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| Fecha del CVA | 12/12/2019 |
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## Parte A. DATOS PERSONALES

|                                      |                      |      |    |
|--------------------------------------|----------------------|------|----|
| Nombre y Apellidos                   | Javier Angulo Frutos |      |    |
| DNI                                  | 51665861H            | Edad | 52 |
| Núm. identificación del investigador | Researcher ID        |      |    |
|                                      | Scopus Author ID     |      |    |
|                                      | Código ORCID         |      |    |

### A.1. Situación profesional actual

|                       |   |                    |  |
|-----------------------|---|--------------------|--|
| Organismo             | Hospital Universitario Ramón y Cajal                                  |                    |  |
| Dpto. / Centro        |   |                    |  |
| Dirección             |   |                    |  |
| Teléfono              | 913368481   | Correo electrónico | <a href="mailto:javier.angulo@hrc.es">javier.angulo@hrc.es</a> |
| Categoría profesional | Técnico Titulado Superior   | Fecha inicio       | 2006   |
| Espec. cód. UNESCO    | 241103 - Fisiología cardiovascular                                    |                    |  |
| Palabras clave        | Envejecimiento (biología); Sexo; Mecanismos moleculares de enfermedad |                    |  |

### A.2. Formación académica (título, institución, fecha)

| Licenciatura/Grado/Doctorado   | Universidad                    | Año  |
|--|--------------------------------|------|
| Doctor en Ciencias Biológicas  | Universidad Autónoma de Madrid | 1996 |
| Licenciado en Ciencias Biológicas<br>Especialidad Biología Molecular y Celular | Universidad Autónoma de Madrid | 1991 |

### A.3. Indicadores generales de calidad de la producción científica

83 publicaciones internacionales - Más del 50% en primer cuartil - 26 como primer autor y 10 como último / h index 27

## Parte B. RESUMEN LIBRE DEL CURRÍCULUM

Doctor en CC. Biológicas por la Universidad Autónoma de Madrid y desde 2006 Técnico Titulado Superior responsable del Servicio de Histología del Departamento de Investigación del Hospital Universitario Ramón y Cajal de Madrid. Adscrito a la Unidad de Investigación Cardiovascular del Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS).

Profesor Honorario del Departamento de Farmacología y Terapéutica de la Facultad de Medicina de la Universidad Autónoma de Madrid de 1999 a 2002. Colaborador Científico en la Fundación para la Investigación Biomédica del Hospital Universitario de Getafe desde 2010. Miembro del CIBER de Fragilidad y Envejecimiento Saludable (CIBERFES).

Director del Laboratorio de Investigación de la Fundación para la Investigación y el Desarrollo de la Andrología (FI+DA) de 1998 a 2006.

Abbot Erectile Dysfunction Research Award 2001 / Award of Excellence de la European Society for Sexual Medicine (ESSM) en 2005 / Premio Sousa-Sampaio al Mérito em Andrologia de la Sociedad Portuguesa de Andrología (2012)

Editor Asociado de la Revista Internacional de Andrología / Miembro del Editorial Board del Journal of Sexual Medicine.

## Parte C. MÉRITOS MÁS RELEVANTES (ordenados por tipología)

### C.1. Publicaciones

**1 Artículo científico.** La Fuente JM; et al. 2019. L-cysteine/hydrogen sulfide pathway induces cGMP-dependent relaxation of corpus cavernosum and penile arteries from patients with erectile dysfunction and improves arterial vasodilation induced by PDE5 inhibition. Eur J Pharmacol. Elsevier. 863, pp.172675.

