Predicting the outcome of coinfection using a model of TB in mice.

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Project description:

Most animals, including humans in the developing world, are simultaneously infected by multiple pathogen species, termed coinfection. Coinfecting pathogens often interact with one another and this can affect: i) the number of pathogens within a host, ii) pathogen transmission between hosts, iii) disease severity and iv) the effectiveness of pathogen control measures (e.g. vaccines).

Despite their importance, we know little about the consequences of the vast majority of coinfections, as there are so many possible pathogen combinations that could occur in any given host. Our research team has developed a way to deal with this complexity, creating a theoretical framework by which the consequences of a wide range of coinfections might be predicted [1,2]. We have already tested this framework in one scenario but for the framework to be useful in a practical context we need to develop it further and test it for a range of pathogen coinfections.

This PhD will test our predictive framework using laboratory mice. The effect of coinfection with the core pathogen Mycobacterium manresensis and a wide range of other pathogen species, including helminths, bacteria and viruses will be assessed. With our collaborator's at Hospital Germans Trias i Pujol in Barcelona, we will first undertake individual pathogen infections, recording the pathogen burdens and host immune response and pathology. We will use these data to develop and parameterise a mathematical model based on our predictive framework and then apply that model to predict the outcome of combined infections of M. manrensis and the other pathogen species. Finally, we will test and validate our model in a series of coinfection experiments. The project will combine in vivo experiments, immunology and pathology assays with statistical and mathematical modelling, providing the successful candidate with unprecedented level of interdisciplinary training.

The project is at the cutting edge of research on coinfection, a rapidly expanding research field. Further, our mouse model of TB mirrors this disease in other animals and humans. TB is a cause of severe economic losses and animal welfare issue within the agricultural industry worldwide. In the UK alone TB management and control cost around £50M per annum. In humans TB is one of the most important infectious diseases killing around 1.5 billion people per year. Overall, therefore, this PhD will provide the student with the skills and knowledge for a wide range of future career choices.

[1] http://dx.doi.org/10.1098/rspb.2017.2610 [2] http://dx.doi.org/10.1017/S003118200800038