

## The level and distribution pattern of HIF-1 $\alpha$ in the embryonic brain correspond to those of E2F1/Ret-1/Smc2 but not of E2F1/Ret-1

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**Abstract** We studied the tissue expression of cell cycle and cell death factors to investigate whether evidence of the involvement of the retinoblastoma gene in tumor formation extends to the control of the level and distribution pattern of E2F1 $\alpha$ , E2F1 $\beta$ , E2F1 $\gamma$ , and HIF-1 $\alpha$  in both embryonic and adult brains. Western blotting showed that during mouse brain development, the levels of E2F1 $\alpha$ , E2F1 $\beta$ , and HIF-1 $\alpha$  exhibited almost identical trends, whereas E2F1 $\gamma$  and Ret-1 were expressed in a cell cycle-dependent manner. The relative levels of E2F1 $\alpha$  in developing stages 10, 12.5, E18, and P14 changed only moderately with age, while those were characterized by several peaks of E2F1 $\alpha$  expression during E18. Despite high cell cycle-dependent expression, strong tissue heterogeneity relative to expression in the cerebellum was observed in the embryonic neocortex. In contrast, E2F1 $\beta$  and HIF-1 $\alpha$  expression was highly similar in both embryonic and adult brains, indicating that the distribution of HIF-1 $\alpha$  in the embryonic mouse brain is consistent with that of E2F1 $\alpha$  but not E2F1 $\beta$ . The tissue level of E2F1 $\beta$  in the brain was confirmed by immunoprecipitation in the presence of the anti-HIF-1 $\alpha$  antibody. However, using the indirect method, E2F1 $\beta$  was the only immunoprecipitated factor coimmunoprecipitating with anti-HIF-1 $\alpha$  in cultures of embryonic neuroblastoma cells.

**Key words:** HIF-1 $\alpha$ ; E2F1 $\alpha$ ; E2F1 $\beta$ ; E2F1 $\gamma$ ; Ret-1; Smc2; cell cycle; cell death; tissue heterogeneity; cell cycle-dependent expression; cell cycle-independent expression; cell cycle-dependent expression; cell cycle-independent expression; cell cycle-dependent expression; cell cycle-independent expression

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