

## PERSONAL INFORMATION

Juan Fernando Martinez Leal

## WORK EXPERIENCE

February 2001-February 2008

**Staff Scientist**

Centro Nacional de Investigaciones Oncológicas (CNIO, Spanish National Cancer Research Center) (Spain)

Member of the team developing new anticancer small molecules. Management of Preclinical Drug Discovery Projects. Leading the screening and development of small molecule inhibitors of the Pim kinases family. Collaboration with other Departments in the CNIO.

March 2008-December 2016

**Mechanism of Action Group Leader**

Pharma Mar SA (Spain)

Management of Preclinical Drug Discovery Projects, controlling time of execution, quality and costs. Leading the Mechanism of Action team, developing the scientific knowledge of new anticancer molecules and marketed anticancer drugs from the company. Managing preclinical research collaborations with academic and industrial partners. Collaboration with other Departments in the Company.

January 2017-September 2020

**Mechanism of Action and Pharmacogenomics Department Manager**

Pharma Mar SA (Spain)

Management of Preclinical Drug Discovery Projects, controlling time of execution, quality and costs. Leading the Mechanism of Action and Pharmacogenomics teams, developing the scientific knowledge of new anticancer molecules and marketed anticancer drugs from the company. Managing preclinical research collaborations with academic and industrial partners.

May 2021- Present

**External Expert**

AEMPS (Spain)

Quality Assessment of Biologics and Advanced Therapies

## EDUCATION AND TRAINING

October 1984-June 1990

**BSc Biology (Specialty in Mol Cell Biology)**

Facultad de Ciencias, Universidad de Córdoba (Spain)

General Biology subjects, Molecular Cell Biology, Genetics, Industrial Microbiology, Physiology, Biological Chemistry

June 1990-June 1991

**MSc Biology**

Departamento de Genética, Universidad de Córdoba (Spain)

Genetic Toxicology, Biochemical Toxicology

January 1991-January 1996

**PhD Biochemistry and Molecular Biology**

Departamento de Bioquímica y Biología Molecular, Universidad de Córdoba (Spain)

Genetic Toxicology, Biochemical Toxicology, Cancer Research

January 1996-December 1997

**Post-Doctoral Fellow**

Unidad de Proteínas y Ácidos Nucléicos, Departamento de Bioquímica y Biología Molecular, Universidad de Córdoba (Spain)

Genetic Toxicology, Biochemical Toxicology, Oxidative Stress

January 1998-January 2000

**Post-Doctoral Fellow**

Molecular Cell Biology Department, The Weizmann Institute of Science (Israel)

Cancer Research, p53 pathway regulation

## ADDITIONAL INFORMATION

**Expertise**

Cancer Research

Molecular Cell Biology

Cell/Biochemical Assay Development  
Pharmacology  
Pharmacogenomics  
Anticancer Therapeutics Development  
Mechanism of Action of Drugs  
Quality Assessment for Biologics and Advanced Therapies  
Genetic and Biochemical Toxicology  
Tissue engineering

