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The immune-expression of P-glycoprotein in Retinoblastoma

Souza Filho JP1,2, Caissie A2, Martins MC1, Callejo SA2, Belfort Jr. R1, Burnier Jr MN2 1- Federal University of Sao Paulo – Department of Ophthalmology – Sao Paulo - Brazil 2- Henry C. Witelson Ocular Pathology Lab. McGill University – Montreal - Canada Purpose: Retinoblastoma (RB) is the most common malignant intra ocular tumor in children. Chemotherapy is frequently used for the treatment of this tumor, however, previous data have indicated that many retinoblastoma tumor cells express the multiple drug resistance phenotype due to P-glycoprotein (P-gp) expression. The objective of this study is to determine the expression of P-gp in retinoblastoma. Methods: Twenty formalin-fixed, paraffin-embedded specimens of RB were collected from The Henry C. Witelson Ocular Pathology Laboratory at McGill University. Twelve patients had undergone enucleation alone while eight patients received chemotherapy before enucleation. Immunohistochemical staining was performed in all cases using a monoclonal antibody against P-gp (clone C494). Slides were reviewed to determine the degree of differentiation, the presence of choroidal and optic nerve (ON) invasion as well as the pattern of P-gp immune-expression. Results: 9 of the 20 RB were of an intermediate degree of differentiation, 8 were considered to be well-differentiated, and the remaining 3 were poorly differentiated tumors. 6 of the 30 tumors showed ON invasion, 1 had choroidal invasion. 6 well differentiated tumors and 2 tumors with an intermediate degree of differentiation were highly positive for P-gp. High P-gp expression in rosette areas was found in 2 well-differentiated tumors and 1 tumor with an intermediate degree of differentiation. High P-gp expression in areas with glial differentiation was found in 6 well-differentiated tumors and 2 with an intermediate degree of differentiation. Five of six tumors with ON invasion were positive for P-gp. Conclusion: We observed that the P-gp expression was seen preferentially in well-differentiated Retinoblastomas. Within the tumor, well-differentiated areas displaying rosettes and areas of glial differentiation expressed high levels of P-gp. These findings may suggest that high levels of P-gp in well-differentiated tumors may correlate with resistance for chemotherapy. Moreover, RB with ON invasion demonstrates expression of P-gp. The role of P-gp is unclear in determining the degree of invasion of such tumors.