UNIVERSITÀ DI SIENA 1240

DIPARTIMENTO DI MEDICINA MOLECOLARE E DELLO SVILUPPO

MODELLO SCHEDA RELAZIONE DOTTORANDI
(da redigere in lingua inglese)

Al collegio docenti del Dottorato in Medicina Molecolare

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Ciclo XXXVII Tutor Prof.ssa Federica Gemignani

Attività scientifica svolta nel 1°/2° anno di Dottorato, Anno Accademico 2022/2023

Pleural mesothelioma (PM) is a rare cancer lacking effective diagnostic and therapeutic strategies. Mesothelin (MSLN) is a cell surface protein with differential expression between healthy and cancer cells; for this reason, MSLN is the most studied target in PM. Non-antibody proteins are an innovative strategy to improve targeted therapies and diagnosis. In this study, the binding between the tenth domain of human fibronectin type III (Fn3, 12 kDa) and MSLN is evaluated to develop a theranostic approach against PM.
Fn3 was previously engineered to bind MSLN by Prof. Sarah Moore's laboratory (Smith College). Fn3 was produced by transforming *E.coli* BL21 cells and purified through cobalt affinity chromatography and dialysis. To obtain a cell line with stable MSLN overexpression, the mesothelioma cells MSTO-211H were transfected with MSLN_OHu21046C pcDNA3.1 plasmid. MSTO with high MSLN expression were selected through fluorescent activated cell sorting (FACS). This cell line was used to evaluate Fn3-MSLN binding through flow cytometry and immunofluorescence. Fn3-MSLN interaction site was also investigated through molecular docking (AlphaFold server, PyMOL).
Fn3 was observed to bind MSLN with nano-molar affinity (K_D~11 nM) in MSTO overexpressing MSLN, in which MSLN expression was 10-fold higher than wild type MSTO. The colocalization of MSLN and Fn3 was observed on MSTO cell surface through immunofluorescence. The docking model confirmed that the Fn3 variable regions were involved in the interaction with MSLN. The model also revealed that Fn3 bound a minimal domain on MSLN that interacts with MUC16. These results will be experimentally validated using MSLN domain mapping through YSD.

Abstracts, conferences, and courses (a.a 2022/2023)

- Graduate seminar, Bio 507, *Recent Advances and Current Problems in the Biological Sciences*, Fall of the 22-23 academic year (course attended at the Department of Biology, Smith College, Northampton, MA, USA).
- *PhD research project presentations.* Research Doctorate in Biology, University of Pisa. 21/10/2022 (seminar).
- *Study skill workshop: writing anxiety.* Jacobson Center, Smith College, Northampton MA. 16/11/2022 (seminar).
- *Hauntings from A Eugenic Past: Race, Gender, and the Practice of Science.* Banu Subramaniam, Smith College, Northampton, MA. 1/12/2022 (seminar).

- *Dialogo sulla Biologia.* Prof. Roberto Giovannoni. Research Professional Skills, Università di Pisa. 02/12/2022 (seminar).
- *Cells, Viscoelasticity, and Medical Devices.* David J. Mooney, PhD, Department of Biomedical Engineering Seminar Series, University of Massachusetts. 2/12/2022 (seminar).
- Guest lecture in Prof. Sarah J. Moore upper-level seminar course in Spring 2023. The course name in Engineering 351: *Introduction to Biomedical Engineering.* I discussed the scientific research regarding my PhD project (guest lecture).
- Pang Sicheng*, Zhao Anya*, Piccardi Margherita*, Ziemba Alexis M, Moore Sarah J., *Engineering and exploring Fn3 for mesothelin targeted cancer therapy.* Poster presentation at Celebrating Collaborations: Students and Faculty Working Together (Smith College, Northampton, MA, USA). April 22, 2023 (poster presentation).
- Piccardi Margherita*, Silvestri Roberto*, Rea Filomena*, *et al., Mesothelin-binding Fn3 for a novel theranostic approach against malignant pleural mesothelioma*. Poster presentation at the 16th internation conference of the international mesothelioma interest group iMig 2023. Lille Grand Palais, France. June 22 – 29, 2023 (conference and poster presentation).
- Piccardi Margherita, Gemignani Federica, Landi Stefano, Moore Sarah J., *Engineering non-antibody proteins for mesothelioma diagnosis and targeted therapy.* Poster presentation at the Gordon Research Conference: Expanding the boundaries of Protein Engineering. Bryant University (Smithfield, RI, USA). July 23 - 28, 2023 (conference and poster presentation).
- *How to exploit your research idea: a quick introduction to EU project design and management.* Dr. Donata Franzi. 27/09/2023 (10-13/14.30-17.30) (soft skills).
- *Crossing Boundaries: Harnessing the Power of Interdisciplinary Approaches in Complex Systems.* Prof. Alessandro Vespignani. 28/09/2023 (14.30-17.30) (soft skills).

Scientific publications (a.a 2022/2023)

Piccardi, M.*, Gentiluomo, M.*, Bertoncini, S. *et al.*, Exploring the Neandertal legacy of pancreatic ductal adenocarcinoma risk in Eurasians. Biol Res 56, 46 (2023). https://doi.org/10.1186/s40659-023-00457-y

Visiting scholar experience

September 2022 – September 2023 (12 months), Prof. Sarah J. Moore laboratory at Smith College, Northampton, MA, USA.