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Cancer stem cell: A new paradigm shift in silibinin efficacy to control colorectal cancer

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Colorectal cancer (CRC) is second leading cause of cancer-related deaths in US. Cancer stem cells (CSC), now recognized as main cause for initiation, promotion and progression of CRC, are inherently resistant to chemo- and radio-therapies which has been the major cause of failure to most of the current therapies. Thus, discovery and development of agents, especially chemopreventive agents, which also target both 'initiated' stem cells and colon CSC, might provide better opportunities to control CRC at both early and advanced stages. We have recently reported the strong preventive and therapeutic efficacy of silibinin in different CRC pre-clinical models. Accordingly, here we assessed silibinin effect on colon CSC and associated mechanisms. The growth kinetics and cycling properties of colon CSC enriched spheres indicated a significant but differential inhibitory effect of silibinin on three different human CRC cell lines. Differentiation assays of these spheroids under serum conditions indicated the formation of more differentiated clones by silibinin treatment. Mechanistic studies showed that silibinin significantly decreases CSC marker CD44 mRNA expression, Notch-mediated signaling, and protein levels of cleaved Notch and its transcriptional target Hes-1. The implications of such an effect are tremendous, since the disruption of homeostasis (regulated in part by Notch signaling) among stem cells and progenitor cells in intestinal region results in the expansion of CSC pool together with an increase in proliferative cell populations.

Biography

Rajesh Agarwal has studied cancer chemoprevention in a wide range of epithelial cancer models including skin, prostate, breast, lung, bladder, colon, etc. for more than 25 years, during which time he has authored more than 320 peer-reviewed publications. He has served (or presently serving) on the editorial boards for the *Cancer Research*, *Cancer Prevention Research*, *Molecular cancer Therapeutics*, *Molecular Carcinogenesis*, etc. He serves on several NIH/NCCAM/NIEHS/NCI Scientific Review Committees related to various aspects of Cancer Research.

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