

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

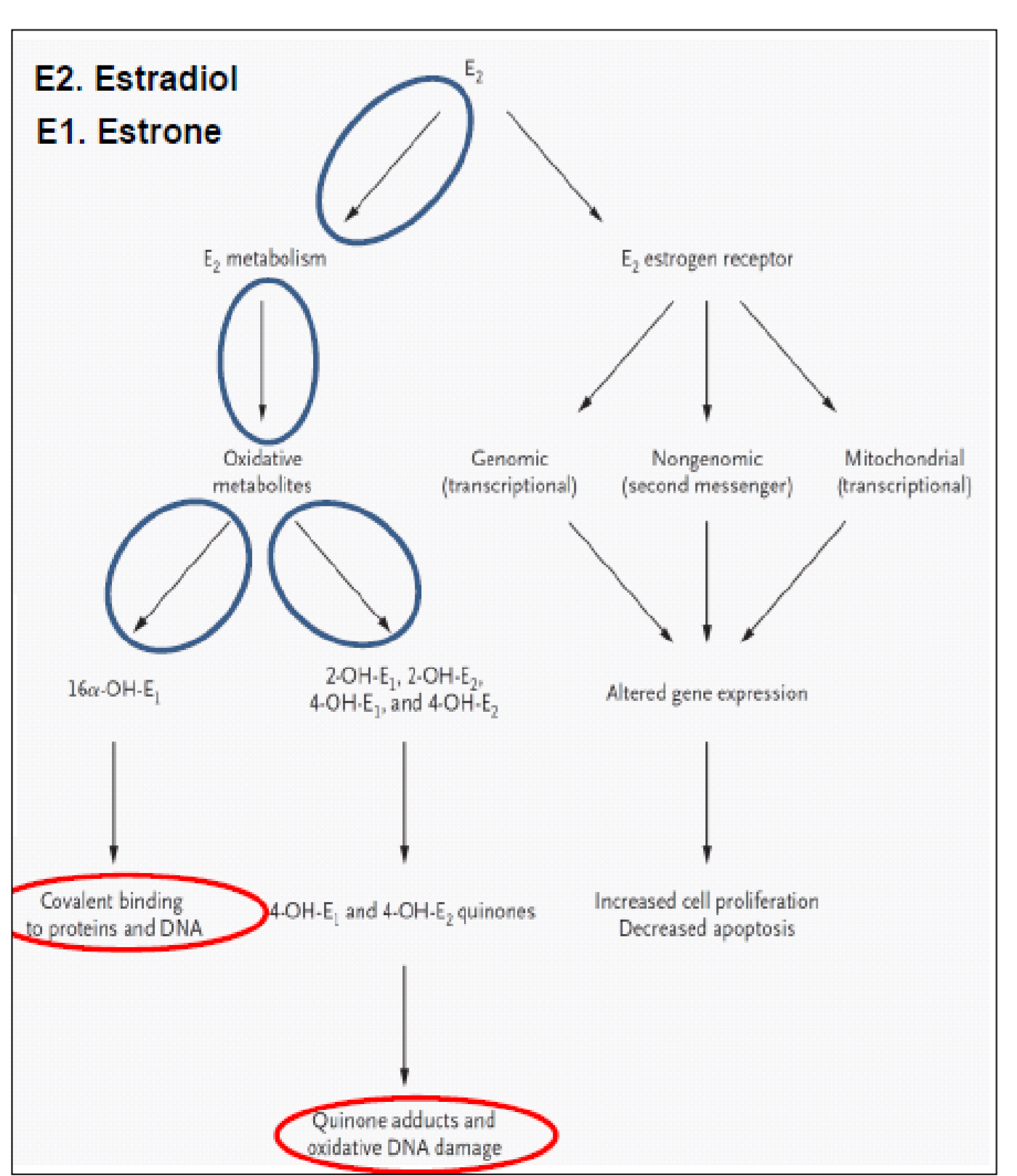


Fig. 4: Pathway for estrogen infertility