

Schistosoma haematobium and host hormones

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08/11/2017



INSTITUTO
DE INVESTIGAÇÃO
E INOVAÇÃO
EM SAÚDE
UNIVERSIDADE
DO PORTO

- What is schistosomiasis?



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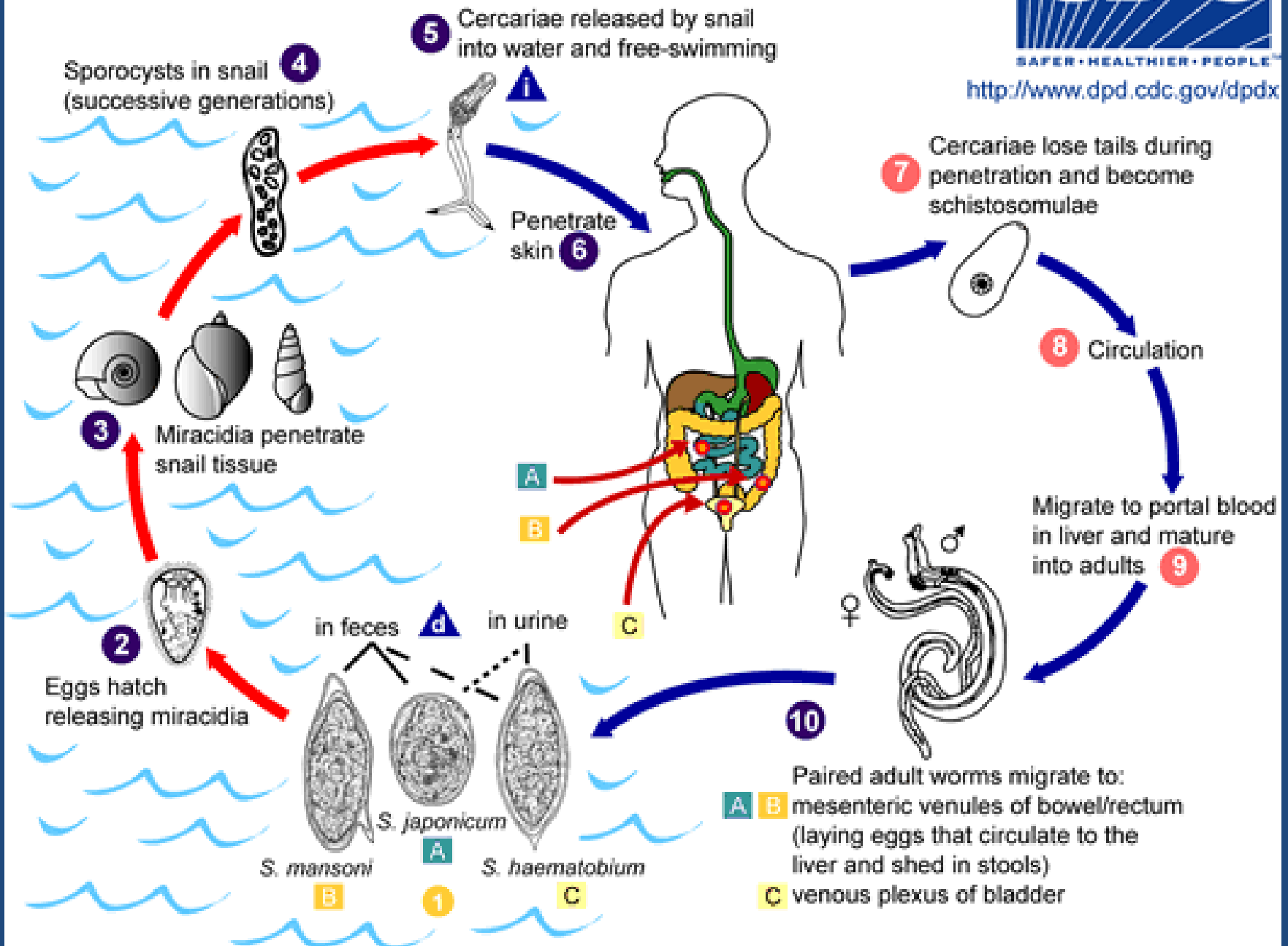
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BEWARE



