

Ignacio Melero	
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Web of Science ResearcherID: <u>T-7600-2019</u>	
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DEGREE	INSTITUTION AND LOCATION	YEAR
MD degree	Universidad de Navarra	1988
Residency in Clinical Immunology	Hospital La Princesa (Madrid)	1993
PhD degree	Universidad Autónoma de Madrid	1994
Full Professor of Immunology	Universidad de Murcia	2004

#### 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 campus 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 serves as full professor of Immunology at the University of Navarra, has directed 15 PhD thesis (8 of them obtained the Outstanding Doctorate Award and one of them the Enrique Fuentes Quintana Award), and has been principal researcher in over 39 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 67 and 267 articles indexed in Medline. For his career he has been awarded the BIAL Medicine award (2004), Conde de Cartagena Award of the Royal Academy of Medicine (2006) and Dr. Durantez award of the LAIR Foundation (2011 and 2019), Francisco Cobos prize(2020), Ciencias de la Salud Fundación Caja Rural Granada award (2020) among other honors. In 2015 he was appointed director of the Immunology and Immunotherapy department of the Clínica Universidad de Navarra and in 2018 he was appointed Corresponding academican at the Royal Nacional Academy of Medicine. The phrase that best defines Dr. Melero's scientific biography is **Translational Research in Cancer Immunotherapy** in collaboration with pharmaceutical industry and with european groups receiving funding in consortia for the development of therapeutic strategies.

#### B. 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
Senior Research	Universidad de Navarra	1998-2005
Full professor of Immunology	Universidad de Navarra	2004-current
Senior Research	Centro de Investigación Médica Aplicada (Cima)	2005-current
Senior consultant	Oncology (Clínica Universidad de Navarra)	2005-current
Co-head Immunology and Immunotherapy	Clínica Universidad de Navarra	2015-current

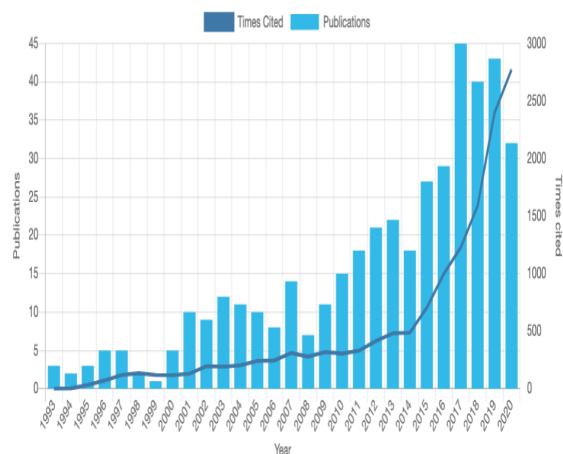
## Other Experience and Professional Memberships

Spanish college of practicing physicians 1988  
 Spanish society of Immunology: 1990 member; 1993 full member.  
 American association of Immunologists: 1996 Regular member.  
 American society of Gene Therapy. Member. 1998  
 Asociación española de Terapia génica y celular (2000) Founding member  
 American Association of Cancer Research (2006).  
 Society for immunotherapy of cancer (SITC) (2016)  
 Member of de Royal Academy of Medicine (RANM) (Spain), 2018

### C. General quality indicators:

	Total
Five six-year research, the last in 2014	
Doctoral thesis directed finalized	16
Doctoral thesis directed in progress	4
Total number of publications	267
Number of publications first decile	143
Number of publications First Quartile	195
Number of publications 1st author	31
Number of publications Last signatory	133
Nº Citations	14400
<b>Index h</b>	<b>67</b>

Source: Web of Science (2020)



### D. Research Support (Ongoing):

Title	Financed	Amount	Role	Year
LINTERNA: liderazgo e innovación en inmunoterapia del cáncer desde Navarra	Gobierno de Navarra	1.674.430 €	PI	2020-2022
Ensayo clínico fase I/II: nuevo enfoque terapéutico para el tratamiento de tumores sólidos con metástasis hepática.	MINECO-Retos colaborativos con empresas	2.183.845,67€/CIMA: 270.481,6€	PI	2020-2023
Personalized Immunotherapy for Endometrial Cancer	Fundació La Marató de TV3	396.684€/ CIMA: 97.500€	PI	2019-2021
Metabolic requirements for immune infiltration in effective cáncer (MINCITH)	BBVA	124.768€	PI	2020-2023
Local Immunoradiotherapy (LIRT) ref. Accelerator Award	Cancer Research UK. AECC. AIRC	£5,000,000/ CIMA-CUN: 1.480.000€	PI and Coordinator	2019-2024
Tumor Treg Targeting	European Commission H2020 ITN	1.279.782€/ CUN 247.872€	PI and Coordinator	2018-2022
Administración intratumoral y dianizada de agentes de inmunoterapia para el tratamiento del cáncer	Plan Nacional Biomedicina	399.300 €	PI	2017-2020
Potenciación de la citotoxicidad dependiente de anticuerpo mediada por linfocitos NK para la inmunoterapia del cáncer	Spanish Association Against Cancer (AECC)	1.200.000 €	Coordinator	2015-2020
Professional cross-priming for ovary and prostate cancer	European Commission H2020 PROCROP	7.572.500€ / FIMA: 1.190.000€	PI and Coordinator	2015-2020

### E. Activity in Clinical Trials:

- Principal investigator in over 39 cancer immunotherapy clinical trials sponsored by pharmaceutical industry.
- Principal investigator in five institution-sponsored immunotherapy clinical trials.
- Coinvestigator in over 15 clinical trials.

## F. Honors:

- **BIAL merit award** in medical sciences 2004. Republic of Portugal. Shared with the Drs. Prieto and Mazzolini, endowed with con 150.000€
- **Conde de Cartagena 2006 award:** The Royal Academy of Medicine (RANM), Spain, endowed with 3.000€.
- **Grant Ortiz de Landazuri 2008**
- **Dr. Durantez Award** Fundación LAIR 2011 and 2019. Endowed with 3.000€
- **European Academy of immunotherapy Life Career Award.** (EATI 2016)
- **CRI Lecture Award.** Cancer Research Institute, New York, 2017.
- **Corresponding member of The Royal Academy of Medicine (RANM).** Spain. 2018
- **EFIS Lecture Award:** European Federation of Immunological Societies, Portugal. 2019
- **Thesis director of Enrique Fuentes Quintana Awards** for Doctoral Theses. Spain. 2019
- **XIV Premio Fundación Francisco Cobos.** Spain. 2020
- **XVI Ciencias de la salud.** Fundación caja rural de Granada. Spain 2020
- **Highly Cited Researcher in the field of Cross-Field 2020**

## G. Patents:

1. 'Uso combinado de la quimiocina IP-10 y la Interleukina-12 en la preparación de composiciones para el tratamiento de tumores malignos' **I. Melero**, I. Narvaiza, G.Mazzolini, C.Qian, J.Prieto. N°Solicitud: **WO0162274**. Country of priority: España; Date: 25/2/2000. Headline: Insitituto científico y tecnológico de Navarra SA.
2. 'Composición farmacéutica para el tratamiento del cáncer' Dubrot J, Hervás-Stubbs S, Le Bon A, **Melero I**. N°Solicitud: **ES 20070296**. Country of priority: Spain; Date: 07/11/ 2007. Headline: Proyecto Biomedicina CIMA.
3. 'Nuevos conjugados y composiciones para inmunoterapia y tratamiento anti-tumoral'. Berraondo P, Bulfone S, Duitman H, Fioravanti J, Medina J, Ochoa MC, Palazon A, **Melero I**. N° Solicitud: **EP20100814739**. Country of priority: España. Date: 11/12/2009. Headline: CIMA (ES) y Research Centre Borstel (DE).

## H. Activity in scientific journals:

Ignacio Melero is Senior editor for Clinical Cancer Research, scientific editor for Cancer Discovery, associate editor in the journal Frontiers in Immunology, section editor for the Journal for Immunotherapy of Cancer JITC. He is Editorial Board Member of the journals Immunotherapy, Autoimmunity, Oncoimmunology, Journal of Translational Medicine, World Journal of Immunology, Cancer Immunology Research and Cancer Research.

Dr. Melero has served as a reviewer for the journals: European Journal of Immunology, Journal of Immunology, Human Gene Therapy, Gene Therapy, Cellular Immunology, Cancer Research, Molecular therapy, Nature Reviews Cancer, Nature Medicine, Nature, Nature Cancer, Nature Communications, Clinical Cancer Research, International Journal of Cancer, Journal of the National Cancer Institute, Expert Opinion in Biological Therapy, Journal of Hepatology, Current gene therapy, Journal of leukocyte Biology, Blood, Surgical Oncology, PlosOne, PLoS Pathogens, Gastroenterology, Clinical immunology Immunotherapy, Cancer immunology Immunotherapy, Clinical and Developmental immunology, British Journal of Cancer Immunotherapy, Hematology, International Immunology, trends in immunology, Science Translational Medicine, Future oncology, Frontiers in Immunology, Journal of Translational Medicine, Journal of Immunotherapy, Future Oncology, Oncoimmunology, FASEB Journal, Immunobiology, Molecular Cancer Therapeutics, Cancer Immunology Research, Journal of Immunotherapy for cancer, New England journal of Medicine, Lancet, Lancet Oncology,

