

Curriculum Vitae Sketch (February 2017)

Name: J. Miguel López-Botet Arbona

Position title: Professor / Head

Institution: Univ. Pompeu Fabra / Immunology Service, Hospital del Mar

Birth date: 17/05/1954 **Citizenship:** Spanish

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1. Education / Training

Degree	Institution	Year(s)
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

2. Professional academic positions

Dates (from-until)	Position	Department & Institution
1983-1985	Postdoctoral fellow	Ludwig Institute for Cancer Research, Lausanne
1985-2000	Staff member	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. Health and Experimental Sciences)
2006-2015	Scientific Director	IMIM (Hospital del Mar Medical Research Institute)
2007-	Head	Immunology Service (Hospital del Mar)

3. Selected past contributions (from a total of 164. PubMed)

Total citations: 10102. H-index: 51 (Web of Science, February 2016)

(IF: impact factor; C: citations.)

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. (IF: 5.6 ; C: 151)
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. (IF: 5.6 ;C: 130)
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. (IF: 5.2; C: 191)
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. (IF: 5.2; C: 224)
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. (IF: 14.5; C: 637)
6. Lee, N., Llano M., Carretero M., Ishitani A., Navarro F., López-Botet M*, and D.E. Geraghty*. (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. (IF: 9.4; C: 593) (* shared credit)
7. Llano, M., Lee N., Navarro F., García P., Albar J.P., Geraghty D.E., and 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. (IF: 5.2; C: 223)
8. Navarro, F., Llano M., Bellón T., Colonna M., Geraghty D.E., and 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. (IF: 5.2; C: 266)

9. López-Botet M, Bellón T. Natural killer cell activation and inhibition by receptors for MHC class I. (1999) Curr Opin Immunol 11: 301-307 (IF:10.8; C: 127)
10. García P., Llano M., Heredia A.B., Willberg C., Caparrós E., Aparicio P., Braud, V.M., and López-Botet M. (2002) Human T cell receptor-mediated recognition of HLA-E. Eur.J. Immunol. 32:936-944 (IF: 5.2; C: 58)
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 (IF: 5.6; C: 37)
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 (IF: 5.2; C: 45)
13. Gumá, M., Angulo, A., Vilches, C., Gómez-Lozano, N., Malats, N., and López-Botet, M. (2004). Imprint of human cytomegalovirus infection on the NK cell receptor repertoire. Blood. 104: 3664-3671. (IF: 10.6; C: 293)
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 (IF: 5.2; C:34)
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 (IF: 10.6; C: 174) (*) 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. (IF: 5.6; C: 115)
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 (IF: 5.2; C:58)

4. Research Grants

As Principal Investigator (last 6 years).

- Characterization of the innate immune response to human cytomegalovirus: implications for the pathogenesis of vascular disease (coordinator). Subproject 1 (PI): Characterization of the innate immune response and viral subversion mechanisms in cytomegalovirus infection. Plan Nacional I+D (SAF2010-22153-C03-01; 2011-2013). Univ. Pompeu Fabra.
- New protocols for immunotherapy: Production of activated NK cells for clinical use. EU SUDOE Program. (SOE2/P1/E341 – CiNK; 2011-2012). IMIM (Hospital del Mar Medical Research Institute).
- Multiple Sclerosis Network (REEM, Instituto de Salud Carlos III, Ministry of Health; 2013-). IMIM (Hospital del Mar Medical Research Institute)
- Natural killer cell-based anti-cancer Immunotherapies. NATURIMMUN: Research training in molecular medicine and biotechnology business. (FP7 Marie Curie Training Network; FP7-PEOPLE- 2012-ITN-3170132013-2016). Univ. Pompeu Fabra.
- Evaluation of NK cell contribution to chronic kidney allograft rejection in response to HLA-specific alloantibodies, genetic mismatch and CMV infection. La Marató TV3 Foundation (137/C/2012; 2013-2015). Univ. Pompeu Fabra
- Analysis of the human NK-cell receptor repertoire and its adaptive reconfiguration by HCMV infection: mechanisms and implications in immunity. Programa Estatal I+D Ministry of Economy and Competitiveness (SAF2013-49063-C2-1-R; 2014-2016). Univ Pompeu Fabra.
- 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). EU-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 ISCIII (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

