MARCOS MALUMBRES
Organismo Fundación Centro Nacional de Investigaciones Oncológicas

Marcos Malumbres studied in the University of Navarra and performed his doctoral studies in the University of León, working in molecular genetics in gram-positive bacteria. After obtaining the Ph.D. degree, he moved for a postdoctoral stay at the New York University Medical Center for training in the field of oncogenes and tumor suppressors. In this institution, his work was focused to the molecular biology of Ras oncogenes in carcinogen induced tumors and the interaction between Ras and the cell cycle regulators in collaboration with A. Pellicer (1994-1998). Dr. Malumbres returned to Spain at the end of 1998 to join M. Barbacid's lab in the then newly created CNIO. His research focused on the generation of mouse models to analyze the in vivo role of cyclin dependent kinases (CDKs) and their inhibitors in cell cycle progression and tumour development. In 2003 he obtained a Staff Scientist position at the Consejo Superior de Investigaciones Científicas (CSIC) and in June 2004 he decided to stay at the CNIO to lead the Cell Division and Cancer Group.

Dr. Malumbres' lab is focused to the in vivo analysis of cell cycle regulators and their therapeutic potential. These studies have addressed the in vivo characterization of the mammalian cell cycle and their deregulation in human cancer (see Malumbres & Barbacid, 2009; Malumbres, 2011 for representative reviews). Dr. Malumbres reported that normal mammalian cell cycles do not need Cdk4/6 kinases opening the possibility of using Cdk4/6 inhibitors specifically for tumor cells. Cdk4/6 inhibitors such as palbociclib have been reently (2015) approved for the treatment of breast tumors. He also investigated the role of specific microRNAs in cell proliferation and he reported a microRNA that controls the protein levels of ABL and the translocation protein BCR-ABL (Bueno et al., 2008). This was the first report of a microRNA controlling a tumor-associated translocation protein and it has relevant implications in cancer therapy.

Recent work in Malumbres' lab is now focused to the analysis of mitotic regulators such as kinases (Plk, Aurora), phosphatases (Cdc14, PP2A-B55), proteins involved in ubiquitin-dependent degradation (Cdh1, Cdc20) and some regulators of the spindle checkpoint (securin, Hec1). His group has established the relevance of the APC/C subunits Cdh1 and Cdc20 in the maintenance of genomic stability (Nat Cell Biol 2008 and Cancer Cell 2010). In the last 5 years, his group has reported the relevance of APC/C complexes in different tissues, as well as new substrates and possible therapeutic uses. His lab also identified a new member of the mammalian Plk family (Mol Cell Biol., 2011) and pioneered the characterization of a new kinase, Mastl, able to inhibit PP2A phosphatases (Alvarez- Fernandez et al., 2013). Recent work from his group has characterized the specific energetic requirements of cancer cells during mitosis (Nat Cell Biol., 2015). Current work includes the analysis of cell cycle kinases and phosphatases such as PP2A-B55 complexes, the regulatory networks between microRNAs and the cell division cycle and its relevance in progenitor cells and tumor development.

Publications

de Cárcer, G., Wachowicz, P., Martínez-Martínez, S., Oller, J., Méndez-Barbero, N., Escobar, B., González-Loyola, A., Takaki, T., El Bakkali, A., Cámara, J.A., Jiménez-Borreguero, L.J., Bustelo, X., Cañamero, M., Mulero, F., Sevilla, M.d.l.A., Montero, M.J., Redondo, J.M. and Malumbres, M. (2017) Plk1 regulates contraction of postmitotic smooth muscle cells and is required for vascular homeostasis. Nat. Med., in press.

Doménech, E., Maestre, C., Esteban-Martínez, L., Partida, D., Pascual, R., Fernández-Miranda, G., Seco, E., Campos-Olivas, R., Pérez, M., Megias, D., Allen, K., López, M., Saha, A.K., Velasco, G., Rial, E., Méndez, R., Boya, P., Salazar-Roa, M. and Malumbres, M. (2015) AMPK and PFKFB3 mediate glycolysis and survival in response to mitophagy during mitotic arrest. Nat. Cell Biol. 17, 1304-1316.

Trakala, M., Rodríguez-Acebes, S., Maroto, M., Symonds, C.E., Santamaría, D., Ortega, S., Barbacid, M., Méndez, J. and Malumbres, M. (2015) Functional reprogramming of polyploidization in megakaryocytes. Dev. Cell 32, 155-167.

Eguren, M., Álvarez-Fernández, M., García, F., López-Contreras, A.J., Fujimitsu, K., Yaguchi, H., Luque-García, J.L., Fernández-Capetillo, O., Muñoz, J., Yamano, H. and Malumbres, M. (2014). A synthetic lethal interaction between APC/C and topoisomerase poisons uncovered by proteomic screens. Cell Reports 6, 670-683.

Eguren, M, Porlan, E., Manchado, E., García-Higuera, I., Cañamero, M., Fariñas, I. and Malumbres, M. (2013) The APC/C cofactor Cdh1 prevents replicative stress and p53-dependent cell death in neural progenitors. Nat. Commun. 4, 2880. doi: 10.1038/ncomms3880.

Álvarez-Fernández, M., Sánchez-Martínez, R., Sanz-Castillo, B., Gan, P.P., Sanz-Flores, M., Trakala, M., Ruiz-Torres, M., Lorca, T., Castro., A. and Malumbres, M. (2013) Greatwall is essential to prevent mitotic collapse after nuclear envelop breakdown in mammals. Proc. Natl. Acad. Sci. USA 110, 17374-17379.

Fernández-Miranda, G., Trakala, M., Martín, J., Escobar, B., González, A., Ghyselinck, N.B., Ortega, S., Cañamero, M., Pérez de Castro, I. and Malumbres, M. (2011) Genetic disruption of Aurora B uncovers an essential role for Aurora C during early mammalian development.Development 138, 2661-2672.

Manchado, E., Guillamot, M., de Cárcer, G., Eguren, M., Trickey, M., García-Higuera, I., Moreno, S., Yamano, H., Cañamero, M. and Malumbres, M. (2010) Targeting mitotic exit leads to tumor regression in vivo: modulation by Cdk1, Mastl, and the PP2A/B55a,d phosphatase. Cancer Cell 18, 641-654.

García-Higuera, I., Manchado, E., Dubus, P., Cañamero, M., Mendez, J., Moreno, S. and Malumbres, M. (2008) Genomic Stability and Tumor Suppression by the APC/C Cofactor Cdh1. Nat. Cell Biol. 10, 802-811.

Bueno, M.J., Pérez de Castro, I., Gómez de Cedrón, M., Santos, J., Calin, G.A., Cigudosa, J.C., Croce, C.M., Fernández-Piqueras, J. and Malumbres, M. (2008) Genetic and Epigenetic Silencing of microRNA-203 Enhances ABL1 and BCR-ABL1 Oncogene Expression. Cancer Cell 13, 496-506.

Projects

"Systems Biology of Cell Proliferation" Red Temática de Excelencia (BFU2014-52125-REDT) IP: Marcos Malumbres (coordinator). Ministerio de Economía y Competitividad (2015-2016).

"New therapeutic strategies by inhibiting Mastl in breast tumors" (WCR #15-0278). IP: Marcos Malumbres. Worldwide Cancer Research (formerly AICR).

"Relevancia fisiológica y terapéutica de las quinasas y fosfatasas mitóticas" (SAF2012-38215). IP: Marcos Malumbres. Ministerio de Economía y Competitividad (2013-2016).

"Ciclo Celular y Cáncer" (S2010/BMD-2470). IP (coordinador): Marcos Malumbres. Comunidad Autónoma de Madrid (2012-2015).

"Systems Biology of Mitosis (MitoSys; HEALTH-F5-2010-241548)". Coordinador: J.M. Peters: IP node Spain: Marcos Malumbres. European Community (2010-2014).

Red Consolider: "Biología del Cancer". Coordinador M. Barbacid. IP group: Marcos Malumbres. Ministerio de Educación y Ciencia. (2008-2012).

Renewal under SAF2014-57791-REDC (2015-2016).
"Control of ABL expression by microRNAs". IP: Marcos Malumbres. Association for International Cancer Research (2008-2011).

Representative reviews and editorial publications

Álvarez-Fernández & Malumbres, J. Natl. Cancer Inst., 2015; Trakala & Malumbres, Nat Cell Biol., 2014. Valcárcel & Malumbres, EMBO J., 2014; Malumbres, Genome Biol., 2014; de Cárcer & Malumbres, Nat. Cell Biol., 2014; Malumbres, Cancer Cell, 2012; Malumbres, Physiol. Rev, 2011; Malumbres, Cancer Cell, 2011; Manchado & Malumbres, Cell 2011; Malumbres et al., Nat Cell Biol, 2009 (unsolicited correspondence); Malumbres & Barbacid, Nat. Rev Cancer 2009; Malumbres & Barbacid, Nat Rev. Cancer 2003; Malumbres & Barbacid, Nat Rev. Cancer 2001.

Editorial activities
Editor-in-Chief: Inside the Cell (Wiley; 2014).
Associate Editor: Mol. Cancer; Frontiers Oncol. (2011-present)
Editorial Board Member: Curr. Med. Chem., Genes & Cancer, microRNA, J. BUON .

Scientific evaluation and International Committees
Member of the Scientific Advisory Committee (SAB):
Institute of Molecular Genetics Academy of Sciences of the Czech Republic (2013). AERES committee member, Institute of Molecular Genetics, Montpellier (2013). SAB Elly-Lilly 2015.

Project evaluation: ERC, VI Framework Programme (Networks and Marie Curie fellowships), Cancer Research UK, London, United Kingdom; Association for International Cancer Research, United Kingdom; Czech Science Foundation; Dutch Cancer Society (The Netherlands); Fundação para Ciência e Tecnologia, Portugal; Agence Nationale de la Recherche, Paris, France; Institut Nacional du Cancer (InCA), Paris, France; Ireland Science Foundation, Dublin; Research Grants Council Collaborative Research Fund (Hong Kong); Asociación Espanola Contra el Cáncer, Madrid, Spain; Instituto de Salud Carlos III, Madrid, Spain; CIRIT, Barcelona, Spain; ANEP (Colaborador 2012-2015) and other agencies (Spain)

Reviewing activities: Bioessays, Cancer Cell, Cancer Res., Current Opinion series, Development, EMBO Reports, EMBO J., EMBO Mol. Med., FEBS Lett., Genes & Dev., J. Cell Science, J. Nat. Cancer Inst., Mol. Cell, Mol. Biol. Cell, Mol. Cell Biol. Nature, Nature Cell Biology, Nature Medicine, Nature Reviews Cancer; Nature Reviews Mol. Cell. Biol., Oncogene, PLoS Biol., PLoS One, PNAS., Science, Trends series, etc.

Organization and participation in International Conferences
Organization of Conferences:
EMBO Workshop on “"Cell division: molecular machineries and cancer targeted therapies" with co-sponsorship from UNIA" (Baeza, España; 19-21 October 2015); “Chromosomal Instability and Cancer”, Madrid 2013; Cell Cycle and Cancer; Montpellier, 2012; “Cell Cycle Regulators/ Inhibitors and Cancer”, Vienna, 2011; “Cancer, stem cells and metastasis”, Salamanca, 2010; “The Cell Cycle and Cancer (CCC Workshop; Madrid 2002).

Invited Conferences: More than 90 conferences or invited seminars in Universities or research institutes in Austria, France, Germany, Italy, Mexico, Portugal, The Netherlands, UK, USA and Spanish Institutions. Participation in more than 100 National or International meetings including Gordon Conferences, Keystone Symposia, EMBO Meetings, and meetings organized by the European and American Associationes for Cancer Research (EACR & AACR).

Honors and other activities

• Elected EMBO member, 2016
• Adjunto Colaborador Agencia Nacional de Evaluación de Proyectos (ANEP), Ministerio de Economía y Competitividad, Madrid (2012-2015)
• Honorary Professor, Departamento de Bioquímica y Biología Molecular de la Universidad Autónoma de Madrid (2008-)
• Honorary member, Balkan Union of Oncology (2007)
• National Research Award Beckman-Coulter 2005 for Young Investigators in Biochemistry and Molecular Biology.
• Juan Abelló" Award (Real Academia de Doctores) to the best Thesis work in Biochemistry 1994.