GLIAL EXPRESSION OF NEUTRAL ENDOPEPTIDASE-24.11 (NEP) IN TUMORS ARISING FROM NEUROTRANSPLANTATION OF RAT FETAL CORTEX CORRELATES WITH EXPRESSION OF TRANSFORMING GROWTH FACTOR-ALPHA

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Authors
BACK, SA
COLON, M
WANG, W
et al.

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DUAL EXPRESSION OF NEUTRAL ENDOCYTOSIS 24:11 (NEP) IN TUMORS ARISING FROM NEPHROTOXIC TRANSPLANTATION OF RAT FETAL CORTEX CORRELATES WITH EXPRESSION OF TRANSFORMING GROWTH FACTOR ALFA. Z.A. Bercu*, W. Wang*, C. Alles*, T. Heil*, and S. Louis†
Depos of Pediatnics, Anatomy and Neurology and the Clinical Cancer Center, University of California, Irvine.

The gene encoding NEP is identical to the common acute lymphoblastic leukemia antigen (CALLA). NEP is a nervous tissue expressed in fetal tissues with high expression in certain human glomerulonephritis. We report here a unique method to study NEP expression in spontaneously-induced tumors arising after nephrotoxicity. A fluorescence histochemical method (Bercu and Ginocchio, A. Cancer, 1991, 76:10-18) was used to localize NEP in brain sections from fetal rat embryos (E17) or adult rats which survived 4-6 weeks after transplantation of a suspension of rr fetal cortical cells (E17) into the rat brain. Tumor morphology was assessed by histological examination of the sections. Tumor sections were stained with nonfluorescent protein (NFP) or transforming growth factor-a (TGF-a). Tumor sections typically contained a mass which compressed the surrounding tissue. The apparent tumor contained several types of cells forming extracellular matrix. A fluorescence double-labeling technique demonstrated several types of cells containing both NEP and NFP: a) Many reactive astrocytes containing muet algin and glioma-specific gymnoctytes within the tumor; and c) occasional nests of cells which stained for NEP and were surrounded by reactive gliocytic processes. Within the tumor, glioma cells for both TGF-a and NEP were often observed in the same region. Occasional satellite clusters of cells, distinct from the main tumor, contained many TGF-a-positive glioma cells surrounded by reactive NEP staining. An examination of NEP staining in fetal rats (E17-21) indicated that there was extensive staining in the CNS which paralleled that which we have previously described in the adult. At a later fetal stage (E17-21), there were few NEP-positive gliomas in the fetal brains, as in the adult brains, we found NEP expression to be largely unassociated with glioma cells.

However, in our surviving fetal rat embryonic tumors, expression of NEP was found in the tumors or tumor tissue. It was significant that the number of glioma cells contained many TGF-a-positive glioma cells which appeared to be needed to maintain the growth of the tumor. Many of these glioma cells contained NEP. Given that TGF-a was shown to be selectively associated with malignant glioma in our series of 20 patients, we concluded that in our tumors, glioma cells may be positive for the proliferative potential of the tumors. This technique may be useful to study the role of NEP in the growth of malignant gliomas and should be useful to aid the potential therapeutic role for NEP inhibitors in slowing the growth of malignant gliomas in children. S.A.B. is a Girouard Foundation Fellow.

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