Heat shock protein 27 determines the neovasculogenic potential of breast cancer stem cells

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Neovascularization is a natural process to form vascular networks during embryogenesis and development via angiogenesis and vasculogenesis and it is also necessary for tumor maintenance and progression. Breast cancer stem cells (BCSCs) have been identified as a subpopulation of breast cancer cells with markers of CD24-CD44+ or high aldehyde dehydrogenase activity (ALDH+) and have been proven to be associated with radiation resistance and metastasis. In the view of differentiation capability of CSCs, some reports indicate that CSCs of ovarian cancer or glioblastoma may involve in tumor neovascularization by direct differentiation into endothelial cells. Here we investigate the neovasculogenic potential of BCSCs. By matrigel-based tube formation analysis, we found that only ALDH+ BCSCs could form tube structures as similar as microvascular endothelial cells. Enrichment of BCSCs by mammosphere culture also increased the tube formation capability. The ALDH+ BCSCs expressed several angiogenic factors, receptors or endothelial markers, such as VEGF-A, VEGFR2, SDF-1, CXCR4, CD31 and CD34. Quercetin, a plant flavonoid compound which is known to suppress heat shock proteins, could suppress tube formation capability of ALDH+ BCSCs. By siRNA mediated gene silencing, knockdown of Hsp27 completely inhibited the neovasculogenic potential of BCSCs. We also found that knockdown of Hsp27 in breast cancer cells could decrease the phosphorylation of insulin-like growth factor-1 receptor. Further investigations of the molecular mechanisms of neovasculogenic potential of BCSCs will provide a new insight in CSC biology and CSC-based targeting therapy

Biography

Wen-Wei Chang, male, cancer biologist, graduated from Institute of Basic Medical Sciences, National Cheng Kung University (Taiwan) in 2006. He worked as a post-doctoral fellow in Genomics Research Center, Academia Sinica (Taiwan) 2006-2009 and became an Assistant Professor in School of Biomedical Sciences, Chung Shan Medical University (Taiwan) from 2009 to present. His major interests are to understand the signal transduction in the maintenance of cancer stem cells and to discover anti-cancer stem cell agents from natural compounds.

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