

# Curriculum Vitae

## Alejo Efeyan

Junior Group Leader  
Centro Nacional de Investigaciones Oncológicas (CNIO)

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### Educación y Experiencia Investigadora

2016 Group Leader en el Centro Nacional de Investigaciones Oncológicas (CNIO), Madrid.

Nov 2008 – Dec 2015 Postdoctoral Fellow en el laboratorio de David M Sabatini. Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology. Cambridge, MA, USA.

Oct 2003 - Nov 2008 Estudiante de Doctorado bajo la supervisión de Manuel Serrano en el Grupo de Supresión Tumoral del Centro Nacional de Investigaciones Oncológicas (CNIO), Madrid.

Nov 2007 Defensa de Tesis Doctoral en Biología Molecular: Disección Genética de la Supresión Tumoral mediada por p53. De Respuestas Celulares a Estrategias Terapéuticas. Sobresaliente *Cum Laude*. Universidad Autónoma de Madrid.

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### Publicaciones

*h*-index: 24. Citas totales (excluyendo las propias): 8000+.

a. Artículos de investigación:

1. Folliculin-interacting protein FNIP2 impacts on overweight and obesity through a polymorphism in a conserved 3' untranslated region. Fernández LP\*, Deleyto-Seldas N\*, Colmenarejo G, Sanz A, Wagner S, Plata-Gómez AB, Gómez-Patiño M, Molina S, Espinosa-Salinas I, Aguilar-Aguilar E, Ortega S, Graña-Castro O, Loria-Kohen V, Fernández-Marcos PJ, **Efeyan A**<sup>#</sup> & Ramírez de Molina A<sup>#</sup>. (#: co-corresponding authors). *under review*.
2. Assessing kinetics and recruitment of DNA repair factors using high content screens. Martinez-Pastor B, Silveira GG, Clarke TL, Chung D, Gu Y, Cosentino C, Davidow LS, Mata G, Hassanieh S, Salsman J, Ciccio A, Bae N, Bedford MT, Megias D, Rubin LL, **Efeyan A**, Dellaire G, Mostoslavsky R. *Cell Reports*. 2021 Dec 28;37(13):110176. doi: 10.1016/j.celrep.2021.110176.
3. Inhibition of Rag GTPase signaling in mice suppresses B cell activation and lymphomagenesis without detrimental tradeoffs. Ortega-Molina A, Lebrero-Fernández C, Deleyto-Seldas N, Sanz A, Menéndez C, Caleiras E, **Efeyan A**. *Cell Reports*. 2021 Jul 13;36(2):109372. doi: 10.1016/j.celrep.2021.109372.
4. Limited survival and impaired hepatic fasting metabolism in mice with constitutive Rag GTPase signaling. de la Calle Arregui C, Plata-Gómez AB, Deleyto-Seldas N, Ortega-Molina A, García F, Muñoz J, Abril-Garrido J, Rodríguez E, Nemazanyy I, de Martino A, Caleiras E, Mulero F, Pende M, Sabio G, Sabatini DM, **Efeyan A**. *Nature Communications*. 2021 Jun 16;12(1):3660. doi: 10.1038/s41467-021-23857-8.
5. Cyclin D3 drives inertial cell cycling in dark zone germinal center B cells. Pae J, Ersching J, Castro TBR, Schips M, Mesin L, Allon SJ, Ordovas-Montanes J, Mlynarczyk C, Melnick A, **Efeyan A**, Shalek AK, Meyer-Hermann M, Victoria GD. *J Exp Med*. 2021 Apr 5;218(4):e20201699. doi: 10.1084/jem.20201699.

