Adipo-NETwork: inside the crosstalk between adipose cells and gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

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A growing body of evidence suggests that adipose cells sustain the development and progression of several solid tumors both at the systemic level and locally, as a part of the tumor microenvironment. In gastroenteropancreatic neuroendocrine tumors (GEP-NETs) a significant association between obesity-related disorders and tumor onset/aggressiveness has been recently described. However, the potential crosstalk between GEP-NETs and adipose tissue is still unknown and no data are available about the characterization of adipose cells in the tumor microenvironment of these neoplasms.
Different platforms combining in vitro co-cultures and in vivo experiments in zebrafish are currently available to study the crosstalk between adipose and cancer cells. In the last years, we have developed an innovative preclinical model to study tumor-induced angiogenesis and invasiveness through the xenotransplantation of NET cells in zebrafish embryos. We took advantage of the Tg(fli1a:EGFP)^{y1} line which expresses enhanced green fluorescent protein (EGFP) in endothelial cells under the control of the fli1a promoter, thus labelling all blood vessels and providing a live visual marker for vascular development due to the optical transparency of zebrafish embryos. This quick transplantable platform resulted particularly suitable for cancer drug testing. Interestingly, we have collected preliminary data on GEP-NET immortalized cell lines and patient-derived adipose cells implanted in zebrafish embryos, demonstrating their attitude to stimulate angiogenesis and migrate far from the injection site within only two days post-injection. These data represent a promising starting point to study the crosstalk between adipose cells and GEP-NETs.

The aims of the present PhD project are:

- To study the reciprocal influence of GEP-NETs and adipose cells on 1) cell viability, cell cycle, apoptosis, migration and secreted factors through an in vitro co-culture model; 2) proangiogenic and invasive potential of both cell populations, using an in vivo zebrafish platform.
- To study the anti-tumor activity of new drugs targeting lipid metabolism in GEP-NETs, taking advantage of previously reported in vitro and in vivo models.