



Schistosoma mansoni infection impairs reproduction in mice

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AIM

To study the effect of *S. mansoni* infection in fertility using a mouse model.

BACKGROUND

- Our group is listed in the Top 10 most publishing authors in the field of schistosomiasis as a cause of infertility (Figure 1).
- Estrogen-like molecules produced by schistosomes haematobia and mansoni induce hormonal imbalances in infected persons (Botelho et al. Trends in Parasitology, 2015; Botelho et al. Letters in Drug Design and Discovery, 2016).
- These estrogenic metabolites down-regulate Estrogen Receptor in an in vitro model (Botelho et al, Experimental Parasitology, 2009, 2010).
- We have identified these estrogenic metabolites as catechol-estrogens (oxidative metabolites derived from estrogens) (Figure 2) (Botelho et al, International Journal for Parasitology, 2013).
- These catechol-estrogens were found to be associated with infertility in women infected with *S. haematobium* (Santos et al, Plos One, 2014).

METHODOLOGICAL STRATEGY

- Mating CD-1 mice infected with *S. mansoni* and controls during one year (\approx 12 cycles).
- Two females with one male per cage and combinations of infected vs. controls (Table 1).
- Female reproductive synchrony of infected females vs. controls (number of days between births from females in the same cage).
- Gestational length of infected females vs. controls (number of days of pregnancy).
- Offspring from infected females vs. controls (number of pups per birth).
- Histopathology of reproductive organs in males and females (infected vs. control).

RESULTS

Table 1: Gestational length (mean number of days), synchrony (mean number of days) and offspring (mean number of pups) of controls vs. infected females.

Animals	Gestational length (mean \pm SD)	Synchrony (mean \pm SD)	Offspring (mean \pm SD)
2FCx1MC	25 \pm 2	0.4 \pm 0.5	15.1 \pm 3.3
2FCx1MI	25.6 \pm 1.86; n.s.	1.5 \pm 0.56; p=0.01	14.5 \pm 2.2; n.s.
2FIX1MC	22.8 \pm 1.47; p=0.05	4.25 \pm 2.36; p=0.007	13.8 \pm 2.6; n.s.
2FIX1MI	21.8 \pm 2.5; p=0.03	6.8 \pm 2.5; p=0.0007	11.9 \pm 2.7; p=0.04

FC - female control; MC - male control; FI - female infected; MI - male infected; SD - standard deviation; n.s. - not statistically significant

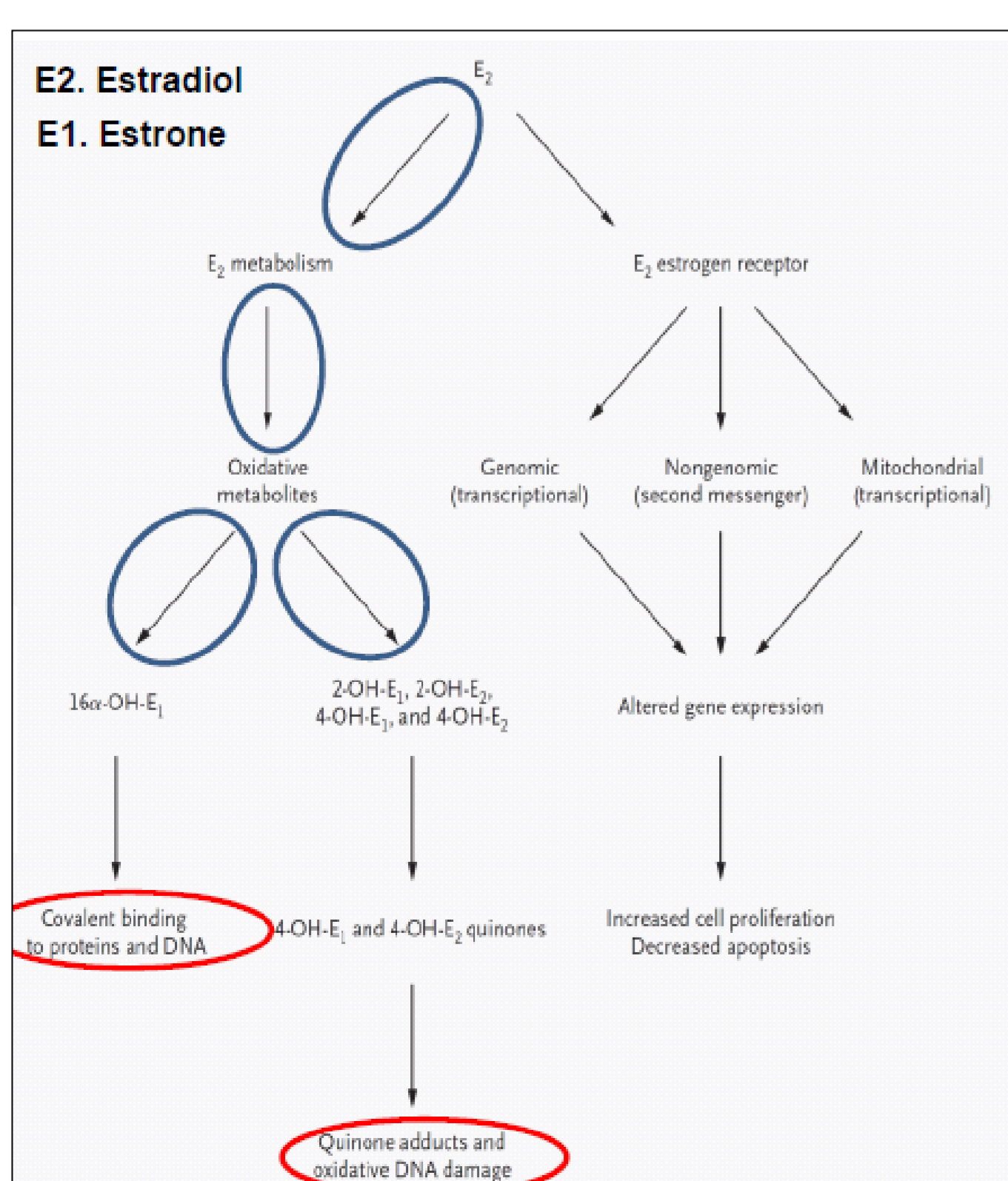


Fig. 4: Pathway for estrogen infertility and carcinogenesis

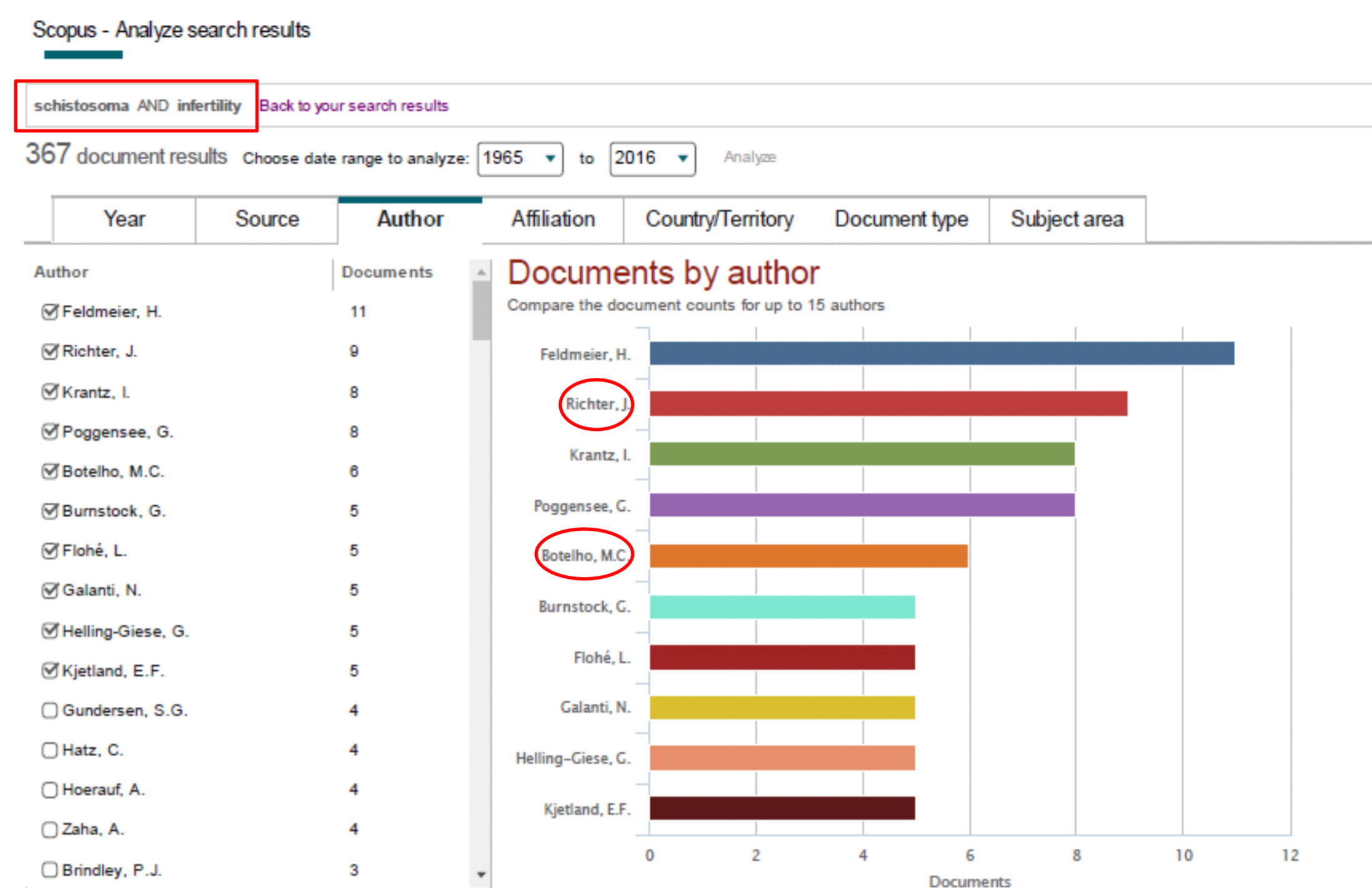


Fig. 1: Scopus data base search results "schistosomiasis AND infertility"

