THERAPEUTIC POTENTIAL IN VITRO OF TELOMERASE INHIBITOR MST-312 IN TUMOR CELL LINES WITH DIFFERENT PROLIFERATIVE PATTERNS

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Currently, there is no effective treatment for all kinds of cancer, and probably this will only be feasible when the cellular immortalization (maintenance of telomeres), a phenomenon common to all types of tumors is better understood. Despite the immortalization is critical for any tumor maintenance, for decades all “new” chemotherapy agents targeted only cell proliferation. It is known that, in 85-90% of cancers, immortalization occurs by telomerase expression. In fact, this enzyme is an important target for development of new anti-cancer drugs. In this work, the cytotoxic action of the telomerase inhibitor MST-312 was evaluated in three different tumor telomerase positive cell lines. Expression of telomerase was confirmed by RT-PCR. Cell viability after 80 hours exposition of increasing concentrations of MST-312 was measured by MTT assay. The same assay was used to determine doubling time (DT) of each culture. The IC50% values calculated by nonlinear regression of the data were: 2.03μM for U251 cells, 7.87μM for HEK-293 cells and 16.21μM for MDA-MB-231 cells. Interestingly, according to the DTs found, during treatment the amount of cells in cultures duplicated 2.38, 2.04, and 3.31 times for U251, HEK-293 and MDA-MB-231 respectively, what is not enough to promote shortening of telomerases. In conclusion, MST-312 exhibits cytotoxic action at high concentration through a mechanism not associated to telomerase inhibition. It is a very important data since anti-telomerase therapy is a current approach. Also, many studies showed that inhibiting telomerase activity in tumor cells leads to a phenomenon known as alternative lengthening of telomeres (ALT), an alternative pathway for immortalization that is not totally understood yet. Our data give parameters (sub-toxic concentrations of telomerase inhibitor) to study this phenomenon in vitro.

Keywords: Cancer, telomeres, telomerase