



104 - DECIPHERING EPIGENETIC ELEMENTS UNDERLYING THYROID CANCER DEDIFFERENTIATION

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Resumen

Differentiated thyroid cancer (DTC) is the most common endocrine malignancy. Despite most patients having an initial good prognosis, some patients progress and become resistant to radioiodine treatment. Importantly, effective markers or therapies are not yet available. Many of these patients present tumours with high levels of dedifferentiation, having lost some or most of their thyrocyte-specific features. As DTC patients present low levels of mutations, epigenetics has been considered as a field to be explored in this disease. Our group has previously reported an increased global DNA hypomethylation in distant metastatic and dedifferentiated thyroid cancer. However, the role of epigenetics in thyroid cancer dedifferentiation is poorly understood. Our aim is to study the epigenetic mechanisms underlying DTC dedifferentiation to identify new prognostic biomarkers as well as potential therapeutic targets. Here, we correlated DTC tumour differentiation to a previously reported set of epigenetics-associated genes, named Epifactors. Tumour differentiation was defined using the Thyroid Differentiation Score (TDS). We correlated the expression of these Epifactors to TDS values of patient samples using different publicly available datasets. DNA methylation levels were also taken into account. Based on these analyses, we selected a group of 14 genes, named EpiGenes. Their expression has a clear link with TDS values, suggesting their potential role in DTC dedifferentiation. Moreover, these EpiGenes are also associated with other clinical prognostic markers, such as risk factor. Our findings are currently being validated *in vitro* in different cell lines. We observed that a change in expression of some of these EpiGenes resulted in a change in TDS gene expression. In conclusion, we have identified candidate epigenetic factors that will help to better understand DTC dedifferentiation and may be future therapeutic targets for advanced thyroid carcinomas.