

*Schistosoma mansoni* infection associated infertility

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17/06/2016

50  $\mu$ m

# OUTLINE

## **1. Schistosomes**

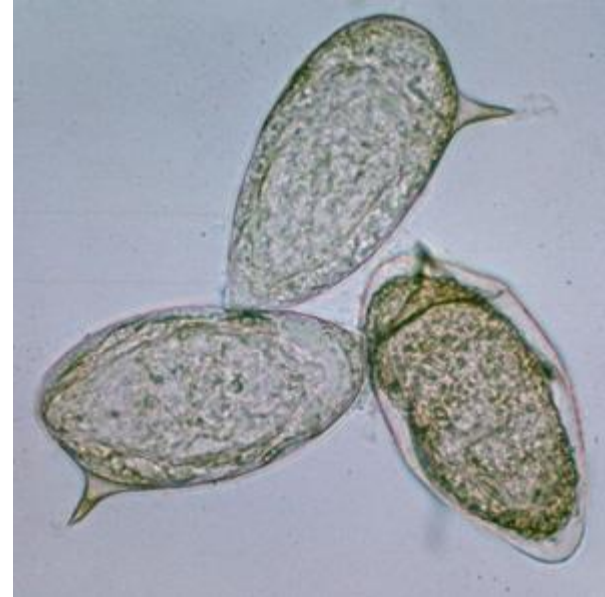
- Facts of figures

## **2. Infertility-associated schistosomiasis**

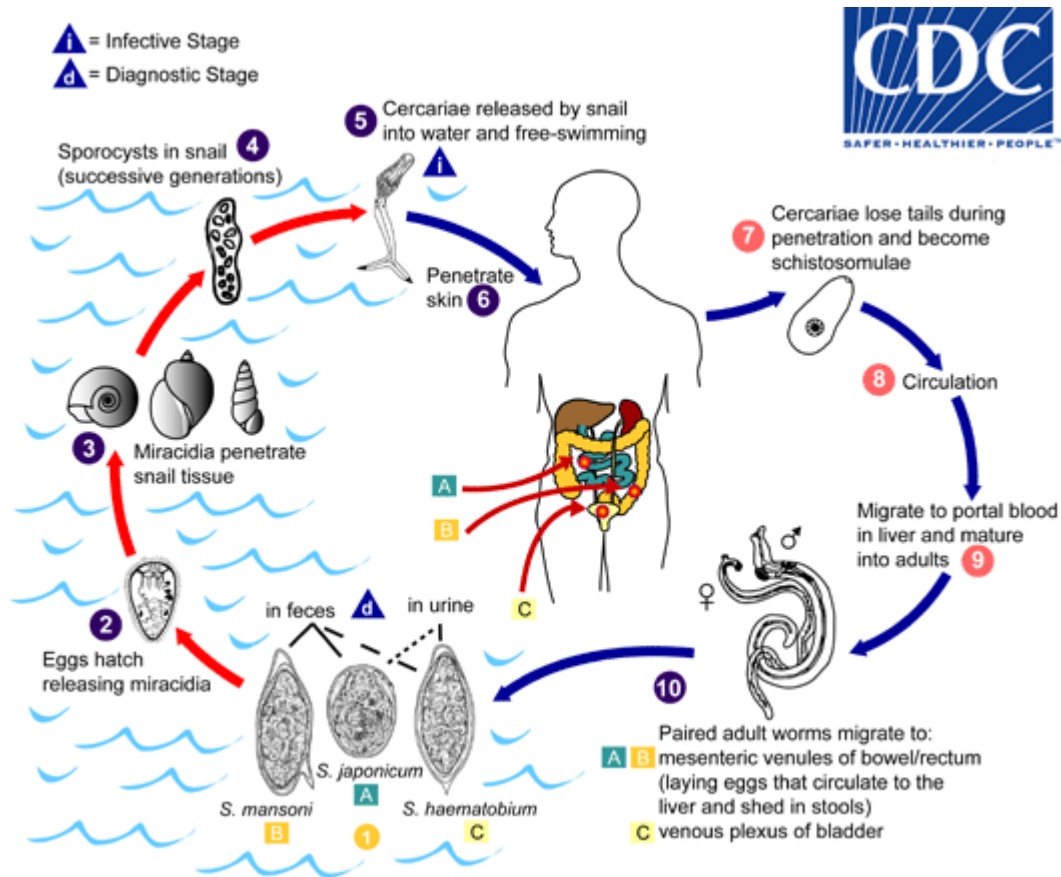
- Pathway of hormonal imbalance induced by schistosomes

