

Targets for drug design in schistosome parasitism

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Schistosomiasis

It is a chronic disease that affects more than 200 million people in 74 tropical and subtropical countries, and over 500 million people are estimated to be at risk of Schistosomiasis (WHO, 2005).

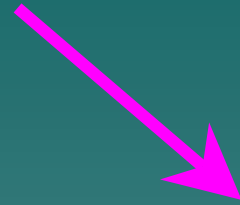
Schistosomes



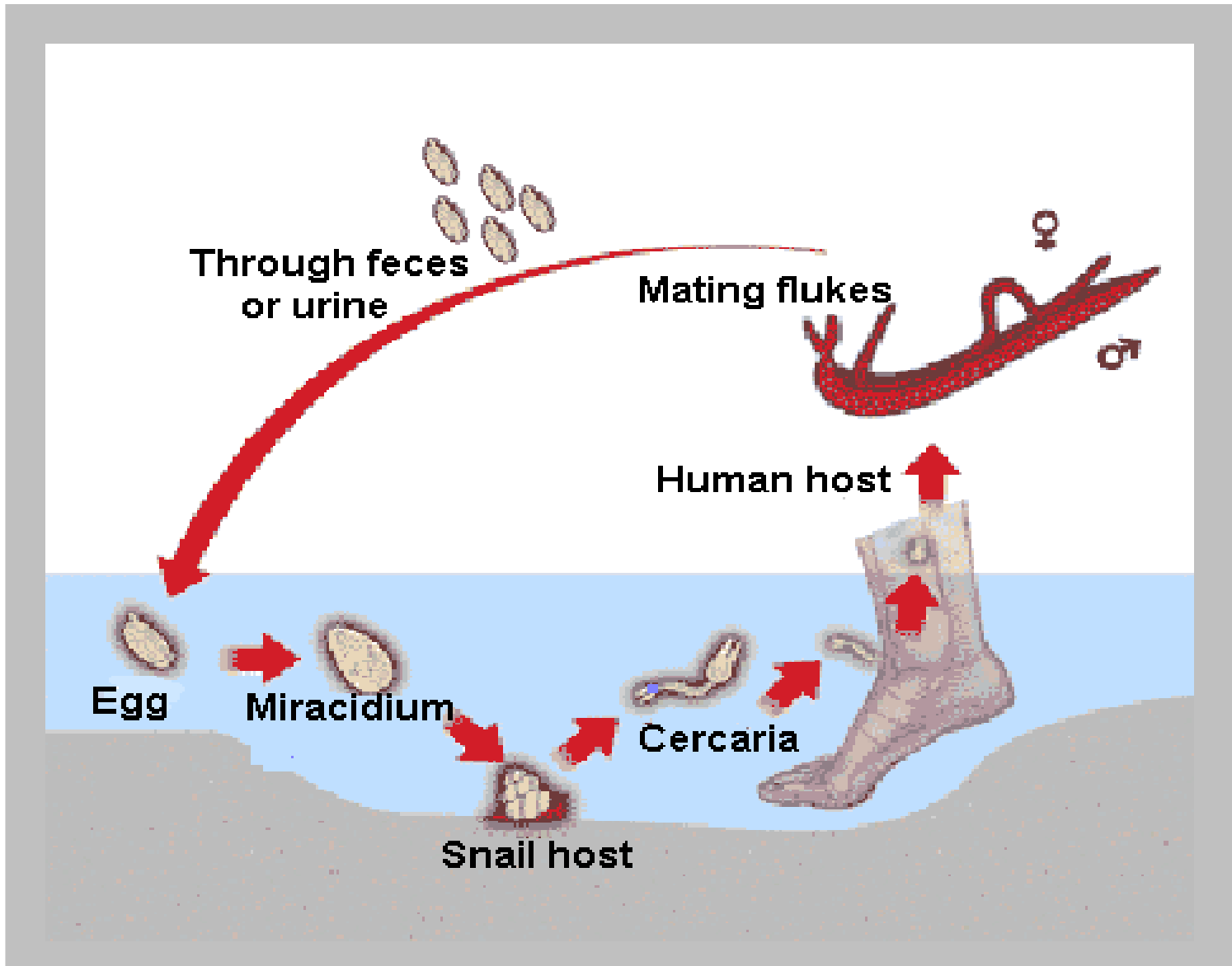
Molluscan Snail Hosts



- *Biomphalaria* (*S.mansoni*)
- *Bulinus* (*S.haematobium*)-



Definitive Human Hosts



Schistosome Life Cycle

Control of Schistosomiasis

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graph TD; A[Control of Schistosomiasis] --> B[Health education]; A --> C[Snail control]; A --> D[Vaccine development]; A --> E[Drugs (Praziquantel)];
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Health education

Snail control

Vaccine development

Drugs
(Praziquantel)

Success in the control of the disease is usually measured by:

- Inhibition of cercarial penetration
- Decreased worm burden (liver & intestinal)
- Reduced egg count
- Reduced number and diameter of granuloma

