Fecha del CVA	21/05/2020

Parte A. DATOS PERSONALES

Nombre y Apellidos	Eugenio Santos		
DNI/NIE/Pasaporte		Edad	
Núm. identificación del investigador	Researcher ID		
	Scopus Author ID	7202142651	
	Código ORCID	0000-0003-3565-0321	

A.1. Situación profesional actual

Organismo	Universidad de Salamanca		
Dpto. / Centro	Departamento de Microbiología y Genética / Universidad de SalamancaDepartamento de Microbiología y Genética		
Dirección			
Teléfono		Correo electrónico	
Categoría profesional	Catedrático de Universidad / Full Professor	Fecha inicio	1999
Espec. cód. UNESCO	240300 - Bioquímica; 240900 - Genética; 241500 - Biología molecular		
Palabras clave			

A.2. Formación académica (titulo, institución, fecha)

Licenciatura/Grado/Doctorado	Universidad	Año
Doctor en Ciencias Biológicas / PhD Biological Sciences	Universidad de Salamanca	1978
Licenciado en Ciencias Biológicas / M Sci Biological Sciences	Universidad de Salamanca	1975

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

A. Scientific Production

Google Scholar Citation Indexes for Eugenio Santos

Citations: 10600. h-index: 47. i10-index: 112

B. Competitive Funding as PI

Individual projects: Intramural NCI (1990–99; 450000$/yr). FEDER 1FD97-1678 (2000-2001; 282355€). FEDER 1FD97-1735 (2000–01; 187624€). SAF2000-0069 (2000-03; 285072€.). FIS PI021570 (2002-05; 219765€). CICYT SAF2003-04177 (2003-06; 200000€). CICYT GEN2003-20239-C06-02 (2004–07; 177100€). FIS PI061274 (2006-09; 422000€). GR93, CyL (2008-10; 197306€). FIS Intrasalud PS09/01979(2010-13; 523325€). BIO/SA03/14(2014; 25110€). SA181U13 (2013-14;35000€) (FIS PI13/02846 (2013-16; 195415€). SA043U16 (2016-18; 120000€). FIS PI/16/02137 (2017-19;147015€). Ciberonc (2017; 72000€). CyL-SA264P18 (2018-20, 12000€). Areces (2019-21, 129357€). FIS/PI19/00934(2020-22, 292820)

Collective projects:MCYT APC1998-0246(1998; 100.000.000Ptas) MCYT APC1999-0154. (1999; 59.000.000Ptas). MCYT APC2000-0003 (2000; 50.000.000Ptas) MCYT-FEDER UNSA00-23-014 (2001; 2055461,40€). MCYT-FEDER (2001; 488623€). MCYT-FEDER. (2002; 485017€). Infraestruct SNS-FIS 01/3634 (2001; 127014,89€). Infraestruct SNS-FIS 02/3632 (2002; 219704€). MCYT-FEDER-UNSA00-23-020 (2003; 1984481,80€). Infraestruct SNS-FIS 03/3613 (2003; 133400€) Fund. M. Botín (2004-09; 200000€/yr). RTICCC(ISCIII)-Nodo CIC C03/10 (2003-06, 734000€/yr). Acción Transversal Cáncer, Mº Sanidad (2008; 800000€). Infraestruct SAF2005-24631-E (2005; 380000€). Infraestruct SNS-FIS (2008; 400000€). RTICC(ISCIII)-RD06/0020/0000 (2007-12; 304000€/yr). RTICC (ISCIII)-RD12/0036/0001(2013-17; 442343€/yr).MCIU-EQC2018-004532P (2018, 166.777€).INFRARED CyL (2019, 201799,20€)