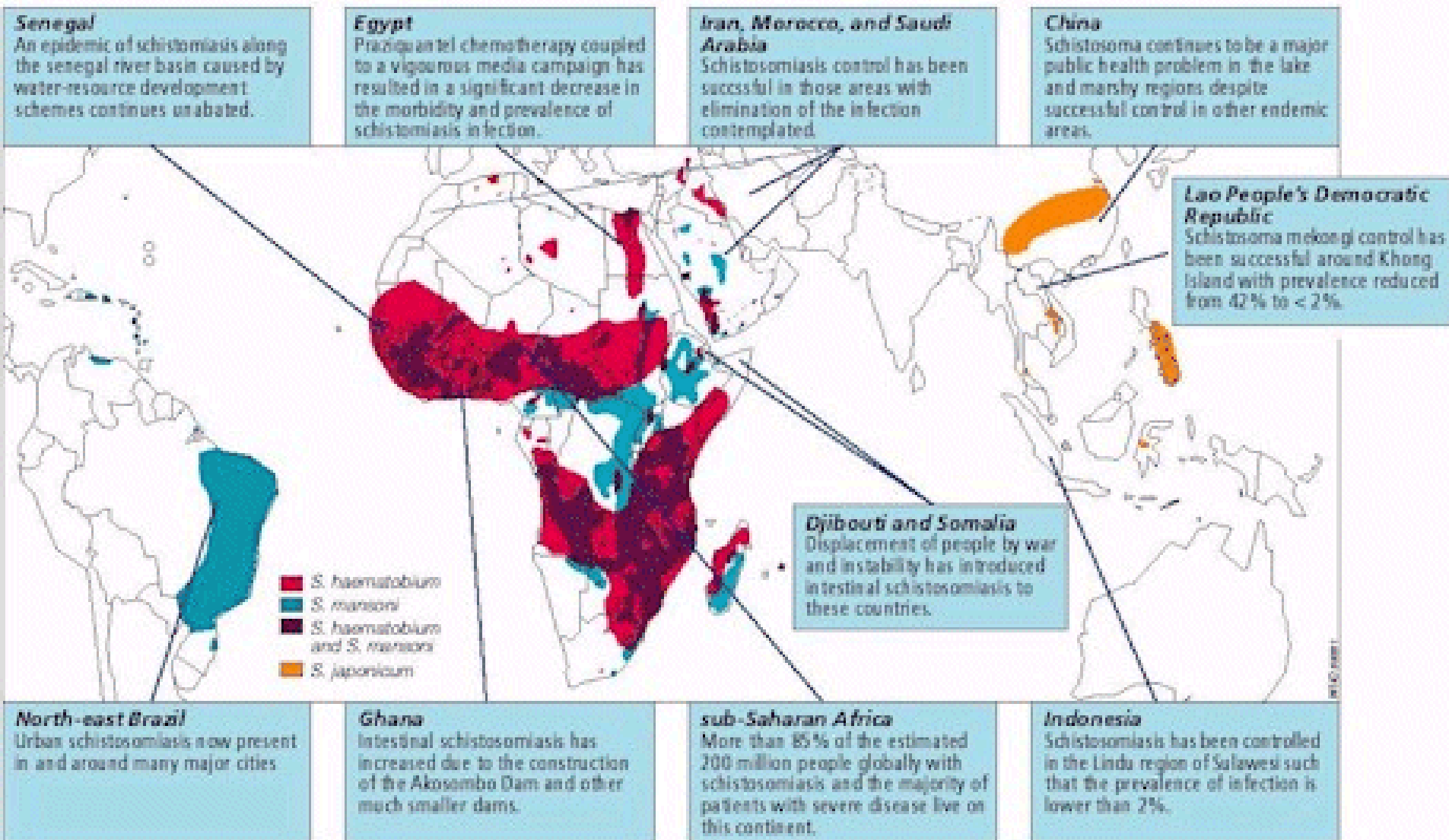
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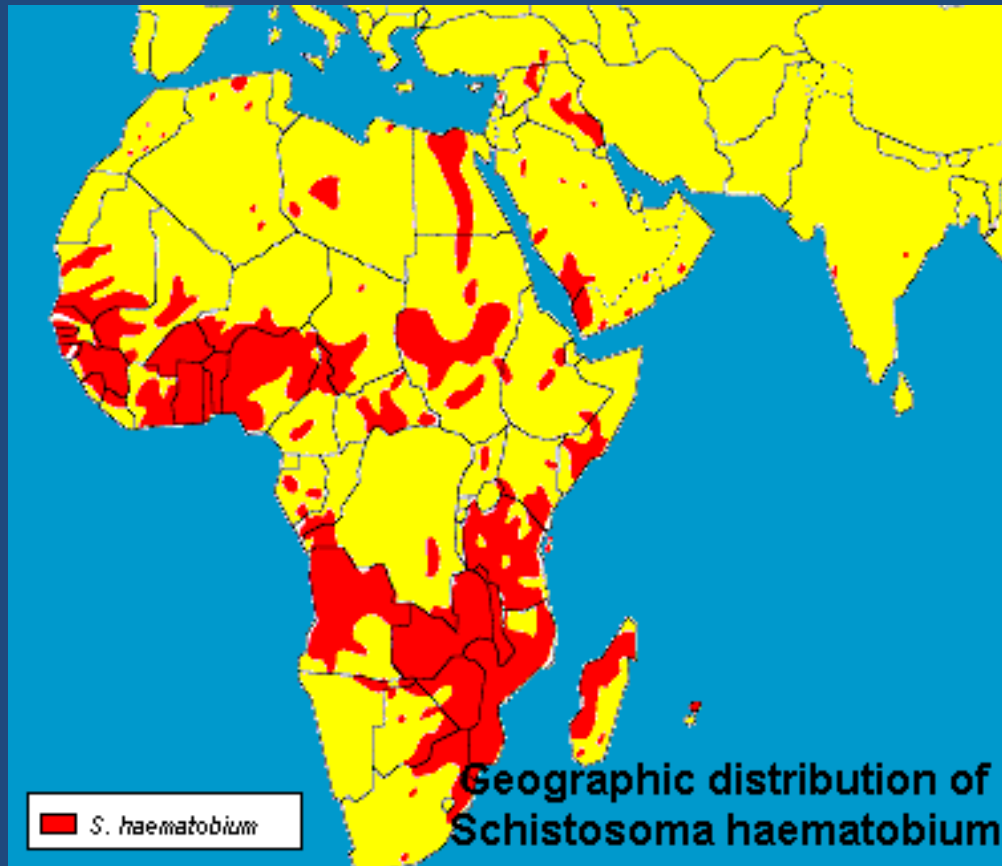
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Schistosomiasis: facts and figures

- Human schistosomes currently infect more than 200 million people in 76 countries worldwide in the endemic areas of Africa, the Caribbean, Central America, South America, East Asia, and the Middle East.

