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RTVP-1 Promotes the mesenchymal transformation of glioma stem cells via the CXCR4 and the IL-6 pathways

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Glioblastoma, the most aggressive primary brain tumors, are categorized into the major subgroups: Proneural, neural, classical and mesenchymal, the latter being characterized by increased invasion and poor prognosis. We recently identified RTVP-1 as a glioma-associated protein that regulates glioma cell migration and invasion. Using ChiP analyses, we found that the RTVP-1 promoter bind STAT3 and C/EBPbeta. Analysis of TCGA tumor specimens demonstrated that the expression of RTVP-1 was higher in the mesenchymal GBM and was inversely correlated with patient survival. We further found that RTVP-1 was expressed in glioma stem cells (GSCs) but not in human neural stem cells (NSCs). Overexpression of RTVP-1 in NSCs induced their mesenchymal transformation, whereas silencing of RTVP-1 in GSCs decreased their mesenchymal signature, increased their neural phenotypes and inhibited their self renewal and stemness. Silencing of RTVP-1 also decreased tumor volume of GSC-derived xenografts and increased animal survival. Using gene array analysis of RTVP-1 silenced cells we identified IL-6 and CXCR4 as major mediators of RTVP-1 effects on the mesenchymal transformation and self-renewal of GSCs. Using a pull down assay with His-tagged RTVP-1 and FRET analysis, we identified HSP27, N-WASP and hnRNPK as novel interacting proteins of RTVP-1, that mediate its effects on GSC migration and invadopodia formation. In summary, RTVP-1 promotes the mesenchymal transformation of GSCs and induces self-renewal and migration by the increased expression of IL-6 and CXCR4 and via its interaction with N-WASP, hnRNPK and HSP27. Collectively, these results implicate RTVP-1 as a novel prognostic marker and therapeutic target in GBM.

Biography

Chaya Brodie has completed her PhD at Bar-Ilan University, Israel and postdoctoral studies at University of Colorado and National Jewish Center for Immunology and Respiratory Medicine. She is a Senior Staff Scientist and the Director of Translational Science in the Hermelin Brain Tumor Center, Henry Ford Hospital, Detroi, MI and a Professor in the Faculty of Life Sciences, Bar-Ilan University, Israel. She has published more than 135 papers in reputed journals and has served as a reviewer in various NIH study sections and in international foundations and societies.

Mesoporous silica based drug delivery systems and their ultrasonic theranostic application

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This lecture will address a variety of mesoporous silica based drug delivery systems (MS-DDS) for pre-clinical evaluations of ultrasonic medicine for tumors theranostic. We mainly focus on constructing multifunctional hollow mesoporous silica nanospheres (HMSNs) as innovative and efficient theranostic/synergistic agents and explore them in a representative non-invasive therapeutic mode HIFU (High Intensity Focused Ultrasound) application. The main topics will include the following four aspects: (1) design, preparation & targeted modification of HMSNs with high dispersity and bio-stability; (2) multifunctionalization of MS-DDS for MR/US imaging and its guided tumor therapy; (3) a novel HIFU-mediated MS-DDS and its repeatedly enhanced HIFU treatment under once injection; and (4) a pH/temperature dual-responsive MS-DDS for inhibiting Panc-1 Pancreatic solid tumor via ultrasound-activated inertial cavitation.

Biography

Hangrong Chen has been a full professor and PhD supervisor in Shanghai institute of Ceramics, Chinese Academy of Sciences, since 2006. Her recent research interest focuses on nano-scale mesoporous and/or specific structures as drug delivery systems for controlled drug release and their ultrasonic theranostic application. She has published more than 140 SCI papers and received 14 authorized Chinese patents. Her work has been cited for more than 3600 times by other scientists with an h-value of 33. She has rewarded the first-class award of Shanghai Natural Science in 2008, the second prize of National Natural Science Award in 2011, and received the China National Funds for Distinguished Young Scientists in 2012.

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