Molecular Pathophysiology of Adrenal and endocrine Tissues Team

Directors: Dr Pierre VAL PhD, Dr Antoine Martinez PhD

Research overview

Our research group entitled "Molecular Pathophysiology of Adrenal and Endocrine Tissues" is hosted by the Genetics Reproduction and Development Institute (iGReD), a multidisciplinary laboratory located in the heart of France. It is currently composed of 14 people encompassing PhD students (3), Postdocs (3), full-time researchers (2), researcher-teachers (2), MDs (2) and technical support (2).

Over the last 15 years our goal has been to decipher the genetic and molecular mechanisms underlying adrenal development, differentiation and disease, using elaborate genetically engineered mouse models. Our work has demonstrated the central role of WNT and PKA signalling antagonism to allow establishment and maintenance of zonal differentiation of the adrenal cortex, which is central to maintain its endocrine activity [1–3]. We have further shown that deregulation of these two pathways resulting from mutations in their key regulators, is associated with tumour development (benign and malignant) and endocrine hyperactivity of the adrenal cortex. Through our strong interactions with clinical groups in France, Germany and the USA we have been able to translate these findings to patients with adrenocortical carcinomas, aldosterone producing adenomas and cortisol producing adenomas [1,4–9]. Building on these findings, we also demonstrated a central role of post-translational modifications (histone methylation and sumoylation) in fine tuning response of PKA/WNT pathways and we found that alterations of these modifications are associated with adrenal insufficiency[10,11]. Our models of WNT pathway deregulation also uncovered an undisclosed sexually dimorphic role of macrophages in preventing tumour progression in the adrenal cortex.

Our current projects funded by ANR and "Ligue Contre le Cancer" grants, aim at understanding how sex-specific regulation of PKA, WNT and SUMO signalling pathways results in sexually dimorphic adrenal differentiation and renewal, and how this may explain the strong female bias in adrenal diseases. We also aim at deciphering the complex interplay between sex hormones, adrenal cortex cells and macrophages in both adrenal differentiation and carcinogenesis. Our ultimate goal is to find new targetable molecular mechanisms and cell populations to develop novel treatments for adrenal diseases. Availability of our large collection of genetically engineered mice, will allow rapid evaluation of these therapeutic options, in clinically relevant models.

Research Environment

The GReD institute is a highly dynamic workplace, setup in a brand-new building hosting state of the art facilities (automated histopathology, high-end confocal and brightfield microscopy, high-capacity mouse facilities, bioinformatics, tissue culture...) (https://www.gred-clermont.fr). The 16 research teams at iGReD (190 employees) aim at understanding the genetic and epigenetic programs associated with development, reproduction, health and disease. Our friendly and international team is part of the Endocrinology, Signalling and Cancer department.

The institute is located in Clermont-Ferrand, a young and vibrant university city (>35 000 students at University Clermont Auvergne) surrounded by the volcanoes of Auvergne (UNESCO world Heritage), providing a perfect mix between the intensity and dynamism of a metropolis (urban area of 500 000 inhabitants) and the serenity of nearby wide-open wild spaces.

Techniques

We routinely use a large array of techniques and approaches that the intern will be able to familiarize with. These include but are not limited to:

-Generation and maintenance of genetically engineered mouse models of diseases
-Experimental manipulation of mouse models
-Histology, immunohistochemistry, RNA in situ hybridization
-Tissue imaging
-RNA sequencing, RTqPCR
-Hormone analysis by ELISA
-Flow cytometry
-Cell sorting
-Cell culture

Contacts

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