C. Other scientific activities and recognition

- **Reviewer scientific Journals** : Biochemistry, BBA, Cancer Biology&Medicine, Cancer Res., Cancer Genet.& Cytog, Cell Cycle, Differentiation, Eur. J. Biochem, Int. J. Oncol., J. Biol Chem, J Cell Biol, Leukemia, Life Science Alliance, Mol Biol of the Cell, Mol Cell Biol, Molecular Reports, Neurosc Letters, Nature, Oncogene, Proc Natl Acad of Sciences USA, Sci Signal.
- **Editorial Boards**: Int J Oncology, Clinical and Translational Oncology, Genes&Cancer, Current Cancer Drug Targets
- **Reviewer Grant proposals**: National Science Foundation (USA), Canadian Fonds de la Recherche en Santé du Quebec, International Science Foundation program (ISF, Washington D.C.), Israel Science Foundation, Asoc.Italiana per la Ricerca sul Cancro (AIRC), Spanish ANEP, FIS, AECC.
- **Tenure Review committees**: National Cancer Institute; Johns Hopkins Med Sch; Mount Sinai Med Sch; Robert Wood Med Sch.
- **Scientific Advisory Board member**: CNIO (Madrid), IIS La Fe, CIPF (Valencia), CIMAGO (Coimbra), IUOPA (Asturias), IDIBAPS, IDIBELL (Barcelona), CIOCC, Fund. Ferrer, Asoc. Española contra el Cáncer (AECC)
- **Invited speaker** at many national and international **meetings** on oncogene research.
- 25 **articles** cited >100 times, 4 articles among most cited of decade 80-90. 3 articles declared ISI Citation Classics (>400 citations). Average citations/article: ~60.
- **6** research **sexenios** and **6** teaching **quinquenios** recognized by **Spanish Ministry of Education and MINECO**.
- Grupo de Excelencia (**GR93**) and Unidad de Investigacion Consolidada (**UIC 076**) by Education Ministry, **Castile&Leon**
- **Scientific personnel trained**: More than 50 postdoctoral fellows, predoctoral students and technicians.
- National Coordinator, Spanish Cancer Research Network (**RTICC, ISCIII**) 2003-2017

Parte B. RESUMEN LIBRE DEL CURRÍCULUM

Ph.D. from Salamanca Univ. (USAL 1978) and postdoc training at the RIMB (79-81) and the NCI (81-84). From 85 to 00 he was a PI at the NIH in the Laboratory of Molecular Microbiology (NIAID, 85-90) and the Laboratory of Cellular and Molecular Biology (NCI, 91-00). Since 2000 he is Professor, Dept Microbiology&Genetics and Director, CIC-IBMCC (USAL-CSIC).

Santos' **scientific career** has progressed in temporal sync with Molecular Oncology since his cloning and characterization of the first human oncogene (HRAS) at the NCI in the early 80's. **During the 80's** his work isolating the HRAS oncogene and demonstrating its malignant activation by point mutation was followed by his demonstration for the first time in humans of an activated KRAS oncogene in tumor but not normal tissue of the same patient (Nature 82a,82b; Science 84). In **the 90's** he contributed to understanding structure and function of RAS proteins (JBC 88; FASEB J 89) and their participation in signaling pathways controlling cell growth and differentiation (PNAS 88; MCB 90) by using various RAS-dependent biological models (Science 91a,91b; Oncogene 93,97; PNAS 93; JBC 94,96; MCB 97). **Since 2000** his work focused on mechanisms of RAS activation by exchange factors (GEF) and ascertainment of functional specificity/redundancy of various RAS and RasGEF isoforms.

Regarding functional specificity of **RAS proteins** (Genes Cancer 11; Sci Signal 14, 18) he showed that only KRAS is necessary and sufficient for development to the adult stage (MCB 01) and documented a critical involvement of NRAS in immune modulation/host defense and apoptotic responses (Oncogene 07; Genome Biol 09; Blood 11; J Exp Med 13); KRAS in cell cycle progression (EMBO J 10; PLosOne 10; BMC Genomics 13); HRAS in systemic vascular pressure (Kidney Int 10; Hypertens 10; AJPCP 12); RRas in germinal center formation (Sci Signal 18); HRAS and NRAS in lung development.

