Potential of Y79 Retinoblastoma as a Model Drug Screening System [MAS]

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Y79 is a human retinoblastoma cell culture line grown optimally in suspensions but also grown in monolayer culture when the growth

surface is pre-treated with attachment factors such as poly D-lysine or fibronectin. Y79 shows many characteristics of normal retinal cells including the presence of enzymes responsible for melatonin synthesis. Both N-acetyltransferase (NAT), which catalyzes the conversion of serotonin to N-acetyl- serotonin, and hydroxyindole-O-methytransferase (HIOMT), which catalyzes the conversion of N-acetylserotonin to melatonin, are active in this culture system. In our attempts to better understand migraine headache and to build superior anti-migraine drugs, we have been attracted to melatonin because light is a regulatory parameter for both melatonin and migraine. One of the chief problems in anti-migraine drug development has been a reliable, relatively straight forward system for evaluating the potential of new drugs. The physiological characteristics of Y79 in concert with the ease of culturing and treating the cells suggest that it has potential as a model in vitro system for screening anti-migraine drugs. In the preliminary studies reported here, Y79 cells were grown in suspension and in some cases in monolayer, in the presence of RPMI 1640 medium containing 10% fetal calf serum. Cultures were incubated in a humidified 5% C02 atmosphere at 37 ° C. Drug treatments were for 24 hours, after which cells were harvested and homogenized by sonication. NAT activity was determined by incubation of homogenates at 30 ° C for 30 minutes in the presence of tryptamine and 14C-acetyl Co-enzyme A. Radiolabeled product was quantified by liquid scintillation spectroscopy and protein was measured by the Bio-Rad procedure. Current anti-migraine drugs were tested for activity in the system. Propranolol and sodium valproate both elevated NAT activity while the calcium channel antagonist flunarizine lowered activity. Dihydroergotamine and buspirone, a 5-HT1a partial agonist both were without activity. Additionally, the 5-HT1a agonist 8-OH-DPAT was used to test for the presence of receptor, and a dose-response curve was obtained with a Kd of approximately 1 nM. These pilot studies warrant further exploration of this system, and hint that the system may be predictive of prophylactic anti-migraine drug activity if not acute activity. Serotonin receptors may be present, but melatonin receptors have not been evaluated at this point.