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Alteration of mammary gland development by bisphenol a and evidence of a mode of action mediated through endocrine disruption

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Abstract:
The development and function of the mammary gland are endocrine-dependent processes, depending on the stage of development. Foetal and/or postnatal exposure to low doses of BPA alters tissue organisation through epithelial proliferation and stroma-epithelial interactions. BPA also alters the expression of E2-dependent epithelial and stroma transcriptomes. Several signalling pathways are consistent with the observed phenotype: proliferation and apoptosis, a focal adhesion pathway indicating changes in biomechanical properties of the extracellular matrix, and immune function. Some of BPA's effects are reversed by oestrogen and/or GPER inhibitors. BPA also alters the expression of epigenetic marks (EZH2, HOTAIR), which would explain the delayed effect of foetal BPA exposure. In conclusion, experimental evidence shows that pre- or postnatal BPA exposure consistently causes endocrine modifications in the mammary tissue of different animal species, disrupting stromal-epithelial interactions and ultimately increasing its susceptibility to carcinogens. An interspecies comparison highlights why and how these effects apply to humans.