Using KO models he documented differential functionality of **GRF1 and GRF2** (BBA Rev Cancer 11) demonstrating specific roles of GRF1 in pancreatic beta cells (EMBO J 03; BMC Genomics 14) and neurosensory/photoreception processes (Neurosci 07; J Neurochem 09; Nat Gen 10); and of GRF2 in T cell signaling (MCB 07; PLosOne 09), addiction behavior (PNAS 11, 12; Psychopharmacol 14), control of nuclear migration required for development and function of retinal cone photoreceptors (J Cell Sci 16, Small GTPases 18), and control of stem cell density and onset of differentiation during adult neurogenesis (Mol Cell Neurosci 17).

Regarding **SOS1/2 isoforms** he demonstrated that SOS1 is essential for embryonic development (EMBO J 00) but Sos2 is dispensable in adult mice (MCB 00). He also demonstrated functional redundancy of SOS1 and SOS2 for survival and homeostasis at the organismal level (MCB 13) and a direct mechanistic link between Sos1 and control of intracellular ROS (Oncogene 16, Oncogenesis 19, J Leuk Biol 19). SOS1 is also critical for bcr-abl leukemogenesis (Leukemia 17) and skin homeostasis and carcinogenesis (MCB 18).

He directs the Salamanca **CIC-IBMCC** and was National Coordinator of the **RTICC** Cooperative Cancer Research Network, ISCIII (2003-17) and ASEICA president (2010-14). Member of editorial & advisory boards, Royal Academy of Medicine and European Academy of Cancer Sciences. Received scientific awards including: Severo Ochoa Biomedical Research Award, Castile&Leon Scientific Research Award, Spanish Health Ministry Encomienda, Echevarne Oncology Award.

Parte C. MÉRITOS MÁS RELEVANTES (ordenados por tipología)

C.1. Publicaciones

1 **Artículo científico**. R Fuentes-Mateos; et al. 2019. Concomitant deletion of HRAS and NRAS leads to pulmonary immaturity, respiratory failure and neonatal death in mice . Cell Death Dis. 10-838.
2 **Artículo científico**. R Spanagel; et al. 2019. The inhibition of RasGRF2, but not RasGRF1, alters cocaine reward in mice Journal of Neuroscience. 39-32.
3 **Artículo científico**. FC Baltanas; et al. 2019. Nucleolin reorganization and nucleolar stress in Purkinje cells of mutant pcd mice Neurobiology of Disease. 127, pp.312-322.
4 **Artículo científico**. S Suire; et al. 2019. TNF? and GM-CSF1 priming augments the role of SOS1/2 in driving activation of Ras, PI3K? and neutrophil proinflammatory responses . J Leukoc. Biol.
5 **Artículo científico**. N Zarich; et al. 2019. The CSN3 subunit of the COP9 signalosome interacts with the HD region of Sos1 regulating stability of this GEF protein Oncogenesis. 8-1.
6 **Artículo científico**. 2018. The RAS-ERK pathway: A route for couples Science Signaling. 11-554, pp.). pii: eaav0917.
7 **Artículo científico**. L Manyes; et al. 2018. Spatial learning and long term memory impairments in RasGrf1 KO, Pttg1 KO and double KO mice Brain and Behavior.
8 **Artículo científico**. 2018. Differential role of the RasGEFs SOS1 and SOS2 in mouse skin homeostasis and carcinogenesis.Molecular and Cellular Biology. In press.
9 **Artículo científico**. C Gomez; et al. 2017. Ras-GRF2 regulates nestin-positive stem cell density and onset of differentiation during adult neurogenesis in the mouse dentate gyrus Molecular and Cellular Neuroscience. 85, pp.127-147.
10 **Artículo científico**. S Gerboth; et al. 2017. Phosphorylation of SOS1 on tyrosine 1196 promotes its RAC GEF activity and contributes to BCR-ABL leukemogenesis Leukemia.
11 **Artículo científico**. Jimeno, D.; et al. 2016. RasGRF2 controls nuclear migration in postnatal retinal cone photoreceptors.Journal of Cell Science. 129-4, pp.729-742. ISSN 1477-9137.
12 **Artículo científico**. Santos E. 2014. Dimerization opens new avenues into Ras signaling research Science Signalling. 7-324, pp.pe12.
13 **Artículo científico**. Baltanás C. F; et al. 2013. Functional redundancy of sos1 and sos2 for lymphopoiesis and organismal homeostasis and survival.Molecular and Cellular Biology. 33-22, pp.4562-4578.