6. Harnessing DNA for nanothermometry. Spicer G, Gutierrez-Erlandsson S, Matesanz R, Bernard H, Adam AP, **Efeyan A\***, Thompson S\* (co-corresponding authors). *J Biophotonics*. 2020 Oct 31:e202000341. doi: 10.1002/jbio.202000341.
7. Nutrient mTORC1 Signaling Underpins Regulatory T Cell Control of Immune Tolerance. Do M, Wang X, Zhang X, Chou C, Nixon B, Capistrano K, Peng M, **Efeyan A**, Sabatini DM, Li M. *Journal of Experimental Medicine*. 2019 Oct 24. DOI: 10.1084/jem.20190848.
8. Oncogenic Rag GTPase signalling enhances B cell activation and drives follicular lymphoma sensitive to pharmacological inhibition of mTOR. Ortega-Molina A, Deleyto-Seldas N, Joaquim Carreras J, Sanz A, Lebrero-Fernández C, Menéndez C, Vandenberg A, Fernández-Ruiz B, Marín-Arraiza L, de la Calle Arregui C, Plata-Gómez AB, Caleiras E, de Martino A, Martínez-Martín N, Troulé K, Piñeiro-Yáñez E, Nakamura N, Araf S, Victora GD, Okosun J, Fitzgibbon J, **Efeyan A**. *Nature Metabolism*. 2019 Aug 19;1:775–789. (N&V en el mismo volumen de *Nature Metabolism*).
9. Universal guidelines for the conversion of proteins and dyes into functional nanothermometers. Spicer G, **Efeyan A**, Adam A, Thompson S. *J Biophotonics*. 2019 Apr 29:e201900044. doi: 10.1002/jbio.201900044.
10. mTORC1-dependent AMD1 regulation sustains polyamine metabolism in prostate cancer. Zabala-Letona A *et al.* (A. Carracedo Lab) *Nature*. 2017 Jul 6;547(7661):109-113.
11. Germinal center selection and affinity maturation require dynamic regulation of mTORC1. Ersching J\*, **Efeyan A\***, Mesin L, Jacobsen JT, Pasqual G, Grabiner BC, Dominguez-Sola D, Sabatini DM, Victora GD. *Immunity*. 2017 Jun 20;46(6):1045-1058 (\*: equal contribution).
12. Indifference to amino acid-induced mTORC1 regulation enables hematopoietic stem cell resilience to nutritional stress. Kalaitzidis D, Lee D, **Efeyan A**, Kfoury Y, Nayyar N, Sykes DB, Mercier F, Papazian A, Baryawno N, Victora GD, Sabatini DM, Scadden DT. *J Clin Invest*. 2017 Apr 3;127(4):1405-1413.
13. Recurrent mTORC1-activating RRAGC mutations in follicular lymphoma. Okosun J, Wolfson RL, Wang J, Araf S, Wilkins L, Castellano BM, Escudero-Ibarz L, Al Seraihi AF, Richter J, Bernhart SH, **Efeyan A**, Iqbal S, Matthews J, Clear A, Guerra-Assunção JA, Bödör C, Quentmeier H, Mansbridge C, Johnson P, Davies A, Strefford JC, Packham G, Barrans S, Jack A, Du MQ, Calaminici M, Lister TA, Auer R, Montoto S, Gribben JG, Siebert R, Chelala C, Zoncu R, Sabatini DM, Fitzgibbon J. *Nat Genet*. 2016 Feb;48(2):183-8.
14. RagA, but not RagB, is essential for embryonic development and adult life. **Efeyan A**, Schweitzer LD, Bilate AM, Chang S, Kirak O, Lamming DW, Sabatini DM. *Dev. Cell*. 2014 May 12;29(3):321-9.
15. Regulation of mTORC1 by the Rag GTPases is necessary for neonatal autophagy and survival. **Efeyan A**, Zoncu R, Chang S, Gumper I, Snitkin H, Wolfson R, Kirak O, Sabatini DD, Sabatini DM. *Nature*. 2013 Jan 31;493(7434):679-83
16. DEPTOR cell-autonomously promotes adipogenesis and associates with obesity. Laplante M, Horvat S, Festuccia WT, Birsoy K, Prevorsek Z, **Efeyan A**, Sabatini DM. *Cell Metab*. 2012 Aug 8;16(2):202-12.
17. mTORC1 senses amino acids through a lysosomal inside-out mechanism that requires the Vacuolar H<sup>+</sup>-ATPase." Zoncu R, Bar-Peled L, **Efeyan A**, Wang S, Sancak Y, Sabatini DM. *Science*. 2011 Nov 4;334(6056):678-83.
18. Pten positively regulates brown adipose function, energy expenditure and longevity. Ortega-Molina A, **Efeyan A**, Muñoz-Martin M, Gomez G, Cañamero C, Mulero F, Pastor J, Martinez S, Valverde AM, Romanos E, Bischoff JR, Serrano M. *Cell Metab*. 2012 Mar 7;15(3):382-94.
19. A minimally invasive assay for individual assessment of the ATM/CHEK2/p53 pathway activity. Kabacik S, Ortega-Molina A, **Efeyan A**, Finnon P, Bouffler S, Serrano M, Badie C. *Cell Cycle*. 2011 Apr 1;10(7):1152-61.
20. Limited evidence for the in vivo role of ATM in the response to oncogenic stress. **Efeyan A\***, Murga M\*, Martinez-Pastor B, Ortega-Molina A, Soria R, Collado M, Fernandez-Capetillo O, Serrano M. *PLoS One*. 2009;4(5):e5475.(\*: equal contribution)
21. Induction of p53-dependent senescence by the MDM2 antagonist nutlin-3a in mouse cells of fibroblast origin. **Efeyan A**, Ortega-Molina A, Velasco-Miguel S, Herranz D, Vassilev LT, Serrano M. *Cancer Res*. 2007 Aug 1;67(15):7350-7.
22. Policing of oncogene activity by p53. **Efeyan A**, Garcia-Cao I, Herranz D, Velasco-Miguel S, Serrano M. *Nature*. 2006 Sep 14;443(7108):159.

