

BIOGRAPHICAL SKETCH

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NAME Ignacio Melero Bermejo	POSITION TITLE		
eRA COMMONS USER NAME (credential, e.g., agency login)	Co-director of Department Senior investigator Professor in Immunology		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Universidad de Navarra, Pamplona, Spain	MD Residency in Clinical Immunology Md degree Professor in Immunology	1988	Medicine

MD degree	Universidad de Navarra	1988
Residency in Clinical Immunology	Hospital La Princesa (Madrid)	1993

Doctorate	Center	Fecha
PhD degree	Universidad Autónoma de Madrid	1994

A. Personal Statement

Dr. Melero started out in biomedical research as a resident of immunology at the prestigious department of this specialty in Hospital Universitario de la Princesa (Madrid). He completed his doctoral thesis with Professor Miguel López-Botet identifying and functionally studying natural killer cell receptors. His work obtained the Outstanding Doctorate Award. In 1994 he joined Bristol Myers Squibb Company as a researcher in cancer immunotherapy in his institute in Seattle (WA). The result of his three years of work in this environment are pioneering publications in the knowledge of costimulation of antitumor immune responses and the use of immunostimulatory monoclonal antibodies. During this period he worked with Professor Lieping Chen in the division led by Professor Karl E. Hellström. In 1998 he returned to Spain in the field of CIMA and Clínica Universidad de Navarra. In these centers he has led a multidisciplinary team working in cancer immunotherapy with cell therapy techniques, gene therapy and monoclonal antibodies. Dr. Melero is a professor of immunology at the University of Navarra, has directed 10 PhD thesis (6 of them obtained the Outstanding Doctorate Award), and has been principal researcher in over 20 clinical trials of immunotherapy (both sponsored by industry and by the center itself). His work has resulted in three patents transferred to industry. From a bibliometric point of view, Dr. Melero has an h-index of 41 and 166 articles indexed in Medline. For his career he has been awarded the Grand Prix BIAL Medicine (2004) the Conde de Cartagena Awards of the Royal Academy of Medicine (2006) and Dr. Durantez of the LAIR Foundation (2011), among other honors. In 2015 he was appointed director of the Immunology and Immunotherapy department of the Clínica Universidad de Navarra. The phrase that best defines Dr. Melero's scientific biography is Translational Research in Cancer Immunotherapy in collaboration with pharmaceutical industry and european groups in consortia with receiving funding for the development of therapeutic strategies.

B. Positions and Honors

Positions and employment:

Medical Resident	Hospital Universitario La Princesa (Madrid)	1989-1993
Research fellow, FIS	Hospital Universitario La Princesa (Madrid)	1994
Postdoctoral Fellow	Bristol Myers Squibb (Seattle, USA)	1994-1995
Investigator	Bristol Myers Squibb (Seattle, USA)	1995-1998
Associate Professor	Facultad de Medicina (Universidad de Navarra)	1998-2004
Investigator	Universidad de Navarra / FIMA	1998-2005
Catedrático (Full professor)	Universidad de Navarra	2004-current
Senior Investigator	Centro de Investigación Médica Aplicada (CIMA)	2005-current
Senior consultant	Oncology (Clínica Universidad de Navarra)	2005-current
Co-Director of Immunology and Immunotherapy Department	Clínica Universidad de Navarra	2015-current

Other Experience and Professional Memberships

Sociedad Española de Inmunología: 1990 socio adherido; 1993 socio numerario.

American association of Immunologists: 1996 Regular member.

American society of Gene Therapy. Member. 1998

Asociación española de Terapia génica y celular (2000) Socio fundador

American Association of Cancer Research (2006).

SENIOR EDITOR: Clinical Cancer Research.

Associate editor in frontiers in immunology

Editorial board Member en: Immunotherapy, Autoimmunity, Oncoimmunology, Journal of translational Medicine, World Journal of Immunology and Cancer Immunology Research.

Referee in more than 40 prestigious journals.

Reviewer for: proyectos de Investigación para la ANEP (CICYT y FIS), "Associazione italiana per la ricerca sul cancro y Referee de Cancer UK (2005, 2006, 2007)". Member of the committee of MEC en el plan nacional (2005 y 2016). Evaluator INSERM (Francia 2008). European Expert (evaluador programa Marie Curie y FP7 2006, 2009). Evaluator on financiación ensayos clínicos (convocatoria de nuevas terapias del ministerio de sanidad 2009 y 2010)

Honors:

Gran Premio BIAL de Medicina 2004. República de Portugal. Compartido con los Dres. Prieto y Mazzolini, endowed with con 150.000 euros.

Premio Conde de Cartagena 2006 de la Real Academia Nacional de Medicina (España), endowed with 3.000 euros.

Beca Ortiz de Landazuri 2008.

Premio Dr. Durantez de la Fundación LAIR 2011. Endowed with 3.000 euros.

Member of the "Immuno-oncology network (Bristol-Myers Squibb)" in which he has been elected chairman in 2015.

C. Selected Peer-reviewed Publications

Abscopal effects of radiotherapy are enhanced by combined immunostimulatory mAbs and are dependent on CD8 T cells crosspriming. Rodríguez-Ruiz ME, Rodríguez I, Garasa S, Barbes B, Solorzano JL, Perez-Gracia JL, Labiano S, Sanmamed MF, Azpilikueta A, Bolaños E, Sanchez-Paulete AR, Aznar MA, Rouzaut A, Schalper KA, Jure-Kunkel M, Melero I. **Cancer Research** 2016 Aug 22.

'Tumor-produced interleukin-8 attracts human myeloid-derived suppressor cells and elicits extrusion of neutrophil extracellular traps (NETs).' Alfaro C, Teijeira A, Oñate C, Pérez G, Fernández de Sanmamed M, Andueza MP, Alignani D, Labiano S, Azpilikueta A, Rodríguez-Paulete A, Garasa S, Fusco JP, Aznar MA, Inoges S, Medina-Echeverz J, Berraondo P, Pérez-Gracia JL, Melero I. 2016 MAR 8. **Clin Cancer Res**. IF: 8.722.

'Cancer Immunosurveillance Caught in the Act.' Berraondo P, Teijeira A, Melero I. **Immunity**. 2016 Mar 15; 44(3):525-5. IF: 21.561.

'Defining the optimal murine models to investigate immune checkpoint blockers and their combination with other immunotherapies.' Sanmamed MF, Chester C, Melero I, Kohrt H. **Ann Oncol**. 2016 FEB 23; IF: 7.040.

Cancer immunotherapy with immunomodulatory anti-CD137 and anti-PD-1 monoclonal antibodies requires Batf3-dependent dendritic cells. Sanchez-Paulete AR, Cueto FJ, Martínez-Lopez M, Labiano S, Morales-Kastresana A, Rodríguez-Ruiz ME, Jure-Kunkel M, Azpilikueta A, Aznar MA, Quetglas JI, Sancho D, Melero I. **Cancer Discov**. 2015 Oct 22. pii: CD-15-0510. IF: 15.929.

PD-L1 expression as a potential predictive biomarker. Fusi A, Festino L, Botti G, Masucci G, Melero I, Lorigan P, Ascierto PA. **Lancet Oncol**. 2015 OCT. 16(13); 1285-7. IF: 24.690.

'Evolving synergistic combinations of targeted immunotherapies to combat cancer.' Melero I, Berman DM, Aznar MA, Korman AJ, Gracia JL, Haanen J. **Nat Rev Cancer**. 2015 Jul 24;15(8):457-72. doi: 10.1038/nrc3973.

'Nivolumab and urelumab enhance antitumor activity of human T lymphocytes engrafted in Rag2^{-/-}IL2R^γ null immunodeficient mice.' Fernández de Sanmamed M, López Rodríguez I, Schalper KA, Oñate C, Azpilikueta A, Rodríguez-Ruiz ME, Morales-Kastresana A, Labiano S, Pérez-Gracia JL, Martín-Algarra S, Alfaro C, Mazzolini G, Sarno F, Hidalgo M, Korman AJ, Jure-Kunkel M, Melero I. **Cancer Res**. 2015 Sep 1;75(17):3466-78.

'Combined immunostimulatory monoclonal antibodies extend survival in an aggressive transgenic hepatocellular carcinoma mouse model.' Morales-Kastresana A, Sanmamed MF, Rodríguez I, Palazón A, Martínez-Forero I, Labiano S, Hervas-Stubbs S, Sangro B, Ochoa C, Rouzaut A, Azpilikueta A, Bolaños E, Jure-Kunkel M, Gütgemann I, Melero I. 2013;19(22); 6151-62. **Clinical Cancer Research** IF:8.7.

'Therapeutic vaccines for cancer: an overview of clinical trials.' Melero I, Gaudernack G, Gerritsen W, Huber C, Parmiani G, Scholl S, Thatcher N, Wagstaff J, Zielinski C, Faulkner I, Mellstedt H. 2014 **Nat Rev Clin Oncol** [doi:10.1038/nrclinonc.2014.111] IF:15.696.

'T cell costimulation with anti-CD137 monoclonal antibodies is mediated by K63-polyubiquitin-dependent signals from endosomes.' Martínez-Forero I, Azpilikueta A, Bolaños-Mateo E, Nistal-Villan E, Palazón A, Teijeira A, Pérez-Chacón G, Morales-Kastresana A, Murillo O, Jure-Kunkel M, Zapata JM, Melero I. 2013.190(12);6694-706. **J Immunol**. IF: 5.362.

'The HIF-1 α hypoxia response in tumor-infiltrating T lymphocytes induces functional CD137 (4-1BB) for immunotherapy.' Palazón A, Martínez-Forero I, Teijeira A, Morales-Kastresana A, Alfaro C, Sanmamed MF, Pérez-Gracia JL, Peñuelas I, Hervás-Stubbs S, Rouzaut A, de Landázuri MO, Jure-Kunkel M, Aragonés J, Melero I. 2012. 2(7);608-23. **Cancer Discov.** IF: 15.929.

'Antitumor immunotherapeutic and toxic properties of an HDL-conjugated chimeric IL-15 fusion protein.' Ochoa MC, Fioravanti J, Rodriguez I, Hervas-Stubbs S, Azpilikueta A, Mazzolini G, Gurrpide A, Prieto J, Pardo J, Berraondo P, Melero I. 2012. 73(1);139-49. **Cancer Res.** IF: 9.284.

'Pilot clinical trial of type-1 dendritic cells loaded with autologous tumor lysates combined to GM-CSF, pegylated interferon and cyclophosphamide for metastatic cancer patients.' Alfaro C, Pérez-Gracia JL, Suárez N, Rodríguez J, Fernández de Sanmamed M, Sangro B, Martín-Algarra S, Calvo A, Redrado M, Agliano A, Gonzalez A, Rodriguez I, Bolaños E, Hervás-Stubbs S, Pérez-Calvo J, Benito A, Peñuelas I, Vigil C, Richter J, Martínez-Forero I, Melero I. 2011. 187(11);6130-42. **Journal of Immunology** IF: 5.362.

'Agonist anti-CD137 mAb act on tumor endothelial cells to enhance recruitment of activated T lymphocytes.' Palazón A, Teijeira A, Martínez-Forero I, Hervás-Stubbs S, Roncal C, Peñuelas I, Dubrot J, Morales-Kastresana A, Pérez-Gracia JL, Ochoa MC, Ochoa-Callejero L, Martínez A, Luque A, Dinchuk J, Rouzaut A, Jure-Kunkel M, Melero I. 2011. 71(3);801-11. **Cancer Research** IF: 9.284.

D. Research Support

Research Support Ongoing:

"Traslational research on combinatorial strategies for cancer immunotherapy".
CIBER (Centro de Investigación Biomédica en Red) Instituto de Salud Carlos III. Ministerio de Economía y Competitividad. 147.000 euros. 2016-2018
Role: PI.

"Potenciación de la citotoxicidad dependiente de anticuerpo mediada por linfocitos NK para la inmunoterapia del cáncer".
Asociación Española Contra el Cáncer (AECC). 1.200.000 €. 2015-2020.
Role: PI.

"Anticuerpos monoclonales inmunoestimulantes anti-PD-1 y anti-CD137 en combinación con terapia celular adoptiva: Efectos sinérgicos e investigación traslacional".
Plan Nacional Biomedicina. 380.000 €. 2015-2019.
Role: PI.

"Professional cross-priming for ovary and prostate cancer PROCROP".
European Commission HORIZON 2020. 7.572.500 € / FIMA: 1.190.000 €. 2015-2020.
Role: PI

"Phase II study with immunotherapy with dendritic cells and hiltonol in patients with advanced solid tumors: evaluation of the abscopal effect".
Fundación BBVA. 145.500 €. 2014-2016.
Role: PI.

"Immunostimulatory Agonist antibodies for Cancer Therapy".
European Commission. 306.304 €. 2013-2017.
Role: PI.

Research Support Completed:

"Estudio fase II mediante células dendríticas e hiltonol en pacientes con tumores sólidos: valoración efecto abscopal de la radioterapia".

Fundación Caja Ahorros Navarra, CAN. 24.473 €. 2014-2015.

Role: PI.

"Investigación Translacional en Inmunología e Inmunoterapia del Cáncer"

Contrato Río Ortega del Instituto de Salud Carlos III para Miguel Fernández de Sanmamed. CM11/00306. 54.800€. 2010-2013

Role: PI.

"La interleukina-8 en la inmunodeficiencia de leucocitos polimorfonucleares de los pacientes con cáncer avanzado".

Departamento de Salud, Gobierno de Navarra. 80.000 € . 2012-2014.

Role: PI.

"Combinaciones de nuevos agentes inmunoterápicos para el tratamiento de tumores malignos espontáneos".

Plan Nacional de Biomedicina. SAF2011-22831. 305.000 €. 2011-2013.

Role: PI.

"Proyecto FIS EC09/90133 'Ensayo clínico fase II con inmunoterapia mediante células dendríticas maduras cargadas con lisado de tejido tumoral autólogo aplicadas por vía intraganglionar a pacientes con carcinoma renal avanzado y melanoma".

FIS EC09/90133. Universidad de Navarra. 147.000 €.

Role: PI.

"Ayuda para contrato Carlos Alfaro en la realización de ensayos clínicos de inmunoterapia celular"

Asociación Española Contra el Cáncer (AECC). 120.000 €. 2010-2013.

Role: PI

Signed by: Ignacio Melero



Date: 17th of October 2016