14 **Artículo científico**. Sami Azrak; et al. 2013. Reversible, interrelated mRNA and miRNA expression patterns in the transcriptome of Rasless fibroblasts: functional and mechanistic implications.BMC Genomics. 14-1, pp.731.
15 **Artículo científico**. Iborra S; et al. 2011. H-ras and N-ras are dispensable for T-cell development and activation but critical for protective Th1 immunity.Blood. 117-19, pp.5102-5511.
16 **Artículo científico**. Fernández-Medarde A; Santos E.2011. Ras in cancer and developmental diseases.Genes Cancer. 2-3, pp.344-358.
17 **Artículo científico**. Fernández-Medarde; et al. 2009. Rasgrf1 Disruption Causes Retinal Photoreception Defects And Associated Transcriptomic Alterations.Journal of Neurochemistry. 110-2, pp.641-652.
18 **Artículo científico**. Castellano; et al. 2007. Transcriptional networks of knockout cell lines identify functional specificities of H-Ras and N-Ras: Significant involvement of N-Ras in biotic and defense responses. PMID: 16909116.Oncogene. 26, pp.917-933.
19 **Artículo científico**. J. Font de Mora; et al. 2003. Ras-GRF1 Signaling is Required for Normal ¿Ò-cell Development and Glucose Homeostasis Embo journal. 22(12), pp.3039-3049. ISSN 0261-4189.
20 **Artículo científico**. ; et al. 2001. Targeted genomic disruption of H-ras and N-ras, individually or in combination, reveals the dispensability of both loci for mouse growth and development Mol. Cell. Biol.21, pp.1444-1452.
21 **Artículo científico**. X. Quian; et al. 2000. The Sos1 and Sos2 Ras-specific Exchange Factors: Differences in Placental Expression and Signaling Properties Embo journal. 19, pp.642-654. ISSN 0261-4189.
22 **Artículo científico**. C. Guerrero; et al. 1996. Expression of alternative forms of Ras exchange factors GRF and SOS1 in different human tissues and cell lines Oncogene. 12, pp.1097-1107. ISSN 0950-9232.
23 **Artículo científico**. M. Benito; et al. 1991. Differentiation of 3T3 L1 fibroblasts to adipocytes induced by transfection of ras oncogenes Science. 253, pp.565-568.
24 **Artículo científico**. Santos, E.; et al. 1988. Malignant transformation by ras and other oncogenes produces common alterations in phosphoinositide signalling pathways Proceedings of the national academy of sciences of the united states of ame. 85, pp.4271-4275. ISSN 0027-8424.
25 **Artículo científico**. Santos, E.; et al. 1983. Spontaneous activation of a human proto-oncogene Proceedings of the national academy of sciences of the united states of ame. 80, pp.4679-4683. ISSN 0027-8424.
26 **Artículo científico**. Santos, E.; et al. 1982. T24 human bladder carcinoma oncogene is an activated form of the normal human homologue of BALB- and Harvey-MSV transforming genes Nature. 298, pp.343-347. ISSN 0028-0836.

C.2. Proyectos

C.3. Contratos

C.4. Patentes