# ANDROGEN-DERIVED COMPOUNDS REGULATE C6 GLIOMA CELLS GROWTH

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Steroid hormones may influence the development and control of glioma growth by interacting with their receptors and regulating the transcription of target genes. C6 glioma cells and many types of glioblastomas were shown to express two types of the classical androgen receptors. Dihydrotestosterone in a concentration-dependent manner could regulate signaling pathways in C6 glioma cells [1]. One of perspective antitumor androgen-derivative drugs is abiraterone acetate (AA). To the best of our knowledge, in spite of the ability of AA to penetrate blood-brain barrier [2], effects of the compound on glioma cells have not been reported.

The aim of this work was to investigate the effects of steroidal and indole derivatives on C6 glioma cells proliferation. Two steroids, N-(indol-3-ylethyl)-3β-hydroxyandrost-5-en-17β-amine (DTPA) and N-methyl-3β-hydroxyandrost-5-en-17β-amine (DAM) were obtained by reductive amination of dehydroepiandrosterone (DHEA) with tryptamine (TRPA) and methylamine hydrochloride, respectively, according to [3]. The structures were confirmed by mass, infrared and nuclear magnetic resonance spectroscopy. C6 glioma cells in monolayer on the 2$^{nd}$ day of growth were exposed to compounds for 24 h and then the number of cells was counted.

Treatment with DTPA, DAM and TRPA for 30-60 min did not affect cell viability. In contrast our study we demonstrated that AA and compound DTPA at $1 \cdot 10^{-5}$ M concentration can inhibit glioma cells proliferation by 55±5% and 45±6%, respectively. At the same time, steroid DAM, being a structural moiety of DTPA, did not cause such pronounced effect, implying the importance of the N-heterocycle in the steroids' side chains. TRPA, another part of DTPA, led to 25 % decrease of glioma cells proliferation.

The effect of DTPA could be due to influence on steroidal signaling, including potentially competing membrane-associated and nuclear androgen receptors, which are confirmed in C6 glioma cells [1]. It was published that DHEA promotes survival of glioma cells [4], whereas its biosynthetic precursor pregnenolone induces their apoptosis [5]. Thus, inhibition of CYP17, which catalyzes pregnenolone-to-DHEA conversion, could be a new therapeutic strategy against this type of cancer. Depending on the specificity of steroid biosynthesis, tranport and reception, the outcome of androgen treatment of glioma might be different. In general, enzymes of steroidogenesis are known to be promising targets for anti-cancer drug developing [6]. Therefore, synthesis of androgen-containing molecules with designed properties is of current interest.

In summary, ability of AA and a newly synthesized DTPA demonstrated glioma growth inhibition, providing opportunity to develop steroidal derivatives as potential drug candidates agains the cancer.

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