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Mycobacterial RD antigens as diagnostic and vaccine candidates

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The currently available diagnostic tools and BCG vaccine for tuberculosis are not adequate. There is an urgent need to identify the novel candidate antigens for specific and early diagnosis as well as effective vaccine. Analysis of virulent *Mycobacteriun tuberculosis* genome has shown the presence of regions of deletion (RD) that are deleted in BCG vaccine and till now 16 such regions (RD1-RD16) have been identified. The immune dominant RD proteins seem to be the ideal candidates for diagnostic and vaccine tools particularly due to absence of many of these from BCG vaccine and environmental mycobacterium. Earlier we have shown the antibodies to four RD antigens in the patients of pulmonary tuberculosis. Epitope mapping of these antigens lead to identification of four immune dominant peptides and antibodies to these peptides were detected in the sera of specifically TB patients not in a closely mimicking disease Sarcoidosis. To identify additional such B–cell epitopes, RD1-RD16 proteins were subjected to bio-informatic analysis and the epitopes from cell surface expressed RD proteins have been identified to be further used for the development of diagnostic assay. The predicted MHC binding T-cell epitopes of RD proteins were also screened in TB patients and healthy household contacts and a combination of three selected peptides has been investigated for its immunogenicity as well as protection against experimental tuberculosis. The results of our study indicate that carefully selected combination of peptides from RD proteins could be used for specific diagnosis as well a potent vaccine against tuberculosis.

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The central role of abscisic acid in regulating egress of two different intracellular stages of malaria parasite *Plasmodium falciparum*

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The release of intra erythrocytic parasites is a fundamental step during blood-stage propagation and transmission of the malaria parasite from the human to the mosquito. Although considerable advances have been made in our understanding of the unique exit mechanisms, the signal that triggers the egress of these different intra erythrocytic stages are not known. Herein, we demonstrate that abscisic acid (ABA) a phyto-hormone that is produced in blood stage parasites plays a critical role in regulation of Ca^{2+}dependent egress of both invasive merozoites and activated gametocytes. Extracts of *Plasmodium falciparum* analyzed by LC-MS/MS at different time points during the blood stage life cycle revealed a marked spike in ABA levels in late schizonts. Use of herbicide fluridone (FLU), an inhibitor of ABA biosynthetic pathway, reduced the levels of ABA and blocked egress of merozoites as well as of activated gametocytes. Further, addition of exogenous ABA triggered intracellular Ca^{2+} release in late stage schizonts and also rescued egress of FLU-treated merozoites and gametocytes from the host erythrocyte *P. falciparum* perforin like proteins PfPLP1 and PfPLP2, which were previously shown to mediate host cell membrane permeabilization during egress of both merozoites and gametocytes, respectively, did not localize to the erythrocyte membrane in FLU-treated infected erythrocytes. These results indicate that ABA synthesis in malaria parasites is a critical step for egress of both merozoites and activated gametocytes. The ABA biosynthesis pathway, which is found in plants and absent in mammalian cells can be explored to identify target to limit blood stage parasite growth and transmission of malaria parasites.

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