Otolaryngology: Open Access

Sun and Wang, Otolaryngol (Sunnyvale) 2018, 8:6
DOI: 10.4172/2161-119X.1000355

Research Article Open Access

A Letter to the Editor on Up-regulation of Insulin Receptor and Insulin-like Growth Factor 1 Receptor Promotes TSCC Tumorigenesis and Metastasis

Jingjing Sun[1] **and Anxun Wang**[2*]

[1]*Department of Stomatology, First Affiliated Hospital, Guangdong Pharmaceutical University, Guangzhou, Guangdong, P.R. China*

[2]*Department of Oral and Maxillofacial Surgery, First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, Guangdong, P.R. China*

[*]**Corresponding author:** Anxun Wang, Department of Oral and Maxillofacial Surgery, First Affiliated Hospital, Sun Yat-Sen University, 510080 Guangzhou, Guangdong, P.R. China, Tel: +86 013724896216; E-mail: wang_anxun@aliyun.com

Received date: November 14, 2018; **Accepted date:** November 20, 2018; **Published date:** November 27, 2018

Letter to the Editor

Our studies, published in "*Biochimica et Biophysica Acta-Molecular Basis of Disease*", have revealed that the up-regulation of both INSR and IGF1R was a frequent event and may be associated with enhanced tumorigenic and metastatic potential in Tongue Squamous Cell Carcinoma (TSCC).

TSCC, as one of the most aggressive type of Oral Squamous Cell Carcinomas (OSCCs), is characterized by its rapid local Lymph Node (LN) metastasis and high rate of proliferation [1]. According to the American Cancer Society, during the past five years, the incidence of new cancers increased by 5.5%, while that is 33% for TSCC [2,3]. Despite the rapid development of cancer diagnosis and treatment technology, the death rate of TSCC has increased by 12.8% during the past five years [2,3]. Importantly, improvement in patient survival requires a better understanding of tumor tumorigenesis and metastasis. Our studies shed new light that both INSR and IGF1R may serve as a biomarker of metastatic potential or as a therapeutic target in patients with TSCC and strategies targeting the C-myc ~ IGF1R/INSR ~ NF-κB pathway may be effective treatments for TSCC.

The Insulin-like Growth Factor (IGF) system is a key factor involved in the growth, proliferation, differentiation, apoptosis, metabolism. Insulin-like growth factor 1 receptor (IGF1R) and insulin receptor (INSR), involved in IGF signaling, are highly homologous molecules that may heterodimerize to form an IGF1R/INSR hybrid [4]. In our previous studies, IGF1R was up-regulated and identified as a direct target of miR-7 in TSCC [5]. EM et al. [6] recommended that therapeutic targeting of both INSR and IGF-IR is likely more effective than targeting IGF1R alone in abrogating endocrine therapy resistance in breast cancer. Ofer et al. [7] underlined the oncogenic functions of IGF1R and INSR in prostate cancer. Similarly, our research indicated that both INSR and IGF1R exhibited similar oncogenic effects on TSCC, as either INSR or IGF1R overexpression dramatically enhanced TSCC cell growth, migration and invasion *in vitro* and tumorigenesis and tumor metastasis *in vivo*.

C-myc is regulator gene and proto-oncogene that code for transcription factors. In our previous studies, we found that superoxide dismutase 2 (SOD2) and Bmi1 are two direct target genes of C-myc and contribute to the migration and invasiveness of TSCC [8,9]. In the present research, C-myc directly targeted INSR and IGF1R and promoted tumorigenesis and metastasis in TSCC.

NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) is a protein complex that controls transcription of DNA, cytokine production and cell survival. NF-κB is found in almost all animal cell types and is involved in cellular responses to stimuli. NF-κB may target INSR/IGF1R to modulate microRNAs in myoblasts [10]. Li et al. [11] suggested that IGF1R expression could alter NF-κB signaling in lung and colon carcinoma cells. Tian et al. [12] found that IGF1R knockdown suppresses tumor growth and enhances chemosensitivity in pancreatic cancer *via* the inhibition of PI3K/AKT and NF-κB pathways and is a promising approach to overcome the chemoresistance of pancreatic cancer. In the signaling pathway, IGF1R and NF-κB signaling are often formed by the pathways cross-talk with each other impacting the cell growth, migration and invasion. The INSR/IGF1R and NF-κB signalling sever as catalysts in cancer, but relatively little is known about possible crosstalk between these pathways in TSCC. In our article, we found that NF-κB is activated and regulated by both INSR and IGF1R, further supplementing and improving the pathway.

References

1. Uzawa K, Ono K, Suzuki H, Tanaka C, Yakushiji T, et al. (2002) High prevalence of decreased expression of KAI1 metastasis suppressor in human oral carcinogenesis. Clin Cancer Res 8: 828-835.
2. Siegel RL, Miller KD, Jemal A (2016) Cancer statistics. CA Cancer J Clin 66: 7-30.
3. Siegel R, Ward E, Brawley O, Jemal A (2011) Cancer statistics, 2011: The impact of eliminating socioeconomic and racial disparities on premature cancer deaths. CA Cancer J Clin 61: 212-236.
4. Singh P, Alex JM, Bast F (2014) Insulin receptor (IR) and insulin-like growth factor receptor 1 (IGF-1R) signaling systems: Novel treatment strategies for cancer. Med Oncol 31: 805.
5. Jiang L, Liu X, Chen Z, Jin Y, Heidbreder CE, et al. (2010) MicroRNA-7 targets IGF1R (insulin-like growth factor 1 receptor) in tongue squamous cell carcinoma cells. Biochem J 432: 199-205.
6. Fox EM, Miller TW, Balko JM, Kuba MG, Sánchez V, et al. (2011) A kinome-wide screen identifies the insulin/IGF-I receptor pathway as a mechanism of escape from hormone dependence in breast cancer. Cancer Res 21: 6773-6784.
7. Ofer P, Heidegger I, Eder IE, Schöpf B, Neuwirt H, et al. (2015) Both IGF1R and INSR knockdown exert antitumorigenic effects in prostate cancer in vitro and in vivo. Mol Endocrinol 29: 1694-1707.
8. Liu Z, He Q, Ding X, Zhao T, Zhao L, et al. (2015) SOD2 is a C-myc target gene that promotes the migration and invasion of tongue squamous cell carcinoma involving cancer stem-like cells. Int J Biochem Cell Biol 60: 139-146.
9. He Q, Liu Z, Zhao T, Zhao L, Zhou X, et al. (2015) Bmi1 drives stem-like properties and is associated with migration, invasion and poor prognosis in tongue squamous cell carcinoma. Int J Biol Sci 11: 1-10.
10. Wei W, Zhang WY, Bai JB, Zhang HX, Zhao YY, et al. (2016) The NF-?B-modulated microRNAs miR-195 and miR-497 inhibit myoblast

proliferation by targeting Igf1r, Insr and cyclin genes. J Cell Sci 129: 39-50.

11. Li S, Pinard M, Wang Y, Yang L, Lin R, et al. (2015) Crosstalk between the TNF and IGF pathways enhances NF-kappaB activation and signaling in cancer cells. Growth Horm IGF Res 25: 253-261.

12. Tian X, Hao K, Qin C, Xie K, Xie X, et al. (2013) Insulin-like growth factor 1 receptor promotes the growth and chemoresistance of pancreatic cancer. Dig Dis Sci 58: 2705-2712.