ISPA - Etude génomique et génétique intégrée de l'hyperaldostéronisme primaire: implications physiopathologiques et pronostiques

ISPA - Integrated study of primary aldosteronism: from genetics and genomics to physiopathology and prognosis

Participating teams

+ Primary aldosteronism (PAL) - Background
  + Prevalence ~ 0.6-1.7% (THA, 2001; Masson 2006)
  + Differences with essential hypertension
  + Con: a sodium (APAR): 30-50% (Kallberg et al. 2005)
  + Con: a aldosterone (APAR): 5-10% (Kallberg et al. 2005)
  + Primary unilateral adrenal hyperplasia (5-10%)

+ Pathophysiology
  + Comparative genetic heterogeneity (GH): little changes in pair 19q and 17
  + Comparative expression of genes involved in sodium reabsorption and in cholesterol and electron supply in the cell (Cartier et al. 2005; Bours et al. 2015)
  + Alterations in transcription factors that enhance expression of steroid metabolizing enzymes (Kallberg et al. 2005)
  + Overexpression of estrogen and androgen receptors (Kallberg et al. 2005)

+ Aim of the study
  We make the hypothesis that activation of particular signalling pathways or transcriptional cascades, via qualitative (mutations) or quantitative (expression) molecular changes may be responsible for the development of PAL.

  The aim of our project is to identify these abnormalities by using a combined approach, integrating genomics and genetics with pathophysiologic, cellular, and molecular investigations.

  Our project includes four research axes:

  1. Transcriptional profiling of PAL and correlation of gene expression signatures with the pathophysiologic profile and therapeutic outcome after surgery.
  2. Study of the role of mast cells in the pathogenesis of PAL
  3. Identification of susceptibility genes by whole genome association studies
  4. Analysis of signaling pathways and transcriptional cascades in model systems

+ Expected outcome
  The project will allow to gain better insight into the pathogenic mechanisms involved in the development of PAL, possibly leading to the identification of susceptibility genes and new therapeutic targets.

  Furthermore, the identification of molecular signatures correlated with therapeutic outcome, the analysis of new factors regulating transcriptional regulation and proliferation in glomerulosa cells and the characterization of relevant pathways, might open new perspectives in the development of novel strategies for therapeutic intervention and follow-up after surgery.

  The originality of our strategy stems from the interdisciplinary approach, which integrates the competences of basic researchers, mathematicians and clinicians, allowing to explore all the aspects of the project and the transfer of relevant results to clinical practice.

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The COMETE network : (COrtico and MEDullo-surrenal: les Tumeurs Endocriennes)