Sm-p80-based schistosomiasis vaccine: Preparation for human clinical trials

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Science ranked schistosomiasis vaccine as one of the top 10 vaccines that need to be urgently developed

(January 1, 2016, 351:16-19)

- Reliance on repeated treatment with praziquantel not adequate, infection rates continue to be high
- Development of drug resistance by the parasite?
- Durable reduction in the disease spectrum and transmission via vaccination linked with chemotherapy?
- A vaccine would contribute to the reduction of schistosomiasis morbidity through induced immune responses

1. ***Neglected Tropical Diseases: Defining Opportunities to Accelerate Translational Research. NIAID/NIH, Bethesda, MD (March 9-11, 2011)***
2. ***Schistosomiasis Elimination Strategy and Potential Role of Vaccine in Achieving Global Health Goals Meeting, NIAID/NIH and the Bill & Melinda Gates Foundation, Seattle, WA (March 12-13, 2013)***

Preferred product characteristics, NIAID/NIH, Bethesda, MD (Vaccine, 2016, 34:995; Trends Parasitol.2017, 33:194)

Acceptable features for a prophylactic schistosomiasis vaccine (Reduction in morbidity, rather than sterile immunity is the immediate target)	
Indication ✓	Prevention of infection by one of the three human schistosome parasites
Target Populations ✓	Population in endemic countries • Adults (18-59 years of age) in high-risk occupations or areas • High risk school age children (3-12 years of age)
Efficacy ✓	Reduce at least 75% infection by one of the schistosome species (Efficacy readout: egg output and/or worm burden)
Duration of Protection ✓	2-3 years after last dosing
Dosage and Cost	Parenteral administration, 2 doses administration Less than $1/dose
Product Criteria ✓	• The vaccine antigen should not react to IgE from target population • Can be co-administered with local MDA/other interventions
Manufacturing ✓	Suitability for human trials: purity > 90% (Yield ~ 50 mg/L) Endotoxin levels < 50 EU/mg

Vaccination strategies using Sm-p80

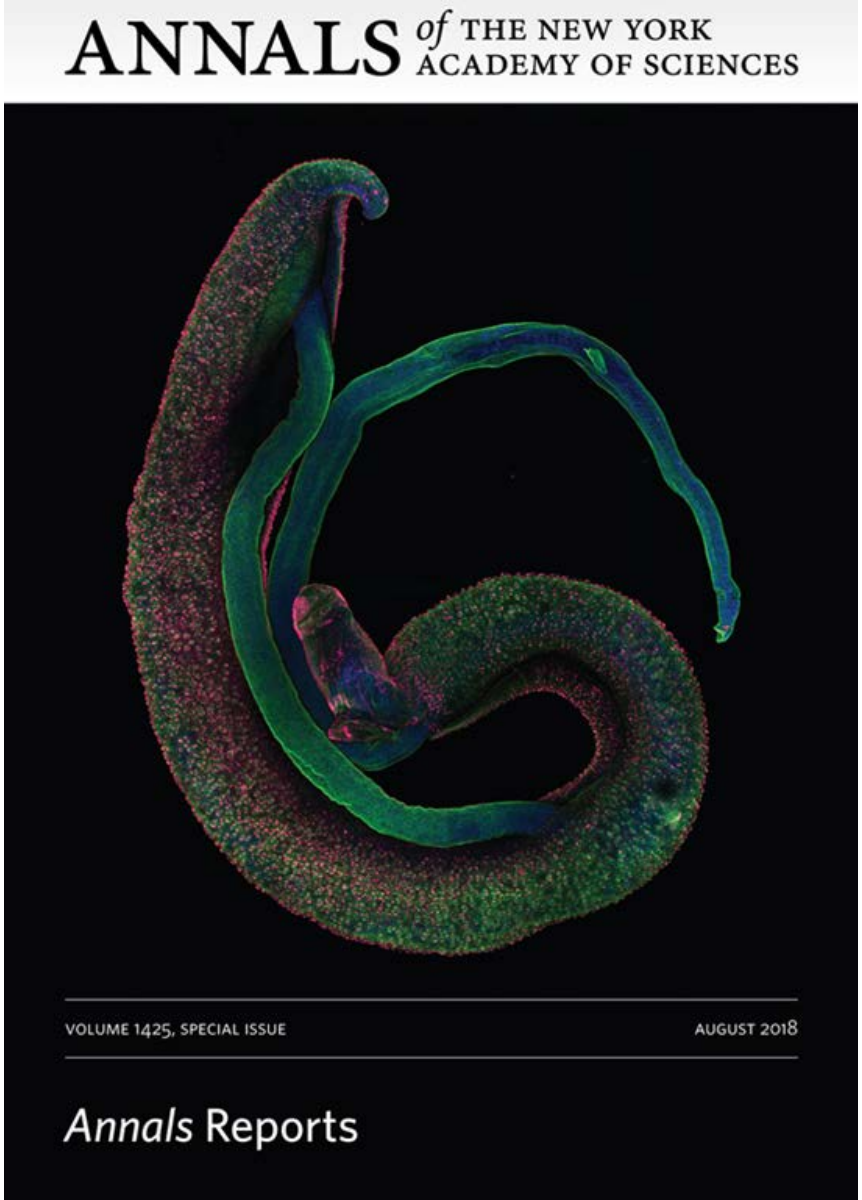
Sm-p80 has been tested for its prophylactic efficacy in different vaccine formulations and approaches