Global distribution of Schistosomiasis

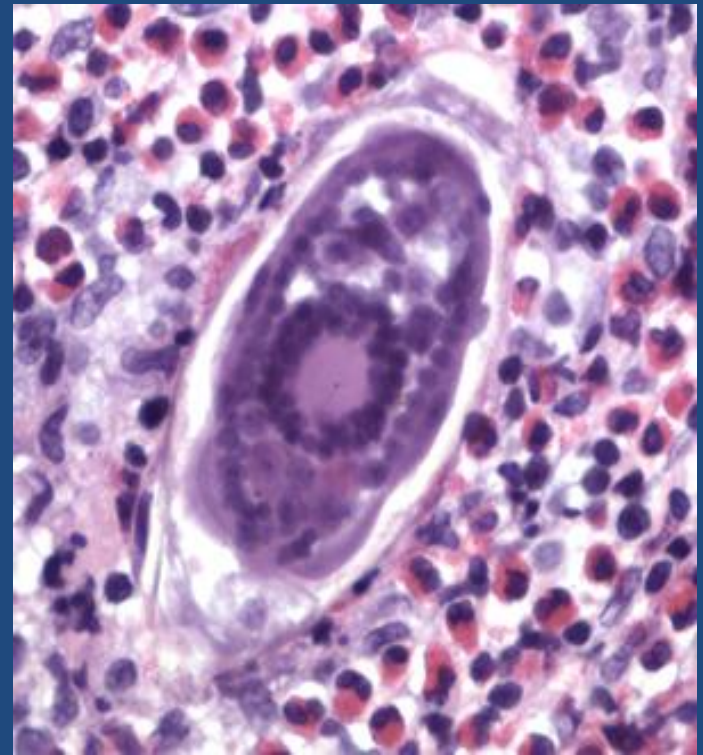




- Is there a role for *S. haematobium* in bladder cancer?

S. haematobium and bladder cancer

- A causal association between the parasite and bladder cancer was postulated in 1911 by Fergusson, but so far proof of this association has remained elusive.



S. haematobium and bladder cancer

Squamous cell carcinoma of the urinary bladder has been associated with *Schistosoma haematobium* infection in many parts of Africa.

A parasite-tumor linkage is further suggested by the predominance of squamous cell (as opposed to transitional cell) morphology of bladder carcinomas seen in *S. haematobium*-endemic areas.

- What about host endocrine system?

Schistosomiasis and host hormones

It has been shown that schistosomes synthesize steroid hormones (Nirde et al, FEBS Letters, 1983).

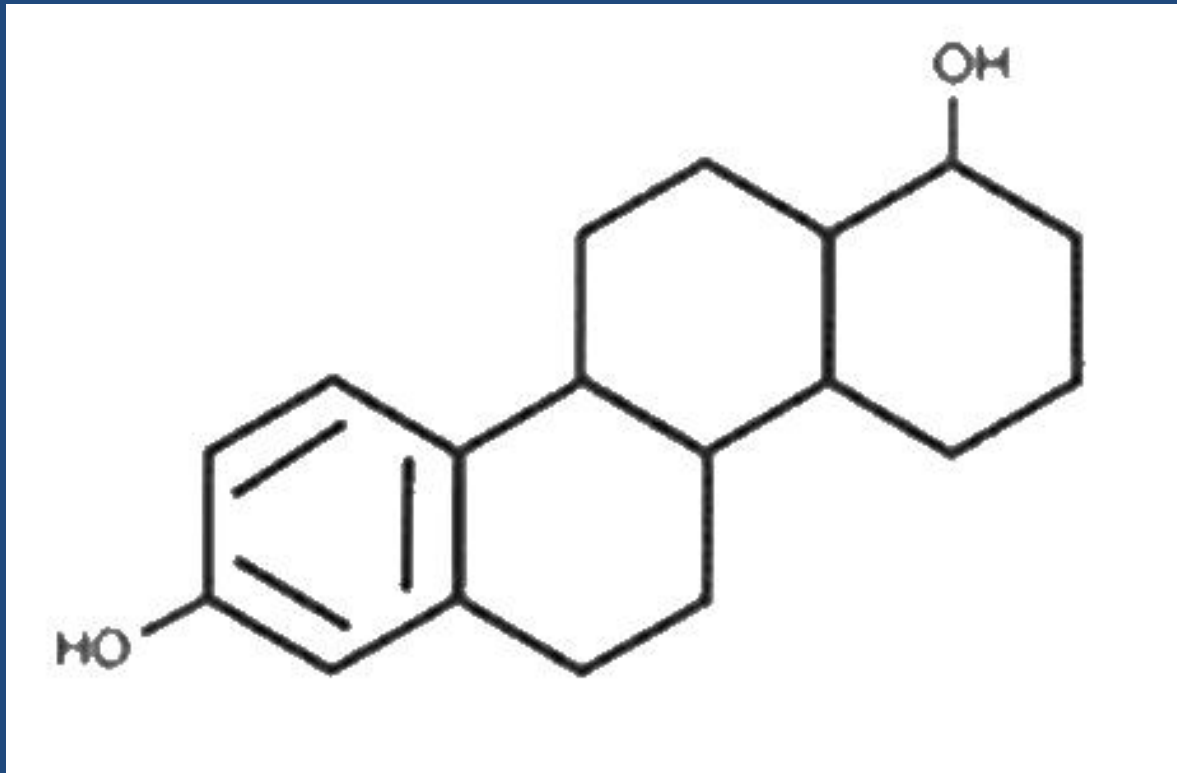
Schistosomes produce hormone-like signals (Mendonça et al, Parasitology Today, 2000).

Existence of receptors able to bind the molecules of estradiol (Barrabes, Ann Parasitol Hum Comp, 1986; Mendonça et al, Parasitology Today, 2000).

Schistosomiasis and host hormones

Recent experimental evidence suggests that schistosomes can not only evade immune responses actively but also exploit the hormonal microenvironment within the host to favor their establishment, growth and reproduction (Escobedo et al, Trends in Parasitology, 2005).