#### Publications

1. Martinez-Leal, JF; Barbancho, M. 1992. Acetaldehyde detoxification mechanisms in *Drosophila melanogaster* adults involving aldehyde dehydrogenase (ALDH) and alcohol dehydrogenase (ADH) enzymes. *Insect Biochemistry and Molecular Biology* 22:885-892
2. Martinez-Leal, JF; Barbancho, M. 1993. Aldehyde dehydrogenase (ALDH) activity in *Drosophila melanogaster* adults: evidence for cytosolic localization. *Insect Biochemistry and Molecular Biology* 23:543-547
3. Steingrimsdottir, H; Beare, D; Cole, J; Martinez-Leal, JF; Kostic, T; Lopez-Barea, J; Dorado, G; Lehmann, A. 1996. Development of new molecular procedures for the detection of genetic alterations in man. *Mutation Research* 353:109-121
4. Gallardo-Madueno, R; Martinez-Leal, JF; Dorado, G; Holmgren, A; Lopez-Barea, J; Pueyo, C. 1998. In Vivo Transcription of *nrdAB* Operon and of *grxA* and *fpg* Genes Is Triggered in *Escherichia coli* Lacking both Thioredoxin and Glutaredoxin 1 or Thioredoxin and Glutathione, Respectively. *Journal of Biological Chemistry* 273:18382-18388
5. Damalas, A; Ben-Ze'ev, A; Simcha, I; Shtutman, M; Martinez-Leal, JF; Zhurinsky, J; Geiger, B; Oren, M. 1999. Excess  $\beta$ -catenin promotes accumulation of transcriptionally active p53. *EMBO Journal* 18:3054-3063
6. Blander, G; Kipnis, J; Martinez-Leal, JF; Yu, Chang-En; S, GD; Oren, M. 1999. Physical and functional interaction between p53 and the Werner's syndrome protein. *Journal of Biological Chemistry* 274:29463-29469
7. Blander, G; Zalle, N; Martinez-Leal, JF; Bar-Or, RL; Yu, CE; Oren, M. 2000. The Werner syndrome protein contributes to induction of p53 by DNA damage. *The FASEB Journal* 14:2138-2140
8. Maya, R; Balass, M; Kim, ST; Shkedy, D; Martinez-Leal, JF; Shifman, O; Moas, M; Buschmann, T; Ronai, Z; Shiloh, Y; Kastan, MB; Katzir, E; Oren, M. 2001. ATM-dependent phosphorylation of Mdm2 on serine 395: role in p53 activation by DNA damage. *Genes & Development* 15:1067-1077
9. Gottlieb, TM; Martinez-Leal, JF; Seger, R; Taya, Y; Oren, M. 2002. Cross-talk between Akt, p53 and Mdm2: possible implications for the regulation of apoptosis. *Oncogene* 21:1299-1303
10. Oren, M; Damalas, A; Gottlieb, T; Michael, D; Taplick, J; Martinez-Leal, JF; Maya, R; Moas, M; Seger, R; Taya, Y. 2002. Regulation of p53. *Annals of the New York Academy of Sciences* 973:374-383
11. Blanco-Aparicio, C; Pequeno, B; Moneo, V; Romero, L; Martinez-Leal, JF; Velasco, J; Fominaya, J; Carnero, A. 2005. Inhibition of phosphatidylinositol-3-kinase synergizes with gemcitabine in low-passage tumor cell lines correlating with Bax translocation to the mitochondria. *Anti-Cancer Drugs* 16:977-987
12. Blanco-Aparicio, C; Renner, O; Martinez-Leal, JF; Carnero, A. 2007. PTEN, more than the AKT pathway. *Carcinogenesis* 28:1379-1386
13. Gujjarro, MV; Martinez-Leal, JF; Blanco-Aparicio, C; Alonso, S; Fominaya, J; Lleonart, M; Castellvi, J; Ramon y Cajal, S; Carnero, A. 2007. MAP17 enhances the malignant behavior of tumor cells through ROS increase. *Carcinogenesis* 28:2096-2104
14. Gujjarro, MV; Link, W; Rosado, A; Martinez-Leal, JF; Carnero, A. 2007. MAP17 inhibits Myc-induced apoptosis through PI3K/AKT pathway activation. *Carcinogenesis* 28:2443-2450
15. Moneo, V; Serelde, B G; Fominaya, J; Martinez-Leal, JF; Blanco-Aparicio, C; Romero, L; Sanchez-Beato, M; Cigudosa, JC; Tercero, JC; Piris, MA; Carnero A. 2007. Extreme sensitivity to Yondelis(R)(Trabectedin, ET-743) in low passaged sarcoma cell lines correlates with mutated p53. *Journal of Cellular Biochemistry* 100:339-348
16. Blanco-Aparicio, C; Perez-Gallego, L; Pequeno, B; Martinez-Leal, JF; Renner, O; Carnero, A. 2007. Mice expressing myrAKT1 in the mammary gland develop carcinogen-induced ER-positive mammary tumors that mimic human breast cancer. *Carcinogenesis* 28:584-594

