( ) R1 ( ) R2 ( ) R3 (X) PG0 ( ) PG1 ( ) Estagiário ( ) Tecnólogo ( ) PIBIC Last Name - Pereira First Name - Patricia Middle - Rusa

Service (sector) Tumor and Pathology - McGill University, Montreal, Canada Nº CEP

Gleevec: a new therapeutic target for Uveal Melanoma?

PR Pereira 12, AN Odashiro 12, JCA Marshall 1, JP Souza Filho 12, Belfort R2, MN Burnier Jr1. 1Ocular Pathology, McGill University, Montreal, Canada; 2Ophthalmology, UNIFESP, Sao Paulo, Brazil. **Purpose.** C-kit (CD117), a tyrosine kinase protein-receptor (TKR), has been recognized as a therapeutic target for some tumors. In a previous study, we demonstrated that 78.2% of uveal melanoma (UM) specimens are c-kit positive. Imatinib mesylate (Gleevec®, Novartis) is a compound that specifically inhibits TKR. The aim of this project is to evaluate the effect of Gleevec® in the proliferation and invasion of human UM cell lines. **Materials & Methods.** The Sulforhodamine-B based assay kit (TOX-6, Sigma) and a Matrigel coated modified Boyden's chamber were performed to compare the proliferation and invasion rate, respectively, of 5 human UM cell lines (92.1, SP6.5, MKT-BR, OCM-1, and UW-1) with and without Gleevec®. Briefly, the UM cell lines were seeded at a concentration of 2.5x103 cells per well, in a minimum of six wells per cell line. Twenty-four hours following seeding, Gleevec® at the concentration of 10mM (highest dose tolerated by humans), were added to the experimental wells. After forty-eight hours of incubation, the cells were fixed to the bottom of the wells using a solution of 50% Trichloroacetic acid for 1 hour at 4° C. Control cell proliferation rate over 48 hours was compared to proliferation rate of cells exposed to Gleevec® during the same time period. The Student's t- test was used. The invasive potential of the UM cell lines was characterized. 10mM of Gleevec® was added to the top layer of each well. Wells were incubated for 24, 48 and 72-hour intervals and observed at these periods as well. **Results.** There was a statistical significant decrease in the proliferation and invasion rates of all 5 cell lines. All 5 UM cell lines (92.1, MKT-BR, OCM-1, SP6.5, UW-1) that were directly exposed Gleevec® showed a decrease in proliferation as compared to control (p value of 0.001354991, 0.012655861, 9.47698x10-7, 0.002754018 and 5.79576x10-6 respectively). The percent invasion of cell lines according to the baseline invasion without and with Gleevec® was, respectively: MKT-BR (38.4% and 1.03%) > OCM-1 (21.7% and 0.1%) > 92.1 (14.4% and 0.2%) > UW-1 (12% and 0%) > SP6.5 (3% and 0%). **Conclusion**. Gleevec® does decrease the proliferation and invasion rates of human UM cell lines. These results justify the need for a clinical trial to investigate in vivo the response of UM toGleevec®.