Validation of Molecular Markers associated to Recurrence in Head and Neck Squamous Cell Carcinoma

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Head and Neck Squamous Cell Carcinomas (HNSCC) represent 5% of malignant tumors worldwide and are strongly associated with tobacco and alcohol exposure. Recent studies also pointed HPV infection as a possible risk factor. These tumors are, in general treated with surgery and/or chemo and radiotherapy. After treatment, disease recurrence is observed in 30-50% of patients within the 5 years, leading to high mortality rate. Molecular changes in HNSCC are mainly due to activation of oncogenes and inactivation of tumor suppressor genes, leading to deregulation of cell proliferation. Our group studied gene expression profile in a set of 120 samples representing HNSCC of different topographies and compared alterations sets of functionally related genes. Among these patients, 55 were treated surgically and had disease-free margins, had neck dissection and received adjuvant radiotherapy. Twenty four patients presented local regional recurrence within 2 to 4 years whereas 31 patients remained disease-free for 2.5 to 9 years. When we compared changes in functional modules in samples from patients with or without recurrence, the functional module cell-cell signaling showed statistically significant difference, being active in recurrent patients and inactive in non-recurrent patients. Seven genes (*EGLN3, IL1F9, INHBA, AREG, BST2, KLK6 and CCL20*) contributed to this difference. Using Q-PCR, three genes were individually validated: *BST2* (p=0,025)*, EGLN3* (p=0,002) *and IL1F9* (p=0,0045). The gene *BST2* is down-regulated in patients with recurrence whereas *EGLN3* and *IL1F9* are up-regulated in recurrent patients (fold= 2,56 and 1,94, respectively). The identification of altered genes potentially associated to a worst behavior of HNSCC might have practical applications for as prognostic markers and also, could define new strategies for disease control.

Keywords: *functional module, head and neck squamous cell carcinoma, prognostic markers, recurrence.*

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