and carcinogenesis

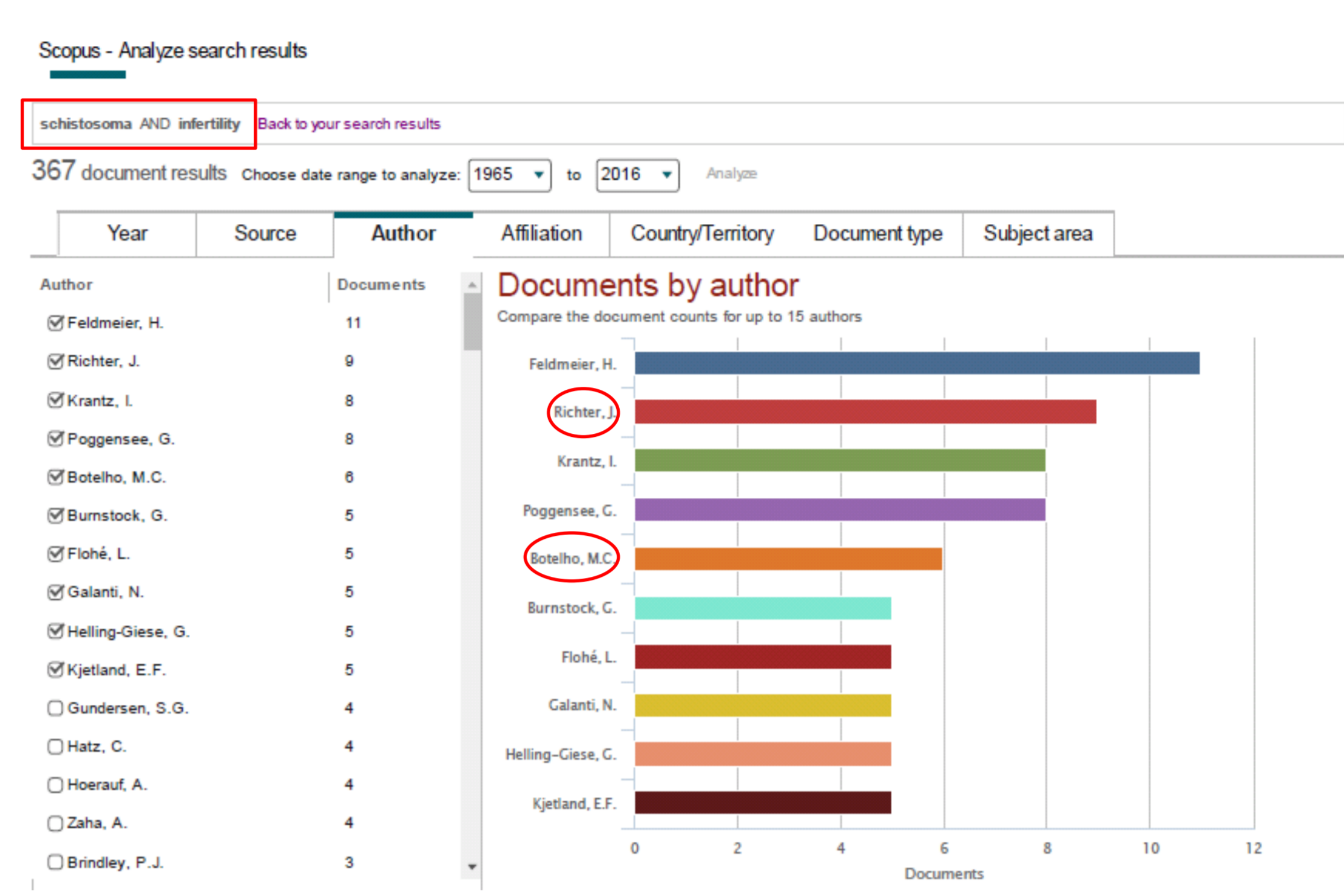


Fig. 1: Scopus data base search results "schistosomiasis AND infertility"

