Of mice, flies - and men? Comparing fungal infection models for large-scale screening efforts.

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Abstract

Studying infectious diseases requires suitable hosts for experimental in vivo infections. Recent years have seen the advent of many alternatives to murine infection models. However, the use of non-mammalian models is still controversial, as it is often unclear how well findings from these systems predict virulence potential in humans or other mammals. Here we compare the commonly used models, fruit fly and mouse (representing invertebrate and mammalian hosts) for their similarities and degree of correlation upon infection with a library of mutants of an important fungal pathogen, the yeast Candida glabrata. Using two indices, for fly survival time and for mouse fungal burden in specific organs, we show a good agreement between the models. We provide a suitable predictive model for estimating the virulence potential of mutants in the mouse from fly survival data. As examples, we found cell wall integrity mutants attenuated in flies and mutants of a MAP

kinase pathway defective in both fly virulence and relative fitness in mice. In addition, mutants with strongly reduced in vitro growth were generally, but not always, reduced in fly virulence. Overall, we demonstrate that surveying Drosophila survival after infection is a suitable model to predict outcome of murine infections, especially for severely attenuated mutants. Pre-screening of mutants in an invertebrate Drosophila model can thus give a good estimate of the probability for finding a strain with reduced microbial burden in the mouse host.

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