Cercarial penetration of mammalian skin



Cercarial targets

Sm Stathmin-Like protein

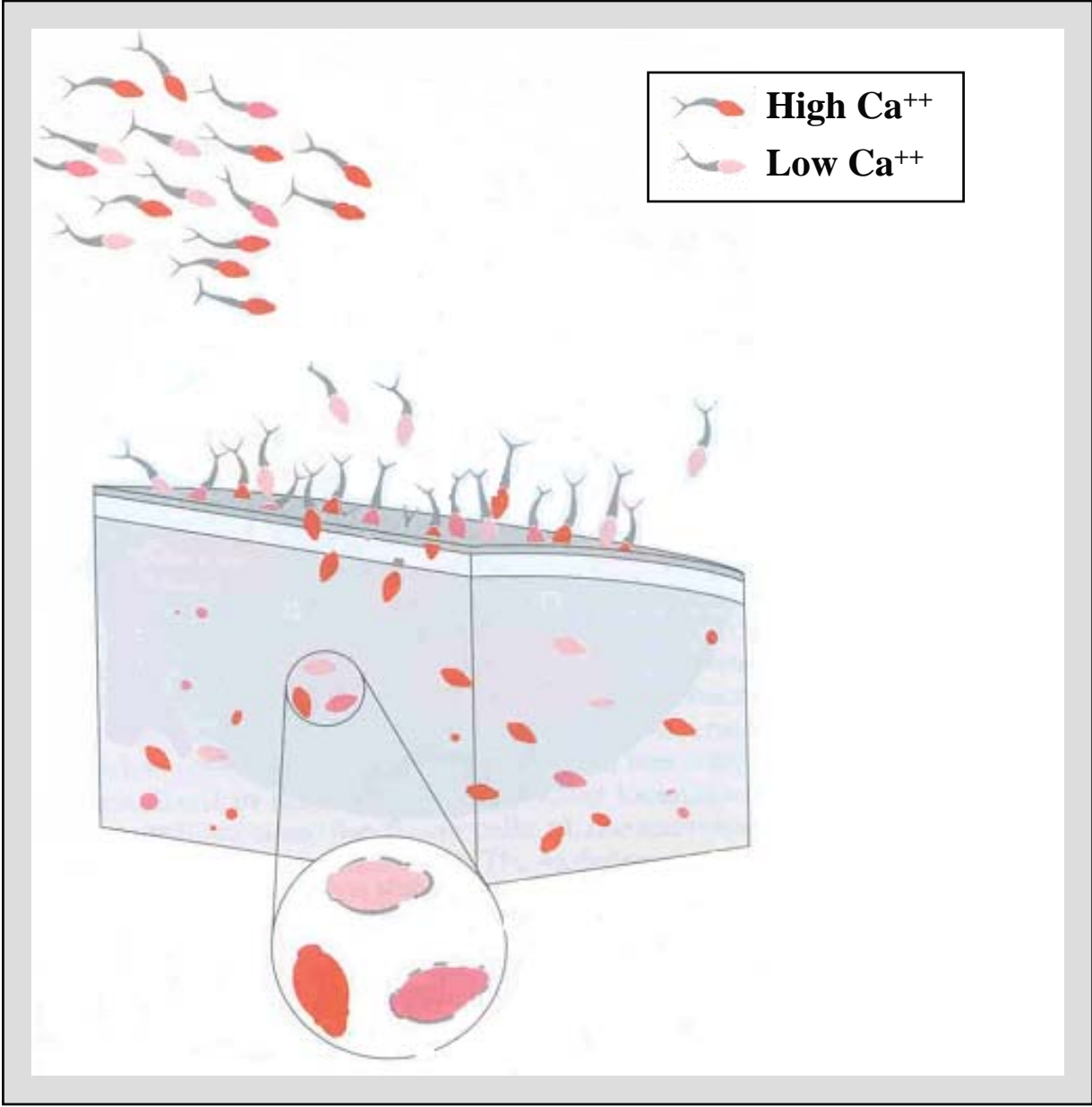
Elastase

Tryptophan hydroxylase

Ca⁺⁺-binding protein 28KDa

Role of Calcium

- Prevent damage of cercarial membrane
- Enhance tail loss
- Prevent dispersal of glycocalyx (i.e. delay presentation of antigens)





Adult Worm Targets