Shistosoma haematobium produces an estradiol-related molecule



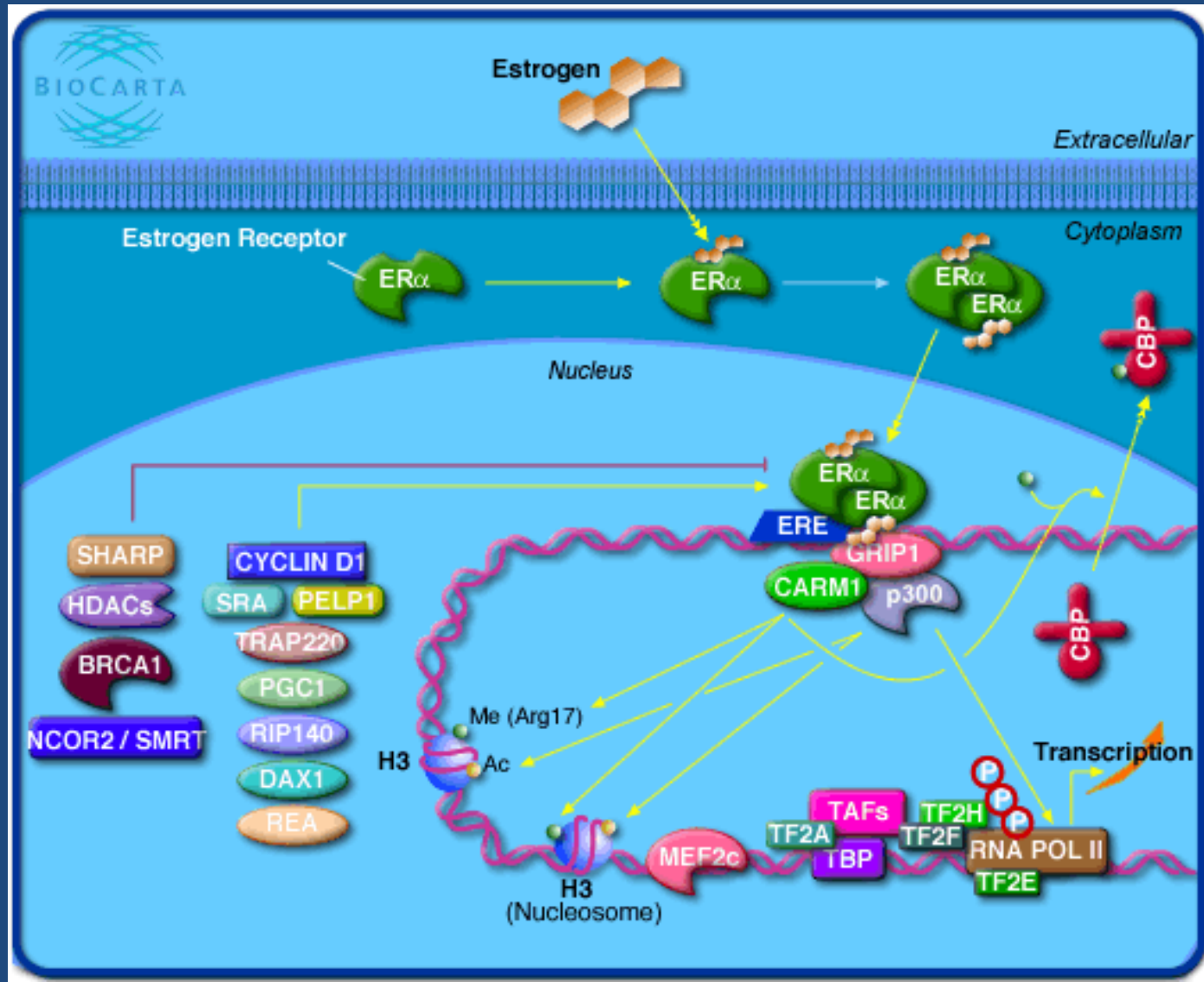
Estradiol (E2)

Shistosoma haematobium produces an estradiol-related molecule

Sex	Age (years)	E2	Range	Testosterone	Range	LH	Range
Female	4	62,8	0-22	<15,0	2-10	0,114	<2,5
Male	12	30,8	0-25	77,5	5-500	1,79	0,2-8,0
Male	14	79,8	0-25	363	5-500	1,89	0,2-8,0
Male	17	45,7	0-25	724	>200	5,89	1,4-7,7
Male	17	31,9	0-25	535	>200	7,65	1,4-7,7
Male	20	68,3	<56,0	982	262-1593	2,87	1,4-7,7

Antigenic preparations	E2 (pg/ml) ± SD
<i>S. haematobium</i>	14,84±0,14
<i>S. mansoni</i>	12,63±0,27
<i>F. hepatica</i>	<10
H ₂ O _d	<10
10 nM E2	1632,99±2,55

S. haematobium produces estrogenic molecules that are able to down-regulate ER alpha and ER beta and repress ER transcriptional activity



