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The road to a sterilizing vaccine for murine schistosomiasis mansoni using larval excretory-secretory molecules and papain or type 2 cytokines as adjuvant

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Schistosome larval excretory-secretory products (ESP) such as glyceraldehyde 3-phosphate dehydrogenase (SG3PDH), aldolase (ALD), 2-cys peroxiredoxin (TPX), readily initiate systemic immune responses and are targets for immune effector antibodies and cells. ESP essentially induce T helper (Th) 1 and Th17 immune responses during natural infection. Such immune environment promotes production of nitric oxide and hydrogen peroxide by interferon-gamma-activated monocytes, and interleukin (IL)-17-mediated recruitment and activation of neutrophils, yet, likely prevents engagement of eosinophils and basophils in the hunt for developing larvae in blood capillaries. We reasoned that polarizing ESP-induced immune responses towards a Th2 phenotype, via the use of papain or type 2 cytokines would lead to almost total parasite elimination. In a series of 8 independent experiments, outbred CD1 mice were immunized with 10 μg recombinant SG3PDH (rSG3PDH) and 15 μg ALD- or TPX-derived peptide in a MAP (multiple antigen peptide) construct in conjunction with 10 μg papain or 300 ng thymic stromal lymphopoietin (TSLP), IL-25, or IL-33 as adjuvant. Two weeks later, untreated, adjuvant controls, and immunized mice were challenged with 100 or 120 cercariae of Schistosoma mansoni. These formulations elicited IgG1 and IgA specific antibodies, and robust increase in ex vivo spleen cells release of IL-4, IL-5, and IL-13. Immunization with rSG3PDH and ALD MAP led to significant ($P < 0.005$ and < 0.002) reduction in challenge worm burden in comparison to untreated, infection control mice of 42% and 47%, respectively with TSLP or papain as adjuvant. Immunization with rSG3PDH and TPX MAP led to significant ($P < 0.0001$) reduction in challenge worm burden of about 66% with either papain, TSLP, or IL-25, and 77% with IL-33 as adjuvant. These results support our assumption that improvement of ESP selection, singly or in a combination, and immunization regimen, namely ESP and cysteine protease or type 2 cytokine dose and injection site and schedule, will likely lead to a sterilizing schistosomiasis vaccine in a foreseeable future.

Biography

Prof. Dr. Rashika A.F. El Ridi, Zoology Department, Faculty of Science, Cairo University, Egypt, 1986- Professor of Immunology, Zoology Department, Faculty of Science, Cairo University, Tenure position, 1981-1986 Associate Professor of Immunology, Zoology Department, Faculty of Science, Cairo University.

1976-1981 Lecturer of Immunology,Zoology Department,Faculty of Science, Cairo University. 1990-2000 Director of Schistosomiasis Research, Biomedical Research Center,Egyptian Organization for Sera and Vaccines, Cairo, Egypt. April through October 1995, Visiting Scientist at the Department of Infectious Diseases, Harvard School of Public Health, Boston, MA, USA. October 1995-July 1996, Visiting Scientist at the Department of Parasitology, Hirosaki University, Hirosaki, Japan Responsibilities involved teaching the different branches of immunology to under- and post-graduate students; directing research in immunology funded by NIH, Sandoz Gerontological Foundation, Schistososomiasis Research Project (SRP), the Egyptian Academy of Scientific Research and Technology; the International Centre for Genetic Engineering and Biotechnology and the World Health Organization; the Arab Foundation for Science and Technology; supervising 60 M. Sc. and 30 Ph.D. Theses. Obtained for these continuous efforts the State Award of Excellence in High-Tech Sciences, 2002,the Cairo University Award for Recognition in Applied Sciences, 2002, and the D.Sc. degree in Immunobiology 2004.

Awards: Egyptian State Award of Excellence in High-Tech Sciences, 2002. The Cairo University Award for Recognition in Applied Sciences, 2002. D.Sc. Degree in Immunobiology, 2004, by Cairo University, following positive evaluation of the D.Sc. Thesis by three independent Referees from the United Kingdom. L'Oreal-Unesco for Women in Science 2010. Egyptian State Award of Merit and Recognition in High-Tech Sciences, 2010.

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