

Defining the signatures of radio-resistance in head and neck squamous cell carcinoma (HNSCC), using artificial intelligence and genomic spatial analysis.

Head and neck squamous cell carcinomas (HNSCC) are a group of diverse diseases that can develop in more than 30 areas within the head and neck encompassing the oral cavity (mouth, tongue, lip), pharynx (throat) and larynx (voice box) area. They are often associated with smoking and alcohol consumption, although there has been increasing incidence of cancer due to human papillomavirus (HPV) infection. HNSCC are divided anatomically according to the primary tumour location, and this determines treatment methods.

With diagnosis at an early stage, the survival rate increases to 80-90%. However, approximately 50% of patients with locally advanced disease, will develop a recurrence and this remains a major cause of failure in HNSCC. Despite improvements in treatment, the prognosis for HNSCC patients remains poor and available treatments often have serious side effects. Surgery and radiation therapy can cause significant side effects, in particular by impairing the capacity for breathing, food intake and articulation. Radiotherapy can damage blood vessels that nourish muscles, nerves, and bones resulting in a progressive “radiation fibrosis syndrome”. Current mechanisms of patient stratification are not fully sufficient to identify those patients who will benefit from radiation therapy. This results in non-optimal use of cancer health services and delay in delivery of potentially curative treatment. At present no clinically useful biomarkers for identifying radio-resistance are available.

Our goal is to investigate digitized histopathological samples (processed surgical specimens), stained with hematoxylin and eosin by applying computational pathology and exploratory methods of artificial intelligence in order to investigate radio-resistance. Furthermore, we are planning to investigate the relationships between the genes responsible for coding proteins, by applying a sophisticated molecular pathology technique with the ability to link genomic information to particular cell populations in the tissue. Thus, we plan to dissect the multiplex hallmark of radio-resistance and at the same time, shed light on the mechanism responsible for radio/chemo sensitivity in some HNSCC entities. Both methods of computational and molecular pathology are experimental and ground breaking methodologies in basic biology research.

HNSCC pathomorphology is thought to play a role in shaping the radio-resistance phenomenon. Preneoplastic lesions often extend into the surgical margins and even when tumours are excised, they can source local recurrences as well as second primary tumours. These changes occur in a background of the extracellular matrix, which provides structural and biochemical support for the surrounding cells. Cancer cells are also accompanied by other cell types (e.g. cells of the immunological system, fibroblasts, endothelial cells that line the blood vessels), which are part of the tumor microenvironment and which can affect the growth of tumor tissue by manipulating the surrounding environment. Therefore, it is important to understand the role of the tumour microenvironment, the “crosstalk” between cancer cells and non-cancer cells in their surrounding extracellular matrix that create their local environment. HNSCC are characterised by extent molecular and phenotypic heterogeneity, along with the presence of multiple mutations.

Our hypothesis is that not only malignant epithelial cells, but also small alterations in what appear to be ‘a normal epithelial’ component, as well as changes in the tumour microenvironment, immune cells and cancer associated stromal cells play a crucial role in regulating tumour cell function, disease progression, radio-resistance or radio-sensitivity. Better understanding of the ways in which the tumour microenvironment affects cancer behavior will eventually lead to new, better and more useful explanations of sensitivity/resistance/recurrence phenomenon. With the help of advanced histopathological methods, such as computational and molecular pathology, we will be able to identify histopathological features and expose cell to cell interactions, as well as to explore the biological processes in the tumour bed that are relevant for cancer cell behavior and radio-resistance.