## **3. Development of functional tools for schistosomes**

- Animal models of *S. mansoni* induced impaired reproduction



# Schistosomes: Life cycle



# Infertility-associated schistosomiasis

Trends in Parasitology, June 2015, Vol. 31, No. 6

Opinion

CellPress

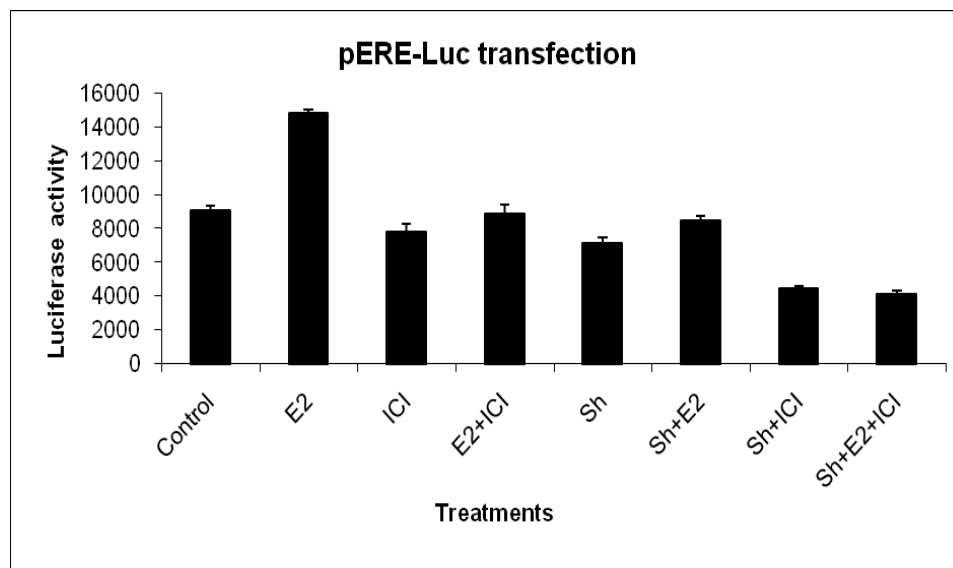
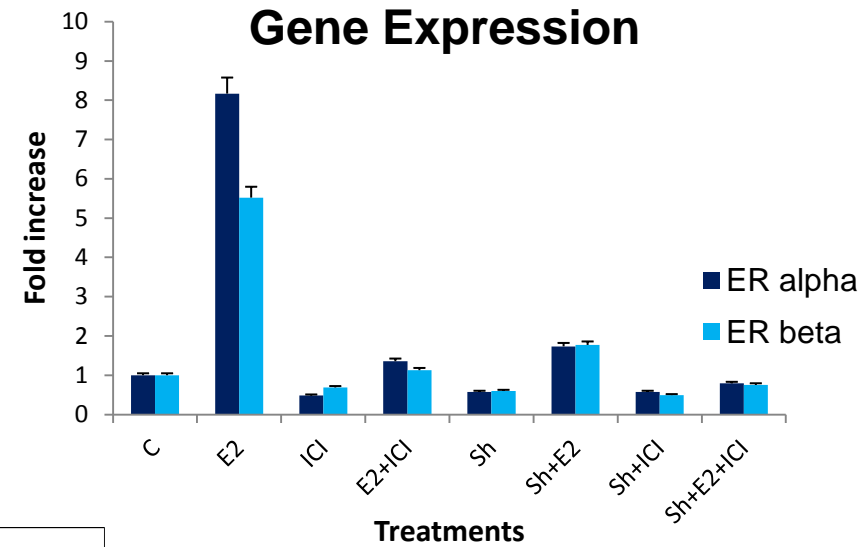
## The role of estrogens and estrogen receptor signaling pathways in cancer and infertility: the case of schistosomes

