Molecular profiling of exosomes in Pancreatic Ductal Adenocarcinoma and Non-Small Cell Lung Cancer. Diagnostic, predictive and prognostic biomarkers.

Introduction

Lung cancer is the first cause of cancer death worldwide, and the pancreatic carcinoma is the tumour with highest mortality worldwide with a 1-year survival rate of approximately 20% and a 5-year survival rate of 6%. This data show the two main problems in cancer, the absence of early detection and the lack of treatments.

Since few years ago and thanks to the research and development in targeted therapies the era of "one fits all" treatments finished. New treatments appear in the routine clinical protocols; however, these treatments would be more effective with an appropriate diagnosis and an easy follow-up.

With this purpose, the liquid biopsy has become one of the most promising tools to make a early diagnosis of the disease and a optima prognosis. Three main elements are under study, Circulating Tumour Cells (CTCs), cell-free DNA (cfDNA) and exosomes. For their stability (lipidic bilayer) and representative cargo of the cell, my PhD is going to be focused on their study.

Aims

- Try to identify a drugable translocation present in about several NSCLC, inside the exosomes, both in RNA and protein.
- Demonstrate the spread of the resistance to Erlotinib inside the tumour through the release of exosomes cargo in sensitive NSCLC cells.
- Identify new biomarkers inside the exosomes in patients with Pancreatic Ductal Adenocarcinoma, both genes and ncRNAs.
- Try to identify a diver mutation inside the exosomes in NSCLC patients resistant to Erlotinib.

Material and Methods

For our experiments, we will use plasma from NSCLC patients with the known translocation and NSCLC patients without mutation as control. The assays will be performed in blind in collaboration with OncoDNA (Gosselies). The isolation of the exosomal RNA for the analysis is done by exoRNeasy kit (Qiagen) and the protein isolation will be performed through exoEasy (Qiagen). Also in a parallel assay, plasma from patients with acquired or naïve resistance to Erlotinib will be used as well as non-mutated patients.

For the discovery of new PDAC biomarkers we will use plasma from patients with PDAC, PDAC with metastasis and healthy volunteers, and the isolation of the different molecules will be done as in the experiment before.