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Artemis inhibitor: A new approach for radiotherapy

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The higher relative biological effectiveness (RBE) or radiation weighting factor (WR) of any prescribed radiotherapy determines the effectiveness of radiation dose to kill the target cells in a biological system. Currently our knowledge limits the effectiveness to the radiation source and type of radiation that deposits energy into the target tissue. However the RBE and WR can be enhanced by two folds if the target tumor mass can be radio-sensitized with small molecule inhibitors that inhibit the DNA repair process, before tumor cells are bombarded with the radiation dose. We propose the development of radio-sensitizers from inhibitors of Artemis and DNA-PKcs as they increase the cancer cell lethality when coupled with ionizing radiation (IR). Inhibitor of non-homologous end-joining repair (NHEJ) pathway enzyme DNA-PKcs (NU7026) at 10 μ M concentration lowers cell viability by up to 50% at 4Gy of the radiation dose (CO60 gamma source). DNA-PKcs inhibition resulted in defects in repair pathway while the novel Artemis inhibitor (purchased from University of California) did not show these effects. Inhibition of artemis followed by IR caused increased cell killing of four primary ductal carcinoma cell lines at low dose of radiation as compared to DNA- PKcs. DNA repair changes were not significant for artemis inhibition. We used 2-hydroxy-5-methoxybenzaldehyde 4-anilino-6-(3, 5-dimethyl-H-pyrazolyl)-, 3, 5-triazin-2-ylhydrazone for the inhibition of Artemis and results were compared to literature where siRNA was used for Artemis inhibition. To achieve improved therapeutic ratio such radio-sensitizers are a need of the hour and should be developed as chemotherapeutic drugs.

Biography

Nasir Jalal has completed his PhD from the Colorado State University, USA and currently engaged in Post-doctoral studies at the School of Pharmaceutical Science and Technology, Tianjin University, China. He is an Academician and Researcher since 2007 working in the field of Radiation Induced DNA Damage and Repair Mechanisms. He has published more than 10 papers in reputed journals and has served as the Expert Committee Member for biological drugs at the Drug Regulatory Authority of Pakistan.

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