Methodological Strategy

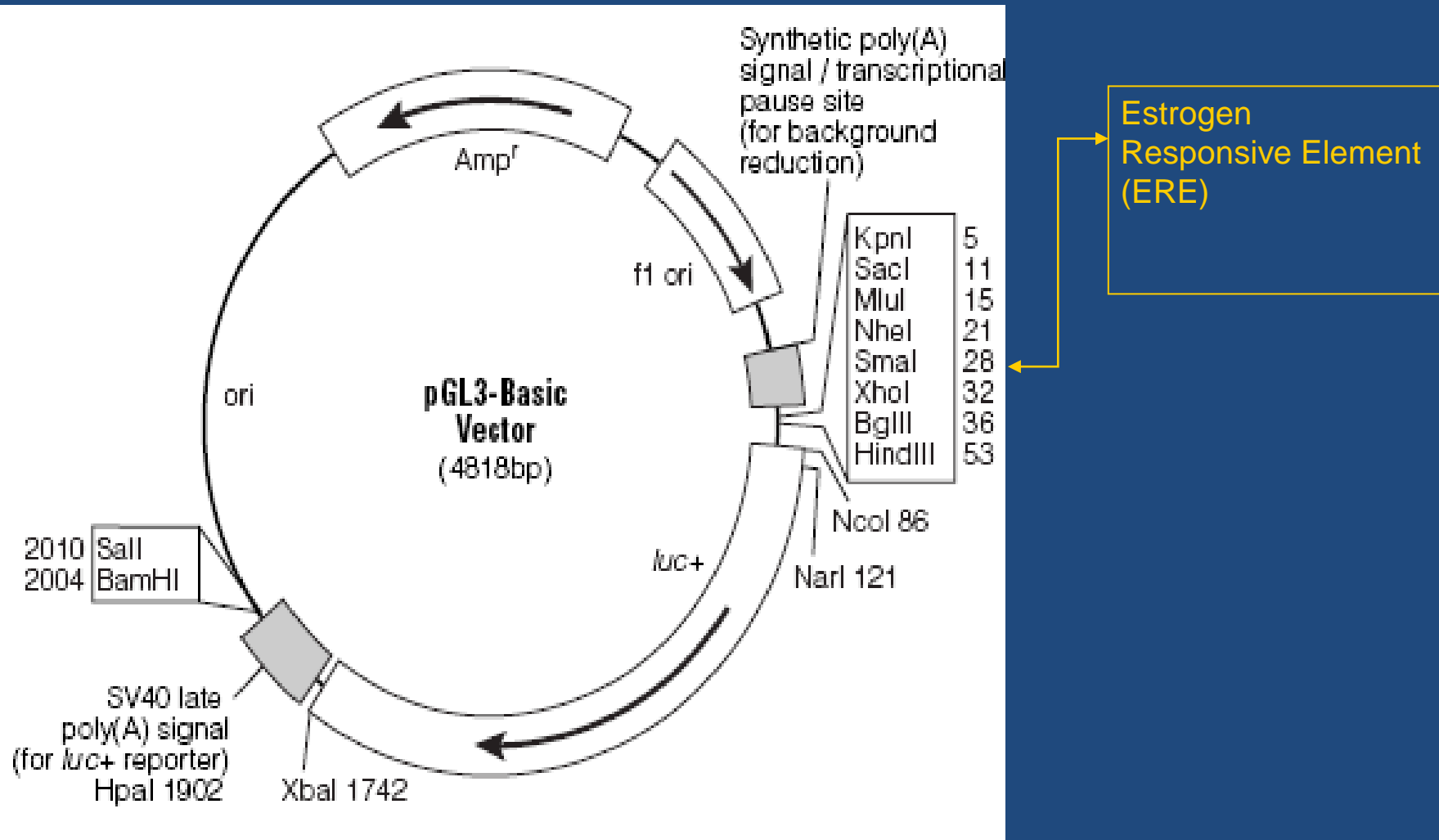
Gene expression Real-Time PCR



Methodological Strategy

Transfection

pERE-Luc

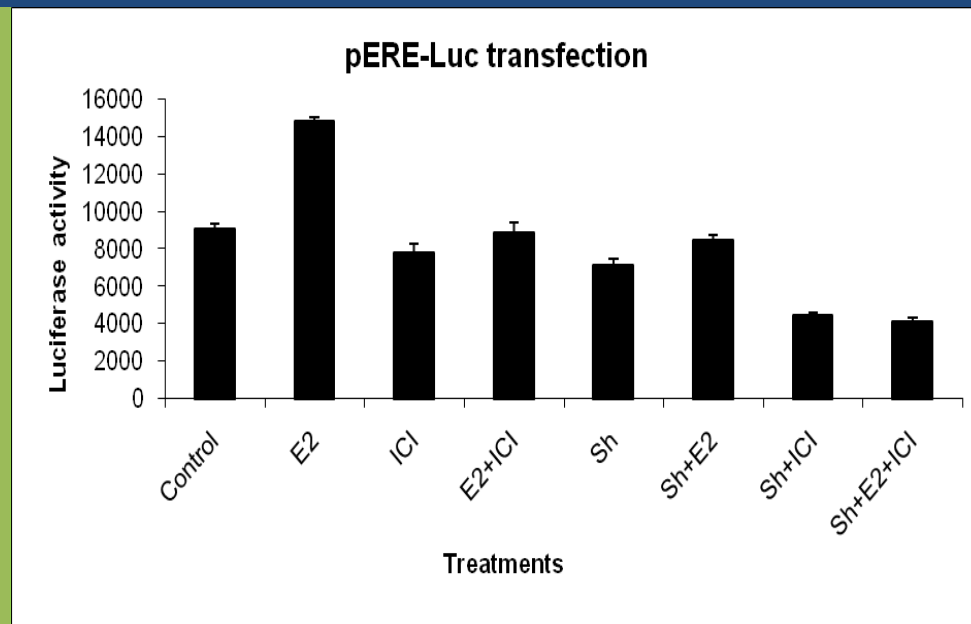
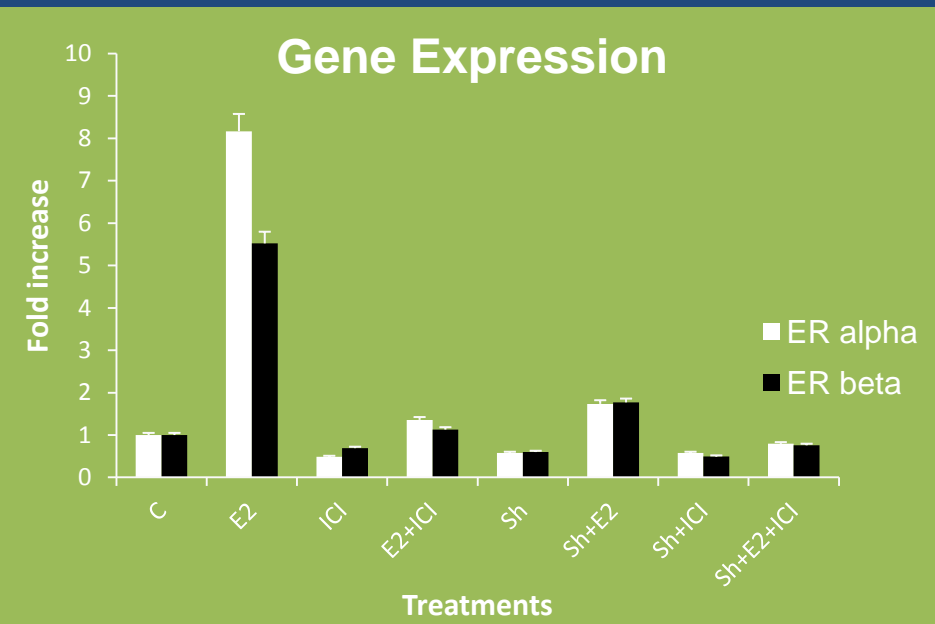


