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 miR-483-5p/ALCAM axis as a new player in pheochromocytoma at the metastatic niche and showed that mTOR pathway mutations correlate with poor prognosis in chromophobe renal cell carcinoma.”
mTORC pathway alterations in chromophobe renal cell carcinoma associated with poor outcome

Overexpression of miR-483-5p is confined to metastases and linked to high circulating levels in chromophoeyctoma/papanglioma patients

Phaeochromocytoma/paranglioma (PPGLs) are rare neuroendocrine tumours. Approximately 15% of PPGL patients present at diagnosis with metastatic disease (n=992) so far, we performed an in-depth characterisation of the mTORC pathway through targeted NGS and immunohistochemistry (Roldán-Borromeo et al. 2020). Furthermore, we investigated mutations in the electron transport chain Complex I genes by developing a bioinformatics approach to identify mitochondrial variants using NGS off-target data (Lanillos et al. 2020). Mutations in key components of the mTORC pathway (mTOR, TSC1, TSC2) occurred in 17% of primary tumours and were associated with the immunohistochemistry staining of phospho-S6 and PTEN, and with chRCCsophisticated variant, supporting their biological relevance. Patients with mTORC pathway mutations had worse outcomes (overall survival: HR=3.5 and P=0.027, confirmed in TCGA with HR=10.3, P<0.006), and mutations in TP53 and telomerase genes were enriched in metastatic chRCC. Overall, we showed that mTORC pathway mutations correlate with poor prognosis in chRCC, suggesting that mTOR inhibitors might be a good therapeutic option for patients with these alterations.

The expression of miR-483-5p is linked to metastatic colonisation, and pinpoints circulating ALCAM-ALCAM interaction in metastatic PPGL (FIGURE). ALCAM/CD166 is member of a subfamily of immunoglobulin receptors that is linked to metastatic colonisation, and pinpoints circulating ALCAM-ALCAM interaction in metastatic PPGL.

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