

Cancer stem cells in head and neck tumors: evidence for metastatic spread and treatment resistance

Virginia Tirino¹, Vincenzo Desiderio¹, Francesca Paino¹, Marcella La Noce and Gianpaolo Papaccio¹

¹ School of Medicine, Department of Experimental Medicine-Section of Histology, Second University of Naples, 80138, Naples, Italy

The major challenge in the management of patients with oral squamous cell carcinomas (OSCC) is the development of resistance to therapy leading to disseminated disease. Since cancer stem cells (CSC) have emerged as important players in OSCC metastasis, our objectives were to explore the implications of CSC in OSCC tumor progression, invasion and response to conventional therapies. Methods: A panel of well-characterized cell lines originated from the most common sites in the head and neck area was used. Cells were cultured as floating spheres or under normal adherent conditions and analyzed for CD44, ALDH, CD24, CD29, CD56 by flow cytometry, PCR arrays for genes related to stemness, metastasis and EMT. We also investigated sLeX expression, known to play a key-role in many cancers metastasis by promoting tumor cells binding to endothelial E-selectin. We analyzed the tumorigenic potential of OSCC cells by invasion assays and in vivo OSCC experimental models comparatively to CSC cells. Moreover resistance to cisplatin and radiation was assessed by annexin V/PI assay and by colony forming assay. Results: The highest levels of sLeX expression were found in cell lines originated from oral cavity (9%-47%) compared to other head and neck locations (0.1%-7%). Cells grown as spheres were 95-100% positive for sLeX compared to 10-40% of adherent counterpart. Although sLeX+ and sLeX- cells were both able to form spheres, sLeX+ spheres were predominant and larger. Flow cytometry and PCR arrays indicated that the spheres were highly enriched in CSC and metastatic markers. Consistently, the spheres showed increased invasive and tumorigenic potential, and resistance to conventional chemotherapy and radiations. *Conclusion:* these studies are the first to unveil a novel link between sLeX expression, stem cell formation and metastatic spread in OSCC, and provide supportive evidence for CSC resistance to treatment. Understanding the mechanisms of tumor invasion and metastasis will improve patient outcome and survival.

Key words

Cancer stem cells, head and neck tumors, metastasis, multidrug resistance, gene expression.