Methodological Strategy

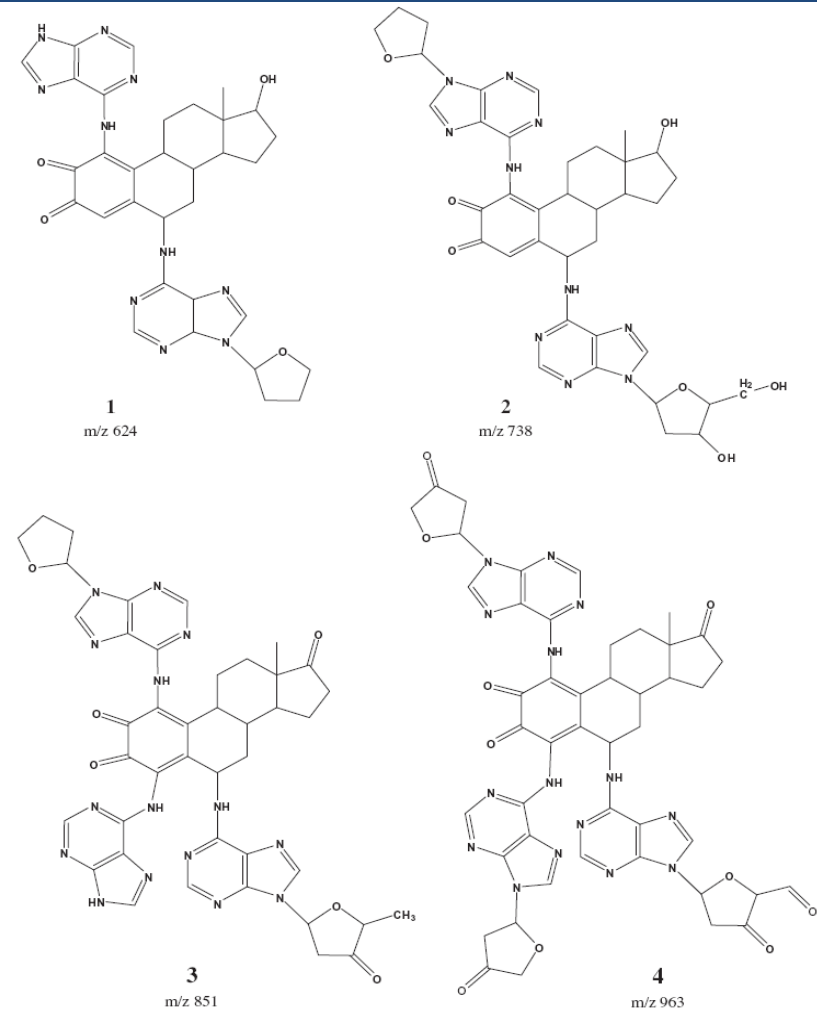
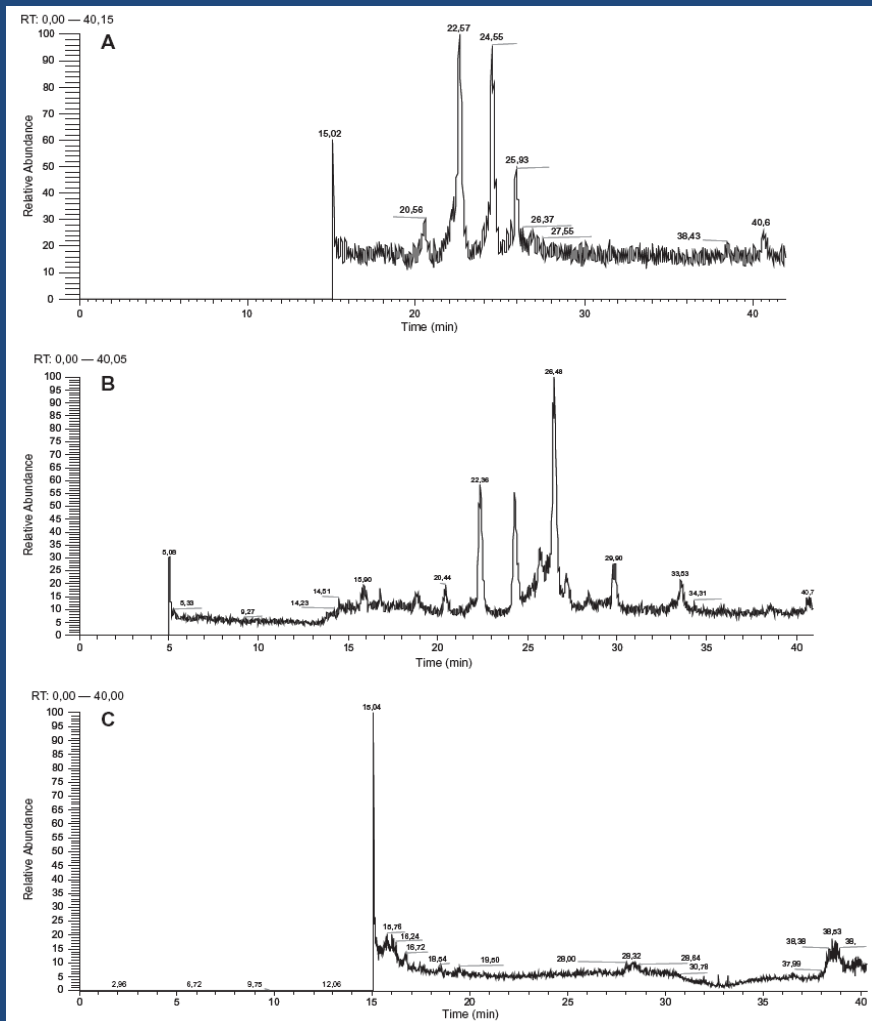
Mass spectrometry LC-ESI-MS



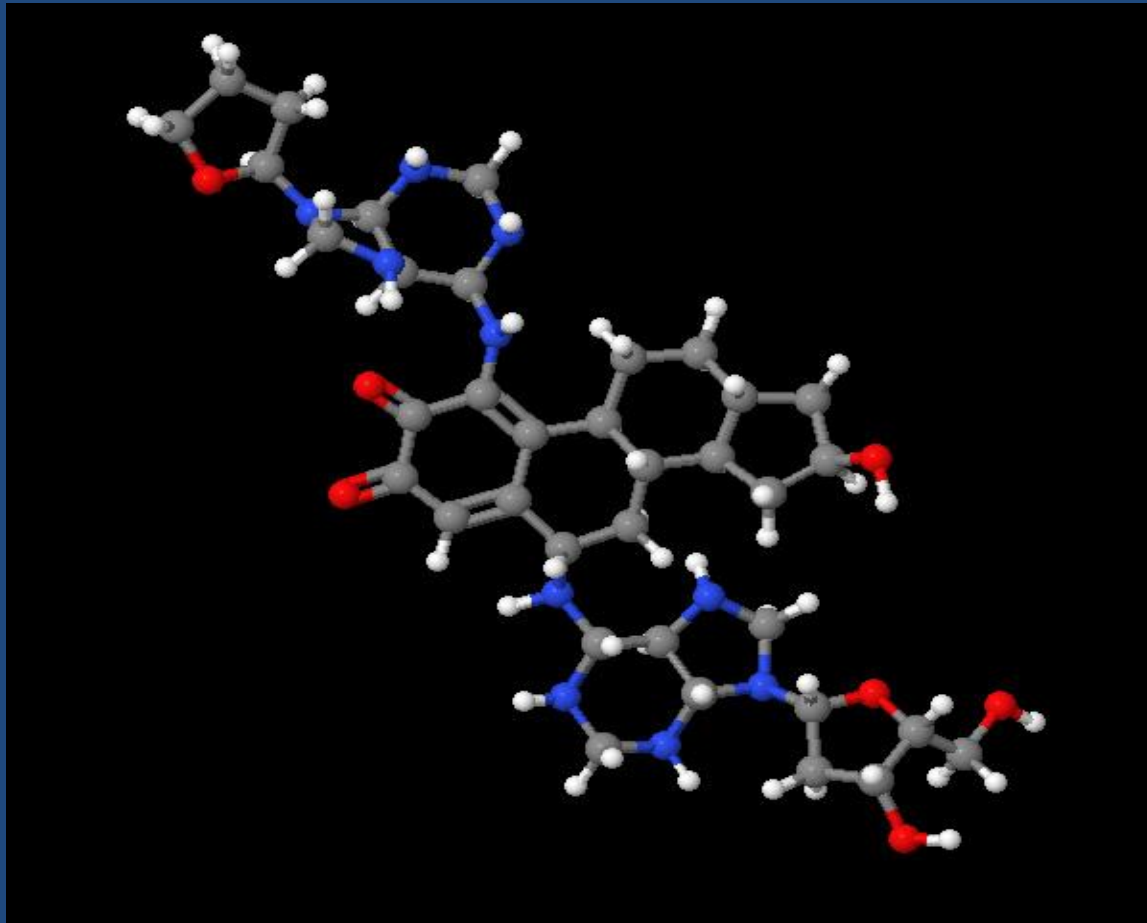
S. haematobium produces estrogenic molecules that are able to down-regulate ER alpha and ER beta and repress ER transcriptional activity



S. haematobium produces estrogenic molecules that are able to down-regulate ER alpha and ER beta and repress ER transcriptional activity

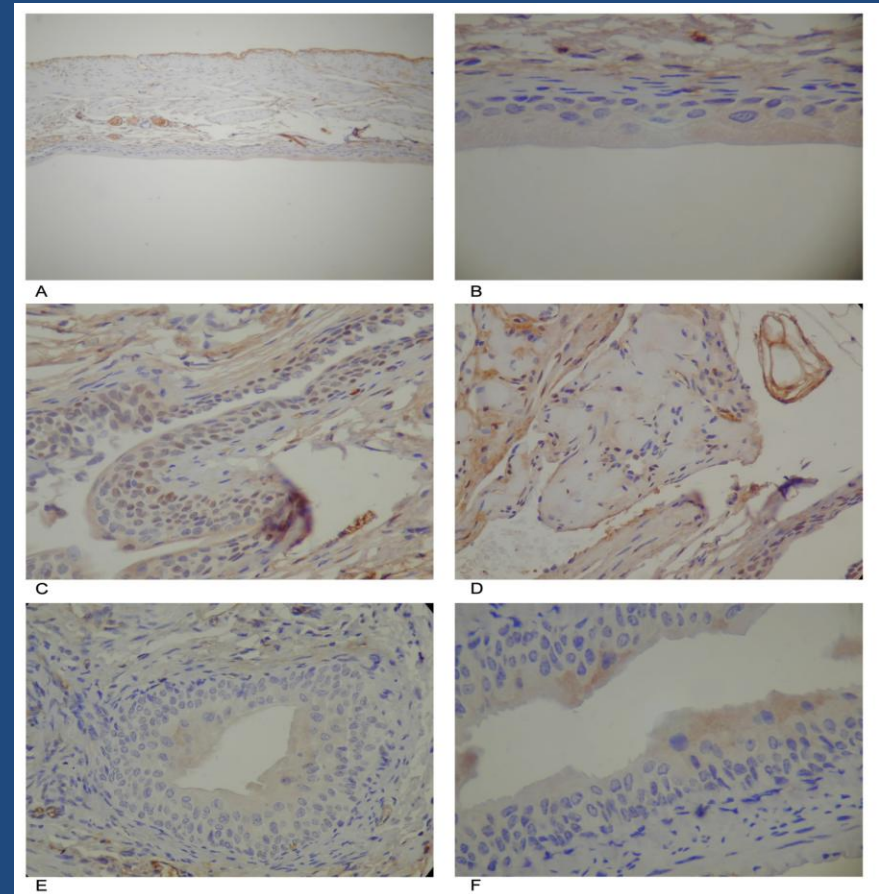
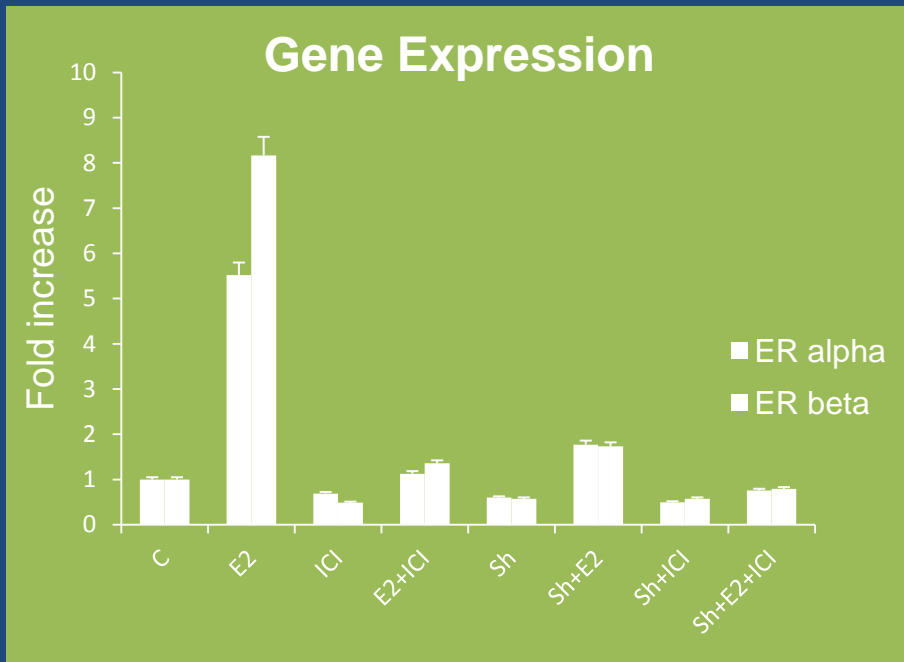


