Identification of Protective Epitopes for a Multiepitope Schistosomiasis Vaccine: Insights from Human and Animal Models

Mariana Ivo Khouri[1], Fernanda Maria Lessa Carvalho[1], Cléber Pereira da Silva[1], Ronald Alves dos Santos[2], Almiro Pires da Silva Neto[1], Bruna Souza Santos Oliveira[2], Robert Alan Wilson[3], Luciana C. C. Leite[4], Ricardo Riccio Oliveira[2], Leonardo Paiva Farias[1]

[1] Laboratório de Medicina e Saúde Pública de Precisão, Instituto Gonçalo Moniz, Fiocruz, Salvador – BA, Brasil.
[2] Laboratório de Investigação em Saúde Global e Doenças Negligenciadas, Instituto Gonçalo Moniz, Fiocruz, Salvador – BA, Brasil
[3] York Biomedical Research Institute, University of York, York, United Kingdom
[4] Laboratório de Desenvolvimento de Vacinas, Instituto Butantan, São Paulo, Brazil

Schistosomiasis is endemic in 78 countries and has the highest morbidity among helminth infections. A vaccine would be a valuable tool for control and elimination. Most vaccines tested so far have targeted single antigens, none reaching final development. We propose using multiple immunogenic epitopes at the host-parasite interface, associated with protective immune responses. Our group mapped protective epitopes in murine models immunized with attenuated cercariae and in auto-cured rhesus macaques. This study aims to identify epitopes uniquely recognized in resistant to reinfection (RR) individuals versus susceptible (SR) ones in a schistosomiasis-endemic area and compares them with those previously identified in animal models. To achieve this, sera collected 18 months after Praziquantel treatment were used to screen peptide microarrays containing 55 secreted or exposed proteins from the alimentary tract or tegument. The most reactive epitopes were found in Sm25 and ADP-ribosyl cyclase (tegument), MEG-12, MEG-4.1, and LAMP (alimentary tract). Notably, two tegument targets (Sm25 and ADP-ribosyl cyclase) displayed three epitopes differentially recognized by RR sera. In general, RR individuals recognized more tegument epitopes, while SR individuals recognized more alimentary tract epitopes. Immunohistochemistry confirmed that RR individuals showed a stronger response against native tegument proteins than SR individuals. We then compared these epitopes with those previously mapped in protected animal models. Mice recognized 126 epitopes, human 56, and rhesus macaques 38. Our findings highlight the specificity and diversity of the humoral response in each model. Despite the high number of epitopes identified, only 11 were shared across all three models - two from the tegument and nine from the alimentary tract. In conclusion, these epitopes warrant further evaluation as vaccine candidates.

Financial Support: Fiocruz VPPCB-007-FIO-18-2-45; PROEP/IGM/2020 - EDITAL N° 01/2020; CNPq 431155/2018-6; FAPESP 2017/24832-6

Keywords: Schistosoma mansoni, vaccine, epitopes