

The Aryl Hydrocarbon Receptor Agonist 3,3',4,4',5-Pentachlorobiphenyl Induces Distinct Patterns of Gene Expression between Hepatoma and Glioma Cells: Chromatin Remodeling as a Mechanism for Selective Effects

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Genome-wide oligonucleotide DNA microarrays and real time reverse transcription-polymerase chain reaction (RT-PCR) were used to compare differential gene expression in rat glioma and hepatoma cell lines after exposure to the aryl hydrocarbon receptor (AhR) agonist 3,3',4,4',5-pentachlorobiphenyl (penta-CB). Under maximal inducing concentrations for cytochrome P450 1A1 (CYP1A1) in H4IIE rat hepatoma cells, both H4IIE and C6 rat glioma cells were exposed to sub-micromolar concentrations of penta-CB for 24 hours. Differential gene expression for approximately 28,000 gene probes were computationally analyzed and compared. As expected, penta-CB potently activated CYP1A1/2 transcription in liver-derived H4IIE hepatoma cells, yet did not do so in brain-derived C6 glioma cells. Additionally, we show that penta-CB causes: (1) distinct patterns of gene expression between tumor cells derived from liver or brain; (2) robust transcriptional activation of select C6 glioma gene ontologies; (3) over-expression of H4IIE hepatoma genes associated with tumor progression in liver; (4) greater than 100-fold over-expression of C6 glioma genes associated with protein processing and programmed cell death and/or metastasis; and, (5) tissue-selective histone deacetylase inhibition in C6 glioma, but not H4IIE hepatoma cells as signaled by galectin-1 over-expression.

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