

Contribution of p63 protein isoforms to the aggressiveness of head and neck squamous cell carcinomas

Medical and scientific context:

Head and Neck Squamous Cell Carcinomas (HNSCC) rank 4th among the most frequent cancers in France with 14,000 new cases each year. The *TP63* gene is very frequently overexpressed in these cancers. *TP63* encodes the transcription factor p63, which belongs to the p53 tumor suppressor family, and which is a major regulator of epithelial proliferation and differentiation. The relationships between *TP63* overexpression and tumorigenesis or tumor aggressiveness is complicated by the existence of many isoforms of the p63 protein. Preliminary results obtained in the laboratory from the bioinformatics analysis of public TCGA data (The Cancer Genome Atlas) demonstrated a correlation between *TP63* splicing and cancer prognosis.

Objective of the internship and methodology:

We propose to study the differential functions of p63 isoforms on cell phenotypes in physiological and pathological contexts. To do this, the recruited student will use different 3D cell models (cell cultures in the form of spheroids) from the HaCat line (immortalized human keratinocytes, physiological context) and the ATCC HNSCC panel (cancerous lines from patients, pathological context). 3D cultures have the advantage of growing cells in an environment closer to physiological and/or tumour conditions than 2D culture and is therefore more relevant to cancer. In these cells, the student will inhibit the expression of the different isoforms of p63, or overexpress them, and assess cell differentiation using specific markers, migratory capacities by cultivating spheroids under adhesion conditions, and invasive capacities by cultivating spheroids within a matrigel matrix.

Relevance of the results obtained to cancer:

All the results generated will allow a better understanding of the involvement of p63 isoforms in tumor processes. In the long term, they will contribute to the opening of new diagnostic and therapeutic avenues for squamous cell carcinomas in the ENT sphere.

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