INTRODUCTION

Tumour Growth Factor β (TGFβ) isoforms belong to a super-family of cytokines that regulate cell growth and differentiation, cell motility, angiogenesis and apoptosis. Signal is transduced by a family of serine-threonine kinase receptors through activation of SMAD proteins. In cancer, activation primarily occurs after the formation of a complex between TGFβRII and TGFβRIII.

Previous in vitro studies have suggested that microglia may promote tumour growth via production of TGFβ family members in the tumour microenvironment.

Our aim is to investigate the expression of TGFβ and TGFβRII in astrocytomas and oligodendrogliomas, identify its cell source and discuss its possible role as therapeutic target in patients with.

METHOD


Fifty supratentorial adult gliomas (10 diffuse astrocytoma, 10 anaplastic astrocytoma, 20 glioblastoma, 4 low grade and 6 anaplastic oligodendrogliomas) were retrieved from the BTRC Tumour Registry at the Charing Cross Hospital. Patients ages ranged between 25 and 68 years; all received surgical debulking. High grade tumours were then treated with radiotherapy and chemotherapy.

TGFβ1 and TGFβ2 expression and the extent of microglial infiltration were assessed on tissue sections by immunohistochemistry using immunoperoxidase and double immunofluorescence. Antibodies used are shown in Table 1.

### TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>Manufacturer</th>
<th>Clone</th>
<th>Dilution</th>
<th>Pre-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGFβ1</td>
<td>Santa Cruz Biotechnology</td>
<td>Poly-clonal (TB21)</td>
<td>1:1200</td>
<td>Citrate buffer + 30min MW</td>
</tr>
<tr>
<td>TGFβII</td>
<td>Santa Cruz Biotechnology</td>
<td>Poly-clonal (V)</td>
<td>1:400</td>
<td>None</td>
</tr>
<tr>
<td>TGFβRII</td>
<td>Santa Cruz Biotechnology</td>
<td>Poly-clonal (V)</td>
<td>1:200</td>
<td>None</td>
</tr>
<tr>
<td>Iba1</td>
<td>Santa Cruz Biotechnology</td>
<td>Mono-clonal (1622-5)</td>
<td>1:75</td>
<td>EDTA + 40min MW</td>
</tr>
</tbody>
</table>

RESULTS

Dataset analysis: The microarray dataset expression of TGFβ genes showed no significant correlation between relative gene expression and glioma grade, either between datasets or within separate probes themselves in each individual dataset.

Immunohistochemistry: In all cases, TGFβI expression was restricted to tumour endothelium and perivascular macrophages. TGFβII expression localised to tumour cells in a subset of 9 astrocytomas (1 low grade astrocytoma, 2 anaplastic astrocytomas and 6 glioblastomas) (Fig. 1). No TGFβII was observed in oligodendrogliomas and no expression was seen in microglial cell (Fig. 2).

Double immunofluorescence studies using Iba1-confirmed the lack of TGFβII in microglia across all tumour subtypes (Fig. 2).

The immunoreaction for TGFβIII was positive in endothelial cells. A non-specific nuclear immunolabelling was seen in neoplastic cells but no obvious expression was observed.

CONCLUDING REMARKS

Our results do not presently support the use of TGFβIII in the treatment of human gliomas.

REFERENCES


