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Gene expression profiling of TB challenge in BCG-vaccinated and unvaccinated Cynomolgus Macaques to identify potential correlates of protection

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AIM: The development of an effective vaccine against tuberculosis would be a significant step in tackling the pandemic currently faced and is a key goal for numerous research groups worldwide. A major hurdle to this development is the lack of biological markers indicative of protective immunity for tuberculosis (correlates of protection). Non-human primates potentially represent the most relevant model for evaluation of new vaccines because of the close similarities to human tuberculosis infection, particularly in the immune responses and disease pathology induced.

METHOD: To identify potential correlates of protection, RNA from PPD-stimulated peripheral blood mononuclear cells taken from BCG-vaccinated and unvaccinated cynomolgus macaques before and after tuberculosis challenge, was analysed using a genome-wide macaque microarray. Differentially expressed (DE) genes were identified and related to the ability to control progression of TB-induced disease.

RESULTS: 825 genes were DE across all groups i.e. vaccinated or unvaccinated animals able to control disease progression and unvaccinated animals in which disease progressed, representing a common response to tuberculosis infection. 327 genes were DE in animals which controlled disease progression, regardless of vaccination status and164 genes were DE only in vaccinated animals which successfully controlled disease, indicating a potential vaccine-induced protective response. Animals unable to control disease progression exhibited an additional 2086 DE genes after challenge, possibly associated with an overall lack of control in response to infection.

CONCLUSIONS: Using a genome-wide microarray to analyse the expression of thousands of genes simultaneously provides an unbiased approach to identifying potential biomarkers of disease and protection.

Biography

Alice Hicks is in the final year of her PhD with the Health Protection Agency and St George's University of London, having previously worked with microarrays in the Diagnostic Technologies department. Alice gained her Masters degree in Medical and Molecular Microbiology in 2007 from University of Manchester, UK, where she came top of her class.