transcriptional switches between variants of the highly polymorphic /var/ gene family which encodes the immunodominant surface protein and virulence factor PfEMP1. To minimise exposure of its limited antigenic repertoire, expression of single gene variants have to be orchestrated across a whole population of parasite clones during infection.

There is experimental evidence of non-random switching hierarchies, both in terms of on/off rates and the order of expression; however, theoretical work indicates that these are insufficient for maintaining this orchestration over long periods of time. Why then have hierarchical switching patterns evolved? Here it will be shown that highly structured switch pathways can arise through evolutionary trade-off's in pathogens which have to optimise between safeguarding their antigenic repertoire and remaining capable of establishing chronic infections, particularly in non-naive hosts. It will further be demonstrated how these predicted switch pathways underlie /var/ expression of /P. falciparum/ by using longitudinal genome-wide expression data in a series of parasite clones. Together, these results provide a unifying theory of antigenic variation in /P. falciparum/ malaria as a balanced process of antigenic switching and immune mediated selection.