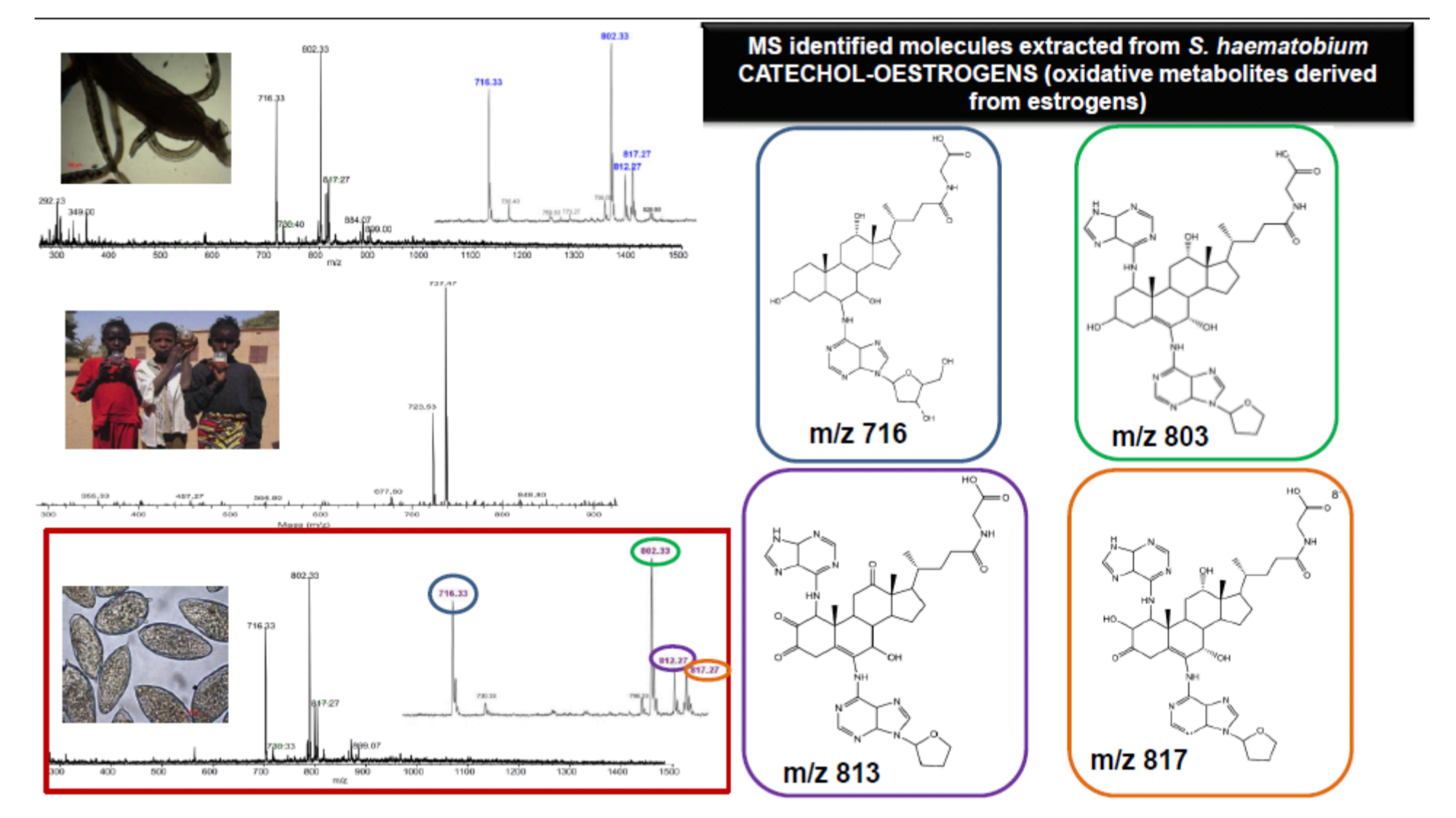


Fig. 2: Catechol-estrogens produced by *S. haematobium*

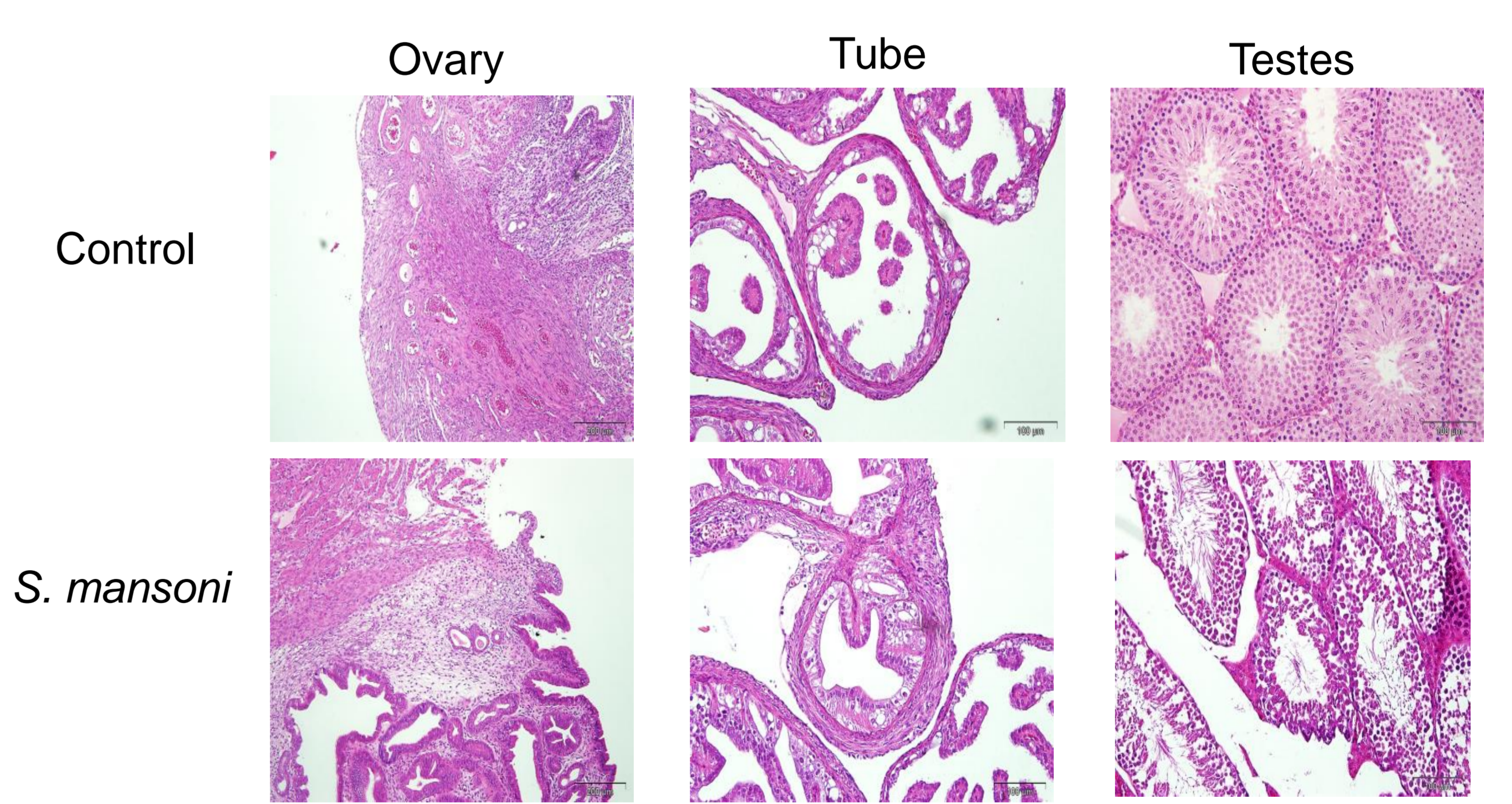


Fig. 3: Histopathology of reproductive organs of males and females (infected vs. control)

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