

# Thrombosis and Haemostasis



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## Main Lines of Research

- ▶ Investigation of the genetic basis of venous and arterial thrombosis. GAIT-1 and GAIT-2 projects.
- ▶ Investigation of new antithrombotic drugs: thrombin inhibitors, molecules against activated factor X, low molecular weight heparin with oral activity, among others.
- ▶ Biomarkers of prothrombotic states in patients under 55 years with venous thromboembolic disease, acute ischaemic stroke, or acute myocardial infarction. VEREMA project.
- ▶ Applied clinical development of the self-management model of oral anticoagulant treatment. ORION project. Retrospective analysis of the clinical outcomes from patient self-management of antivitamin-K treatment at the Hospital de Sant Pau. NCT3532724
- ▶ Mathematical models of prediction of the individual risk of thromboembolic disease in general population (RETROVE Project) and in cancer patients (MIRTO Project).
- ▶ CITA project. Centre for Antithrombotic Therapy Management. Research into a new ambulatory management model for patients receiving any kind of antithrombotic therapy (anti vitamin-K, new oral anticoagulants, low molecular weight heparins, antiplatelets) by incorporating new educational programmes, specialized nursing and new communication technologies.

## Challenges

- ▶ Study QTL detected in GAIT-1 families in relation to phenotypes of haemostasis with thrombosis risk (resistance to activated protein C, factor VIII, homocysteine, factor XII, body mass index and others).
- ▶ Replicate QTL related to thrombosis in GAIT-1 families by means of the linkage analysis using new GAIT-2 families.
- ▶ Conduct genome-wide association study (GWAS) of phenotypes involved in GAIT-1.
- ▶ GWAS of phenotypes included in GAIT-2.
- ▶ Analyse RNA expression in the GAIT-2 families.
- ▶ Investigate miRNA associated with thromboembolic disease in GAIT-2.
- ▶ To complete the recruitment of the cohorts included in MIRTO Project (Modeling the Individual Risk of Thrombosis in Oncology), with the goal of establishing an individual risk score for venous thromboembolism (RETROVO sub-project) and for ischaemic stroke (SINO subproject) in patients with cancer.
- ▶ Research plasma proteins associated with the risk of venous thromboembolism by using high affinity proteomics developed at Karolinska Institutet. VEREMA project, joint collaboration between the European case-control studies VEBIOS (Sweden), RETROVE (from our unit) and MARTHA (France).
- ▶ Investigation on laboratory management of DOACs.
- ▶ Search for new universal laboratory methods for the assessment of any kind of oral anticoagulant (AVK and DOACs).
- ▶ To finish the recruitment of patients for the ORION project.

## Active Grants

- ▶ Joan Carles Souto Andrés. Red Cardiovascular. RD12/0042/0032. Instituto de Salud Carlos III. Duration: 2013-2017. 181,000.00 €.
- ▶ Joan Carles Souto Andrés. Continuación de la búsqueda de algoritmos aplicables en la clínica para definir el perfil individual de Riesgo de Enfermedad Tromboembólica Venosa (RETROVE). PI15/00269. Instituto de Salud Carlos III. Duration: 2016-2018. 86,500.00 €.

Note: Total amount granted to PI. It does not include indirect costs.

## Grants Awarded in 2017

- ▶ Concepción Muñoz Lozano, Predisposición genética a la trombosis en pacientes oncológicos (ONCOTHROMB). SLT002/16/00113. Departament de Salut. Duration: 2017-2019. 63,311.05 €.

Note: Total amount granted to PI. It does not include indirect costs.

## Theses

- ▶ Miguel Vázquez Santiago, Plaquetas y enfermedad tromboembólica. Aspectos genéticos, biológicos y clínicos. Universitat Autònoma de Barcelona. Directors: Juan Carlos Souto and Nuria Pujol-Moix. Date of defense: 26/09/2017.

Collaborations

**Collaborations with other IIB Sant Pau Groups**

- ▶ Genomics of Complex Diseases (GAIT1, GAIT2, RETROVE, VEREMA and MIRTO Project).
- ▶ Stroke Unit (HERO and MIRTO Project).
- ▶ Vascular Surgery (GAIT2, genetics of venous insufficiency).
- ▶ Medical Oncology (MIRTO Project).
- ▶ Clinical Haematology (MIRTO Project).
- ▶ Digestive Diseases (HEPACO).

**External Collaborations**

- ▶ Cardiovascular Research Network (RIC).
- ▶ Karolinska Institutet, Stockholm, Sweden: GAIT2 and VEREMA.
- ▶ La Timone Hospital, Marseille, France: GAIT2 and VEREMA.

