International PhD Course in Molecular Medicine 2016/2017

PhD project tile: **Effects of Endoscopic Ultrasound-guided (EUS) Cryothermal Ablation (CTA) for Pancreatic Ductal Adenocarcinoma (PDAC) on Systemic and Antitumor Immunity.**

PhD Curriculum: **Experimental and Clinical Medicine (ECM)**

Director of Studies: **Dr. Paolo Giorgio Arcidiacono**

Link to the OSR website:

**Background.** Radiofrequency ablation (RFA) and cryotherapy (CrT) are therapeutic options for unresectable PDAC. RFA and CrT induce cell death, vascular and endothelial injury, but post-necrotic amplification of tumor-induced immune response is also possible. Although immune-mediated mechanisms are likely to be implicated in the anti-tumor properties of these procedures, the effects on the immune system are poorly understood (1,2). EUS permits targeting lesions easily wherever they are located in the pancreas. EUS-guided CTA combines bipolar RFA with cryogenic cooling and is a new minimally invasive therapeutic tool, leading to a significant tumor mass reduction (3).

**Aim.** The aim of the present research project is to demonstrate that EUS-CTA for unresectable locally advanced not metastatic PDAC induces a systemic and anti-tumor immune response. To this purpose, serum and peripheral blood mononuclear cells (PBMCs) from patients with PDAC undergoing EUS-CTA will be sampled before and after treatment at different time points (up to three CTA treatments, and 2- and 4-month re-staging). Patients will be evaluated clinically and tumor mass volume will be radiologically assessed within a prospective randomized trial comparing EUS-CTA + chemotherapy (CT) vs. CT alone. Flow cytometry studies will be performed in order to assess the frequency of cytotoxic, helper, and regulatory T cells. The frequency of these cells will be also evaluated on cyto-histological samples from fine-needle pancreatic biopsies obtained before each CTA treatment, and on surgical specimens. T cells will be screened with a pool of tumor antigens in order to track their frequency before and after treatment (4). ELISA/Luminex studies on serum samples will be performed in order to characterize the cytokine profile of the patients before and after treatment. Our ultimate goal is to identify immune-modulating cells that can be injected under EUS guide into the PDAC mass as a potential anti-tumor therapy (5).

**References**