23. Genetic dissection of the role of p21Cip1/Waf1 in p53-mediated tumour suppression. **Efeyan A**, Collado M, Velasco-Miguel S, Serrano M. *Oncogene*. 2007 Mar 8;26(11):1645-9.
  24. A high-throughput loss-of-function screening identifies novel p53 regulators. Llanos S, **Efeyan A**, Monsech J, Dominguez O, Serrano M. *Cell Cycle*. 2006 Aug;5(16):1880-5.
  25. Senescence in premalignant tumours. Collado M, Gil J, **Efeyan A**, Guerra C, Schuhmacher AJ, Barradas M, Benguria A, Zaballos A, Flores JM, Barbacid M, Beach D, Serrano M. *Nature*. 2005 Aug 4;436(7051):642.
  26. Increased gene dosage of Ink4a/Arf results in cancer resistance and normal aging. Matheu A, Pantoja C, **Efeyan A**, Criado LM, Martin-Caballero J, Flores JM, Klatt P, Serrano M. *Genes Dev*. 2004 Nov 15;18(22):2736-46.
  27. Isolation of a stromal cell line from an early passage of a mouse mammary tumor line: a model for stromal parenchymal interactions. Lamb CA, Fabris V, Gorostiaga MA, Helguero LA, **Efeyan A**, Bottino MC, Simian M, Soldati R, Sanjuan N, Molinolo A, Lanari C. *J Cell Physiol*. 2005 Mar;202(3):672-82.
  28. Establishment of two hormone responsive mouse mammary carcinoma cell lines derived from a metastatic mammary tumor line. **Efeyan A**, Fabris V, Merani S, Lanari C, Molinolo A. *Breast Cancer Res Treat*. 2004 Feb;83(3):233-44.
  29. p21 and p27 in estrogen and antiprogesterin-induced tumor regression of experimental mouse ductal carcinomas. Vanzulli S, **Efeyan A**, Benavides F, Helguero LA, Peters G, Shen J, Conti CJ, Lanari C, Molinolo A. *Carcinogenesis*. 2002 May;23(5):749-58.
- b. Revisiones y otros artículos
30. From mouse genetics to targeting the Rag GTPase pathway. Ortega-Molina A & **Efeyan A**. *Molecular & Cellular Oncology*. 2021 Sep 24 <https://doi.org/10.1080/23723556.2021.1979370>.
  31. Protocol for the assessment of mTOR activity in mouse primary hepatocytes. Plata-Gómez AB, Crespo M, de la Calle Arregui C, de Prado-Rivas L, Sabio G, **Efeyan A**. *STAR Protocols*. 2021 Oct 29;2(4):100918. doi: 10.1016/j.xpro.2021.100918.
  32. The mTOR – autophagy axis and the control of metabolism. Deleyto-Seldas, **Efeyan A**. *Front Cell Dev Biol*. 2021 Jul 1;9:655731. doi: 10.3389/fcell.2021.655731.
  33. A spotlight on cancer researchers in Spain: new paradigms and disruptive ideas. Ramón Y Cajal S, Sancho P, Soucek L, Peinado H, Abad M, Valiente M, **Efeyan A**, Pardo J, Quesada V, Jimeno J, Duque PM, Antón A, Varela I, Schuhmacher AJ. *Clin Transl Oncol*. 2019 Aug 9. doi: 10.1007/s12094-019-02199-4.
  34. Nutrient-sensing mechanisms and pathways. **Efeyan A**, Comb WC, Sabatini DM. *Nature*. 2015 Jan 15; 517(7534):302-310.
  35. Nutrients and growth factors in mTORC1 activation. **Efeyan A**, Sabatini DM. *Biochem Soc Trans*. 2013 Aug 1;41(4):902-5.
  36. Amino acids and mTORC1: from lysosomes to disease. **Efeyan A\***, Zoncu R\*, Sabatini DM. *Trends in Molecular Medicine*. 2012 Sep;18(9):524-33. (\*: equal contribution)
  37. mTOR: from growth signal integration to cancer, diabetes and ageing. Zoncu R\*, **Efeyan A\*\$**, Sabatini DM\$. *Nat Rev Mol Cell Biol*. 2011 Jan;12(1):21-35. (\*: equal contribution; \$: corresponding authors)
  38. mTOR and cancer: many loops in one pathway. **Efeyan A**, Sabatini DM. *Curr Opin Cell Biol*. 2010 Apr;22(2):169-76.
  39. p53: guardian of the genome and policeman of the oncogenes. **Efeyan A**, Serrano M. *Cell Cycle*. 2007 May;6(9):1006-10.