- DNA
- Recombinant protein/adjuvant
- Prime/boost

Sm-p80-based vaccine formulations have been tested in three experimental animal models of infection and disease

- Mouse
- Hamster
- Baboon

Sm-p80-based schistosomiasis vaccine: double-blind preclinical trial in baboons demonstrates comprehensive prophylactic and parasite transmission-blocking efficacy
Ann. N.Y. Acad. Sci. 1425 (2018) 38–51.



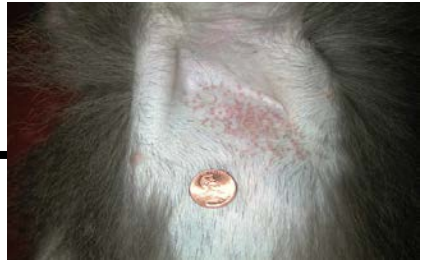
A typical prophylactic vaccine efficacy protocol

Week 0 — Primary immunization

Week 4 — First boost

Week 8 — Second boost

Week 12 — Challenge with schistosome cercariae



Week 20-24 — Necropsy

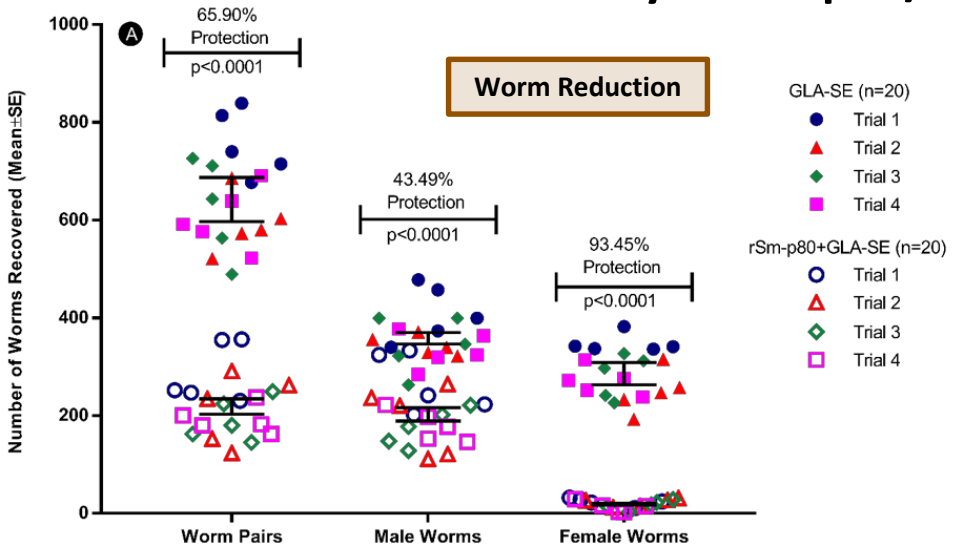
Control groups of baboons:

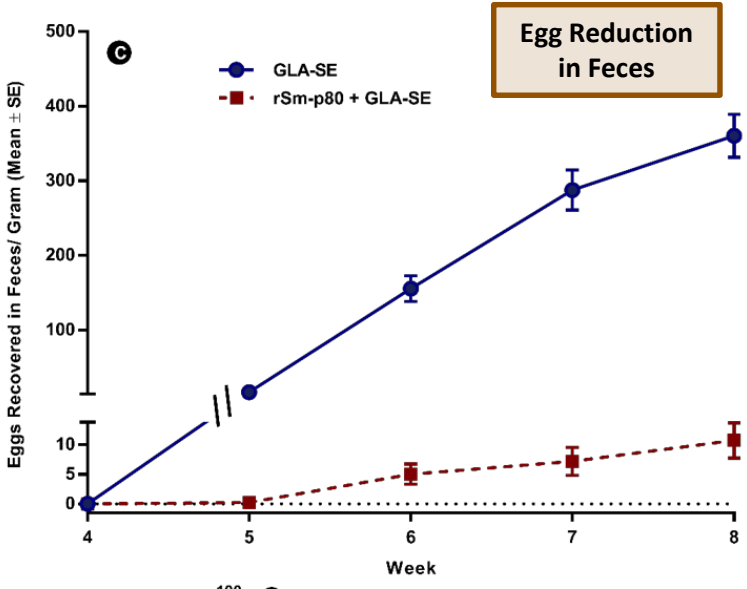
- Received only the delivery vehicle and no antigen
- Were challenged with the same number of larvae

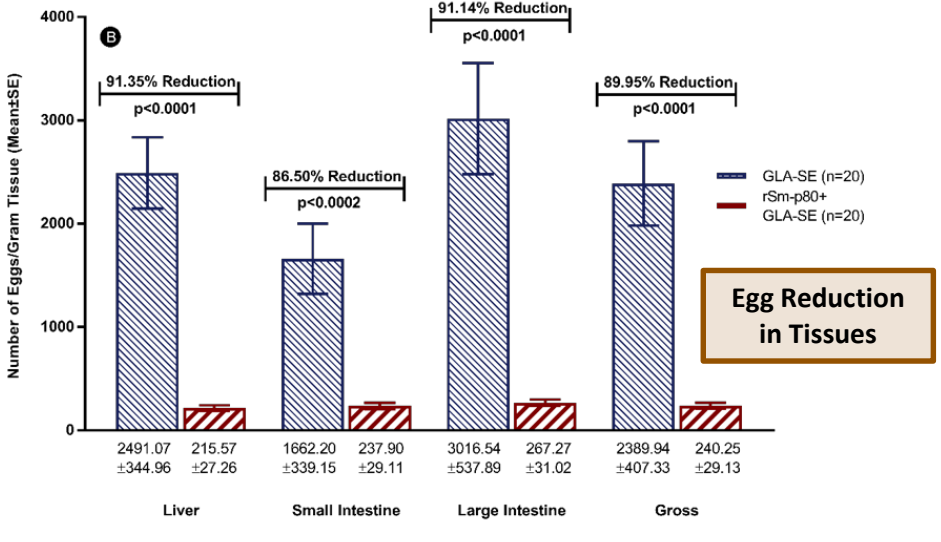
Number of worms recorded and compared with controls and % reduction in number of worms was determined

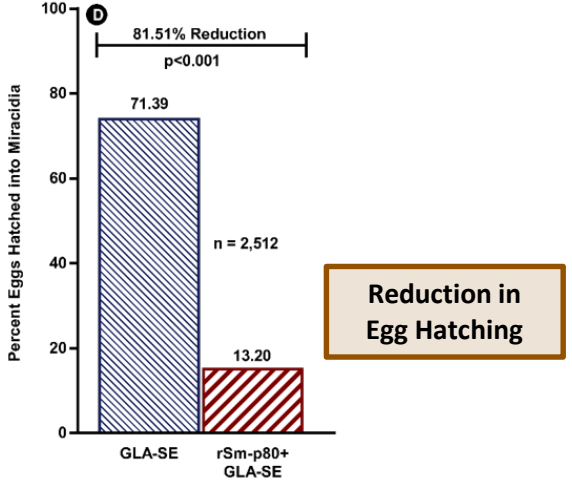
Reduction in the number of eggs in tissues (liver and intestine) and egg hatching ability was determined

Efficacy of Sm-p80/GLA-SE Vaccine





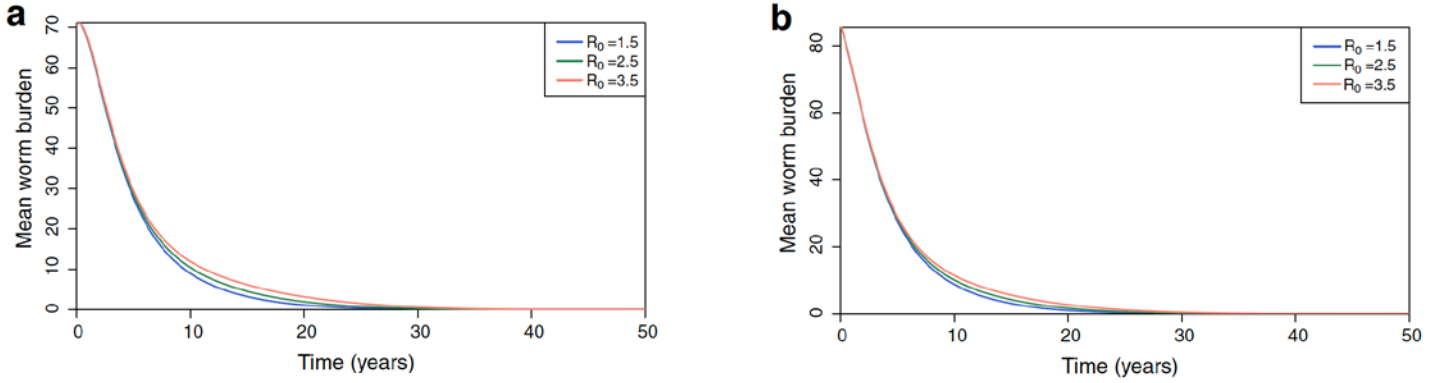




Modeling Studies Using Our Sm-p80/GLA-SE Data

Imperial College: Sir Roy Anderson

Mathematical model for the evaluation of the potential impact of a partially efficacious vaccine on the transmission dynamics of Schistosoma mansoni in human communities (Parasites & Vectors 201710:294).



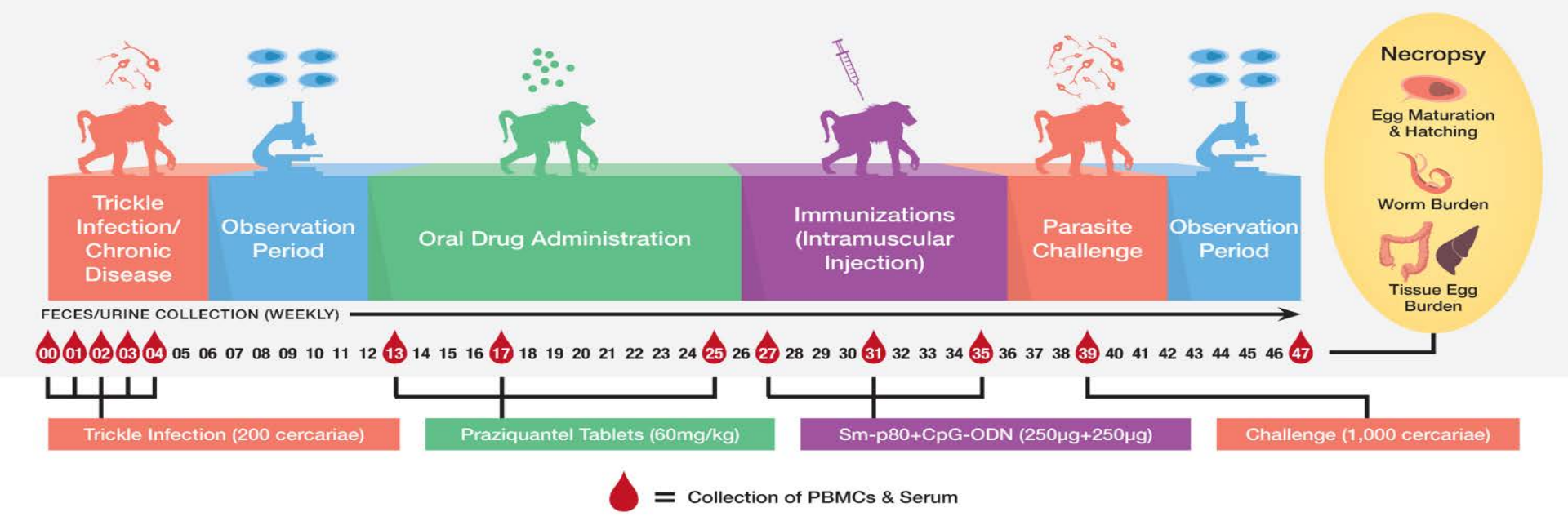
The impact of the transmission setting, R_0, for Model 1 on the temporal trend in the mean worm burden M, with 80% vaccine efficacy on parasite establishment only, i.e. $v_1 = 0$, $v_2 = 0$, $v_3 = 0.80$, for (a) p = 70% and (b) p = 85%. The starting value for the mean worm burden is M_0 = 100 per host and the vaccine protection is assumed to be lifelong, i.e. $\omega = 0$

- Vaccine efficacy of 60% will interrupt transmission in communities with low and moderate transmission.
- For high transmission settings, higher vaccine efficacies are required to interrupt transmission or multiple booster vaccine doses each year may be necessary.
- Vaccine that impacts either on worm establishment, worm fecundity or adult parasite survival in the human host is almost equally beneficial [all of theses are targeted by Sm-p80-based vaccine].
- Model shows that breaking transmission in even low intensity transmission areas, may take 18 years or more.

Deployment of Sm-p80-based vaccine

- **Approach:** Mass Drug/ Vaccine Administration or MDVA

Schematic representation of experimental design mimicking natural conditions of schistosomiasis in field conditions



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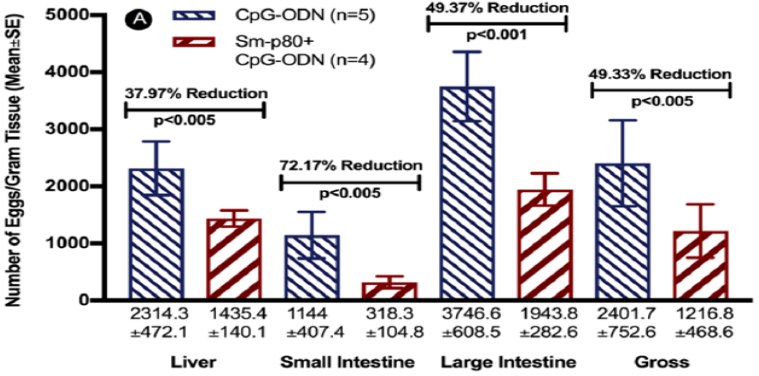
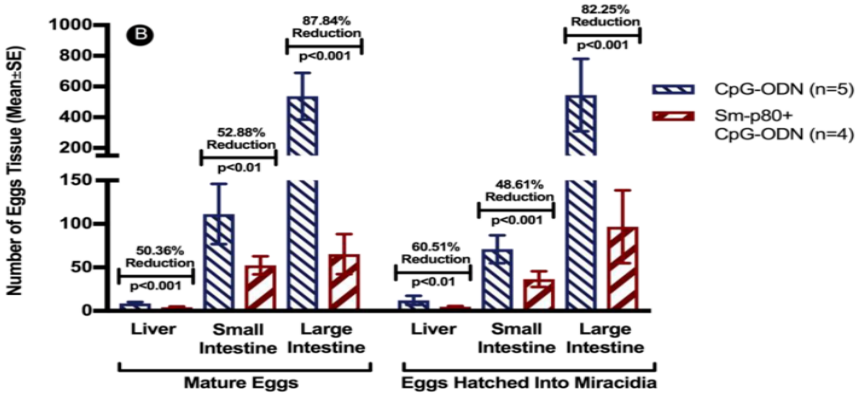
Vaccine efficacy in simulated conditions of endemic areas