Ignacio Melero is a regular reviewer of research projects for the ANEP (CICYT and FIS), Member of the Committee of Experts of MEC in the national plan (2005 and 2009), reviewer of the Italian Associazione per la ricierca sul Cancro and Referee Cancer UK (2005 2006, 2007). INSERM Evaluator (France 2008). European expert (evaluator and FP7 Marie Curie 2006, 2009 program). Evaluator of funding clinical trials (call for new therapies of the Health Ministry 2009 and 2010). Member of the scientific advisory boards of institute Curie (Paris), institute the investigación biomédica de Granada, and Netherlands cancer Institute (NKI).

## I. Scientific publications: (15 Most relevant)

1. Elevated serum interleukin-8 is associated with enhanced intratumor neutrophils and reduced clinical benefit of immune-checkpoint inhibitors. Schalper KA, Carleton M, Zhou M, Chen T, Feng Y, Huang SP, Walsh AM, Baxi V, Pandya D, Baradet T, Locke D, Wu Q, Reilly TP, Phillips P, Nagineni V, Gianino N, Gu J, Zhao H, Perez-Gracia JL, Sanmamed MF, **Melero I**. **Nature Medicine** 2020. May;26(5):688-692. Epub 2020 May 11. PMID: 32405062

2. Marquez-Rodas I, Longo F, Rodriguez-Ruiz ME, Calles A, Ponce S, Jove M, Rubio-Viqueira B, Perez-Gracia JL, Gomez-Rueda A, Lopez-Tarruella S, Ponz-Sarvisé M, Alvarez R, Soria-Rivas A, de Miguel E, Ramos-Medina R, Castañón E, Gajate P, Sempere-Ortega C, Jimenez-Aguilar E, Aznar MA, Calvo A, Lopez-Casas PP, Martin-Algarra S, Martin M, Tersago D, Quintero M, **Melero I**. Intratumoral nanoplexed poly I:C BO-112 in combination with systemic anti-PD-1 for patients with anti-PD-1-refractory tumors. **Science Translational Medicine**. 2020 Oct 14;12(565):eabb0391. PMID: 33055241
3. CXCR1 and CXCR2 Chemokine Receptor Agonists Produced by Tumors Induce Neutrophil Extracellular Traps that Interfere with Immune Cytotoxicity. Teijeira Á, Garasa S, Gato M, Alfaro C, Migueliz I, Cirella A, de Andrea C, Ochoa MC, Otano I, Etxeberria I, Andueza MP, Nieto CP, Resano L, Azpilikueta A, Allegretti M, de Pizzol M, Ponz-Sarvisé M, Rouzaut A, Sanmamed MF, Schalper K, Carleton M, Mellado M, Rodriguez-Ruiz ME, Berraondo P, Perez-Gracia JL, **Melero I**. **Immunity**. 2020 Apr 6. pii: S1074-7613(20)30089-3. PMID: 3228925
4. Intratumor Adoptive Transfer of IL-12 mRNA Transiently Engineered Antitumor CD8+T Cells. Etxeberria I, Bolaños E, Quetglas JI, Gros A, Villanueva A, Palomero J, Sánchez-Paulete AR, Piulats JM, Matias-Guiu X, Olivera I, Ochoa MC, Labiano S, Garasa S, Rodriguez I, Vidal A, Mancheño U, Hervás-Stubbs S, Azpilikueta A, Otano I, Aznar MA, Sanmamed MF, Inogés S, Berraondo P, Teijeira Á, **Melero I**. **Cancer Cell**. 2019 Dec 9;36(6):613-629.e7. PMID: 31761658
5. Prophylactic TNF blockade uncouples efficacy and toxicity in dual CTLA-4 and PD-1 immunotherapy. Perez-Ruiz E, Minute L, Otano I, Alvarez M, Ochoa MC, Belsue V, de Andrea C, Rodriguez-Ruiz ME, Perez-Gracia JL, Marquez-Rodas I, Llacer C, Alvarez M, de Luque V, Molina C, Teijeira A, Berraondo P, **Melero I**. **Nature**. 2019 May;569(7756):428-432.. PMID: 31043740
