The lecture of Prof. Rob Coppes 13.06.2017

Radiation induced damage to the salivary glands: protection and treatment. Tumor-derived organoids and radiation therapy

- **Clinical relevance:** patients who are treated with radiotherapy for head and neck cancer have relatively high survival rates. However, about 40% of these patients develope hyposalivation and xerostomia (dry mouth syndrome) which severely compromise the quality of life.
- **Discoveries and Areas of research:**
  - *Sparing the region of the salivary glands that contains salivary stem/progenitor cells responsible for long-term regeneration during radiation therapy:*

    The distribution of the stem/progenitor cell population is non-uniform within the salivary glands (particularily partiod). Sparing the cranial 50% of the parotid gland, the area containing the major ducts, is associated with a better saliva production after one year, and it is the radiation dose applied to this region that determines the degree of radiation induced parotid dysfunction. This was demonstrated in:

      - Cohorts of patients who had received head and neck radiation therapy with no tumor involvement in the salivary glands.
      - Rat-experiments: irradiation of specific subsections of rat parotid gland using high precision proton setup.

  - *The opportunity of adult stem cell therapy for radiation induced hyposalivation:*

    Developement of novel 3D culture methods to isolate and expand murine and human salivary stem/progenitor cells and confirming their nature based on the ability of single cells to self-renew and

differentiate into organoids (salivary gland-like structures with acinar and ductal components) in 3D cultures, the importance of Wnt signaling in this process, and using them successfully to restore the long-term functionality of the salivary gland in animal models:

- Murine salivary gland cells to murine recipients.
- Human salivary gland cells to murine recipients in xenotransplantation models

o *Finally, the ex vivo expansion of patient-derived tumor organoids, e.g. esophageal cancer in 3D culture and the possibility to use them for the prognosis and prediction of response to radiation therapy and developing personalized treatment.*