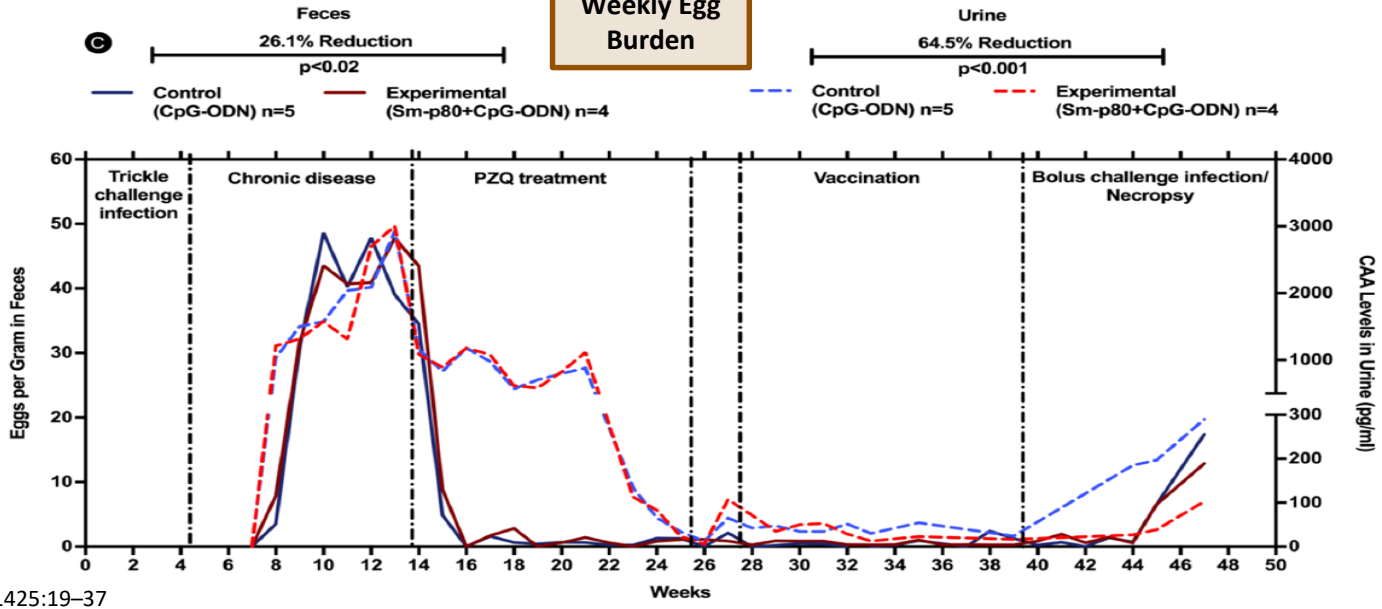
Egg Reduction in Tissues



Reduction in Egg Hatching



Weekly Egg Burden



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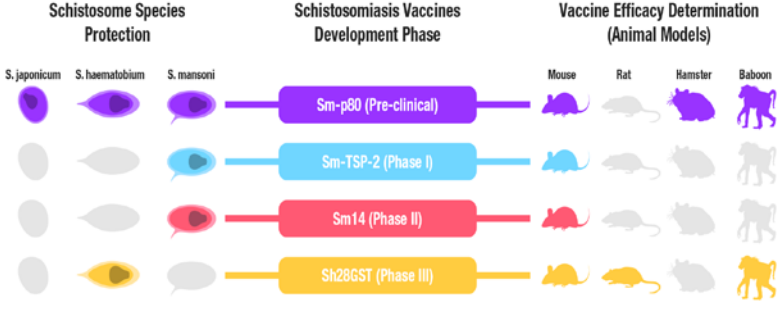