Mónica C. Botelho<sup>1,2</sup>, Helena Alves<sup>1</sup>, Alberto Barros<sup>3,4</sup>, Gabriel Rinaldi<sup>5</sup>, Paul J. Brindley<sup>5</sup>, and Mário Sousa<sup>6</sup>

- Homonal imbalance caused by estrogen-like molecules produced by schistosomes

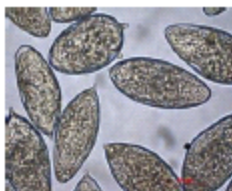
# Schistosomes estrogen-like molecules and down-regulation of estrogen receptor

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

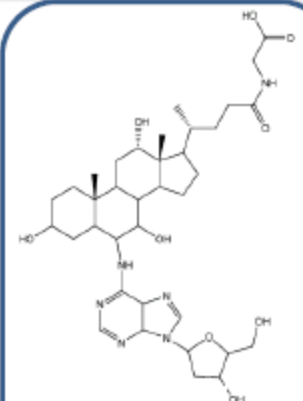


Botelho *et al.* Exp Parasitol 2009, 2010

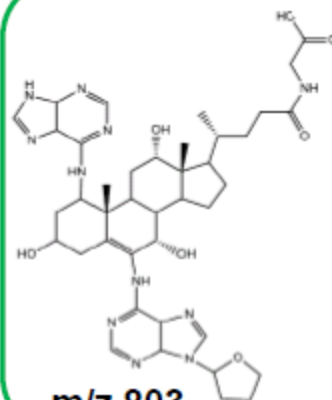




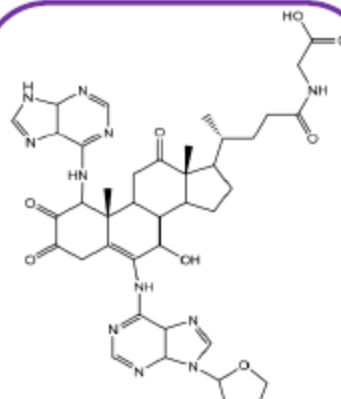
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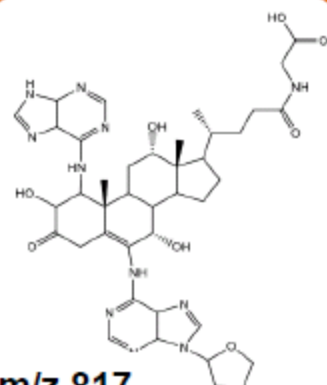
m/z 716



**m/z 803**



**m/z 813**



**m/z 817**

# Infertility-associated *Schistosomiasis haematobia* in women

## Urinary Estrogen Metabolites and Self-Reported Infertility in Women Infected with *Schistosoma haematobium*

Júlio Santos<sup>1</sup>, Maria João Gouveia<sup>2</sup>, Nuno Vale<sup>2</sup>, Maria de Lurdes Delgado<sup>3</sup>, Ana Gonçalves<sup>4</sup>, José M. Teixeira da Silva<sup>4</sup>, Cristiano Oliveira<sup>4</sup>, Pedro Xavier<sup>4</sup>, Paula Gomes<sup>2</sup>, Lúcio L. Santos<sup>1,5</sup>, Carlos Lopes<sup>1,6</sup>, Alberto Barros<sup>4,7</sup>, Gabriel Rinaldi<sup>8,9</sup>, Paul J. Brindley<sup>8</sup>, José M. Correia da Costa<sup>3,10</sup>, Mário Sousa<sup>11</sup>, Mónica C. Botelho<sup>3,10\*</sup>

Plos One 9 (2014) e96774

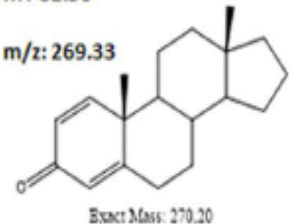
	E + (n= 25)	E - (n= 21)	OR	95% CI	P-value
Fertile women (ages)	2 (29, 63)	6 (28–94)			
Group 2+3 (ages)	15 (19–41)	2 (21–34)	4.33	1.13–16.70	0.03
Group 2 (ages)	9 (18–20)	1 (21)	2.67	0.60–11.80	n.a.
Group 3 (ages)	6 (27–41)	1 (34)	4.75	0.51–44.50	n.a.
Total	17	8			
≤12 years	8	13			
Total	25	21			

Women unable to become pregnant after one year of trial (Self-reported primary infertility - Group 2) and those who had borne fewer children than desired (Self-reported secondary infertility - Group 3).

