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Assessment of the stemness-suppressive effects of several SHP-1 activators in human colorectal cancer cells

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STAT3 activation has been shown to be associated with enhanced malignancy and metastasis in human colorectal cancer (CRC). Moreover, active STAT3 was reported to be critical for the proliferation and survival of human colorectal cancer stem cells (CRSCs). Accordingly, several STAT3 inhibitors have been shown to block both the viability and self-renewal of CRSCs. Therefore, novel agents capable of reducing the levels of active STAT3 may help in treating CRC more effectively.

Because STAT3 is activated mainly by the phosphorylation of its tyrosine 705, a dephos-phorylation of this phosphor-residue executed primarily by the SH2 domain-containing phosphatase 1 (SHP-1), results in its inactivation. In this study, we assessed whether three novel SHP-1 activators including Sorafenib, SC-43, and SC-2001 could suppress the stemness of HCT-116 and HT-29 human CRC cells. Even though all three SHP-1 activators not only inhibited sphere formation but also induced sphere shrinkage of both cell lines, SC-2001 was excluded due to its low potency. Subsequently, Sorafenib and SC-43 were shown to suppress the anchorage-independent growth in both CRC lines. Furthermore, two agents could inhibit the expression of several CRSC markers as well as reduce the CD133+/CD44+ subpopulations in these cells. Interestingly, SC-43 was much more potent than Sorafenib in reducing the stemness properties of two CRC lines which could be accounted by its higher efficacy in reducing their active STAT3 levels. Since the dosages of both Sorafenib and SC-43 required for suppressing the stemness were significantly lower than those for diminishing the active STAT3 levels, investigation of the possible involvement of some "off-target" effects in their CRSC-suppressive activities is currently underway.

Biography

Yeu Su has completed his PhD. from University of Wisconsin-Madison and postdoctoral studies from the Oncology Center of Johns Hopkins University in 1991 and 1993, respectively. He is currently a full professor of the Institute of Biopharmaceutical Sciences of National Yang-Ming University, a premier Medical University in Taiwan. He has published more than 50 papers in reputed journals such as Oncogen and Stem Cells, and has been serving as an editorial board member of the World Journal of Biological Chemistry.

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