- 2 **Artículo científico.** El Assar M; Angulo J; Rodríguez-Mañas L. 2019. Frailty as a phenotypic manifestation of underlying oxidative stress *Free Radicals in Biology and Medicine*. pii: S0891-5849(19)3.
- 3 **Artículo científico.** Angulo J; et al. 2019. Short-term pharmacological activation of Nrf2 ameliorates vascular dysfunction in aged rats and in pathological human vasculature. A potential target for therapeutic intervention *Redox Biol.* 26, pp.101271.
- 4 **Artículo científico.** Fernandez-Pascual E; et al. 2019. Optimizing collagenase *Clostridium histolyticum* therapy for Peyronie's disease using a novel approach with percutaneous needle tunnelling *BJU Int.* Wiley. 124-6, pp.1055-1062.
- 5 **Artículo científico.** El Assar M; et al. (8/2). 2018. Better Nutritional Status Is Positively Associated with mRNA Expression of SIRT1 in Community-Dwelling Older Adults in the Toledo Study for Healthy Aging *Journal of Nutrition*. Oxford Academic. 148-9, pp.1408-1414.
- 6 **Artículo científico.** El Assar M; et al. 2018. Multivessel analysis of progressive vascular aging in the rat: Asynchronous vulnerability among vascular territories. *Mechanisms of Ageing and Development*. 173, pp.39-49.
- 7 **Artículo científico.** Cobo-Nuñez MY; et al. 2018. Haemostatic agent etamsylate in vitro and in vivo antagonizes anti-coagulant activity of heparin *European Journal of Pharmacology*. Elsevier. 827, pp.167-172.
- 8 **Artículo científico.** El Assar M; et al. 2017. Frailty is associated with lower expression of genes involved in cellular response to stress: Results from the Toledo Study of Healthy Aging *Journal of the American Medical Directors Association*. Elsevier. 18, pp.734.e1-734.e7.
- 9 **Artículo científico.** Martínez-Salamanca JI; et al. 2016.  $\alpha$ 1A-adrenergic receptor antagonism improves erectile and cavernosal responses in rats with cavernous nerve injury and enhances neurogenic responses in human corpus cavernosum from patients with erectile dysfunction secondary to radical prostatectomy *The journal of sexual medicine*. Elsevier. 13-12, pp.1844-1857.
- 10 **Artículo científico.** Angulo, J.; El Assar, M.; Rodríguez Mañas, L. 2016. Frailty and sarcopenia as the basis for the phenotypic manifestation of chronic diseases in older adults. *Molecular Aspects of Medicine*. 50, pp.1-32. ISSN 1872-9452.
- 11 **Artículo científico.** Assar, ME.; Angulo, J.; Rodríguez Mañas, L. 2016. Diabetes and ageing-induced vascular inflammation. *The Journal of physiology*. 594-8, pp.2125-2171. ISSN 1469-7793.
- 12 **Artículo científico.** El Assar, M.; et al. 2016. ADMA elevation and arginase up-regulation contribute to endothelial dysfunction related to insulin resistance in rats and morbid obese humans. *The Journal of physiology*. ISSN 1469-7793.
- 13 **Artículo científico.** Martínez Salamanca, JI.; et al. 2016. Dual Strategy With Oral Phosphodiesterase Type 5 Inhibition and Intracavernosal Implantation of Mesenchymal Stem Cells Is Superior to Individual Approaches in the Recovery of Erectile and Cavernosal Functions After Cavernous Nerve Injury in Rats. *The journal of sexual medicine*. 13-1, pp.1-12. ISSN 1743-6109.
- 14 **Artículo científico.** El Assar, M.; et al. 2015. FM19G11 reverses endothelial dysfunction in rat and human arteries through stimulation of the PI3K/Akt/eNOS pathway, independently of mTOR/HIF-1 $\alpha$  activation. *British journal of pharmacology*. 172-5, pp.1277-1368. ISSN 1476-5381.
- 15 **Artículo científico.** Martínez Salamanca, JI.; et al. 2015. Nitric function is lost but endothelial function is preserved in the corpus cavernosum and penile resistance arteries of men after radical prostatectomy. *The journal of sexual medicine*. 12-3, pp.590-599. ISSN 1743-6109.
- 16 **Artículo científico.** Angulo, J.; et al. 2015. Diacetyloxyl derivatization of the fibroblast growth factor inhibitor dobesilate enhances its anti-inflammatory, anti-angiogenic and anti-tumoral activities. *Journal of translational medicine*. 13, pp.48. ISSN 1479-5876.
- 17 **Artículo científico.** El Assar, M.; et al. 2015. Differential effect of amylin on endothelial-dependent vasodilation in mesenteric arteries from control and insulin resistant rats. *PloS one*. 10-3, pp.e0120479. ISSN 1932-6203.