OR, odds ratio; CI, confidence interval.

RT: 32.96

m/z: 269.33



## Infertility associated *Schistosomiasis mansoni*

*Schistosoma mansoni* infection impairs reproduction in mice (In Preparation)

- Mating (1 year)
- Gestational period
- Synchronization
- Number pups



# Infertility associated *Schistosomiasis mansoni*

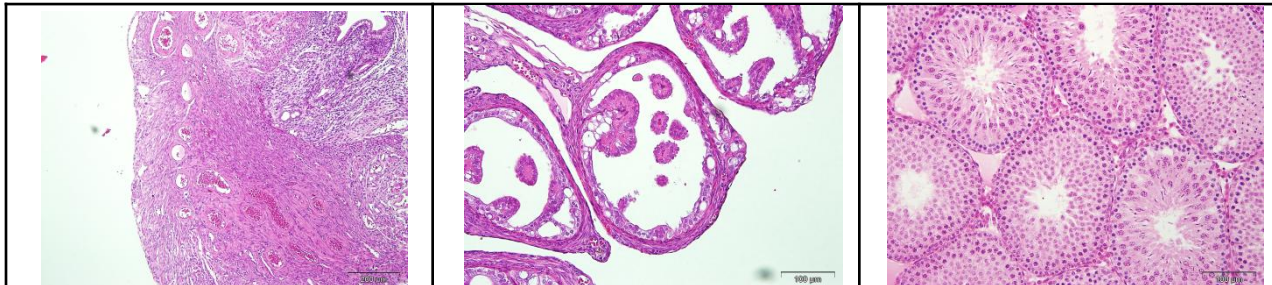
Animals	Gestational length (days)	Synchronicity (days)	Number of pups
2FCx1MC	25	0-1	15.1
2FCX1MI	25.6	0-2	14.5
2FIX1MC	22.8	1-6	13.8
2FIX1MI	21.8	3-8	11.9

