Findings of the Independent Academic Prostate Studies in CLARITY-BPA

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Early-life BPA Exposure Increases Prostate Cancer Susceptibility

BPA (10 µg/kg BW)

Birth

Puberty

↑ PCa incidence

→ No PCa

↑ Adult Estrogen

↑ E/T in aging men

Ho, et al, Cancer Research, 2006; Prins, et al, Repro Toxicology, 2011; Prins et al, Environ Health Perspectives, 2017
**SUMMARY**

- Repeated previous findings:
  - Increased prostate cancer risk
  - Greatest effect at lowest BPA dose i.e. 2.5 µg/kg BPA
Low-dose BPA increased E$_2$-induced adenocarcinoma multiplicity

Dorso-Lateral Prostate Ducts:

- Increased *multiplicity* of ductal adenocarcinoma in 2.5µg BPA (P<0.01 vs Vehicle).

  Trending for higher doses; borderline significance in parametric analysis.
How might early-life BPA exposure affect prostate cancer susceptibility later in life, long after BPA is cleared from the body?

Prostate Epithelial Cell Hierarchy

- Stem Cell
- Basal progenitor
- Bipotent progenitor
- Unipotent basal progenitor
- Unipotent luminal progenitor
- Luminal
- Neuroendocrine

- Self-renewal
- Transit amplification
- Differentiation

Questions: BPA

[Diagram showing the prostate epithelial cell hierarchy with labeled cell types and processes.]
CLARITY-BPA: Examined the stem and progenitor cells from BPA-exposed rat prostates.

Animal Tx at FDA-NCTR

Workflow at UIC

Prostasphere (PS) Assay and Passage
Chronic exposure to low-dose BPA increased prostate stem cell numbers and progenitor cell proliferation.

Passage 3 – Total PS #

Passage 3 – PS > 80 µM

Representative of stem cell number

Representative of progenitor cell proliferation

Symmetric Self-renewal

Symmetric Committed division
Chronic low-dose EE and BPA (25 and 250 µg/kg) exposures alter progenitor cell lineage commitment

See a shift towards increased basal progenitor lineage at the expense of decreased luminal progenitor lineage.
Propose: Chronic in vivo low-dose BPA exposures ↑ prostate stem cell numbers and altered lineage commitment underpinning an increased carcinogenic risk with aging.