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## Honos y Premios

Dic 2020	EMBO Young Investigator.
Nov 2007	Premio Extraordinario de Tesis en Biología Molecular de la Universidad Autónoma de Madrid.

Nov 2001 Premio Eufemio Uballes de la Academia Nacional de Medicina Argentina. "Novel breast cancer cell lines with hormone receptors. The utility in the evaluation of therapeutic drugs." **Efeyan A**, Lanari C, Lamb C, Fabris V, Helguero L, Molinolo A.

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### **Financiación a la Investigación**

Jul 2021 LaCaixa Foundation Research Grant. Leader de Consorcio (€992581)  
Jun 2021 Beca Leonardo FBBVA 2021 (€40000).  
Dic 2020 EMBO Young Investigator Program (€15000 + viajes & organización de congresos).  
Jun 2020 Plan Nacional *Retos* de España (€229000 + 1 beca predoctoral FPI).  
Dec 2018 XV Beca Fundación Fero (€80000).  
Sep 2017 Asociación Española Contra el Cáncer (AECC) Lab Grant (€300000).  
Feb 2017 Red de Excelencia Temática (MINECO). PI - Coordinador. (€20000).  
Feb 2016 Plan Nacional *Retos* de España (€ 169400 + 1 beca predoctoral FPI).  
Nov 2014 Starting Grant del European Research Council (€1846493).  
Jul 2014 Seleccionado en 1<sup>era</sup> posición en Biomedicina en Proyecto Ramón y Cajal (€308600).  
2013 - 2015 Charles King's Trust - Simeon J. Fortin Charitable Foundation Beca Postdoctoral (US\$ 98000).  
2009 - 2012 Human Frontiers Science Program Long-Term Beca Postdoctoral (US\$149840).  
2004 - 2008 Beca Predoctoral FPU del Ministerio de Ciencia Español.  
2002 - 2003 Beca Predoctoral FPI del Ministerio de Ciencia y Tecnología Español.

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### **Organización de R&D&I**

May 2022 Co-organizador (A Efeyan, M Blasco, T Rando) del CNIO Frontiers Meeting Molecular, cellular and organismal hallmarks of aging v2.0. 9 – 10 Mayo 2022.  
Mar 2022 Co-organizador (A Efeyan, G Sabio) EMBO YIP Sectorial Meeting. 7 – 9 Marzo 2022, Malaga.  
Nov 2021 Moderador EMBO YIP Virtual Seminar. Stress kinases in Cardiometabolic Diseases, by G Sabio.  
Jul 2021 Organizador del Simposio *The mTOR pathway in health and disease*, 43<sup>er</sup> Congreso de la SEBBM.  
May 2019 Organizador de Metabocancer *Closing meeting*. CNIO, Madrid, España.  
Oct 2018 Co-organizador (A Carracedo, A Efeyan, N Chandel, R DeBerardinis, J Seoane, J Carmona) del EACR Meeting Mechanisms to Therapies, Innovations in Cancer Metabolism). 9-11 Octubre Bilbao, País Vasco.  
May 2018 Co-organizador (A Efeyan, M Blasco, T Rando, K Collins) del CNIO Frontiers Meeting Molecular, cellular and organismal hallmarks of aging. 2-4 Mayo, Madrid.  
Dic 2017 Organizador de Metabocancer *Kick-off meeting*. CNIO, Madrid, España.  
2017 - 2019 Coordinador / PI de Red de Excelencia del MINECO "Metabocancer".

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### **Patentes y Transferencia**

**Licencia a Genentech para el uso de ratones KO condicionales para las Rag GTPasas.** Arancel compartido entre el laboratorio de DM Sabatini en el Whitehead Institute y el laboratorio de A Efeyan.

**Título:** MTORC1 modulation by amino acids and uses thereof.  
**Inventores:** Wang S, Comb W, Efeyan A, Zoncu R, Sabatini DM.  
**ID:** WO/2015/061607. International Application number: PCT/US2014/062031