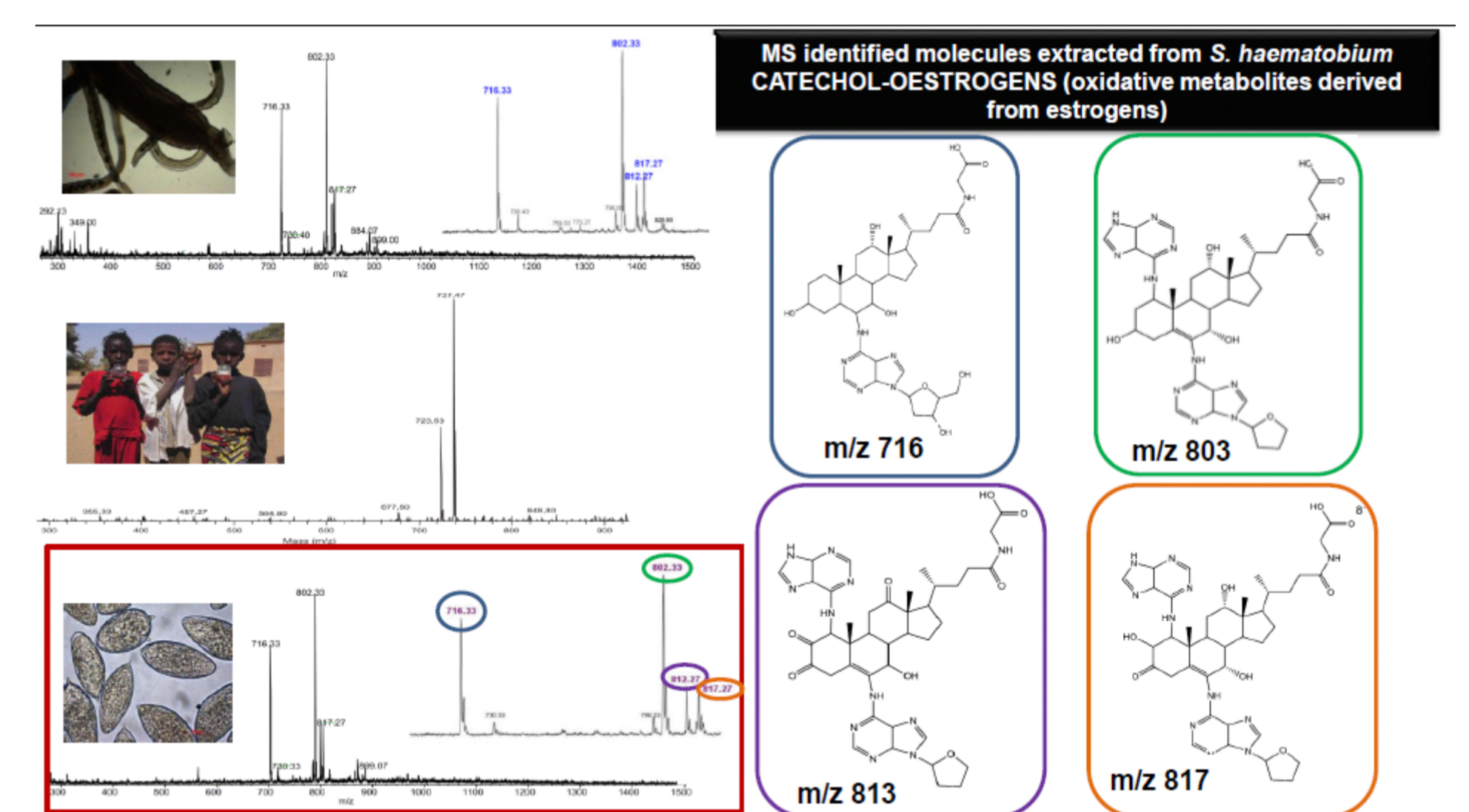


Fig. 2: Catechol-estrogens produced by *S. haematobium*

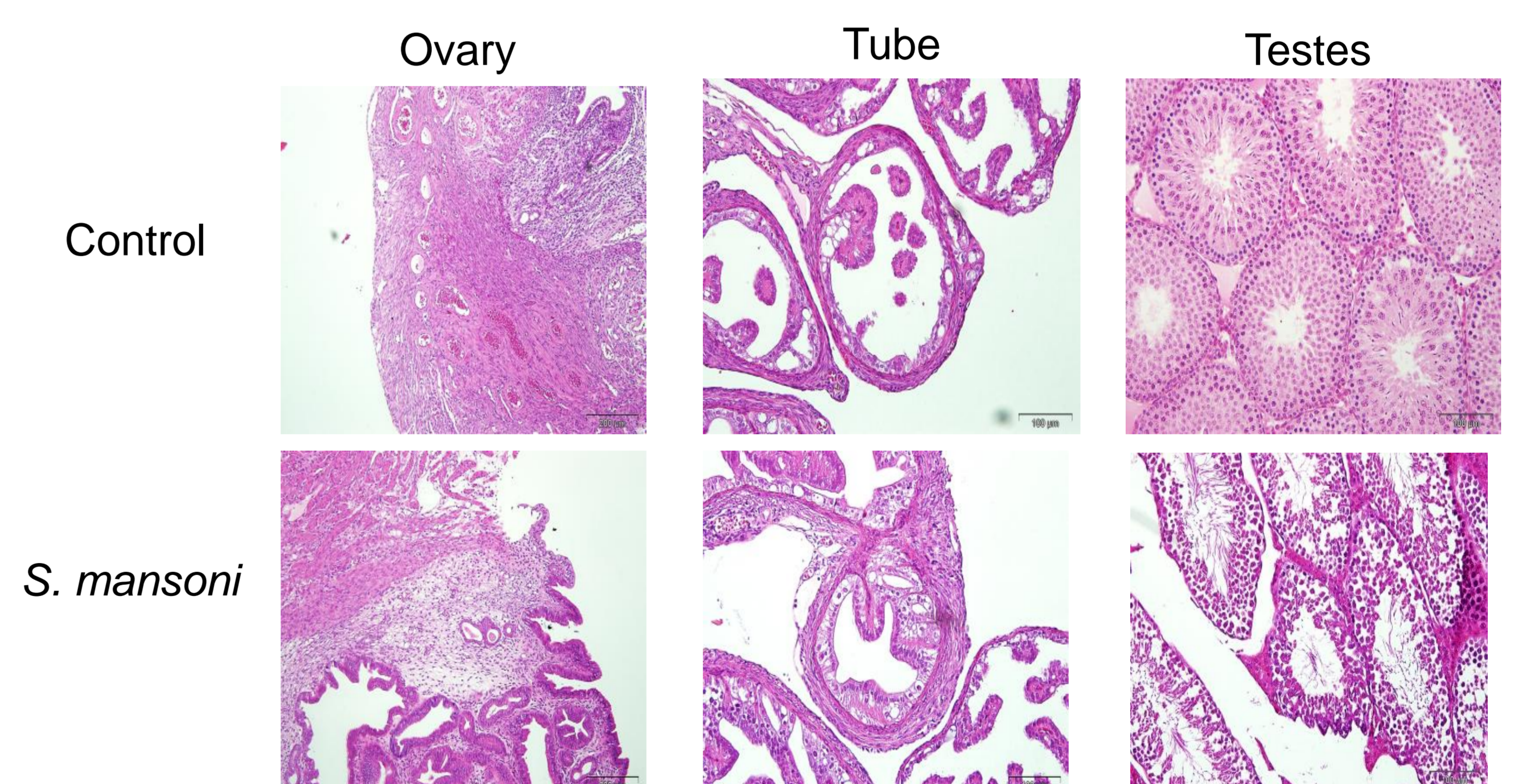


Fig. 3: Histopathology of reproductive organs of males and females (infected vs. control)

CONCLUSIONS

1. *S. mansoni* induced impaired reproduction in animal models
2. Novel catechol-oestrogen molecules derived from the eggs could be involved in infertility
3. Two different complementary pathways probably contribute to estrogen imbalance leading to:

- Infertility
- Initiation and promotion of cancer progression