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Alterations of DNA methylation seem to be an early event in the development of tumors from the upper aero digestive tract

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Statement of the Problem: Tumors from the upper aerodigestive tract (UADT) rank among the 10 most frequent neoplasias worldwide. These tumors are more prevalent in developing countries, arising from a squamous epithelium and are usually associated with tobacco, alcohol consumption and HPV infection. The most common histological type is squamous cell carcinoma and the most commonly affected sub sites include larynx, oral cavity, pharynx and esophagus. Although they share similarities, UADT cancer comprises a group of neoplasias with high clinical and phenotypic heterogeneity and inspite of the recent advances in the identification of biomarkers and new therapeutic targets, no significant gains in overall survival have been observed. Between the associated causes, the development of second primary tumors in the UADT stands out. It is hypothesized that the squamous epithelium lining the affected organs goes through a process known as cancerization field, in which different morphologically normal areas acquire molecular alterations, making them prone to become neoplastic. Based on this, we have been interested in understanding the epigenetic mechanisms that lead to the development of each of these tumors.

Methodology & Theoretical Orientation: Microarrays have been used to determine the DNA methylation signature of UADT tumors with further validation by pyro-sequencing in independent samples.

Findings: Interestingly, we showed that each subtype of UADT cancer carries a specific DNA methylation signature. They differ in terms of hyper/hypomethylation frequency; affected genomic regions, genes and pathways and transcription factor networks. We have also shown that aberrant DNA methylation of genes involved in epithelium protection and in apoptosis control is an early event in the development of UADT tumors. Therefore, our data indicates that these neoplasias show an epigenetic convergence with respect to early changes, but also diverge in terms of carcinogenic pathways, which may have an impact on prognosis and response to therapy.

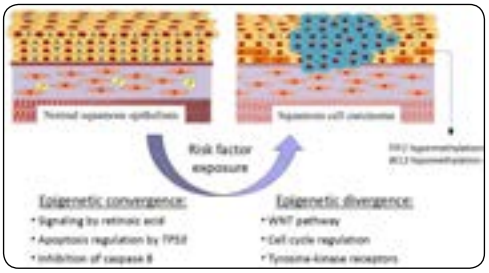

Figure 1: Epigenetic alterations involved in the development of UADT tumors.

Recent Publications

1. Degli Esposti D, et al. (2017) Unique DNA methylation signature in HPV-positive head and neck squamous cell carcinomas. Genome Medicine 9:33.
2. Herceg Z, et al. (2017) Roadmap for investigating epigenome deregulation and environmental origins of cancer. International Journal of Cancer 142(5): 874-882.
3. Gonzaga I M, et al. (2017) TFF1 hypermethylation and decreased expression in esophageal squamous cell carcinoma and histologically normal tumor surrounding esophageal cells. Clinical Epigenetics 9:130.
4. Lima S, et al. (2011) Identification of a DNA methylome signature of esophageal squamous cell carcinoma and potential epigenetic biomarkers. Epigenetics 6(10):1217-1227.

Biography

Sheila Coelho Soares Lima is a Researcher at the Brazilian National Cancer Institute, where she is the Head of the Epigenetics group. She has her expertise in evaluating alterations of DNA methylation in tumors with the objective of understanding molecular carcinogenic mechanisms, identifying biomarkers of diagnosis, prognosis and response to therapy and determining new therapeutic strategies. Based on this, she aims to improve cancer patient diagnosis, treatment and life quality. She has shown some of the first evidences of the epigenetic cancerization field in the upper aerodigestive tract and is currently working on tumor stem cells and epigenetic therapy.

Notes: