

BMPR-IB reduces the malignancy of glioblastoma cells by upregulation of p21 and p27Kip1

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In the present study, we detected decreased expression of phospho-Smad1/5/8 and its upstream signaling molecule, bone morphogenetic protein receptor IB subunit (BMPR-IB), in certain glioblastoma cell lines compared to normal astrocytes. Forced BMPR-IB expression in malignant human glioma cells, which exhibit lower expression of BMPR-IB, induced the phosphorylation and nuclear localization of smad1/5/8 and arrested the cell cycle in G1. Additionally, colony formation analysis and immunofluorescence showed that BMPR-IB overexpression could suppress anchorage-independent growth and promote differentiation of these glioblastoma cells. We also observed significant accumulation of p21 and p27kip1 proteins in response to BMPR-IB overexpression, whereas the expression level of Skp2 protein decreased during this growth arrest and differentiation process. The results were consistent with real-time RT-PCR data. Furthermore, overexpression of BMPR-IB also inhibited the growth of subcutaneous and intracranial tumor xenografts and prolonged the survival of mice injected intracranially with BMPR-IB-overexpressing glioblastoma cells. Conversely, inhibition of BMPR-IB caused SF763 malignant glioma cells, a line known to exhibit high BMPR-IB expression that does not form tumors when used for xenografts, to show increased growth and regain tumorigenicity in a nude mouse model system, ultimately shortening the survival of these mice. Our results suggest that decreased expression of BMPR-IB in most human glioblastoma cells contributes to glioma tumorigenicity and that overexpression of BMPR-IB may induce growth arrest and differentiation of glioblastoma cells due to upregulation of p21 and p27kip1 *in vitro* and *in vivo*. BMPR-IB could represent a new potential therapeutic target for malignant human gliomas.

Biography

Shuang Liu has studied molecular biology and molecular therapeutics of brain tumor and stem cells for 10+ years, during which time she has been in charge many research projects about glioma and cancer stem cells, including two Chinese National Science Foundation (No: 30873029 and No: 81172384). She authored more than 20 peer-reviewed reports. Dr. Shuang is a member of the Chinese Neuroscience Society, and has served on the editorial boards for Chinese Journal of Integrated Traditional and Western Medicine for about 10 years.

Aberrant epigenetics and nanomedicine: Right therapeutic target and new paradigm for leukemia treatment

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This lecture will address a variety of topics related to the therapeutic application of nanomedicine in leukemia characterized by aberrant epigenetics, and will include discussion of: the oncogenic role of DNA hypermethylation in leukemogenesis; the molecular mechanisms of abnormal DNA methyltransferase (DNMT) activity and acquired resistance to chemotherapy; the factors affecting experimental outcomes from current available DNA hypomethylating agents; the implications of imbalanced microRNA-protein network; the rationale of developing new DNMT inhibitor; the potential benefit of DNMT protein abundance in drug design and development; the pitfalls of current drug delivery for small molecule compounds and oligos (siRNA, microRNA); the importance of appropriate drug delivery via therapeutic nanoparticles; the better clinical outcomes in leukemia accomplished by suitable drug delivery; and novel concept of combination therapies. Additionally, attendees of this lecture will be aware of the imperativeness for the precise and strict selection of candidate drug targets as well as drug formulations, in order to greatly improve the management of leukemia disease.

Biography

Shujun Liu has studied leukemia molecular biology, cancer epigenetics and therapeutics for 10+ years, during which time he has authored about 80 peer-reviewed reports. He currently serves as section leader of Cancer Epigenetics & Experimental Therapeutics and director, Epigenetics Laboratory, at the Hormel Institute, University of Minnesota. Dr. Liu is a member of Editorial Review Board, Journal of Hematological Malignancies, and he has served as peer reviewer on NIH study section, India Alliance fellowship, and Bankhead-Coley Cancer Research Program.