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The anti-tumour effect of induced pluripotent stem cells against submandibular gland carcinoma in rats is achieved via modulation of the apoptotic response and the expression of Sirt-1, TGF-β, and MALAT-1 in cancer cells

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Abstract:

The era of induced pluripotent stem cells (iPSCs) was used as novel biotechnology to replace embryonic stem cells bypassing the ethical concerns and problems of stem cell transplant rejection. The anti-tumour potential of iPSCs against many tumours including salivary cancer was proven in previous studies. The current study aimed to investigate the contribution of the Bax, Sirt-1, TGF-β, and MALAT genes and/or their protein expression to the pathogenesis of submandibular carcinogenesis before and after iPSCs treatment. Thirty Wistar albino rats were equally assigned into three groups: group I (control), group II (Squamous cell carcinoma (SCC)): submandibular glands were injected SCC cells, and group III (SCC/iPSCs): SCC rats were treated by 5×10^6 iPSCs. Submandibular gland sections were subjected to histological and immunohistochemical analyses to detect mucopolysaccharides, Bax, and TGF-β expression as well as PCR quantification for TGF-β, Sirt-1, and lncRNA MALAT-1 gene expressions. Western blotting was also used to detect Sirt-1 and TGF-β protein expressions. SCC group revealed infiltration by sheets of malignant squamous cells with or without keratin pearls and inflammatory cells, in addition to upregulation of TGF-β, Sirt-1, MALAT-1, and Bax, whereas SCC/iPSCs group showed an improved submandibular histoarchitecture with the maintenance of the secretory function. Bax and TGF-β immunoexpression were significantly reduced. The upregulated TGF-β, Sirt-1, and MALAT-1 genes were significantly decreased. iPSCs protected against the experimentally induced submandibular gland carcinoma that might be achieved via their regenerative potential and their regulatory modulation of Sirt-1, TGF-β, and MALAT-1 gene/protein expressions and of the apoptotic response in cancer cells.

Keywords: Immunohistochemistry, Induced pluripotent stem cells, lncRNA, MALAT-1, Submandibular salivary cancer, Sirt-1, TGF-β gene expressions