The Rocco laboratory works to improve treatment of head and neck cancers. Tumors of the tonsil and the back of the throat—a region called the oropharynx—are occurring more frequently due to human papillomavirus (HPV), the virus that causes most cervical cancer. Although oropharyngeal tumors often respond to combined chemotherapy and radiation, about 2,000 people in the United States die of them every year, and those who are cured can suffer severe long-term consequences of treatment. Being able to predict outcome before treatment would help personalize therapy and identify patients who need more aggressive treatment. We have found, in the laboratory, that high tumor levels of the protein Bcl2 are related to resistance to chemotherapy and, in the clinic, to worse outcomes. In the laboratory, we are investigating whether inhibitors of Bcl2 function might provide an alternative treatment for oropharyngeal tumors that fail to respond to standard therapies. In the clinic, we are studying whether analysis of Bcl2 function in patients’ tumors improves predictions about responses to therapy.
Bcl2 expression and HPV status are both related to outcome in oropharyngeal cancer. Tumor sections from a patient who was cured by concurrent chemoradiation treatment (right) and from a patient who died of disease despite treatment (left), stained with hematoxylin/eosin (H&E) or for human papilloma virus (HPV), the p16 protein (typically high in HPV-positive cases), or the antiapoptotic protein Bcl2. Overall, Bcl2-high/HPV-negative tumors have poor outcomes, while >90% of patients with Bcl2-low/HPV-positive tumors are cured. Patients with Bcl2-high/HPV-positive or Bcl2-low/HPV-negative tumors have intermediate risk of recurrence. From Nichols et al, Clinical Cancer Research 16: 2138-46, 2010.

Selected Publications:


failure. We are currently validating these findings in a large, prospective clinical study, while applying the novel technology of BH3 profiling to examine the functional status of Bcl2 and related proteins that regulate cell death.

Regulation of p16 expression in tumor suppression and senescence

The p16INK4A protein helps prevent division of tumor-prone cells by slowing the cell cycle and inducing cellular senescence. This process costs the organism, however, by reducing the regenerative potential of stem cells required for tissue maintenance and increasing the risk of tissue damage from senescent cells. We discovered that the C-terminal binding protein (CtBP), a target of several stress-signaling pathways, regulates p16 expression through loss of Polycomb-based repression. This epigenetic memory is likely a major tumor-suppressive mechanism that is inherited by a cell’s progeny and may explain how gradual minor insults to tissues can lead to eventual growth arrest and senescence. Finding ways to reset this memory could help prevent or reverse some forms of tissue damage and aging.

Phase II clinical trial of AZD2171 in unresectable head and neck cancer

Many patients with head and neck cancer have advanced disease that recurs after treatment; recurrences usually cannot be removed surgically and are resistant to other standard therapy. Drugs that target development of blood vessels required for tumor growth and metastasis offer new hope for these patients. We are measuring clinical responses to AZD2171 (NSC 732208), an orally administered VEGFR2 inhibitor. This trial will test our prediction that AZD2171 will prevent or slow the growth of cancer by blocking the formation of new blood vessels.