17. Gujjarro, MV; Martinez-Leal, JF; Fominaya, J; Blanco-Aparicio, C; Alonso, S; Leonart, M; Castellvi, J; Ruiz, L; Ramon y Cajal, S; Carnero, A. 2007. MAP17 overexpression is a common characteristic of carcinomas. *Carcinogenesis* 28:1646-1652
18. Renner, O; Fominaya, J; Alonso, S; Blanco-Aparicio, C; Martinez-Leal, JF; Carnero, A. 2007. Mst1, RanBP2 and eIF4G are new markers for in vivo PI3K activation in murine and human prostate. *Carcinogenesis* 28:1418-1425
19. Castro, ME; Martinez-Leal, JF; Leonart, M; Ramon y Cajal, S; Carnero, A. 2008. Loss-of-function genetic screening identifies a cluster of ribosomal proteins regulating p53 function. *Carcinogenesis* 29:1343-1350
20. Carnero, A; Blanco-Aparicio, C; Renner, O; Link, W; Martinez-Leal, JF. 2008. The PTEN/PI3K/AKT signalling pathway in cancer, therapeutic implications. *Current Cancer Drug Targets* 8:187-198
21. Martinez-Leal, JF; Ferrer, I; Blanco-Aparicio, C; Hernandez-Losa, J; Ramon y Cajal, S; Carnero, A; Leonart, ME. 2008. S-adenosylhomocysteine hydrolase downregulation contributes to tumorigenesis. *Carcinogenesis* 29:2089-2095
22. Moneo, V; Serelde, BG; Martinez-Leal, JF; Blanco-Aparicio, C; Diaz-Uriarte, R; Aracil, M; Tercero, JC; Jimeno, J; Carnero, A. 2008. Levels of p27kip1 determine Aplidin sensitivity. *Molecular Cancer Therapeutics* 6:1310-1316
23. Renner, O; Blanco-Aparicio, C; Grassow, M; Canamero, M; Martinez-Leal, JF; Carnero, A. 2008. Activation of phosphatidylinositol 3-kinase by membrane localization of p110 predisposes mammary glands to neoplastic transformation. *Cancer Research* 68:9643-9653
24. Castro, ME; Ferrer, I; Cascon, A; Gujjarro, MV; Leonart, M; Ramon y Cajal, S; Martinez-Leal, JF; Robledo, M; Carnero, A. 2008. PPP1CA contributes to the senescence program induced by oncogenic Ras. *Carcinogenesis* 29:491-499
25. Ruiz, L; Traskine, M; Ferrer, I; Castro, E; Martinez Leal, JF; Kaufman, M; Carnero, A. 2008. Characterization of the p53 response to oncogene-induced senescence. *PloS One* 3:e3230
26. Martinez-Leal, JF; Fominaya, J; Cascon, A; Gujjarro, MV; Blanco-Aparicio, C; Leonart, M; Castro, ME; y Cajal, S Ramon; Robledo, M; Beach, DH. 2008. Cellular senescence bypass screen identifies new putative tumor suppressor genes. *Oncogene* 27:1961-1970
