Laryngeal carcinoma (largely (95%) squamous cell carcinoma) is the second most common head and neck cancer. Comprehensive treatment measures such as surgery, radiotherapy, chemotherapy, and gene therapy have gained a higher 5-year survival rate for patients with laryngeal cancer. However, 30-40% of these patients still dies for tumor recurrence or local (mainly) and distant metastasis. The identification of the transduction pathways involved in this tumor progression and of novel independent prognostic markers is of paramount importance for the advancement of research, accuracy of preoperative diagnosis and improvement of survival rate in patients with laryngeal cancer. To this aim, by the use of oropharyngeal squamous cell lines, human primary tumor bioptic tissues and blood samples from the same patients, we are investigating the following aspects:

1. **Molecular and cellular mechanism involved in carcinogenesis (p75NTR pathway)**

   The low-affinity p75 neurotrophin receptor (p75NTR) has been recently found to be overexpressed in primary tumour cells from several squamous cancers, including Laryngeal Squamous Cell Carcinoma. Accordingly, p75NTR has been proposed as a reliable index of tumorigenicity, invasiveness and chemotherapy resistance [see Triaca et al.(2019) for review ]. Considering the pivot role suggested for p75NTR in the regulation of cell survival and functions, in both healthy and pathological conditions, the study of p75 pathway to the acquisition and maintenance of stem cell properties in LSCC might contribute to better profiling of LSCC patients, and to improve their outcome.

2. **Identification of potential laryngeal carcinoma biomarkers (VGF-derived peptides and other neuropeptides)**

   Chromogranin A is commonly used as a marker of neuroendocrine tumors, including laryngeal tumors. A member of the Chromogranins family, the Secretogranin VGF (Bartolomucci et al., 2011), has been shown to trigger epithelial-to-mesenchymal transition in non-neuroendocrine tumors (lung adenocarcinoma), suggesting its potential utility as a marker for acquisition of tumor invasiveness (Rindi et al., 2007). The aim of this study is to potentially identify the VGF precursor and its derived peptides as new markers of the active/proliferating status of the tumor, thus detecting neoplastic lesions with higher risk of tumor invasiveness also in non-neuroendocrine tumors.

3. **RNA metabolism and related proteins in HN cancer.**

   Alterations of RNA homeostasis can lead to severe pathological conditions. Our ongoing findings highlight a potential role of the RNA-binding protein SMN in tumorigenesis of HN cancer. By in vitro studies, using cell lines derived from human larynx carcinoma, we observed that SMN could be implicated in cell adhesion and motility. Taking into account the key role of SMN in local translation control (Gabanella et al., 2016, 2020), we suppose that SMN could promote the local expression of invasiveness-related mRNAs affecting cell adherence and polarity. Although preliminary, these results point to SMN as a novel therapeutic target for larynx carcinomas.

**References:**
Rindi G et al. 2007. Peptide products of the neurotrophin-inducible gene vgf are produced in human neuroendocrine cells from early development and increase in hyperplasia and neoplasia. J Clin Endocrinol Metab. 92:2811-5.

**Keywords:** Cancer; invasiveness; growth factors; neuropeptides; vgf; stem cells; human tumor bioptic tissues

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**Other:** Studies founded by Projects Sapienza: 1) Characterization of laryngeal squamous cell carcinoma: molecular profiling of p75 neurotrophic receptor in cancer stem cells and circulating tumour cells to predict tumour aggressiveness and treatment response to Prof. Antonio Greco (PI) prot. RG11816436834B1; 2) Ion mobility mass spectrometry: a new high-potential device for new life science ways. to Prof.R. Currini prot. GA11816492EF0E14; 3) Characterization of the secretogranin VGF (SgVII) nerve growth factor inducible gene in laryngeal carcinoma to identify a new potential tumor marker and independent prognostic factor to Dr. M. Ralli, prot. RM11916B7E5A0D24.