S. haematobium produces estrogenic molecules that are able to down-regulate ER alpha and ER beta and repress ER transcriptional activity



Schistosomiasis, bladder cancer and host hormones

Schistosoma haematobium total antigen down-regulates ER alpha and ER beta in HCV29 normal urothelial cells and down-regulates ER expression in the bladders of CD1 mice



Conclusions

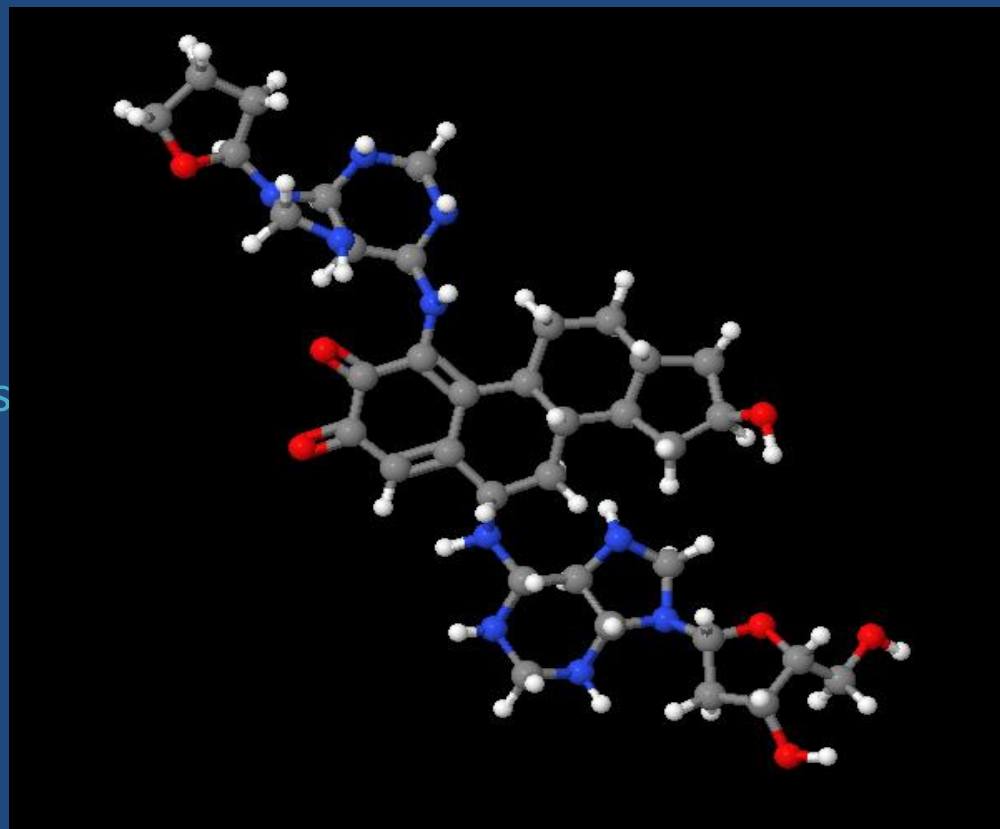
S. haematobium and hormones

S. haematobium total antigen expresses estradiol-related molecules that down regulate Estrogen Receptor alpha and beta in estrogen responsive cells. These estrogens are also present in the sera of *Schistosoma*-infected individuals, and they have the ability to repress Estrogen Receptor transcriptional activity.

The estrogenic molecules present in *S. haematobium* extracts could have a carcinogenic effect possibly through estrogen adduct-mediated pathway and could further explain the link between this parasite and squamous cell carcinoma of the bladder..

OVERALL

Therefore, these results may open potential new strategies for cancer diagnosis by using these estrogens as biomarkers in schistosomiasis-associated bladder cancer.





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