11 beta Hydroxysteroid Dehydrogenase Type 2 is a Key Component of Neoangiogenesis in Renal Carcinoma and Glioma

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11 beta hydroxysteroid dehydrogenase type 2 (11HSD2) converts active cortisol to inactive corticosterone to protect mineralocorticoid and glucocorticoid receptors from illicit activation by high levels of circulating glucocorticoids. It has an important role in salt and water regulation in the distal tubule, is important in the maturation of the developing vasculature but may also limit the effectiveness of steroid based therapy.

In a study of expression of 11HSD2 in carcinomas derived from mineralocorticoid responsive tissue we noted 11HSD2 in new blood vessels in some tumours. This study was undertaken to systematically examine for the expression of 11 HSD2 and mineralocorticoid receptor in tumour vasculature during neoangiogenesis. We used immunocytochemistry on tissue microarrays of renal, ovarian, prostate and colorectal carcinoma and whole section staining of glioblastoma.

We found strong 11 HSD2 reactivity in pericytes of new blood vessels in 5/5glioblastomas and 29/30 clear cell carcinomas of kidney. Nuclear reactivity for the mineralocorticoid receptor was seen in the same cells. 11HSD2 was found infrequently (<10%) in other renal carcinoma subtypes and in the prostate, ovarian and colorectal carcinomas. RNA was extracted from frozen glioblastoma samples and 11HSD2 specific mRNA identified by rtPCR.

11HSD2 is crucial for normal artery and arteriole formation during development and these data suggest it may be important in protecting the mineralocorticoid receptor in tumour neoangiogenesis from the growth inhibitory effects of endogenous or, importantly, therapeutic glucocorticoids