6. Neoadjuvant nivolumab modifies the tumor immune microenvironment in resectable glioblastoma. Schalper KA, Rodriguez-Ruiz ME, Diez-Valle R, López-Janeiro A, Porciuncula A, Idoate MA, Inogés S, de Andrea C, López-Díaz de Cerio A, Tejada S, Berraondo P, Villarroya-Espindola F, Choi J, Gúrpide A, Giraldez M, Goicoechea I, Gallego Perez-Larraya J, Sanmamed MF, Perez-Gracia JL, **Melero I**. **Nature Medicine**. 2019 Mar;25(3):470-476. doi: 10.1038/s41591-018-0339-5. PMID: 30742120
7. Immunotherapeutic effects of intratumoral nanoplexed poly I:C. Aznar MA, Planelles L, Perez-Olivares M, Molina C, Garasa S, Etxeberria I, Perez G, Rodriguez I, Bolaños E, Lopez-Casas P, Rodriguez-Ruiz ME, Perez-Gracia JL, Marquez-Rodas I, Teijeira A, Quintero M, **Melero I**. **J Immunother Cancer**. 2019 May 2;7(1):116. PMID: 31046839.
8. An RNA toolbox for cancer immunotherapy. Pastor F, Berraondo P, Etxeberria I, Frederick J, Sahin U, Gilboa E, **Melero I**. **Nat Rev Drug Discov**. 2018 Oct;17(10):751-767. Review. PMID: 30190565
9. Combined immunotherapy encompassing intratumoral poly-ICLC, dendritic-cell vaccination and radiotherapy in advanced cancer patients. Rodríguez-Ruiz ME, Perez-Gracia JL, Rodríguez I, Alfaro C, Oñate C, Pérez G, Gil-Bazo I, Benito A, Inogés S, López-Díaz de Cerio A, Ponz-Sarvisé M, Resano L, Berraondo P, Barbés B, Martin-Algarra S, Gúrpide A, Sanmamed MF, de Andrea C, Salazar AM, **Melero I**. **Ann Oncol**. 2018 May 1;29(5):1312-1319. PMID: 29554212
10. Changes in serum interleukin-8 (IL-8) levels reflect and predict response to anti-PD-1 treatment in melanoma and non-small-cell lung cancer patients. Sanmamed MF, Perez-Gracia JL, Schalper KA, Fusco JP, Gonzalez A, Rodriguez-Ruiz ME, Oñate C, Perez G, Alfaro C, Martín-Algarra S, Andueza MP, Gúrpide A, Morgado M, Wang J, Bacchiocchi A, Halaban R, Kluger H, Chen L, Szoln M, **Melero I**. **Ann Oncol**. 2017 Aug 1;28(8):1988-1995. PMID: 28595336
11. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial. El-Khoueiry AB, Sangro B, Yau T, (...) Dastani HB, **Melero I**. **Lancet**. 2017 Jun 24;389(10088):2492-2502. PMID: 28434648
12. Cancer Immunotherapy with Immunomodulatory Anti-CD137 and Anti-PD-1 Monoclonal Antibodies Requires BATF3-Dependent Dendritic Cells. Sánchez-Paulete AR, Cueto FJ, Martínez-López M, Labiano S, Morales-Kastresana A, Rodríguez-Ruiz ME, Jure-Kunkel M, Azpilikueta A, Aznar MA, Quetglas JI, Sancho D, **Melero I**. **Cancer Discov**. 2016 Jan;6(1):71-9. doi: 10.1158/2159-8290.CD-15-0510. Epub 2015 Oct 22.
13. Evolving synergistic combinations of targeted immunotherapies to combat cancer. **Melero I**, Berman DM, Aznar MA, Korman AJ, Pérez Gracia JL, Haanen J. **Nat Rev Cancer**. 2015 Aug;15(8):457-72. Review. PMID: 26205340
14. Focusing and sustaining the antitumor CTL effector killer response by agonist anti-CD137 mAb. Weigel B, Bolaños E, Teijeira A, Martínez-Forero I, Labiano S, Azpilikueta A, Morales-Kastresana A, Quetglas JI, Wagena E, Sánchez-Paulete AR, Chen L, Friedl P, **Melero I**. **Proc Natl Acad Sci U S A**. 2015 Jun 16;112(24):7551-6. PMID: 26034288
15. Monoclonal antibodies against the 4-1BB T-cell activation molecule eradicate established tumors. Melero I, Shuford WW, Newby SA, Aruffo A, Ledbetter JA, Hellström KE, Mittler RS, Chen L. **Nature Medicine**. 1997 Jun;3(6):682-5. PMID: 9176498