

CHARACTERIZATION OF VEGF RECEPTOR TWO EXPRESSION IN THE RETINOBLASTOMA MOUSE MODEL LH β Tag

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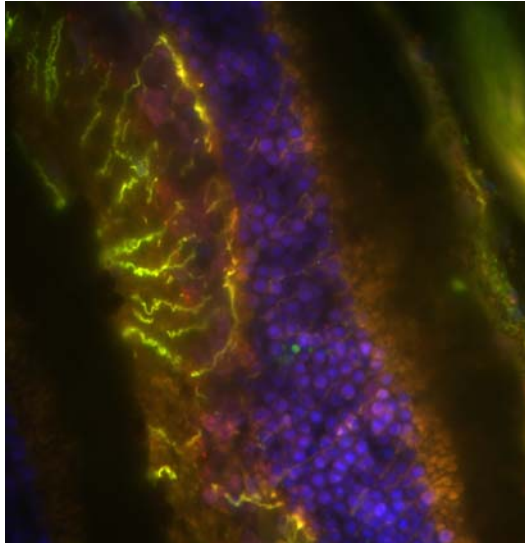
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PURPOSE. Angiogenesis is important in determining the invasive potential of retinoblastoma. VEGF receptor 2 (VEGFR-2) is similarly important in promoting pathologic angiogenic states, and may provide a “survival signal” for retinal cells. We previously showed that VEGFR-2 was strongly upregulated in the LH β Tag mouse model of retinoblastoma. Interestingly, the morphology of the VEGFR-2 positive cells was most consistent with muller cells. We tested the hypothesis that VEGFR-2 is expressed primarily on muller cells.

METHODS. Eight week old LH β Tag mice and background mice were enucleated and eyes were snap frozen and fixed in 4% paraformaldehyde. Five micron sections were obtained. Antibodies specific for VEGFR-2, muller cell marker vimentin and newly formed blood vessels (endoglin) were reacted with the sections. Secondary antibodies bound to FITC or Rhodamine were reacted with the sections. In some experiments, vimentin and VEGFR-2 primary antibodies were reacted with the same section for direct co-localization analysis. Negative controls, with omission of the primary antibody or use of the wrong secondary antibody in the dual staining sections, were performed.

RESULTS. The VEGFR-2 immunostaining was most intense in the ganglion cell layer, inner plexiform layer, outer plexiform layer, and within the body of the tumor in eyes with large tumors. The morphology of most VEGFR-2 positive cells was most consistent with muller cells (see Figure 1). VEGFR-2 co-localized with muller cell marker vimentin (Figure 1). In general, VEGFR-2 did not co-localize with endoglin staining.

Figure 1



Co-localization of muller-glial marker vimentin and VEGFR-2

CONCLUSIONS. VEGFR-2 is upregulated on muller cells in the LH β Tag model of retinoblastoma. The upregulation of VEGFR-2 on muller cells could indicate a more active role for these glial cells in supporting retinoblastoma growth and survival.

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