Ovary

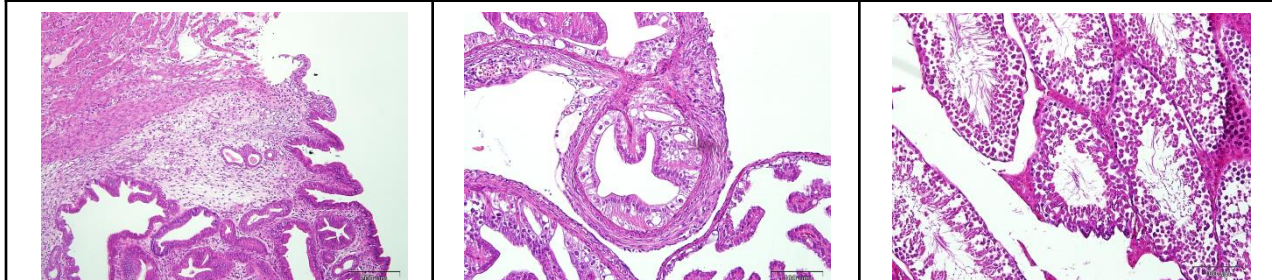
Tube

Testes

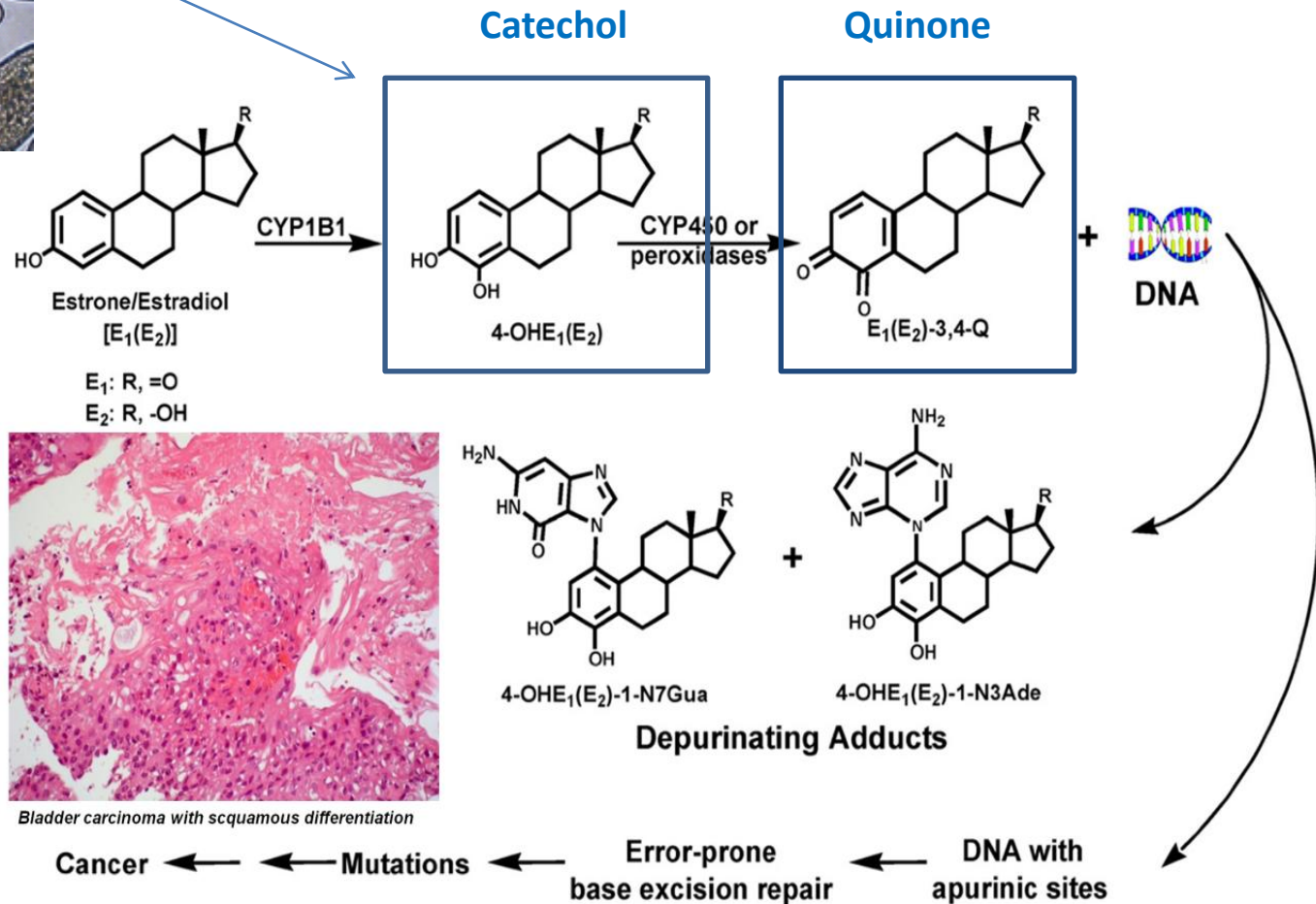
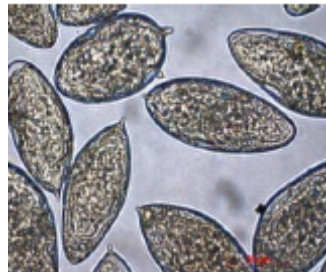
Control