27. Martinez-Leal, JF; Garcia-Hernandez, V; Moneo, V; Domingo, A; Bueren-Calabuig, JA; Negri, A; Gago, F; Guillen-Navarro, MJ; Aviles, P; Cuevas, C. 2009. Molecular pharmacology and antitumor activity of Zalypsis(R) in several human cancer cell lines. *Biochemical Pharmacology* 78:162-170
28. Martinez-Leal, JF; Martinez-Diez, M; Garcia-Hernandez, V; Moneo, V; Domingo, A; Bueren-Calabuig, JA; Negri, A; Gago, F; Guillen-Navarro, MJ; Aviles, P; Cuevas, C; Garcia-Fernandez, LF; Galmarini, CM. 2010. PM01183, a new DNA minor-groove covalent binder with potent in vitro and in vivo antitumor activity. *British Journal of Pharmacology* 161:1099-1110
29. Wozniak, MB; Villuendas, R; Bischoff, JR; Blanco-Aparicio, C; Martinez-Leal, JF; de La Cueva, P; Rodriguez, ME; Herreros, B; Martin-Perez, D; Longo, MI; Herrera, M; Piris, MA; Ortiz-Romero, PL. 2010. Vorinostat interferes with the signaling transduction pathway of T-cell receptor and synergizes with phosphoinositide-3 kinase inhibitors in cutaneous T-cell lymphoma. *Haematologica* 95:613
30. Blanco-Aparicio, C; Garcia-Collazo, AM; Oyarzabal, J; Martinez-Leal, JF; Albaran, MI; Ramos-Lima, F; Pequeno, B; Ajenjo, N; Becerra, M; Alfonso, P; Carnero, A. 2011. Pim 1 kinase inhibitor ETP-45299 suppresses cellular proliferation and synergizes with PI3K inhibition. *Cancer Letters* 300:145-153
31. Gomez-Abad, C; Pisonero, H; Blanco-Aparicio, C; Roncador, G; Gonzalez-Menchen, A; Martinez-Climent, JA; Mata, E; Rodriguez, ME; Munoz-Gonzalez, G; Sanchez-Beato, M; Martinez-Leal JF, Bischoff, JR; Piris, MA. 2011. PIM2 inhibition as a rational therapeutic approach in B-cell lymphoma. *Blood* 118:5517-5527
32. Molina-Gujjarro, JM; Macias, A; Garcia, C; Munoz, E; Garcia-Fernandez, LF; David, M; Nunez, L; Martinez-Leal, JF; Moneo, V; Cuevas, C; Lillo, MP; Villalobos, C; Valenzuela, C; Galmarini, CM. 2011. Irvalec inserts into the plasma membrane causing rapid loss of integrity and necrotic cell death in tumor cells. *PLoS One* 6:e19042
33. Aracil, M; Dauffenbach, LM; Martinez-Diez, M; Richeh, R; Moneo, V; Martinez-Leal, JF; Garcia-Fernandez, LF; Kerfoot, CA; Galmarini, CM. 2013. Expression of XPG protein in human normal and tumor tissues. *International Journal of Clinical and Experimental Pathology* 6:199
34. Martinez-Diez, M; Guillen-Navarro, MJ; Pera, B; Bouchet, BP; Martinez-Leal, JF; Barasoain, I; Cuevas, C; Andreu, JM; Garcia-Fernandez, LF; Diaz, JF; Aviles, P; Galmarini, CM. 2014. PM060184,

