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Rational vaccine design against complex pathogens in the OMICS era

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Vaccines are the most efficient health care intervention for global public health but vaccines against many diseases caused by complex pathogens are still not available despite intense research. A significant advance of the past decade has been the elucidation of the genome, proteome and transcriptome of many pathogens. These datasets provide the foundation for genome-based approaches to identify target antigens for rational vaccine design. Using malaria as a model, we are pursuing a multi-pronged approach using technology platforms including protein microarrays, high throughput protein production, and epitope prediction algorithms, with specimens from humans, or animals naturally or experimentally exposed to malaria. We have established that T cell and antibody responses to the Plasmodium parasite are broadly distributed throughout the proteome, and have identified many novel antigens that are more immunogenic than antigens currently considered as high priority vaccine antigens. Importantly, the subsets of antigens preferentially recognized by T cells are distinct from the subset targeted by antibodies. We have further integrated and analyzed our comprehensive antibody and T cell datasets to identify specific features associated with antibody or T cell immune reactivity. Our data significantly expand our knowledge base of targets of host-parasite immunity and suggest that distinct vaccine approaches and antigen targets are required depending on whether antibodies or T cells are the desired vaccination outcome. Such genome-based vaccine approaches may overcome the problem of poorly efficacious vaccines that has plagued vaccine developers for many years.

Biography

Denise Doolan is a molecular immunologist who heads the Molecular Vaccinology Laboratory at the QIMR Berghofer Medical Research Institute. She is an NHMRC Principal Research Fellow and was previously a Pfizer Australia Senior Research Fellow. Her research investigates the molecular basis of immunity, with a focus on malaria and rational vaccine development. Her research program encompasses core themes of: (i) immune mechanisms; (ii) antigen and epitope discovery from genomic sequence data; and (iii) molecular vaccine technologies. She has published over 120 research articles, is an inventor on a number of patents, and has been a consultant for a number of biotechnology companies.

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