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Chromosomal instability in human osteosarcoma is mediated through Hypoxic inducible factor 1α (HIF-1α)

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Abstract

Osteosarcoma is a rare bone malignancy with fast tumour progression disrupting tumour mass oxygen supply. As to ameliorate the hypoxic environment, new blood vessel developed from the existing vasculature through angiogenesis. However, in the literature, the role of Hypoxic inducible factor 1α (HIF-1α) in human osteosarcoma is unclear. Although osteosarcoma tissue cultures study suggested that the chromosomal instability is due to disturbance of the chromosomal segregation mechanisms and a defective mitotic checkpoint affecting cellular proliferation. However, not much is known about the underlying signalling pathways mediating chromosomal instability in human osteosarcoma. The aim of this study was to investigate the involvement of HIF-1α as the mediating signalling pathway leading to chromosomal instability in human osteosarcoma. The methods used were micronuclei staining, Fluorescent *in situ* hybridization (FISH) and immunohistochemistry. Our results showed increased micronuclei formation (24/31) 77.4% and amplification of 6p21 chromosome region (16/22) 72.7% in human osteosarcoma. This was related to increased HIF-1α and VEGF protein expression ($p<0.05$). In addition, there were also occurrence of PAS positive blood vessel (vasculogenic mimicry, VM) in those cases (12/29) 41.4% compared to (6/26) 20.7% non-VM blood vessel ($p<0.05$). It was concluded that hypoxic tumour microenvironment partly contributes in chromosomal instability, leading to increase angiogenic factor which further decreased patient's survival.

Keywords: Osteosarcoma; chromosomal instability; Hypoxic Inducible Factor 1α (HIF-1α);Vascular Endothelial Growth Factor (VEGF).

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