**Sm Gynecophoral
Protein**

**Sm Fatty acids
Binding
Protein**

Glucose uptake

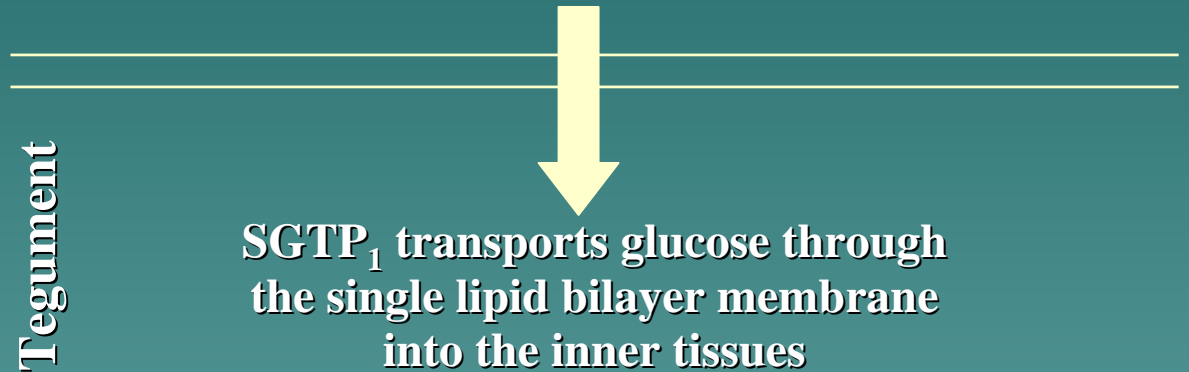
Host immunity

Glucose transporter

➤ SGTP1

SGTP₄ transports glucose from the bloodstream through the apical double bilayer membrane into the tegument

➤ SGTP2



➤ SGTP4

SGTP₁ transports glucose through the single lipid bilayer membrane into the inner tissues

