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Dissecting the functional roles of CD44 in human colorectal cancer stem cells and identifying novel agents capable of selectively eradicating this population

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This lecture will first address the functional roles of CD44 in the initiation and/or maintenance of human colorectal cancer stem cells (CRSCs) present in several established human colorectal carcinoma (CRC) cell lines. The author will present the results showing that much higher soft agar colony-forming ability and *in vivo* tumorigenicity are associated with the CD44⁺ HCT-15 CRC cells than their CD44⁻ counterparts. In addition, significant upregulation of Snail protein and marked downregulation of miR-203, a well-known stemness inhibitory microRNA, are found in CD44⁺ HCT-15 cells. Accordingly, the expression levels of Snail (other EMT inducers as well) and miR-203 in both HCT-15 and HCT-116 cells can be positively and negatively modulated by CD44 overexpression, respectively. Further analyses show that Snail suppresses miR-203 expression by binding directly to a specific E-box in the miR-203 promoter and c-Src activity stimulated by the interaction between CD44 and hyaluronan (HA) appears to be crucial for the activation of Snail. Further supporting the importance of miR-203 in diminishing the stemness of these CRSCs, significant increases of their respective stemness are observed after the function of this microRNA in HCT-116 and HT-29 cells being disrupted. Besides above findings, attendees of this lecture will learn the utility of Connectivity map (CMap) analysis in accelerating the identification of agent(s) capable of selectively eradicating CRSCs. Using this novel bioinformatics approach, several “old” drugs with such activity were identified and the effect(s) as well as the molecular mechanism(s) of one compound will be discussed thoroughly in this meeting.

Biography

Yeu Su is currently working in the Institute of Biopharmaceutical Sciences of NYMU. After getting his PhD from the University of Wisconsin-Madison, he went to the Johns Hopkins Oncology Center for his Post-doctoral training. He has studied the molecular mechanism of colorectal carcinogenesis for almost 15 years and his recent research has focused on understanding the origin of colorectal cancer stem cells as well as identifying novel agents capable of selectively eradicating them. Besides being the reviewers of a number of international journals, he now also serves on the editorial board for the *World Journal of Biological Chemistry*.

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