DNA Damage Response profiles in reprogrammed osteosarcoma cell lines

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Abstract

Osteosarcoma (OS) is a malignancy of the bone occurring mostly in children and adolescents. Alterations and mutations to genes associated with proliferation and differentiation increase the risk of OS tumourigenicity. Reprogramming of OS cells to a more primitive stage could be useful to study and understand OS pathogenesis. By using retroviral OSKM, the Yamanaka factors, two OS cell lines, G-292 and Saos-2, were reprogrammed to pluripotency. Colonies from the reprogrammed OS, designated as iG-292 and iSaos-2, showed ESC-like morphology, expressed pluripotency markers, formed embryoid body-like spheres, expressed markers from three germ layers and showed the ability to differentiate into adipocytes and osteocytes. However, \textit{in vivo} study showed teratoma formation only in iG-292. Hierarchical clustering analysis from global gene expression profile of both parental and reprogrammed OS demonstrated distinctive separation of two clusters of population. Differentially expressed genes (DEGs) were further grouped into DNA repair, cell cycle and apoptosis pathways. Our data showed that iG-292 displayed more DEGs than iSaos-2 in these three pathways. The ability to repair DNA damage in cells is regarded as a crucial process to protect genome integrity and to suppress tumourigenesis. There are no reports on DNA Damage Response (DDR) pathways of reprogrammed cancer cells. OS has been linked to DNA mutation and are known to be resistant to DDR. Thus, this study is essential to gather valuable and novel information on OS pathogenesis, in particular DDR, for future therapeutic intervention.

\textbf{Keywords:} Osteosarcoma, DDR

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