To the Academic Board of the doctoral program in Molecular Medicine

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Cicle XXXV **Tutor** Prof. Federica Gemignani

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Introduction

Malignant pleural mesothelioma (MPM) is a rare and severe tumor arising in the pleura. At the date no approved second line therapy is available for MPM patients due to its extreme drug resistance. The goal of my project is to detect novel genes playing a role for the maintenance of the malignant phenotype of MPM. My research started with a bioinformatics analysis by leveraging the online accessible data like TGCA (The Cancer Genome Atlas) and GEO database (Gene Expression Omnibus). During this year I have developed a new pipeline that would allow us to find the genes differentially expressed and correlated with MPM patient's prognosis. Comparing RNAseq data of MPM patients to RNAseq of healthy lung samples, three molecular signatures defined by 15 genes were detected. To investigate the role of these genes in the tumorigenesis, we carried out a systematic siRNA transfection and functional analysis on different mesothelioma cell lines. During this year I'll start from scratch comparing, this time, the tumor samples to the normal mesothelium tissue, to have a more precise expression profile of the MPM.

Methods

We analyzed *in vitro* the expression of the 15 proteins encoded by the detected genes in MPM cell lines (Mero-14, Mero-41, Mero-95, ZL-55, REN, and MSTO) and in non-malignant cell line (Met-5A) through western blot and siRNA transfection for gene silencing. We used commercial kits for the functional analyses. Bioinformatics analysis was carried out using the R language.

Result

All the proteins are overexpressed in one or more cell lines comparing to the control line. Nevertheless, the siRNA transfection of the genes caused a slower growth and an activation of the caspase pathways, only in some malignant cell lines. Confirming the hypothesis that cell lines represent only a part of patients differentially susceptible to treatment. Deeper functional analysis is underway. Other bioinformatics analysis on the validation of the new signature is ongoing.

Congress

- **Congress** : iMig 2021
  Abstract and ePoster: In-silico analysis reveals novel potential molecular targets associated with MPM patient's survival
  Date: 7-9 May 2021

- **Congress** : SIGU 2020
  Date : 11-13 Novembre 2020
  Abstract and ePoster: In-silico analysis reveals novel genes associated with MPM patient's survival

- **Course** : Igene 2020
  Date: 11-13 Novembre 2020

Pubblication

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