演題番号 8

Stromal cells in the tumor microenvironment promote the progression of oral squamous cell carcinoma

○Shan Qiusheng[1,2)], 高畠清文[2)], 大森悠加[2)], 河合穂高[2)], May Wathone Oo[2)], 中野敬介[2)],
伊原木聰一郎[1)]、佐々木　朗[1)]、長塚　仁[2)]
[1)]岡山大学学術研究院医歯薬学域　口腔顎顔面外科学分野
[2)]岡山大学学術研究院医歯薬学域　口腔病理学分野

[Background]The stromal cells in the tumor microenvironment (TME) can influence the progression of multiple types of cancer; however, data on oral squamous cell carcinoma (OSCC) are limited. Clinically, various subtypes of OSCC exist, including invasive carcinoma and verrucous carcinoma. Differences in the invasive ability of these subtypes results in marked differences in prognosis, progression and metastasis and so on. However, no studies available to date have examined the mechanisms through which differences in these subtypes affect the tumor stroma. Therefore, it was hypothesized that different subtypes of stromal cells in the TME differentially affect the progression of OSCC.

[Materials and Methods] The moderately differentiated human oral cancer cell line, HSC-3, was used as a cell model and verrucous squamous cell carcinoma-associated stromal cells (VSCC-SCs) and squamous cell carcinoma-associated stromal cells (SCC-SCs) were extracted from patients with OSCC. The effects of verrucous VSCC SCs, SCC SCs and human dermal fibroblasts (HDFs) on the tumor nest formation, proliferation, invasion and migration of HSC 3 cells were examined in vitro using Giemsa staining, MTS, and Transwell (invasion and migration) assays, respectively. And also in vivo, mixed cells including HSC-3 and stromal cells were injected into the head of mice, the tumor tissues were extracted after 4 weeks. We examined in vivo using HE staining, TRAP staining and Ki-67 labeling index. Finally, microarray data were used to predict genes in VSCC SCs and SCC SCs that may influence the progression of OSCC, and those with potential to influence the differential effects of VSCC SCs and SCC SCs on the differentiation of OSCC.

[Results]The results revealed that both VSCC SCs and SCC SCs promoted the proliferation, invasion and migration of OSCC cells in vitro. The results demonstrated that VSCC SCs promoted the differentiation, proliferation, invasion and migration of OSCC cells, while the SCC SCs inhibited the differentiation, and promoted the proliferation, invasion and migration of OSCC cells in vivo. It was found that C X C motif chemokine ligand 8 (CXCL8), mitogen activated protein kinase 3 (MAPK3), phosphatidylinositol 4,5 bisphosphate 3 kinase catalytic subunit alpha (PIK3CA), C-X-C motif chemokine ligand 1 (CXCL1) and C C motif chemokine ligand 2 (CCL2) may be involved in the crosstalk between VSCC SCs, SCC SCs and OSCC cells, which regulates the progression of OSCC. Intercellular adhesion molecule 1 (ICAM1), interleukin (IL)1B, Fos proto oncogene, AP 1 transcription factor subunit (FOS), bone morphogenetic protein 4 (BMP4), insulin (INS) and nerve growth factor (NGF) may be responsible for the differential effects of VSCC SCs and SCC SCs on the differentiation of OSCC.

[Discussion] The present study demonstrates that both VSCC SCs and SCC SCs may promote the progression of OSCC, and SCC SCs were found to exert a more prominent promoting effect; this may represent a potential regulatory mechanism for the progression of OSCC.