- a new tubulin binding agent with potent antitumor activity including P-glycoprotein over-expressing tumors. *Biochemical Pharmacology* 88:291-302
35. Carnero, Blanco-Aparicio, C; Kondoh, H; Leonart, ME; Martinez-Leal, JF; Mondello, C; Scovassi, IA; Bisson, WH; Amedei, A; Roy, R; Woodrick, J; Colacci, A; Vaccari, M; Raju, J; Al-Mulla, F; Al-Temaimi, R; Salem, HK; Memeo, L; Forte, S; Singh, N; Hamid, RA; Ryan, EP; Brown, DG; Wise JP Sr; Wise, SS; Yasaei, H. 2015. Disruptive chemicals, senescence and immortality". *Carcinogenesis* 36(Suppl\_1):S19-S37
36. Goodson III, WH; Lowe, L; Carpenter, DO; Gilbertson, M; Manaf A; Lopez de Cerain-Salsamendi, A; Lasfar, A; Carnero, A; Azqueta, A; Amedei, A;(…) Martinez-Leal, JF; (...) et al. 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures in the environment: the challenge ahead. *Carcinogenesis* 36(Suppl\_1):S254-S296
37. Molina-Guijarro, JMI; Garcia, C; Macias, A; Garcia-Fernandez, LF; Moreno, C; Reyes, F; Martinez-Leal, JF; Fernandez, Rogelio; M, Valentin; Valenzuela, C; Lillo, MP; Galmarini, CM. 2015. Elisidepsin interacts directly with glycosylceramides in the plasma membrane of tumor cells to induce necrotic cell death. *PLoS One* 10:e0140782
38. Santamaria-Nunez, G; Genes-Robles, CM; Giraudon, C; Martinez-Leal, JF; Compe, E; Coin, F; Aviles, P; Galmarini, CM; Egly, JM. 2016. Lurbinectedin specifically triggers the degradation of phosphorylated RNA polymerase II and the formation of DNA breaks in cancer cells. *Molecular Cancer Therapeutics* 15:2399-2412
39. Losada, A; Munoz-Alonso, MJ; Garcia, C; Sanchez-Murcia, PA; Martinez-Leal, JF; Dominguez, JM; Lillo, MP; Gago, F; Galmarini, CM. 2016. Translation elongation factor eEF1A2 is a novel anticancer target for the marine natural product plitidepsin. *Scientific Reports* 6:1-15
40. Tarazona, G; Santamaria, G; Cruz, PG; Fernandez, R; Perez, M; Martinez-Leal, JF; Rodriguez, J; Jimenez, C; Cuevas, C. 2017. Cytotoxic anomoian B and aplyzanzine B, new bromotyrosine alkaloids from Indonesian sponges. *ACS Omega* 2,:3494-3501
41. Garcia, C; Losada, A; Sacristan, MA; Martinez-Leal, JF; Galmarini, CM; Lillo, MP. 2018. Dynamic cellular maps of molecular species: Application to drug-target interactions. *Scientific Reports* 8:1-11
42. Galmarini, CM; Martin, M; Bouchet, BP; Guillen-Navarro, MJ; Martinez-Diez, M; Martinez-Leal, JF; Akhmanova, A; Aviles, P. 2018. Plocabulin, a novel tubulin-binding agent, inhibits angiogenesis by modulation of microtubule dynamics in endothelial cells. *BMC Cancer* 18:1-13
43. Aviles, P; Dominguez, JM; Guillen, MJ; Munoz-Alonso, MJ; Mateo, C; Rodriguez-Acebes, R; Molina-Guijarro, JM; Francesch, A; Martinez-Leal, JF; Munt, S; Galmarini, CM; Cuevas, C. 2018. MI130004, a novel antibody-drug conjugate combining trastuzumab with a molecule of marine origin, shows outstanding In Vivo activity against HER2-expressing tumors. *Molecular Cancer Therapeutics* 17:786-794
44. Cruz, PG; Martinez Leal, JF; Hernandez-Daranas, A; Perez, M; Cuevas, C. 2018. On the mechanism of action of dragmacidins I and J, two new representatives of a new class of protein phosphatase 1 and 2A inhibitors. *ACS Omega* 3:3760-3767
45. Losada, A; Munoz-Alonso, MJ; Martinez-Diez, M; Gago, F; Dominguez, JM; Martinez-Leal, JF; Galmarini, CM. 2018. Binding of eEF1A2 to the RNA-dependent protein kinase PKR modulates its activity and promotes tumour cell survival. *British Journal of Cancer* 119:1410-1420
46. Xie, W; Forveille, S; Iribarren, K; Sauvat, A; Senovilla, L; Wang, Y; Humeau, J; Perez-Lanzon, M; Zhou, H; Martinez-Leal, JF; Kroemer, G; Kepp, O. 2019. Lurbinectedin synergizes with immune checkpoint blockade to generate anticancer immunity. *Oncoimmunology* 8(11):e1656502
47. Losada, A; Berlanga, JJ; Molina-Guijarro, JM; Jimenez-Ruiz, A; Gago, F; Aviles, P; de Haro, C; Martinez-Leal, JF. 2020. Generation of endoplasmic reticulum stress and inhibition of autophagy by plitidepsin induces proteotoxic apoptosis in cancer cells. *Biochemical Pharmacology* 172:113744
48. Povo-Retana, A; Mojena, M; Stremtan, AB; Fernandez-Garcia, VB; Gomez-Saez, A; Nuevo-Tapioles, C; Molina-Guijarro, JM; Avendano-Ortiz, J; Cuezva, JM; Lopez-Collazo, E; Martinez-Leal, JF; Bosca, L. 2020. Specific Effects of Trabectedin and Lurbinectedin on Human Macrophage Function and Fate-Novel Insights. *Cancers* 12:3060

[Projects](#)

[Memberships](#)

[Other Relevant Information](#)