- 18 **Artículo científico.** La Fuente, JM.; et al. 2014. Stimulation of large-conductance calcium-activated potassium channels inhibits neurogenic contraction of human bladder from patients with urinary symptoms and reverses acetic acid-induced bladder hyperactivity in rats. *European journal of pharmacology.* 735, pp.68-144. ISSN 1879-0712.
- 19 Martínez Salamanca, JI.; et al. 2014. Nebivolol potentiates the efficacy of PDE5 inhibitors to relax corpus cavernosum and penile arteries from diabetic patients by enhancing the NO/cGMP pathway. *The journal of sexual medicine.* 11-5, pp.1182-1274. ISSN 1743-6109.
- 20 González Peña, D.; et al. 2014. High-cholesterol diet enriched with onion affects endothelium-dependent relaxation and NADPH oxidase activity in mesenteric microvessels from Wistar rats. *Nutrition & metabolism.* 11, pp.57. ISSN 1743-7075.
- 21 El Assar, M.; Angulo, J.; Rodríguez Mañas, L.2013. Oxidative stress and vascular inflammation in aging. *Free radical biology & medicine.* 65, pp.380-781. ISSN 1873-4596.
- 22 González Corrochano, R.; et al. 2013. Ca<sup>2+</sup>-activated K<sup>+</sup> channel (KCa) stimulation improves relaxant capacity of PDE5 inhibitors in human penile arteries and recovers the reduced efficacy of PDE5 inhibition in diabetic erectile dysfunction. *British journal of pharmacology.* 169-2, pp.449-510. ISSN 1476-5381.
- 23 El Assar, M.; et al. 2013. Preserved endothelial function in human obesity in the absence of insulin resistance. *Journal of translational medicine.* 11, pp.263. ISSN 1479-5876.
- 24 Angulo, J.; et al. 2012. Age-related differences in the effects of  $\alpha$  and  $\beta$  peroxisome proliferator-activated receptor subtype agonists on endothelial vasodilation in human microvessels. *Experimental gerontology.* 47-9, pp.734-774. ISSN 1873-6815.
- 25 Angulo, J.; et al. 2012. Tadalafil enhances the inhibitory effects of tamsulosin on neurogenic contractions of human prostate and bladder neck. *The journal of sexual medicine.* 9-9, pp.2293-2599. ISSN 1743-6109.
- 26 Cuevas, P.; et al. 2012. Chronic cystoid macular oedema treated with intravitreal dobesilate. *BMJ case reports.* 2012. ISSN 1757-790X.
- 27 Cuevas, P.; et al. 2012. Clearance of seborrheic keratoses with topical dobesilate. *BMJ case reports.* 2012. ISSN 1757-790X.
- 28 El Assar, M.; et al. 2012. Mechanisms involved in the aging-induced vascular dysfunction. *Frontiers in physiology.* 3, pp.132. ISSN 1664-042X.
- 29 Cuevas, P.; et al. 2012. Short-term efficacy of intravitreal dobesilate in central serous chorioretinopathy. *European journal of medical research.* 17, pp.22. ISSN 2047-783X.
- 30 Cuevas, P.; et al. 2012. Topical dobesilate eye drops for ophthalmic primary pterygium. *BMJ case reports.* 2012. ISSN 1757-790X.
- 31 Cuevas, P.; et al. 2012. Treatment of Stargardt disease with dobesilate. *BMJ case reports.* 2012. ISSN 1757-790X.
- 32 Cuevas, P.; et al. 2012. Treatment of dry age-related macular degeneration with dobesilate. *BMJ case reports.* 2012. ISSN 1757-790X.
- 33 Cuevas, P.; et al. 2011. Efficacy of the fibroblast growth factor inhibitor 2,5-dihydroxyphenylsulfonate in basal cell carcinoma: a histopathological and immunohistochemical study. *The Journal of dermatological treatment.* 22-6, pp.348-400. ISSN 1471-1753.
- 34 Angulo, J.; et al. 2011. Inhibition of vascular endothelial growth factor (VEGF)-induced endothelial proliferation, arterial relaxation, vascular permeability and angiogenesis by dobesilate. *European journal of pharmacology.* 667-1-3, pp.153-162. ISSN 1879-0712.
- 35 Cuevas, P.; et al. 2011. Antiglioma effects of a new, low molecular mass, inhibitor of fibroblast growth factor. *Neuroscience letters.* 491-1, pp.1-8. ISSN 1872-7972.
- 36 Cuevas, P.; Angulo, J.; Giménez Gallego, G.2011. Long-term effectiveness of dobesilate in the treatment of papulopustular rosacea. *BMJ case reports.* 2011. ISSN 1757-790X.
- 37 Cuevas, P.; Angulo, J.; Giménez Gallego, G.2011. Topical treatment of contact dermatitis by pine processionary caterpillar. *BMJ case reports.* 2011. ISSN 1757-790X.
- 38 Vallejo, S.; et al. 2011. Visfatin impairs endothelium-dependent relaxation in rat and human mesenteric microvessels through nicotinamide phosphoribosyltransferase activity. *PloS one.* 6-11, pp.e27299. ISSN 1932-6203.
- 39 Angulo, J.; et al. 2010. Nebivolol dilates human penile arteries and reverses erectile dysfunction in diabetic rats through enhancement of nitric oxide signaling. *The journal of sexual medicine.* 7-8, pp.2681-2778. ISSN 1743-6109.

