Discovery of CD109 as radio-resistance marker in glioblastoma

In glioblastoma (GBM), Proneural (PN) and Mesenchymal (MES) cancer stem cells (CSCs) were identified as distinct subtypes with their individual progenies (non-CSCs). Here, we report that following irradiation, intercellular extrinsic signals from senescent non-CSCs provoke PN CSCs’ compensatory growth, thereby resulting in persistent transcriptomic and phenotypic transformation toward more malignant MES CSCs (PN-MES transition: PMT). PMT of CSCs is accompanied with the activated wound healing pathway, which is significantly associated with poorer prognosis of GBM patients. During PMT of CSCs, a CSC marker CD133 is lost, while CD109 expression evolves. These CD109-positive, but not CD109-negative GBM cells are highly tumorigenic and multipotent in vivo, suggesting CD109 as a novel MES CSC marker. Inhibition of CD109 attenuates clonogenicity and radioresistance. Lastly, CD109 and CD133 expressions are independently instructive for poorer prognosis of MES and PN GBM, respectively. Together, irradiation to GBM tumors induces damaged non-CSC-driven PMT of CSCs developing a malignant phenotype, and CD109 is a clinically relevant functional marker for MES GBM stemness.

Biography

Krishna P L Bhat obtained his PhD from the University of Illinois at Chicago, followed by a Post-doctoral fellowship at the MD Anderson Cancer Center. He was promoted in the ranks and is currently an Assistant Professor in the Department of Translational Molecular Pathology at MD Anderson. He is an authority in the field of brain tumor research and was instrumental in identifying master transcriptional regulators of the mesenchymal subtype of glioblastoma. His work has been published in prestigious journals such as Cancer Cell, Molecular Cell, and Genes and Development and has been cited in commentaries in Nature and Nature Reviews Cancer. He is also the recipient of the adult basic science award at the Society of Neuro-oncology Annual meeting held in Montreal in 2010.

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