Poster #22

The Mycoestrogen Zearalenone Affects the Proliferation of Mouse Primordial Germ Cells in Culture and Activates the *Steel* Gene Promoter via an AP-1 Response Element.

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The increased incidence of testicular cancer could be due to an increased in utero exposure to exogeneous estrogens, like the wide spread mycotoxin zearalenone (ZEA).

Primordial germ cell (PGCs) were isolated from 129/Sv-Sl/+ and CD-1 mice embryos obtained at 11.5 day post coitum (dpc) and cultured in the presence of endogenous somatic cells and on fibroblast feeder layers. ZEA (1 and 10 uM) significantly increased the number of PGCs after 1 and 3 days in culture. The "anti-estrogen" ICI 182.780 blocked this effect. The number of BrdU positive cells increased after ZEA treatment, suggesting that ZEA increased proliferation of PGCs. RT-PCR analysis showed expression of estrogen receptor alpha (ERalpha) mRNA in the somatic cells of the gonadal ridge at dpc 11.5.

The *Steel* gene product, Stem cell factor (SCF), is an important factor for the regulation of proliferation/survival and migration of PGCs. A murine Sertoli cell line (TM4) expressing ERalpha, was transfected with a reporter plasmid expressing the luciferase gene under the transcriptional control of a Steel promoter AP-1 response element. In this system, 10 uM ZEA was shown to activate reporter gene expression 6-fold compared to control levels.

Our findings show that ZEA increases the proliferation of mouse PGCs at 11.5 dpc, which is a critical period for the formation of testicular tumors. Such an effect is likely mediated by ERalpha expressed by the somatic cells of the gonadal ridge and could be due to an increased activity of *Steel* gene promoter mediated by ERalpha under ZEA stimulation.