Our Group is mainly interested in identifying genetic risk factors involved in endocrine tumour susceptibility. Through a comprehensive analysis of tumour genomic features we have been able to propose diagnostic and prognostic markers, to identify altered pathways that could be therapeutically targeted, and to identify new major susceptibility genes.

We are also interested in defining markers associated with differences in anticancer drug response and toxicity. We are applying targeted and whole-exome next-generation sequencing to a large series of clinically well-characterised patients. The aim is to identify new therapeutic approaches to personalise cancer treatment. These efforts will collectively improve the diagnosis, prognosis and treatment of patients.

“We identified a new susceptibility gene for paraganglioma, discovered predictive markers of mTORi response, and uncovered the Hsa-miR-139-5p/HNRNPF axis as a critical modulator of thyroid tumour virulence.”

HEREDITARY ENDOCRINE CANCER GROUP

Mercedes Robledo
Group Leader

Staff Scientists
Alberto Cascón, Cristina Rodríguez

Post-Doctoral Fellows
Cristina Montero, Ángel Mario Martínez (since July)

Graduate Students
Bruna Calsina, Lucía Inglada, Laura Remacha (until June), Marta Pulgarín (since October), Juan M. Roldán, María Santos

Technicians
Javier Lanillos (TS)*(since June), Rocío Letón

Titulado Superior (Advanced Degree)
**ROCKEN MUTATIONS**

Deep sequencing of small RNAs reveals a prognostic marker functionally associated with alternative splicing modulation in thyroid cancer. It is urgent to identify biomarkers and functional networks associated with aggressive thyroid cancer as in order to anticipate disease progression and facilitate patient-personalised management. The mRNA sequencing of thyroid tumour series enriched for advanced disease patients uncovers miRNA profiles correlated with tumour-specific histopathological and molecular features, such as stromal cell infiltration and tumour-driver mutation. Differential analysis considering disease progression revealed a significant miRNA signature associated with alternative splicing modulation of patients from recent/metastatic disease. Exon expression of hsa-miR-139-5p significantly reduced migration and proliferation abilities of anaplastic thyroid cancer cells. Proteomic analysis pointed to RICTOR, SMAD3, and HNRNPF as miRNA targets putative in vitro.

**HUMAN CANCER GENETICS PROGRAMME**

Significantly, many available hnrnpf, an alternative splicing factor mainly involved in cryptic exon inclusion/exclusion, showed an anti-correlation with hsa-miR-139-5p gene expression in thyroid tumours. Analysis of alternative splicing from RNA sequencing data revealed 174 events differentially regulated upon hnrnpf repression in genes and signalling cascades critical for thyroid cancer (FIGURE). These results point at hsa-miR-139-5p/HNRNPF-gene trans- and cell-based transcription as a novel regulatory axis associated with tumour virulence and modulation of major thyroid cancer signalling pathways.

**PUBLICATIONS**