

## Curriculum Vitae sketch (October 2023)

**Name:** J. Miguel López-Botet Arbona

**Institution:** Univ. Pompeu Fabra / Hospital del Mar Research Institute

**Position title:** Professor / Staff

**Birth date:**

**Address:**

**Phone:**

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### 1. Education / Training

Degree	Institution	Dates
M.D.	Univ. de Valencia	1971-1977
Ph.D.	Univ. Autónoma de Madrid (UAM)	1979-1982
Medical Resident in Immunology	Hospital Puerta de Hierro (UAM)	1979-1982

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### 2. Professional academic positions

Dates	Position	Department & Institution
1983-1985	Postdoctoral fellow	Ludwig Institute for Cancer Research, Lausanne
1985-2000	Staff	Dept. of Immunology, Hospital de la Princesa (UAM)
1987-1999	Assistant Professor	Univ. Autónoma de Madrid (UAM)
2000-	Full Professor of Immunology	Univ. Pompeu Fabra (Dpt. of Medicine and Life Sciences)
2006-2015	Scientific Director	Hospital del Mar Research Institute (IMIM)
2007-2019	Head	Immunology Service (Hospital del Mar)
2019-	Staff	Immunology Lab. (Dpt. of Pathology, Hospital del Mar)

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### 3. Past publications (Web of Science, October 2023)

Selected out of a **total of 199** articles/reviews, **117** as main author (first, senior and/or corresponding).

Citations: **13324**. H-index: **64** (as main author C: **8378**. H-index: **50**)

(C: citations)

#### Original articles

1. Aramburu J., Balboa M.A., Ramírez A., Silva A., Acevedo A., Sánchez-Madrid F., O. de Landázuri M., López-Botet M. (1990). A novel functional cell surface dimer (Kp43) expressed by natural killer cell and g/d TCR+ T lymphocytes. I. Inhibition of the Interleukin-2 dependent proliferation by anti Kp43 monoclonal antibody. J. Immunol. 144: 3238-3247. (C: 165)
2. Pérez-Villar J.J., Melero I, Rodríguez A., Carretero M., Aramburu J., Sivori S., Orengo A.M., Moretta A., López-Botet M. (1995). Functional ambivalence of the kp43 (CD94) NK cell-associated surface antigen. J. Immunol. 154:5779-5788. (C: 127)
3. Chang C., Rodríguez A., Carretero M., López-Botet M., Phillips J.H., Lanier L.L. (1995). Molecular characterization of human CD94: a type II membrane glycoprotein related to the C-type lectin superfamily Eur. J. Immunol. 25:2433-2437. (C: 208)
4. Carretero M., Cantoni C., Bellón T., Bottino C., Biassoni R., Rodríguez A., Pérez-Villar J.J., Moretta A., Moretta L., López-Botet M. (1997). The CD94 and NKG2-A C-type lectins covalently assemble to form an inhibitory receptor for HLA class I molecules. Eur. J. Immunol. 27:563-567. (C: 262)
5. Colonna M\*, Navarro F., Bellón T., Llano M., García P., Samaridis J., Angman L., Cella M., López-Botet M\*. (1997) A common inhibitory receptor for Major Histocompatibility Complex Class I molecules on human lymphoid and myelomonocytic cells. J. Exp. Med. 186:1809-1818. (C: 796) (\* shared credit)

6. Lee N., Llano M., Carretero M., Ishitani A., Navarro F., López-Botet M\*, Geraghty DE.\* (1998). HLA-E is a major ligand for the natural killer inhibitory receptor CD94/NKG2A. Proc.Natl.Acad.Sci.U.S.A. 95:5199-5204. (C: 832) (\* shared credit)
7. Carretero M, Palmieri G, Llano M, Tullio V, Santoni A, Geraghty DE, López-Botet M. (1998) Specific engagement of the CD94/NKG2-A killer inhibitory receptor by the HLA-E class Ib molecule induces SHP-1 phosphatase recruitment to tyrosine-phosphorylated NKG2A: evidence for receptor function in heterologous transfectants. Eur J Immunol. 28:1280-91. (C:106)
8. Llano, M., Lee N., Navarro F., García P., Albar J.P., Geraghty D.E., López-Botet M. (1998). HLA-E-bound peptides influence recognition by inhibitory and triggering CD94/NKG2 receptors: preferential response to an HLA-G-derived nonamer. Eur J Immunol 28:2854-2863. (C: 311)
9. Navarro, F., Llano M., Bellón T., Colonna M., Geraghty D.E., López-Botet M. (1999). The ILT2 (LIR-1) and CD94/NKG2A NK cell receptors respectively recognize HLA-G1 and HLA-E molecules co-expressed on target cells. Eur. J.Immunol. 29:277-283. (C: 315)
10. García P., Llano M., Heredia A.B., Willberg C., Caparrós E., Aparicio P., Braud, V.M., López-Botet M. (2002) Human T cell receptor-mediated recognition of HLA-E. Eur.J. Immunol. 32:936-944 (C: 87)
11. Bellón T., Kitzig F., Sayós J., and López-Botet M. (2002) Mutational analysis of Immunoreceptor Tyrosine-based Inhibition Motifs of the Ig-like transcript 2 (CD85j) leukocyte receptor. J. Immunol. 168:3351-3359 (C: 43)
12. Llano M., Gumá M., Ortega M., Angulo A., López-Botet M. (2003). Differential effects of US2, US6 and US11 human cytomegalovirus proteins on HLA class Ia and HLA-E expression: impact on target susceptibility to NK cell subsets. Eur J Immunol. 33:2744-2754 (C: 54)
13. Gumá M., Angulo, A., Vilches, C., Gómez-Lozano N., Malats N., López-Botet M. (2004). Imprint of human cytomegalovirus infection on the NK cell receptor repertoire. Blood. 104: 3664-3671. (C: 637)
14. Gumá M., Busch L.K., Salazar-Fontana L.I., Bellosillo B., Morte C., García P., López-Botet M. (2005) The CD94/NKG2C killer lectin-like receptor constitutes an alternative activation pathway for a subset of CD8(+) T cells. Eur.J.Immunol. 35: 2071-2080 (C:67)
15. Gumá M, Budt M, Sáez A, Brckalo T, Hengel H, Angulo A\*, López-Botet M\*. (2006) Expansion of CD94/NKG2C+ NK cells in response to human cytomegalovirus-infected fibroblasts. Blood. 107:3624-3631 (C: 324) (\* shared credit)
16. Gumá M, Cabrera C, Erkizia I, Bofill M, Clotet B, Ruiz L, López-Botet M (2006) Human cytomegalovirus infection is associated with increased proportions of NK cells that express the CD94/NKG2C receptor in aviremic HIV-1 infected patients. J. Inf. Dis. 194:38-41. (C: 200)
17. Sáez-Borderías A, Gumá M, Angulo A, Bellosillo B, Pende D, López-Botet M. (2006) Expression and function of NKG2D in CD4+ T cells specific for human cytomegalovirus. Eur. J. Immunol. 36:3198-206 (C:100)
18. Magri G, Muntasell A, Romo N, Sáez-Borderías A, Pende D, Geraghty DE, Hengel H, Angulo A, Moretta A, López-Botet M. (2011) NKp46 and DNAM-1 NK cell receptors drive the response to human cytomegalovirus infected myeloid dendritic cells overcoming viral immune evasion strategies. Blood 117:848-56. (C:104)
19. Noyola DE, Fortuny C, Muntasell A, Noguera-Julian A, Muñoz-Almagro C, Alarcón A, Juncosa T, Moraru M, Vilches C, López-Botet M. (2012) Influence of congenital human cytomegalovirus infection and the NKG2C genotype on NK-cell subset distribution in children. Eur. J. Immunol. 42:3256-66. (C:74)

## Reviews

1. López-Botet M, Bellón T. Natural killer cell activation and inhibition by receptors for MHC class I. (1999) Curr. Opin. Immunol. 11: 301-307 (C: 140)
2. López-Botet M; Llano M; Navarro F; Bellón T. (2000) NK cell recognition of non-classical HLA class I molecules Sem. Immunol. 12::109-119 (C: 152)

## **4. Recent publications** (Web of Science, October 2023)

Selected out of 49 articles/reviews in the last 10 years

(C: citations WOS 10/2023)

## Original articles

1. Muntasell A, López-Montañés M, Vera A, Heredia G, Romo N, Peñafiel J, Moraru M, Vila J, Vilches C, López-Botet M. (2013) NKG2C zygosity influences CD94/NKG2C receptor function and the NK-cell compartment redistribution in response to human cytomegalovirus. Eur J Immunol. 43:3268-78. (C:69)

2. Crespo M, Yelamos J, Redondo D, Muntasell A, Perez-Saéz MJ, López-Montañés M, García C, Torio A, Mir M, Hernández JJ, López-Botet M\*, Pascual J\*. (2015) Circulating NK-cell subsets in renal allograft recipients with anti-HLA donor-specific antibodies. Am. J. Transplant. 15:806-14. **(C:41)** (\*) shared credit
3. Costa-García M, Vera A, Moraru M, Vilches C, López-Botet M\*, Muntasell A\*. (2015) Antibody-mediated response of NKG2Cbright NK cells against human cytomegalovirus. J. Immunol. 194:2715-24. **(C:83)** (\*) shared credit
4. Muntasell A, Pupuleku A, Cisneros E, Vera A, Moraru M, Vilches C, López-Botet M. (2016) Relationship of NKG2C Copy Number with the Distribution of Distinct Cytomegalovirus-Induced Adaptive NK Cell Subsets. J. Immunol. 196:3818-27. **(C:47)**
5. Redondo-Pachón D\*, Crespo M\*, Yélamos J, Muntasell A, Pérez-Sáez MJ, Pérez-Fernández S, Vila J, Vilches C, Pascual J\*, López-Botet M.\* (2017) Adaptive NKG2C+ NK cell response and the risk of cytomegalovirus infection in kidney transplant recipients. J. Immunol. 198:94-101. **(C:45)** (\*) shared credit
6. López-Montañés M, Alari-Pahissa E, Sintés J, Martínez-Rodríguez JE, Muntasell A, López-Botet M. (2017) Antibody-Dependent NK Cell Activation Differentially Targets EBV-Infected Cells in Lytic Cycle and Bystander B Lymphocytes Bound to Viral Antigen-Containing Particles. J. Immunol. 15:199 :656-665. **(C:21)**
7. Pupuleku A, Costa-García M, Farré D, Hengel H, Angulo A, Muntasell A\*, López-Botet M\*. (2017) Elusive Role of the CD94/NKG2C NK Cell Receptor in the Response to Cytomegalovirus: Novel Experimental Observations in a Reporter Cell System. Front. Immunol. 24; 8:1317. (\*) shared credit **(C:18)**
8. Muntasell A\*, Rojo F\*, Servitja S, Rubio-Pérez C, Cabo M, Tamborero D, Costa-García M, Martínez-García M, Menéndez S, Vázquez I, Lluch A, González-Pérez A, Rovira A, López-Botet M\*, Albanell J\*. (2018) NK cell infiltrates and HLA class I expression in primary HER2+ breast cancer predict and uncouple pathological response and disease-free survival. Clin. Cancer Res. 25:1535-1545. (\*) shared credit **(C:65)**
9. Muntasell A\*, Servitja S\*, Cabo M, Bermejo B, Pérez-Buira S, Rojo F, Costa-García M, Arpi O, Moraru M, Serrano L, Tusquets I, Martínez MT, Heredia G, Vera A, Martínez-García M, Soria L, Comerma L, Santana-Hernández S, Eroles P, Rovira A, Vilches C, Lluch A, Albanell J\*, López-Botet M\*. (2019) High Numbers of Circulating CD57+ NK Cells Associate with Resistance to HER2-Specific Therapeutic Antibodies in HER2+ Primary Breast Cancer. Cancer Immunol. Res. 7:1280-1292. (\*shared credit) **(C:22)**
10. Ataya M\*, Redondo-Pachón D\*, Llinàs-Mallol L, Yélamos J, Heredia G, Pérez-Sáez MJ, Vila J, Costa-García M, Raich-Regué D, Vilches C, Pascual J, Crespo M\*, López-Botet M\*. (2020) Pretransplant adaptive NKG2C+ NK cells protect against cytomegalovirus infection in kidney transplant recipients. Am. J. Transplant. 20:663-676. **(C:14)** (\*shared credit)
11. Alari-Pahissa E, Ataya M, Moraitis I, Campos-Ruiz M, Altadill M, Muntasell A, Moles A, López-Botet M. (2021) NK cells eliminate Epstein-Barr virus bound to B cells through a specific antibody-mediated uptake. PLoS Pathog. 17:e1009868. **(C:10)**
12. Ataya M\*, Redondo-Pachón D\*, Llinàs-Mallol L, Yélamos J, Alari-Pahissa E, Pérez-Sáez MJ, Altadill M, Raich-Regué D, Vilches C, Pascual J, Crespo M\*, López-Botet M\*. (2021) Long-Term Evolution of the Adaptive NKG2C+ NK Cell Response to Cytomegalovirus Infection in Kidney Transplantation: An Insight on the Diversity of Host-Pathogen Interaction. J. Immunol. 207:1882-1890. (\*shared credit) **(C:1)**
13. Cabo M, Santana-Hernández S, Costa-García M, Rea A, Lozano-Rodríguez R, Ataya M, Balaguer F, Juan M, Ochoa MC, Menéndez S, Comerma L, Rovira A, Berraondo P, Albanell J, Melero I, López-Botet M., Muntasell A. (2021) CD137 Co-stimulation Counteracts TGFβ Inhibition of NK-cell Antitumor Function. Cancer Immunol. Res. 9:1476-1490. **(C:13)**
14. Falco M, Meazza R, Alicata C, Canevali P, Muntasell A, Bottino C, Moretta L, Pende D, Lopez-Botet M. (2022) Epitope characterization of a monoclonal antibody that selectively recognizes KIR2DL1 allotypes. HLA. 100:107-118. **(C:2)**

## Reviews

1. López-Botet M, Muntasell A, Vilches C. (2014) The CD94/NKG2C+ NK-cell subset on the edge of innate and adaptive immunity to human cytomegalovirus infection. Semin. Immunol. 26:145-51. **(C:82)**
2. Muntasell A, Cabo M, Servitja S, Tusquets I, Martínez-García M, Rovira A, Rojo F, Albanell\* J, López-Botet M\*. (2017) Interplay between Natural Killer Cells and Anti-HER2 Antibodies: Perspectives for Breast Cancer Immunotherapy. Front. Immunol. 13; 8:1544. **(C:37)** (\*) shared credit
3. Muntasell A, Ochoa MC, Cordeiro L, Berraondo P, López-Díaz de Cerio A, Cabo M, López-Botet M., Melero I. (2017) Targeting NK-cell checkpoints for cancer immunotherapy. Curr. Opin. Immunol. 45:73-81. **(C:126)**
4. López-Botet M, Vilches C, Redondo-Pachón D, Muntasell A, Pupuleku A, Yélamos J, Pascual J, Crespo M (2017) Dual role of Natural Killer cells on graft rejection and control of cytomegalovirus infection in renal transplantation. Front. Immunol. 8:166 **(C:36)**
5. López-Botet M, De Maria A, Muntasell A, Della Chiesa M, Vilches C. (2023) Adaptive NK cell response to human cytomegalovirus: Facts and open issues. Semin. Immunol. 65:101706. **(C:5)**

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## **5. Research Grants**

Continued funding obtained as PI since 1986: 28 grants from public (national: FIS-ISCI, MEC/MINECO/AEI; international: EC, SUDOE) and private (Marató TV3, AECC, UK WCR)

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### Active in the last 6 years

- Development of molecular tools to enhance NK cell-mediated ADCC responses elicited by trastuzumab against breast cancer (M. López-Botet, coordinator). Worldwide Cancer Research (Formerly AICR, 15-1146) (2015-2018). Co-PI: A. Muntasell. IMIM
  - Targeting Natural Killer cells against cytomegalovirus (TANKACY; coordinated). EC-Ministry of Economy and Competitiveness. Infect ERA program. (PCIN-2015-191-C02-01; 2015-2018). IMIM
  - Potenciación de la citotoxicidad dependiente de anticuerpo mediada por linfocitos NK para la inmunoterapia del cáncer (coordinated). Fundación Científica Asociación Española contra el Cáncer (AECC GCB15152947MELE; 2015-2019). Co-PI: A. Muntasell. Univ. Pompeu Fabra
  - Uncovering resistance to monoclonal antibodies in colorectal and breast cancer. (J. Albanell coordinator). Proyecto Integrado de Excelencia ISCI (PIE 2015/00008, 2015-2019). Co-PI: A. Muntasell IMIM
  - Molecular basis of the adaptive NK cell response to human cytomegalovirus: role of viral factors. (M. López-Botet, coordinator). Programa Estatal I+D Retos, Ministry of Economy and Competitiveness (SAF2016-80363-C2-1-R; 2017-2019). Univ. Pompeu Fabra
  - Manufacturing tumor-reactive Natural Killer cells (MATURE-NK). Coordinator: Ulrike Köhl (Hannover) EC Horizon 2020. Marie Skłodowska Curie-Innovative Training Network No. 765104 (2019-2022). Univ. Pompeu Fabra Co-PI A.Muntasell. UPF.
  - Adaptive NK cell-mediated response to cytomegalovirus in the context of immunosuppression: clinical implications in renal transplantation. Fundació La Marató de TV3 (P 105/U/2018) (2019-2022). IMIM.
  - Involvement of HLA-E in the adaptive NKG2C+ NK cell response to cytomegalovirus infection: lessons from immunosuppression and clinical implications (M. López-Botet, coordinator). Agencia Estatal de Investigación PID2019-110609RB-C21 (2020-2023). Univ. Pompeu Fabra.
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## **6. License agreements, clinical trials (phase I-II), other contracts with companies**

Active license agreements (UPF Business Shuttle) (n:17) for the commercialization of hybridomas producing monoclonal antibodies established with the following companies: Beckman-Coulter (USA); Miltenyi Biotech (Germany); Becton-Dickinson/Pharmingen (USA); Tonbo Biotech/Cytex (USA); ExBio (Czech Republic); e-Bioscience (Affimetrix) (USA), Biologend (USA), Immunostep (Spain).