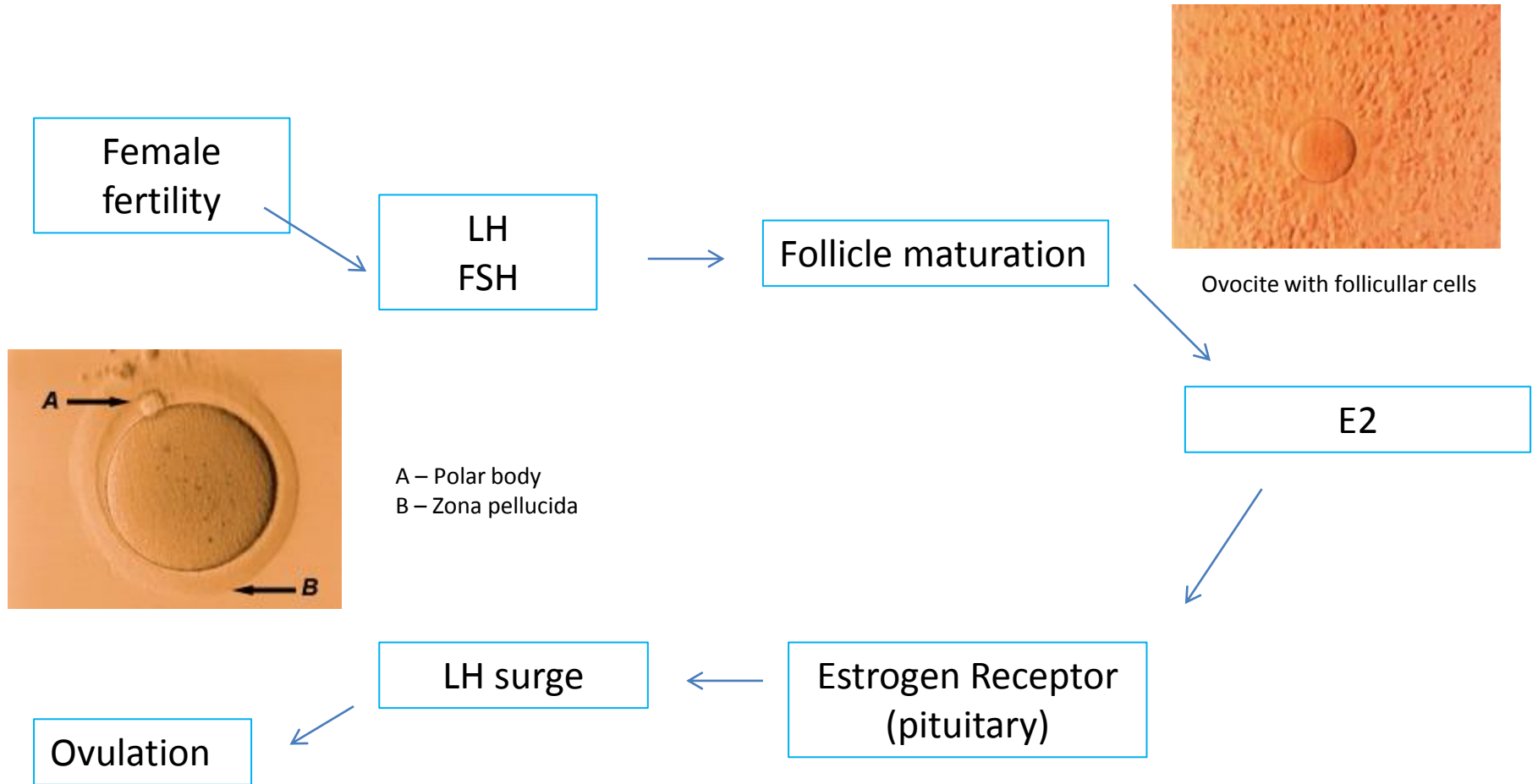
*S. mansoni*