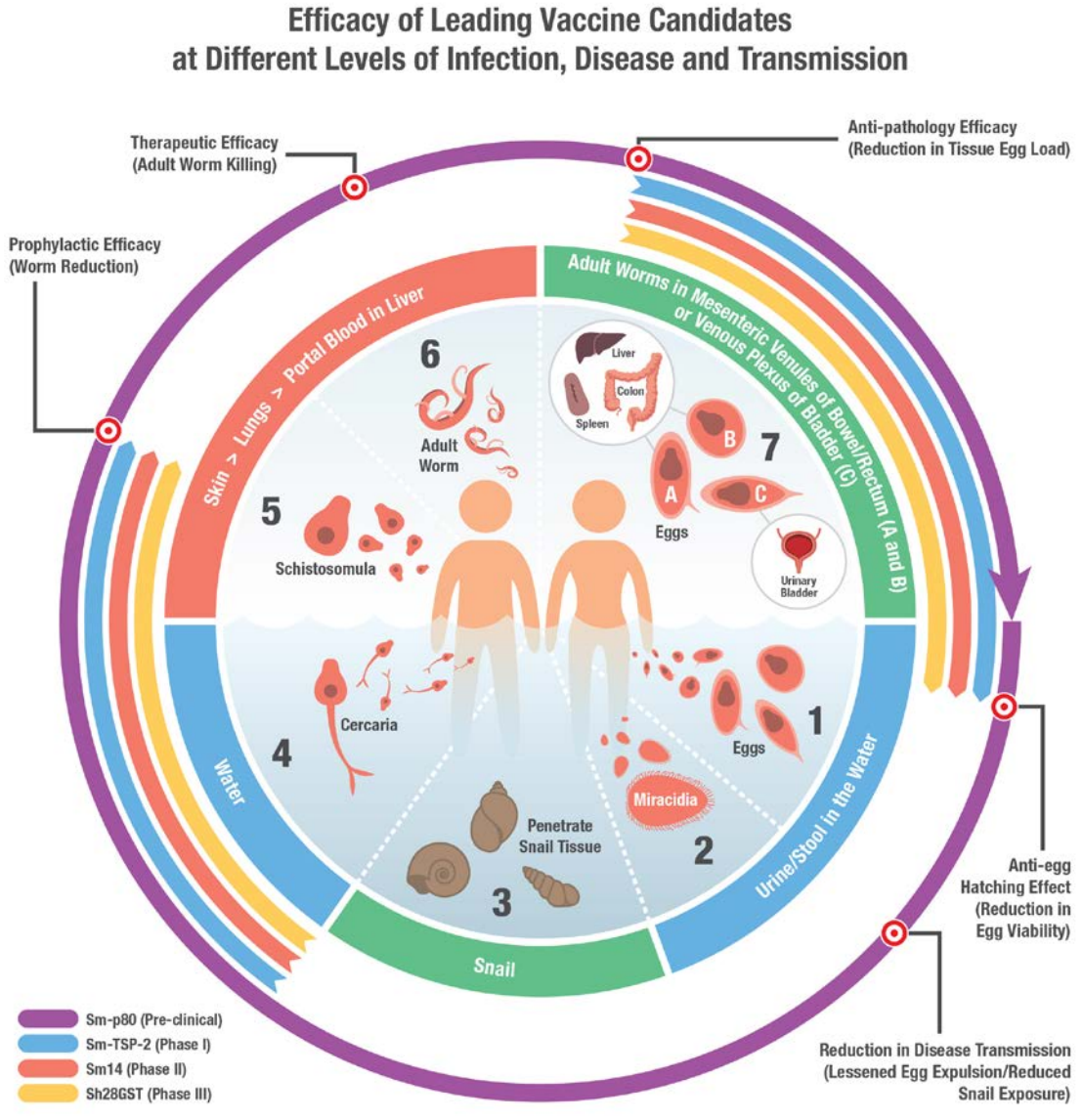
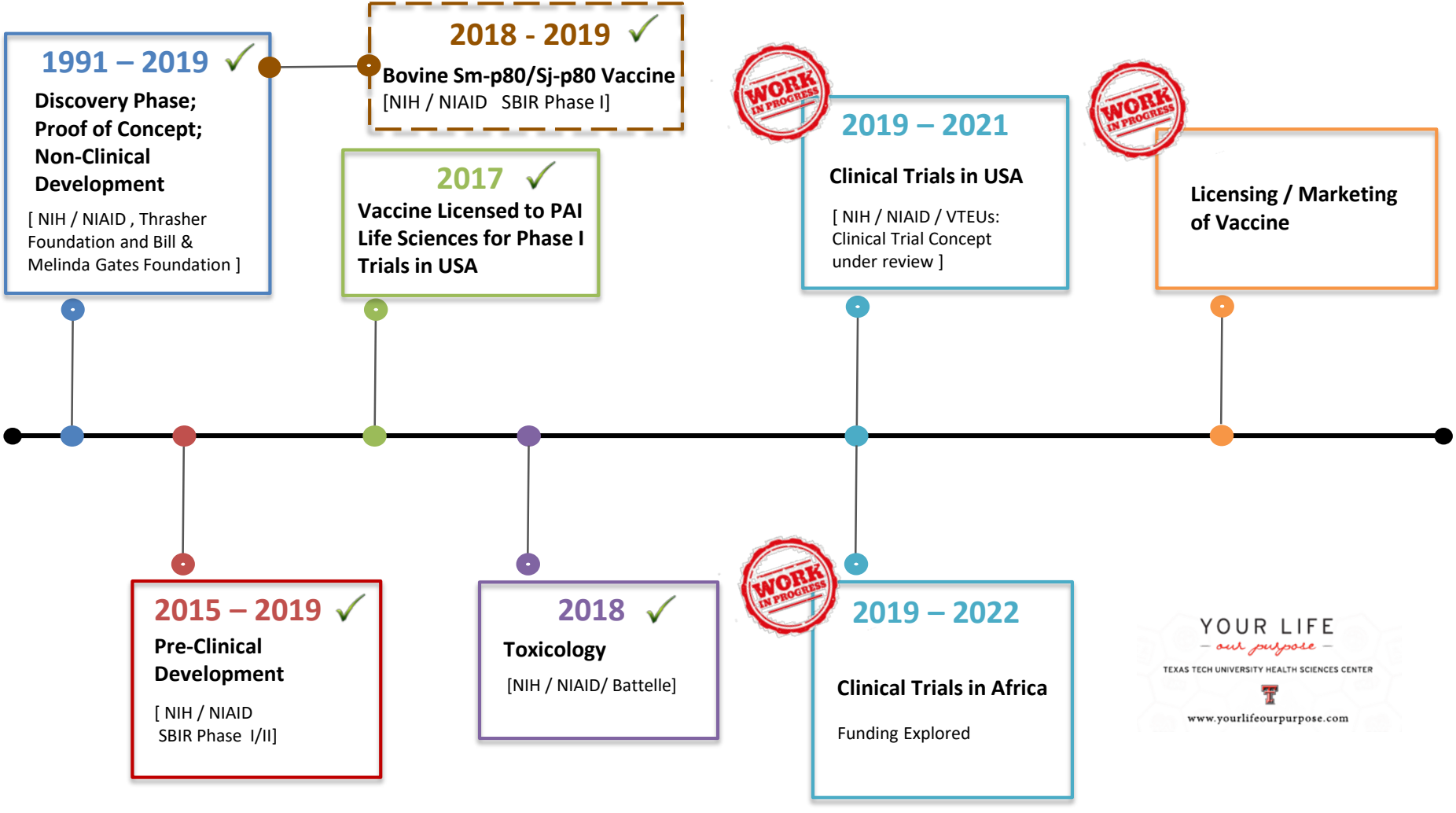
Summary from Published Literature





Roadmap for Sm-p80/GLA-SE Vaccine (SchistoShield®)

(U.S. Patent No. 9,248,169; India Patent No. 10079/DELNP; Chinese Patent No. 201080035900X; Brazilian Patent No. 1015136-2)



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