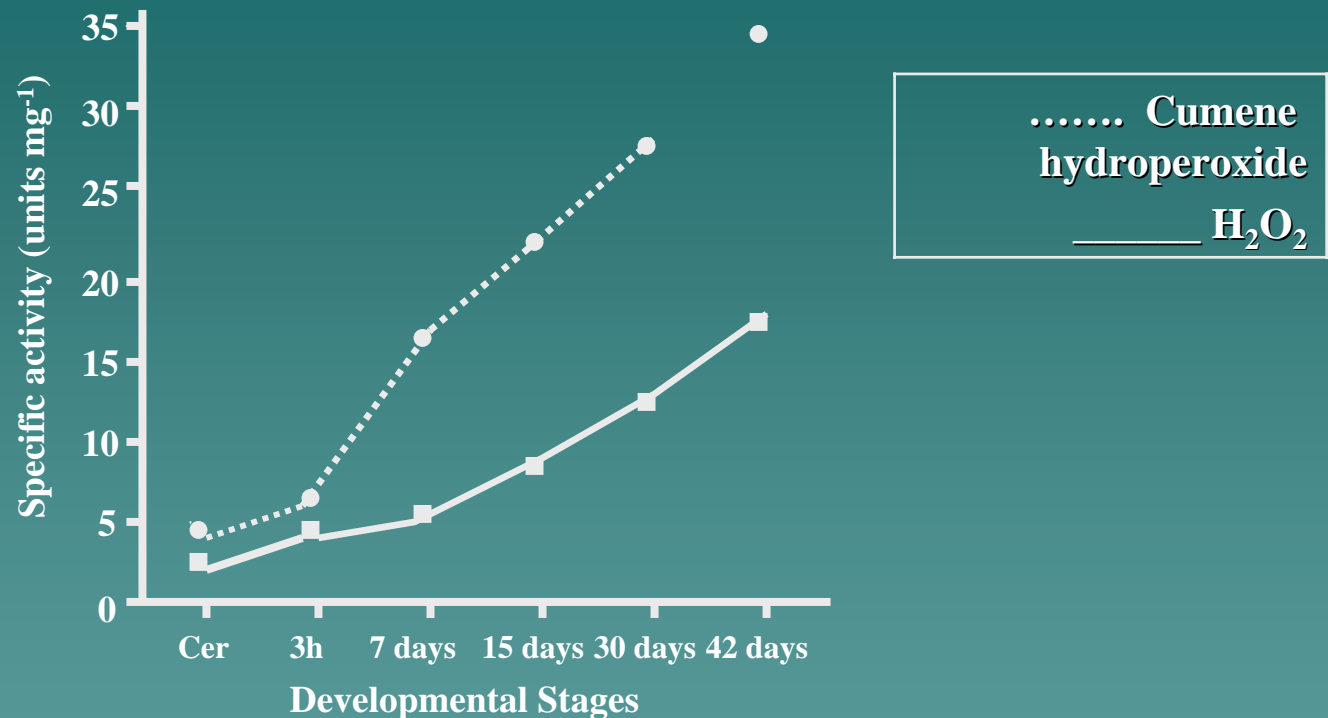
Diagrammatic representation of glucose movement through the tegument.

