

LÍNEA DE INVESTIGACIÓN:

Papel de ncRNAs exosomales en la biología vascular

Investigador Principal: Dr. Francisco Javier Blanco (fjblanco@ugr.es)

Centro de Investigación Biomédica (CIBM, UGR). Departamento de Bioquímica y Biología Molecular III e Inmunología, Universidad de Granada.

LÍNEA DE INVESTIGACIÓN

Hereditary Hemorrhagic Telangiectasia (HHT), or Rendu-Osler-Weber syndrome, is a dominant autosomic rare disease. HHT is a vascular dysplasia characterized by a serious alteration of the Transforming Growth Factor (TGF)-beta signaling pathway affecting mainly to the angiogenesis process. Also, since HHT exhibits incomplete penetrance, other factors are suggested to be involved in its physiopathology. In this sense, some recent studies point out differentially expressed small non-coding RNA molecules (ncRNA; including miRNAs and lncRNA, among others) in plasma of HHT patients related to the angiogenesis process. Recently, it has been reported that ncRNAs are transported by membrane-derived small vesicles named exosomes, which mediate a novel mechanism of cell-to-cell communication linking disparate cell types and tissues. Therefore, exosomal ncRNAs have a high diagnosis value as clinical biomarkers, as well as a putative role as therapeutic vehicle focused on targeted pharmacological manipulation.

This Project combines the interest in the prediction of new biomarkers and therapeutic targets and strategies for the treatment of HHT patients, as well as making progress in the knowledge of the molecular bases of the disease and in vascular biology.

Keywords: Hereditary Hemorrhagic Telangiectasia; Exosomes; miRNAs; lncRNA; CRISPR/Cas9

PUBLICACIONES RECIENTES (5 ÚLTIMOS AÑOS)

Ojeda-Fernández L, Recio-Poveda L, Aristorena M, Lastres P, [Blanco FJ](#), Sanz-Rodríguez F, Gallardo-Vara E, de las Casas-Engel M, Corbí Á, Arthur HM, Bernabeu C, Botella LM. Mice Lacking Endoglin in Macrophages Show an Impaired Immune Response. *PLoS Genet.* 2016 Mar 24;12(3):e1005935.

Gallardo-Vara E, [Blanco FJ](#), Roqué M, Friedman SL, Suzuki T, Botella LM, Bernabeu C. Transcription factor KLF6 upregulates expression of metalloprotease MMP14 and subsequent release of soluble endoglin during vascular injury. *Angiogenesis.* 2016 Apr;19(2):155-71.

[Blanco FJ](#), Deng L, Stevens H, Lu R, Caudrillier A, McBride M, McClure JD, Grant J, Thomas M, Frid M, Stenmark K, White K, Seto AG, Morrell NW, Bradshaw AC, MacLean MR, Baker AH. MicroRNA-143 Activation Regulates Smooth Muscle and Endothelial Cell Crosstalk in Pulmonary Arterial Hypertension. *Circ Res.* 2015 Oct 23;117(10):870-83

Blanco FJ, Ojeda-Fernandez L, Aristorena M, Gallardo-Vara E, Benguria A, Dopazo A, Langa C, Botella LM, Bernabeu C. Genome-wide transcriptional and functional analysis of endoglin isoforms in the human promonocytic cell line U937. *J Cell Physiol*. 2015 Apr;230(4):947-58. doi: 10.1002/jcp.24827.

Aristorena M, Blanco FJ, de Las Casas-Engel M, Ojeda-Fernandez L, Gallardo-Vara E, Corbi A, Botella LM, Bernabeu C. Expression of endoglin isoforms in the myeloid lineage and their role during aging and macrophage polarization. *J Cell Sci*. 2014 Jun 15;127(Pt 12):2723-35.

Valbuena-Diez AC, Blanco FJ, Ojuo B, Langa C, Gonzalez-Nuñez M, Llano E, Pendas AM, Díaz M, Castrillo A, Lopez-Novoa JM, Bernabeu C. Oxysterol-induced soluble endoglin release and its involvement in hypertension. *Circulation*. 2012 Nov 27;126(22):2612-24.

Rossi E, Sanz-Rodriguez F, Eleno N, Düwell A, Blanco FJ, Langa C, Botella LM, Cabañas C, Lopez-Novoa JM, Bernabeu C. Endothelial endoglin is involved in inflammation: role in leukocyte adhesion and transmigration. *Blood*. 2013 Jan 10;121(2):403-15.

Garrido-Martín EM, Blanco FJ, Roquè M, Novensà L, Tarocchi M, Lang UE, Suzuki T, Friedman SL, Botella LM, Bernabéu C. Vascular injury triggers Krüppel-like factor 6 mobilization and cooperation with specificity protein 1 to promote endothelial activation through upregulation of the activin receptor-like kinase 1 gene. *Circ Res*. 2013 Jan 4;112(1):113-27.

Blanco FJ, Bernabéu C. The Splicing Factor SRSF1 as a Marker for Endothelial Senescence. *Front Physiol*. 2012 Mar 28;3:54.

Alt A, Miguel-Romero L, Donderis J, Aristorena M, Blanco FJ, Round A, Rubio V, Bernabeu C, Marina A. Structural and functional insights into endoglin ligand recognition and binding. *PLoS One*. 2012;7(2):e29948.

Blanco FJ, Bernabeu C. Alternative splicing in endothelial senescence. Role of the TGF- β co-receptor endoglin. In: Senescence. Ed. T. Nagata. (2012). InTech, Rijeka, Croacia. ISBN 978-953-51-0144-4.

TESIS DIRIGIDAS (5 ÚLTIMOS AÑOS)

“Papel de las isoformas de endoglina en el linaje mielóide”. Universidad Complutense de Madrid. Mikel Aristorena San Adrián (14/03/2014). Sobresaliente, Cum laude

“Estudio del mecanismo de liberación de endoglina soluble y su relevancia en homeostasis vascular”. Universidad Complutense de Madrid. Ana Cristina Valbuena Diez (11/12/2012). Sobresaliente, Cum laude

PROYECTOS (5 ÚLTIMOS AÑOS)

Título: Análisis funcional de miRNAs exosomales asociados a la Telangiectasia Hemorrágica Hereditaria.

Investigador Principal: Francisco Javier Blanco

Programa: Programa Estatal de I+D+i Orientados a los Retos de la Sociedad

Referencia: SAF2015-74313-JIN

Periodo: 2017 - 2019

Título: Análisis funcional de miRNAs exosomales asociados a la Telangiectasia Hemorrágica Hereditaria.

Investigador Principal: Francisco Javier Blanco

Programa: Plan Propio de Investigación de la UGR

Periodo: 2017 - 2021

Título: Development of miR-145 antagonism as a novel therapeutic strategy for application to the treatment of pulmonary arterial hypertension.

Investigador Principal: Margaret R. MacLean; Andrew H. Baker

Programa: British Heart Foundation (UK)

Referencia: SP/12/9/29593

Periodo: 2013 - 2015

Título: Estudios moleculares sobre endoglina y ALK1, dos componentes del receptor de TGF-beta endotelial implicados en la fisiopatología vascular.

Investigador Principal: Carmelo Bernabéu Quirante

Programa: Plan Nacional de I+D+i

Referencia: SAF2010-19222

Periodo: 2010 - 2013

Título: Mecanismos moleculares y celulares en enfermedades crónicas inflamatorias y autoinmunes.

Investigador Principal: Carmelo Bernabéu Quirante; Francisco Sánchez Madrid

Programa: MEICA

Periodo: 2009 - 2012