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Sorafenib effect on human colon cancer cells HCT116 and HCT116 p53-/-M Al Hassan¹, A Baltaji¹, J Borjac¹, R Fakhouri¹ and J Usta²¹Beirut Arab University, Lebanon²American University of Beirut, Lebanon

Sorafenib, a kinase inhibitor, has been approved among the drugs for the treatment of radioactive iodine resistant thyroid carcinoma, primary kidney and liver cancer. Reported targets of sorafenib include VEGFR, Raf family, and PDGFR belonging to the general class of tyrosine kinases. Blocking growth signals in kidney and breast cancers underlie one of the mechanisms of sorafenib anti-tumor effects leading to cell death. We hereby examine the effect of sorafenib on human colon carcinoma cell-line HCT116. We also investigate the possible role of p53 in mediating this effect using mutant HCT116 p53^{-/-} cells. Cultured wild and mutant cells are treated with sorafenib (0-75 μM) for 24 hr. This is followed by assessing the viability of cells using MTT and trypan blue exclusion assays. We also examined if sorafenib mode of action is mediated by ROS. Levels of ROS were determined in the presence and absence of antioxidants using the colorimetric NBT assay. Our preliminary results show a concentration dependent decrease in viability (trypan blue) with an estimated EC₅₀ of 10 and 25 μM for HCT116 and HCT116 p53^{-/-} respectively. Compared to trypan blue, MTT results were similar in case of HCT116 p53^{-/-} but were significantly different with HCT116. Furthermore we obtained a significant increase in level of ROS of: 37.11% and 31.30% for HCT116 and HCT116p53^{-/-} respectively. However, 2 hr. pre-incubation of cells with antioxidants, Trolox, N-acetylcysteine (NAC), and catalase, prior to sorafenib treatment, exerted no different effect. No restoration of viability or decrease in generated ROS level was noted. Our preliminary findings show that sorafenib action is independent of ROS level and p53 expression and further investigations on the mechanism(s) of sorafenib action are ongoing.

Biography

M Al Hassan is a current PhD candidate at the Beirut Arab University, working in collaboration with the American University of Beirut on Sorafenib and its *in-vitro* and *in-vivo* effects on colorectal cancer. She has graduated from the Lebanese American University with a Master's degree in Cells and Molecular Biology. Her MS thesis was about the effect of metformin on the metastasis and the 3D motility of glioblastoma cancer cells.

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