Host immunity

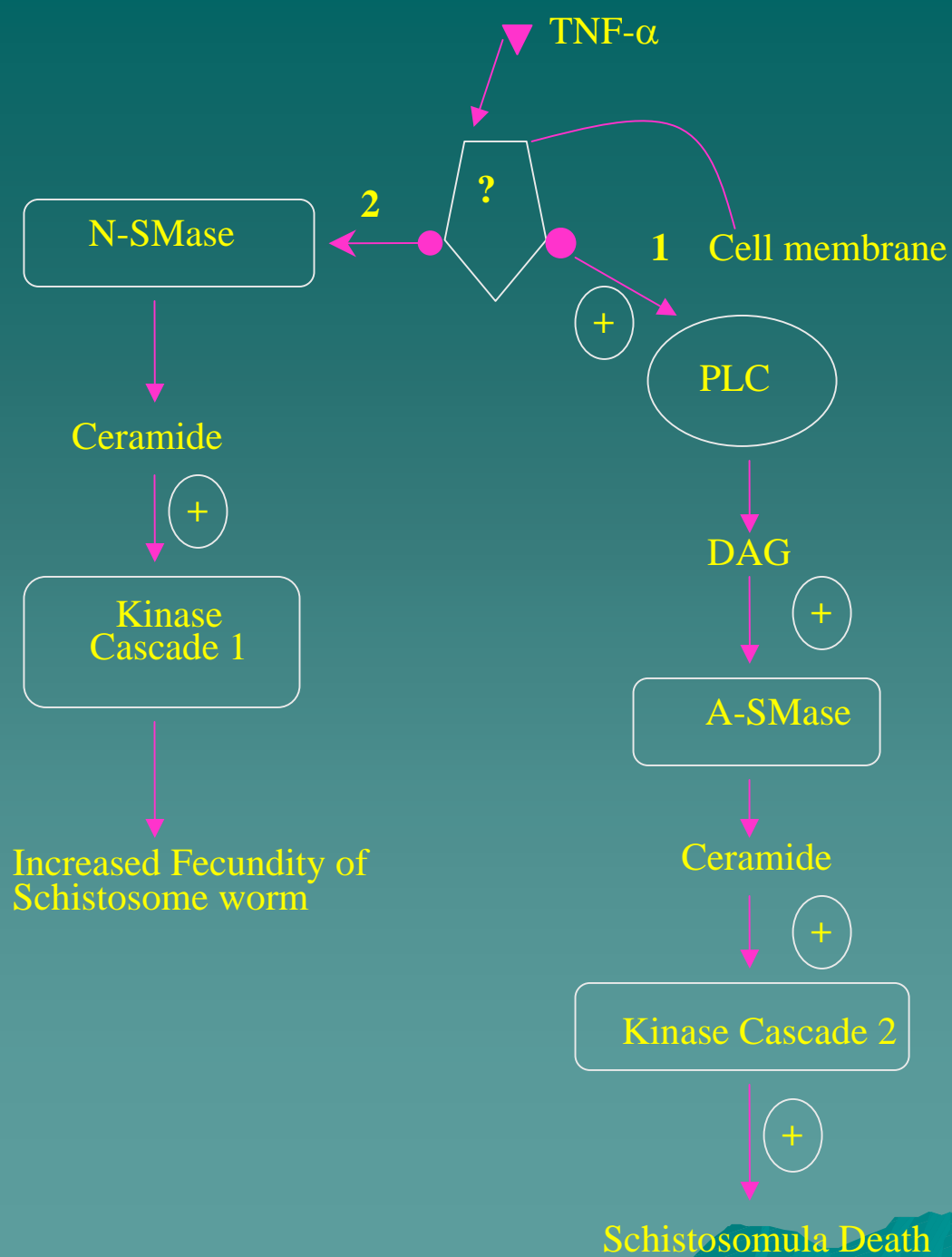
➤ *Sm* Glutathione peroxidase and *Sm* peroxidoxins

➤ TNF- α

Sm Glutathione peroxidase



Specific activity of glutathione peroxidase during developmental stages of schistosomes demonstrating higher activities in the extract of adult worms than in the larval stages.

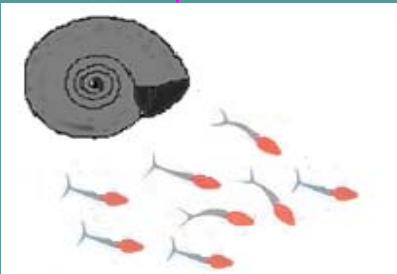


Molluscan snail hosts

Susceptible

No cellular
reactions

Physiologically
suitable



Non-Susceptible

Strong cellular
reactions

Physiologically
unsuitable

Parasite killing

**Intra molluscan
Stage target**

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graph TD; A["Intra molluscan Stage target"] --- B["Serotonin receptors"]; A --- C["Schistosomin"]; A --- D["Phenol-oxidase"]; A --- E["Snail's glycolytic enzymes"];
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**Serotonin
receptors**

Schistosomin

Phenol-oxidase

**Snail's glycolytic
enzymes**



Solanum nigrum

Callistemon lanceolatus



Sublethal concentration
(LC25 and LC10)

Inhibition of glycolytic enzymes (**HK, PK, PGI**)

Less compatible snails (Less adapted to anaerobiosis)

Reduced number of attenuated cercariae

Fail to penetrate

Able to penetrate human skin

Less pathogenic

Less No and small diameter granulomas

Reduced worm burden

Reduced egg count