Endogenous cortisol biosynthesis in human gliomas


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Abstract #6022

**BACKGROUND**

Human astrocytomas express the translocator protein (TSPO), which transfers cholesterol through the mitochondrial membrane and initiates Steroidogenesis.

Previous in vitro studies have reported steroid biosynthesis by glioma cell lines.

Synthetic glucocorticoids may interfere with the apoptotic effects of chemotherapeutic drugs.

Glucocorticoids may suppress microglial immune response in vitro.

**METHOD**

We investigated 30 human infiltrating astrocytomas and 20 oligodendrogliomas (10 examples of each WHO grade) (Table 1) for the expression of the proteins involved in cortisol biosynthesis peroxidase immunohistochemistry.

The expression of TSPO, P450scc, P450c17A1 and P450c11B1 in formalin fixed paraffin embedded tissue samples was assessed immunohistochemically using an avidin-biotin peroxidase method with a 3,3'-diaminobenzidine chromatogen. For pGR, the Super Sensitive Polymer HRP IHC Detection System (Biogenex Laboratories) was used.

Using immunohistochemistry on frozen sections, 24 were examined for the presence of cortisol with a polyclonal anti-cortisol antibody (Sigma Aldrich) intended for radiommunoassay. Sections were post-fixed in formalin after 2 hr incubation in primary antibody. The reaction product was revealed using Super Sensitive Polymer HRP IHC Detection System (Biogenex Laboratories).

Immunoblotting was performed on one histologically representative tissue sample from each tumor grade and histotype.

**RESULTS AND CONCLUDING REMARKS**

- The expression of corticosteroidogenic molecules, cortisol and glucocorticoid receptors increases with grade in astrocytic tumors but remained low in oligodendrogliomas.
- Our results unveil a novel autocrine / paracrine mechanism Endogenous cortisol synthesis in neoplastic cells of human high grade.
- Endogenous cortisol synthesis may explain chemoresistance of high grade astrocytomas.
- Endogenous production of cortisol may explain the suppression of microglial immune response against tumor cells.

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<th>TSPO</th>
<th>P450scc</th>
<th>P450c17A1</th>
<th>P450c11B1</th>
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<tr>
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**Figure 1.** TSPO in gliomas Grade II oligodendroglialomia (a); Diffuse astrocytoma (b); Glioblastoma (c); (ABC x20).
Boxplot (d) represents the distribution of TSPO in tumors of each grade and histotype - * represents outliers and the divider of the box indicates the median.

**Figure 2.** Western blotting analysis of P450scc, P450c17A1 and P450c11B1 in gliomas (OII - oligodendroglialoma, OII - anaplastic oligodendroglialoma, AII - diffuse astrocytoma, AIII - anaplastic astrocytoma, GBM - glioblastoma, AG - adrenal tissue).

**Figure 3.** Key steroidogenic enzymes in glioblastoma P450scc, P450c17A1 and P450c11B1 colocalize with GFAP - bottom panel - negative control (omitting the primary antibody), original magnification 20x.

**Figure 4.** Phosphorylated glucocorticoid receptors (a, x20) and cortisol in a glioblastoma (b, x40).

Acknowledgments

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