

<b>Principal Investigator</b>	<b>Elisei Rossella</b>
<b>Hosting institution</b>	Università di Pisa
<b>Proposal title</b>	GENETIC HALLMARKS OF INVASIVE AND NON-INVASIVE MEDULLARY THYROID CANCER
<b>Keywords</b>	Genomic/Genetic instability; Thyroid ca.; Metastasis; RET; Circulating tumor DNA
<b>PhD project description</b>	<p>The proposed PhD research project for the candidate is part of the bigger IG-2024 project that, at this moment, and hopefully for more 4 years, is now running at the Department of Clinical and Experimental Medicine of Pisa University under the supervision of . He/she will be involved in the IG-2024 project whose PI is Prof.ssa Rossella Elisei. The global project is aimed at identifying genetic features involved in tumoral progression of medullary thyroid carcinoma (MTC). The proposed project for the candidate is regarding the evaluation of the role of ESR1 and ESR2 genes in the pathogenesis and aggressiveness of MTC. ESR1 and ESR2 genes encode for 2 estrogen receptors involved in cell survival and proliferation. Despite the well-known role of these 2 genes in breast cancer, a few data are available for MTC but it is already known that, when mutated, they can upregulate the wild-type RET activity that is the gene whose activation is responsible for 98% of hereditary MTC and 50% of sporadic MTC. Moreover, an ESR2 germline mutation was already reported in a case of hereditary MTC. The candidate will be involved in this part of the project and in particular he/she will identify MTC patients to be enrolled in the study and maintain the database with the clinical and pathological. The candidate will be also involved in the search for ESR1 and ESR2 mutations. ESR1 and ESR2 mutated cases will be then studied for the expression levels of RET transcript by droplet digital PCR and RET transcript levels detected in ESR1 or ESR2 mutated cases will be compared with RET transcript levels in a matched non mutated control group.</p>
<b>Main topics of the lab</b>	Thyroid cancer studies
<b>Short description of the lab activity</b>	<p>The laboratory of the Endocrine Unit of the Department of Clinical and Experimental Medicine of Pisa University headed by Prof.ssa Rossella Elisei is involved since several years in the study of thyroid carcinoma and in particular of medullary thyroid carcinoma. Since our Endocrine Unit is a referral center for the diagnosis and treatment of thyroid carcinoma, a very large series of thyroid cancer patients have been followed over the years and very many are still in follow up. In addition, about 200 new diagnosis per year (including all thyroid cancer histotype) are obtained. Due to the large number of thyroid cancer patients followed at this Unit and thank to the collaboration with the surgery and pathology Unit of this University Hospital more than 2000 thyroid cancer tissues have been biobanked. In most cases,</p>

	<p>peripheral blood has been also collected. In the last 10 years we have also started the collection of plasma samples for the analysis of the mutation profile in the circulating tumoral DNA (ctDNA). The laboratory has all the facilities for the detection of genetic alterations in tumoral tissue, blood and ctDNA (i.e. sequencing analyzer, IOS5 system for next generation sequencing, digital droplet PCR) and also for the analysis of expression of genes involved in thyroid tumorigenesis and progression (digital droplet PCR). We have also a very good cellular biology expertise and the necessary equipments. Since the beginning of our work we have been deeply interested and involved in the identification of driver mutations in all histotype of thyroid cancer to clarify the molecular mechanisms leading to thyroid cancer tumorigenesis taking advantage of the newest technique for sequencing. The identification of these mutations has had an important clinical impact: first some mutations, and in particular RET somatic mutations, are good factor of poor prognosis and have an important role in the monitoring of tumor progression; second, some mutations represent the target of new therapies with molecularly targeted drugs. The characterization of the mutational profile of these patients has therefore allowed the identification of those who could benefit from that specific treatment, resulting in a significant improvement in their prognosis. Once the molecular profile of thyroid cancer cases has been almost deciphered, we started to investigate the molecular profile characterizing tumor progression. Our lab has also contributed to the identification of the relevant role of the analysis of the mutation profile for monitoring the progression of the disease in advanced case. An important focus of our lab has been and is the search of germline RET mutations in patients affected with medullary thyroid carcinoma to unveil hereditary cases erroneously diagnosed as sporadic. Once the germline RET mutation is identified in the proband of the family is identified, family members are investigated and those found to be positive are strictly followed to monitor tumor development.</p>
<b>Main research area</b>	Cancer biology
<b>Group composition</b>	RESEARCH GROUP COMPOSITION: Chief: Prof.ssa Rossella Elisei, MD Laboratory staff: 2 experienced biologist that are involved in all the steps of lab work starting from the definition of protocols, analysis of data, and preparation of manuscripts; 1 postdoc biologist that is mainly involved in a dedicated project; 1 biology fellow whose work is dedicated to different projects ongoing in the laboratory
<b>Institutional page link</b>	<a href="https://endocrinologia.med.unipi.it/">https://endocrinologia.med.unipi.it/</a>
<b>Lab website link</b>	
<b>Social media link</b>	
<b>Lab bibliography</b>	Higher RET Gene Expression Levels Do Not Represent an Alternative RET Activation Mechanism in Medullary Thyroid Carcinoma. Mulè C, Ciampi R, Ramone T, Prete A, Matrone A, Cappagli V, Torregrossa L, Basolo F, Elisei R, Romei C BIOMOLECULES 2021 Oct; 11: