E-1 (EPA)

Mortalin contributes to cancer cell stemness: molecular evidence to its role in drug resistance

Priyanshu BHARGAVA[1,2], Motomichi DOI[1,2], Sunil KAUL[1], Renu WADHWA[1]

[1]DAILAB, National Institute of Advanced Industrial Science & Technology, Tsukuba - 305 8565
[2]Graduate School of Life & Environmental Sciences, University of Tsukuba

Cancer Stem Cells (CSCs) have been identified as rare population in many cancers, including leukemia and solid tumors. Current evidence suggests that the CSCs are capable of self-renewal and differentiate into various types of cancer cells with metastasis and drug resistance properties. Over the years, discovery and development of CSC-related therapies, including finding novel chemotherapeutic drugs such as small molecules, nano-medicines and combinational therapies are in forefront of medical research. We herein induced the properties of CSC by exogenous expression of mortalin, a chaperone, in MCF-7, MDA-MB-231 and U2OS cancer cells. It has earlier been established that mortalin is enriched in a variety of cancers and contributes to the process of carcinogenesis by inactivation of tumor suppressor p53 protein, de-regulation of apoptosis and activation of EMT signaling. For confirming the CSC properties, we examined the expression of several marker proteins including ABCG2, OCT4, CD133, ALDH1, CD9, MRP1 and connexin. We report that the cells transduced with mortalin overexpression possessed enhanced CSC properties including high efficacy of spheroid formation, chemoresistance and migration. Furthermore, knockdown of mortalin by specific shRNA or anti-mortalin small molecules (a rhodacynine dye, MKT-077 and a major component of New Zealand propolis, CAPE) sensitized these cells to several conventional chemotherapeutic drugs.

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Priyanshu BHARGAVA (Graduate School of Life & Environmental Sciences, University of Tsukuba -305 8572)
<e-mail: bhargava.priyanshu@aist.go.jp >