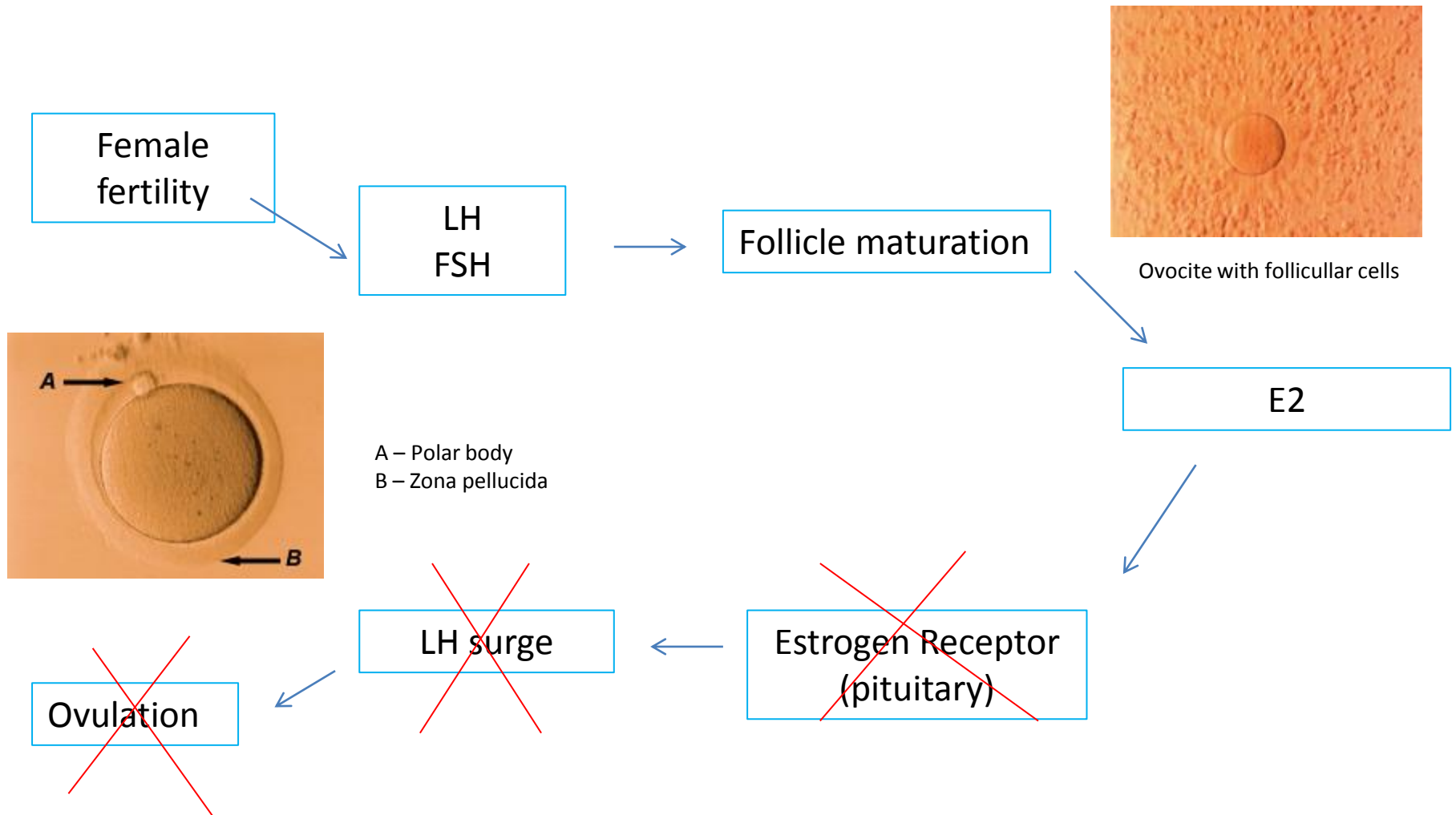
# Pathway for Schistosomiasis Bladder Cancer



# Pathway for Female Fertility



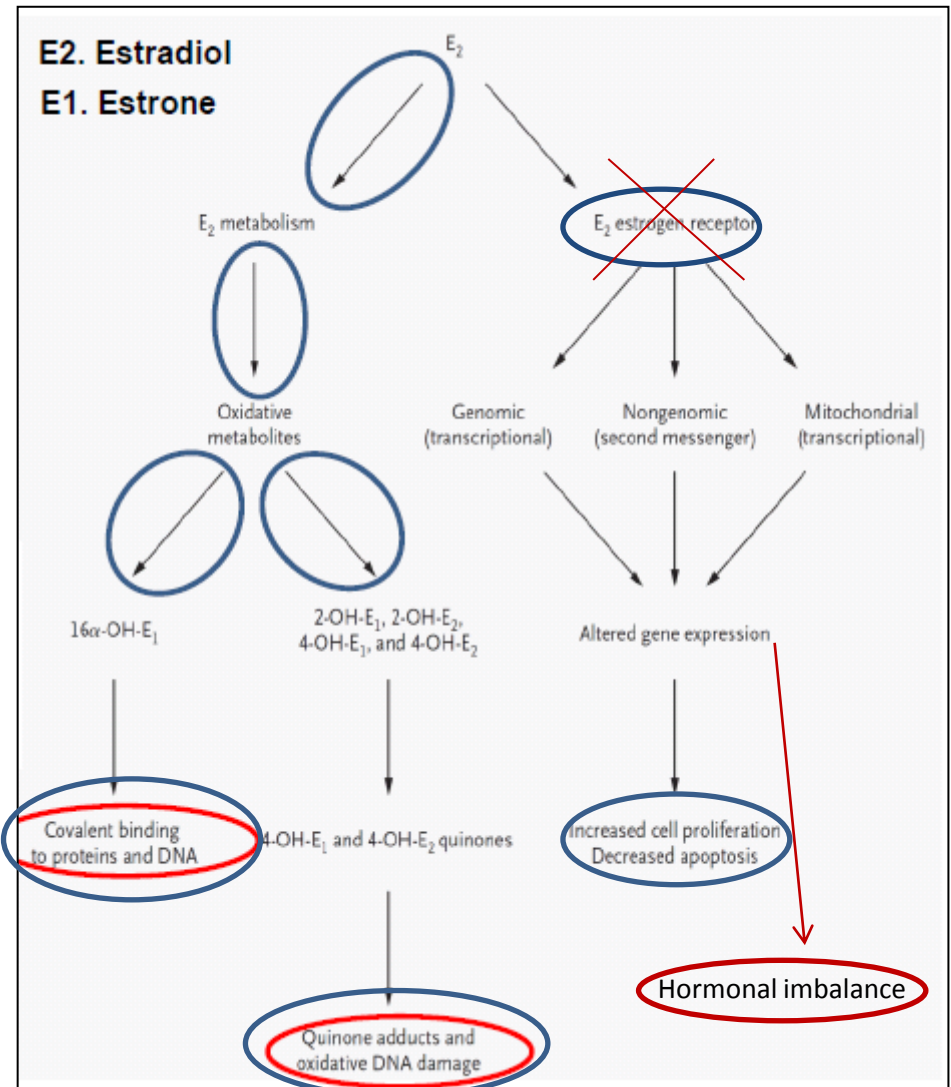
# Mechanism for Schistosomiasis Female Infertility



# Pathways for Estrogen Carcinogenesis and Infertility

Two different complementary pathways probably contribute to estrogen imbalance leading to:

- Initiation and promotion of cancer progression
- Infertility



# Conclusions

- 1. *S. mansoni* induced impaired reproduction in animal models**
- 2. Novel catechol-oestrogen molecules derived from the eggs could be involved in infertility**



# Future Perspectives

- 1.Synthesize and/or purify and/or isolate reactive catechol-estrogens.**
- 2.Evaluate impact of catechol estrogens on culture cells *in vitro*, at the phenotypic and gene expression levels.**
- 3.Evaluate impact of catechol estrogens in an informative mouse model.**
- 4.Investigate schistosome catechol estrogen–DNA adducts in informative human cases from a schistosomiasis haematobia endemic regions. (Potential for Biomarkers screening)**

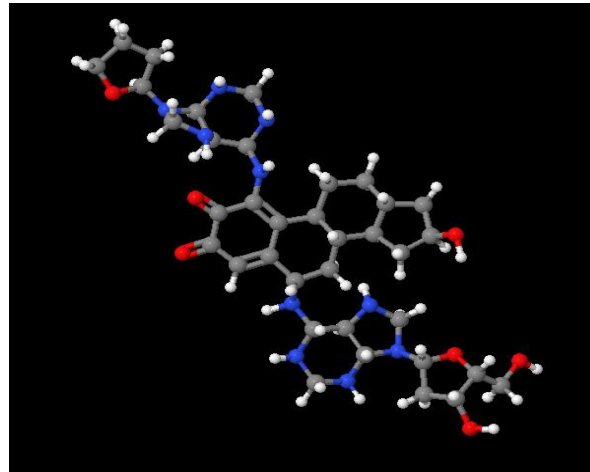
# Collaborations



Paula Oliveira



Joachim Richter



Alberto Barros