- 40 Angulo, J.2010. Neutral endopeptidase inhibition: could it have a role in the treatment of female sexual arousal disorder? *British journal of pharmacology*. 160-1, pp.48-98. ISSN 1476-5381.
- 41 Fernández, IS.; et al. 2010. Gentisic acid, a compound associated with plant defense and a metabolite of aspirin, heads a new class of in vivo fibroblast growth factor inhibitors. *The Journal of biological chemistry*. 285-15, pp.11714-11743. ISSN 1083-351X.
- 42 Angulo, J.; et al. 2010. Diabetes exacerbates the functional deficiency of NO/cGMP pathway associated with erectile dysfunction in human corpus cavernosum and penile arteries. *The journal of sexual medicine*. 7-2 Pt 1, pp.758-826. ISSN 1743-6109.
- 43 Gratzke, C.; et al. 2010. Anatomy, physiology, and pathophysiology of erectile dysfunction. *The journal of sexual medicine*. 7-1 Pt 2, pp.445-520. ISSN 1743-6109.

## C.2. Proyectos

- 1 STIM/Orai inhibition as a strategy to facilitate relaxation of human corpus cavernosum and penile arteries and to relieve ED in diabetic rats *European Society for Sexual Medicine*. (Hospital Universitario Ramón y Cajal). 03/2018-03/2019.
- 2 Papel de STIM/Orai en las alteraciones de diferentes lechos vasculares en el envejecimiento vascular humano. Susceptibilidad del lecho peneano *Instituto de Salud Carlos III*. Javier Angulo Frutos. (Hospital Universitario Ramón y Cajal). 01/2016-12/2018. 60.500 €.
- 3 Modulation of adrenergic system as a novel strategy for the treatment of erectile dysfunction secondary to cavernous nerve injury *European Society for Sexual Medicine*. Javier Angulo Frutos. (Hospital Universitario Ramón y Cajal). 06/2014-06/2015. 30.000 €.
- 4 Intracavernosal bone marrow-derived mesenchymal stem cell therapy combined with tadalafil administration for the recovery of erectile function after cavernous nerve injury. *European Society for Sexual Medicine*. Javier Angulo Frutos. (Hospital Universitario Ramón y Cajal). 01/2011-12/2012. 35.000 €.

## C.3. Contratos

- 1 Effects of the combination of lycopene and N tangutorum Bobr extract on urodynamics and prostate growth in rats with testosterone-induced BPH *Beijing Boxin Nature Biotech*. Javier Angulo Frutos. 2017-01/01/2018.
- 2 Evaluation of the ability of herbal formulation to relax and to influence responses of human prostate and bladder neck and evaluation of its anti-androgenic activity in human prostate cancer cells. *Beijing Boxin Nature Biotech*. Javier Angulo Frutos. 2016-P1Y6M.
- 3 Caracterización del efecto anti-hemorrágico del etamsilato. Relación con su capacidad de interferir con la heparina *Laboratorios Dr. Esteve, S.A.*. Javier Angulo Frutos. 2015-P9M. 24.000 €.
- 4 Oral tadalafil administration combined with bone marrow-derived mesenchymal stem cell cavernous nerve therapy for the recovery of erectile function after cavernous nerve injury *Eli Lilly and Company*. Javier Angulo Frutos. 2011-P1Y. 10.000 €.
- 5 Evaluation of the effects of nebivolol on relaxation and cGMP accumulation induced by PDE5 inhibitors sildenafil, tadalafil and vardenafil in human corpus cavernosum and penile arteries from diabetic patients. *Forest Research Institute*. Javier Angulo Frutos. 2010-P1Y. 40.000 €.

## C.4. Patentes

- 1 Cuevas P; Gimenez-Gallego G; Saenz de Tejada I; Angulo J; Valverde S; Romero A; Lozano RM. US 2014/0328778. Use of 2,5-dihydroxybenzene derivatives for the treatment of dermatitis *Estados Unidos de América*. 06/11/2014. Amderma Pharmaceuticals.
- 2 José María Sánvchez Puelles; Leocadio Rodríguez Mañas; Javier Angulo Frutos; Mariam El Assar De la Fuente. P201230376. Compuestos moduladores del factor de transcripción inducible por hipoxia (HIF) para el tratamiento de diabetes y patologías asociadas *España*. 2012. CSIC-IMSALUD.