- ▶ Pierre and Marie Curie University, INSERM, UMR-S 1166, Paris, France: GAIT2 and VEREMA.
- ▶ Université de Genève, Switzerland: GAIT2.
- ▶ Texas Research Institute (formerly Southwest Foundation for Biomedical Research), San Antonio, USA: GAIT1 and GAIT2.
- ▶ Universitat Politècnica de Catalunya, Barcelona, Spain. Centre for Biomedical Engineering Research: RETROVE and MIRTO design.
- ▶ Thrombosis Group of the Spanish Medical Oncology Society (SEOM): ONCOTHROMB and MIRTO.
- ▶ Institut of Biological Psychiatry, Mental Health Snc. Hans. Roskilde (Denmark).
- ▶ Haematology Service of Hospital Sant Joan de Déu (Clinical modeling for the management of haemophilic patients and patients under self-management of VKA therapy)

\*TIF: 27.083 \*\*MIF: 3.3853

Scientific Production

Barrios V., Egocheaga-Cabello M.I., Gallego-Cullere J., Ignacio-Garcia E., Manzano-Espinosa L., Martin-Martinez A., Mateo-Arranz J., Polo-Garcia J., Vargas-Ortega D., Healthcare resources and needs in anticoagulant therapy for patients with nonvalvular atrial fibrillation. SAMOA Study Recursos y necesidades asistenciales en el tratamiento anticoagulante de los pacientes con fibrilación auricular no valvular. Estudio SAMOA (2017) REV CLIN ESP, 217 (4), 193-200.

**IF: 0.796**

Borras N., Batlle J., Perez-Rodriguez A., Lopez-Fernandez M.F., Rodriguez-Trillo A., Loures E., Cid A.R., Bonanad S., Cabrera N., Moret A., et al. Molecular and clinical profile of von willebrand disease in Spain (PCM-EVW-ES): Comprehensive genetic analysis by next-generation sequencing of 480 patients (2017) HAEMATOLOGICA, 102 (12), 2005-2014.

**IF: 8.725**

Jimenez-Fonseca P., Carmona-Bayonas A., Calderon C., Fontcuberta Boj J., Font C., Lecumberri R., Monreal M., Munoz Martin A.J., Otero R., Rubio A., Ruiz-Artacho P., Suarez Fernandez C., Colome E., Perez Segura P., FOTROCAN Delphi consensus statement

regarding the prevention and treatment of cancer-associated thrombosis in areas of uncertainty and low quality of evidence (2017) CLIN TRANSL ONCOL, 19 (8), 997-1009.

**IF: 2.339**

Llobet D, Tirado I, Vilalta N, Vallvé C, Oliver A, Vázquez-Santiago M, Mateo J, Millón J, Fontcuberta J, Souto JC. Low ADAMTS13 levels are associated with venous thrombosis risk in women. (2017) THROMB RES, 157, 38-40.

**IF: 2.779**

Martin-Fernandez L., Gavidia-Bovadilla G., Corrales I., Brunel H., Ramirez L., Lopez S., Souto J.C., Vidal F., Soria J.M., Next generation sequencing to dissect the genetic architecture of KNG1 and F11 loci using factor XI levels as an intermediate phenotype of thrombosis (2017) PLOS ONE, 12 (4), -.

**IF: 2.600**

Sennblad B, Basu S., Mazur J., Suchon P, Martinez-Perez A., Vlieg A.H., Truong V., Li Y., Gadin J.R., Tang W., Grossman V., de Haan H.G., Handin N., Silveira A., Souto J.C., Franco-Cereceda A., Morange P.-E., Gagnon F., Soria J.M., Eriksson P., Hamsten A., Maegdefessel L., Rosendaal F.R., Wild P., Folsom A.R., Tregouet D.-A., Sabater-Lleal M., Ge-

nome-wide association study with additional genetic and post-transcriptional analyses reveals novel regulators of plasma factor XI levels (2017) HUM MOL GENET, 26 (3), 637-649.

**IF: 4.702**

Vázquez-Santiago M, Vilalta N, Ziyatdinov A, Cuevas B, Macho R, Pujol-Moix N, Carrasco M, Mateo J, Fontcuberta J, Soria JM, Souto JC. Platelet count and plateletcrit are associated with an increased risk of venous thrombosis in females. Results from the RETROVE study. (2017) THROMB RES, 157, 162-164.

**IF: 2.779**

Vicente V., Martin A., Lecumberri R., Coll-Vinent B., Suero C., Gonzalez-Porras J.R., Marco P., Mateo J., Roldan V., Soulard S., Crespo C., Camats M., Clinical perspectives on the management of bleeding in patients on oral anticoagulants: The DECOVER Study (DELphi Consensus on oral COagulation and therapy action reVERsa Perspectivas clínicas del manejo de la hemorragia en el paciente tratado con anticoagulante oral: Estudio DECOVER (2017) EMERGENCIAS, 29 (1), 18-26.

**IF: 2.363**

Other Publications

- ▶ López S, Soria JM, Souto JC. Genética en trombosis. Ponencia en el XXXIII Congreso Nacional de la SETH. Málaga 2017. Libro de Ponencia y Comunicaciones. Arán Ediciones SL. DL: M-34026-2012. P 68-74.
- ▶ Pujol-Moix N, Español I, Hernández A, Vázquez Santiago M, Souto JC, Muñoz-Díaz E. Platelet Ultrastructural Morphology and Morphometry in 10 Patients with MYH9- Related Disease (2017) J Hematol Transfus, 5, 1065.

- ▶ Vilalta N, Vázquez-Santiago M, Cuevas B, Macho R, Remacha A, Carrasco M, Mateo J, Millón J, Soria JM, Souto JC. The relationship between leukocyte counts and venous thromboembolism: results from RETROVE Study (2017) BIOL MED (ALIGARH), 9, 4.
- ▶ Vilalta N, Tirado I , Mateo J, Romero L, Carrasco M, Souto JC, Fontcuberta J. The c.1787G>T and c.1787G>A mutations are not found in the prothrombin gene in a Spanish population. (2017) BIOL MED (ALIGARH), 9, 4.