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### **Decreased Camptothecin sensitivity of cancer stem-like cell population correlates with phosphorylation state of DNA topoisomerase-I**

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Cancer stem cells are characterized by indefinite self-renewal potential and capacity to differentiate into progeny cells that constitute the bulk of tumor. Moreover, they are frequently refractory to anti-cancer therapy. The present study addressed the molecular mechanism behind resistance towards the anti-tumor drugs like camptothecin. The CD44+ and CD44- subpopulations of colorectal cancer cell line Caco-2 were analyzed separately for their sensitivities to camptothecin. Cancer stem-like cell subpopulation CD44+ is significantly less sensitive towards treatment with camptothecin than CD44- cell subpopulation. Topoisomerase-I from the two subpopulations were differentially phosphorylated in a manner that appeared to determine the drug sensitivity and activity of the enzyme. This finding was further supported by the fact that phosphorylation of topoisomerase-I in CD44+ cell extract by protein kinase CK2 converted the enzyme to a camptothecin sensitive, more active form mimicking topoisomerase-I in extracts from CD44- cells. Therefore, the reduced activity level and insensitivity towards camptothecin could be ascribed directly to hypo-phosphorylation of topoisomerase-I in the cancer stem-like cell subpopulation. This is the first example of the phosphorylation state of topoisomerase-I modifying both activity and camptothecin sensitivity of the enzyme. In conclusion, to our knowledge this is the first report of an altered topoisomerase-I activity in cancer stem-like cells relative to progeny cells of a cancer cell line that can explain the camptothecin resistant phenotype of the cancer stem cell subpopulation.

#### **Biography**

Amit Roy has completed his PhD in 2009 from CSIR-Indian Institute of Chemical Biology, Kolkata, India and Postdoctoral studies from Aarhus University, Denmark. He is now an Assistant Professor at Department of Biotechnology, National Institute of Pharmaceutical Education & Research, India. He has published more than 21 research papers in reputed peer-reviewed international journals. His PhD work was highly recognized by Indian National Science Academy (INSA) and he has been awarded the INSA Young Scientist Medal and Professor LSS Kumar Memorial Award in the year 2011. Apart from that, he got many awards including Best Award, Best Presentation Awards, etc.

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