Hospital Universitario La Paz
Paseo de La Castellana, 261
Edificio Norte, 4ªPlanta
28046 - Madrid

POSITION

Project Title/ Job position title

Relevance of the factor H protein family in Complement-associated nephropathies / Pre-doctoral Position

Area of Knowledge

Life Science Panel

Human Biology, Microbiology, Genetics, Cell Biology, Genomics and Proteomics, Biochemestry

Research Project/Research Group Description

This is a translational research project to increase our knowledge on genetic predisposing factors in severe renal diseases, and to help improve patients' clinical management and treatment. Dysregulation of the Complement Alternative Pathway is a relevant pathogenic mechanism in the rare and severe kidney diseases atypical Haemolytic Uraemic Syndrome (aHUS) and C3 Glomerulopathies (C3G), and it likely contributes to the more prevalent IgA nephropathy (IgAN). Early identification of patients with genetic or acquired Complement defects has diagnostic and prognostic value, allowing implementation of therapeutic strategies with Complement inhibitors that drastically improve disease evolution.

Our main objective is to identify and characterize disease-associated genetic variants and protein isoforms of the Complement regulator factor H (FH) and their homologous Factor H-Related Proteins (FHRs), collectively known as "Factor H protein family". We will perform genetic and protein studies in aHUS, C3G and IgAN patients to analyze whether disease-associated variants change protein levels, or whether they give rise to functional changes that modulate the Complement regulatory activity of FH. We will also develop a genetic test for the quick identification of risk variants and haplotypes. For these studies, we have plasma, serum and DNA samples from aHUS, C3G or IgAN patients recruited during the last 15 years, and from unrelated healthy controls. The experimental design includes: 1) Quantitative analysis of FH/FHRs variants by immunological techniques (Western-blot and E.L.I.S.A.). A quantitative SRM-Mass Spectrometry assay will also be done in selected samples. 2) Functional analysis of genetic variants and abnormal protein isoforms. Proteins will be purified from plasma samples by chromatographic techniques, and further characterized in functional Complement assays. 3) Development of a SNapShot assay for genotyping of disease-relevant haplotypes of the FH and FHRs genes.

Job position description.

The job will be done within the *Hospital La Paz Institute for Health Research* (IdiPAZ) in Madrid. The candidate will join the Research Group "Diagnosis and treatment of diseases associated with abnormalities of the Complement system", a national reference group for the study of primary or acquired defects in the Complement system. The work proposed is integrated into the research line of "Complement and renal pathology", and it will allow the candidate to perform translational research and to obtain a Ph.D.

The candidate will be responsible for the following experimental tasks: 1) Isolation of plasma, serum and DNA from blood samples from patients and controls. 2) Western-blot analysis of FH/FHRs to identify protein deficiencies and abnormal protein isoforms. 3)

Quantitation of FH/FHRs by Western-Blot and ELISA. 4) Purification of genetic variants or abnormal proteins of pathological relevance from plasma samples. 5) Functional assays with purified proteins or serum samples. 6) Genotyping of FH/FHRs genetic variants.

The candidate will present and discuss his/her results in lab meetings, and he/she will also attend the IdiPAZ Lecture Programme.

Skills required: Academic background in Immunology Research. Technical competence in Quantitative Western-blot analysis of plasma proteins, PCR and Sanger sequencing. Competence in *Access, Excell* and *Powerpoint* software. Intermediate to advanced level of English.

Valuable skills: Professional and academic background in Complement Research. Technical competence in ELISA assays, chromatographic techniques for protein purification, and MLPA analysis. Competence in *SPSS* software for statistical analysis. Advanced level of English.

GROUP LEADER

Title: PhD.

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Research project/Research group website:
http://www.idipaz.es/PaginaDinamica.aspx?IdPag=161&Lang=ES