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## **7. Patents**

Title: "Nucleic acids encoding KP43 protein and antigenic fragments thereof" (U.S. patent n. 5811284). Divisional U.S. Patent Application (n. 09/156.527) "Purified mammalian NK antigens and related reagents" (filed September 17, 1998)  
Inventors: Chiwen Chang, José Aramburu, Miguel López-Botet, Joseph H. Phillips and Lewis L. Lanier.

Exploitation:  No  Yes

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## **8. International Conferences**

*Invited speaker in the last 10 years.*

1. International Congress of Immunology (ICI-2013) "Adaptive reconfiguration of the human NK cell compartment in response to cytomegalovirus" (Milan 2013)
2. 4th International workshop on CMV and Immunosenescence "Adaptive reconfiguration of the human NK cell compartment in response to cytomegalovirus: a different perspective of the host-pathogen interaction" (Parma 2013)

3. Natural Killer cell symposium. German Society for Immunology. "Adaptive reconfiguration of the human NK-cell compartment in response to cytomegalovirus infection" (Hannover 2014)
  4. European Congress of Immunology (ECI). "Role of the CD94/NKG2C activating receptor in the adaptive-like human NK cell response to cytomegalovirus" (Vienna 2015)
  5. 8th International Congenital CMV Conference and 18th International CMV Workshop. "NK cell response to HCMV infection: overview and studies in immunosuppressed kidney transplant recipients" (Cambridge 2022)
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## **9. PhD Thesis Director**

Total number of thesis accomplished: 28 (8 co-supervised).  
See details at: <https://producciocientifica.upf.edu>

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## **10. Other professional activities**

### **Management**

- Director. Department of Experimental and Health Sciences (DCEXS-UPF) (2002-2004)
- Director. Hospital del Mar Medical Research Institute (IMIM) (2006-2015)
- Program Director. Hospital del Mar Medical Research Institute (IMIM) (2015-2019)
- Research Group Leader DCEXS/MELIS (UPF 2000-) and IMIM (2007- )

### **Committees**

- President. Research Committee. University Hospital La Princesa. Madrid (1988-91). Development of Research Unit
- Research and teaching coordinator. University Hospital La Princesa. Madrid (1995-1996).
- President. Research Committee. University Hospital La Princesa (1996-1998).
- Member. National Immunology Committee (Ministry of Health) (1998-1999)
- Member. Scientific Committee of Barcelona Biomedical Research Park Foundation (PRBB) (2002-2004; 2007-2011)
- Member. Committee for Research and Innovation in Health (Generalitat de Catalunya) (2011- 2015)
- Member. Scientific Advisory Committee. Fundació La Marató de TV3 (2008-2015)
- Member. Committee of Medical Sciences and Health. AQU (Generalitat de Catalunya (2014-2018)
- External Scientific Advisory Board of Hospital Research Institutes (ISCIII): Valdecilla, Santander (2011-2019); La Princesa, Madrid (2010- )

### **Scientific societies membership**

- Member: Spanish Society for Immunology (SEI); American Association of Immunologists (AAI); Spanish Society of Allergy and Clinical Immunology (SEAIC); Society for Natural Immunity (SNI); Henry Kunkel Society (HKS).
- Vice President. Spanish Society for Immunology (1996-1999).
- President. Spanish Society for Immunology (2004-2008).
- President. Society for Natural Immunity (2005-2008)

### **Teaching:**

- Immunology courses for undergraduate and PhD students. UAM (1987-1999)
- Immunology course for undergraduate students UPF. Human Biology (2000- ) and Medicine degrees (2010- )
- International Master and PhD Program. UPF (2003-)
- PhD Thesis supervisor (see section 9)

### **Clinical duties:**

Staff responsible of diagnostic laboratories (Autoimmunity and Flow Cytometry). Dept. of Immunology, Hospital de la Princesa (1985-1999)

### **Reviewer:**

FIS-ISCIII (Ministry of Health, Spain), ANEP/MEC (Ministry of Education and Science, Spain), AEI (State Research Agency, Spain), Wellcome Trust (UK), Medical Research Council (UK), Telethon (Italy), AIRC (Italy), INSERM (France), ANR (France). H