5. License agreements, clinical trials (phase I-II), other contracts with companies

(Last 6 years) Indicate whether it is a service contract or it is a research collaboration

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

6. 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

7. Selected recent publications (2010-2017)

Articles

1. 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. (*) shared credit
2. Baía D, Pou J, Jones D, Mandelboim O, Trowsdale J, Muntasell A*, López-Botet M.* (2016) Interaction of the LILRB1 inhibitory receptor with HLA class Ia dimers. *Eur J Immunol.* 46:1681-90. (*) shared credit
3. 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.
4. Martínez-Rodríguez JE, Cobo-Calvo A, Villar LM, Munteis E, Blanco Y, Rasal R, Vera A, Muntasell A, Alvarez-Lafuente R, Saiz A, Alvarez-Cermeño JC, Martínez-Yélamos S, Roquer J, López-Botet M. (2016) Adaptive natural killer cell response to cytomegalovirus and disability progression in multiple sclerosis. *Mult Scler.* 22:741-52.
5. Costa-Garcia 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. (*) shared credit
6. 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. (*) shared credit
7. Noyola DE, Alarcón A, Noguera-Julian A, Muntasell A, Muñoz-Almagro C, García J, Mur A, Fortuny C, López-Botet M. (2015) Dynamics of the NK-cell subset redistribution induced by cytomegalovirus infection in preterm infants. *Hum Immunol.* 76:118-23.
8. 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:26)
9. 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:38)
10. Romo, N., G. Magri, A. Muntasell, G. Heredia, D. Baia, A. Angulo, M. Gumá, and M. Lopez-Botet. (2011). Natural killer cell-mediated response to human cytomegalovirus-infected macrophages is modulated by their functional polarization. *J. Leukoc. Biol.* 90: 717-726. (C:37)
11. 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:73)
12. Muntasell A, Magri G, Pende D, Angulo A, López-Botet M. (2010). Inhibition of NKG2D expression in NK cells by cytokines secreted in response to human cytomegalovirus infection. *Blood.* 115:5170-9. (C:31)

Reviews

1. 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.
 2. 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
 3. López-Botet M, Muntasell A, Martínez-Rodríguez JE, López-Montañés M, Costa-García M, Pupuleku A. (2016). Development of the adaptive NK cell response to human cytomegalovirus in the context of aging. *Mech Ageing Dev.* 158:23-6.
 4. 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:20)
 5. Muntasell A, Vilches C, Angulo A, López-Botet M. (2013) Adaptive reconfiguration of the human NK-cell compartment in response to cytomegalovirus: a different perspective of the host-pathogen interaction. *Eur J Immunol.* 43:1133-41 (C:45)
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8. International Conferences

Max. of 10 as invited speaker in the last 6 years.

1. Human Leukocyte Differentiation Antigen (HLDA) Conference. "CD94/NKG2 C-type lectin-like receptors" (Barcelona 2010)
 2. 7th International Innate Immunity Conference. "Characterization of the human NK cell response to cytomegalovirus-infected myelomonocytic cells" (Rhodes, 2010)
 3. NK2010 and 12th Meeting of the Society for Natural Immunity. "Human NK cell response to HCMV-infected myelomonocytic cells" (Dubrovnik, 2010)
 4. SIICA Workshop Innate immunity in the pathogenesis of immune-mediated human diseases. "NK cells and human cytomegalovirus". (Milano, 2010)
 5. European Congress of Immunology (ECI-2012) "Cytomegalovirus infection reshapes the human NK cell compartment promoting a persistent expansion of CD94/NKG2C+ cells" (Glasgow, 2012)
 6. International Congress of Immunology (ICI-2013) "Adaptive reconfiguration of the human NK cell compartment in response to cytomegalovirus" (Milan, 2013)
 7. 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)
 8. Natural Killer cell symposium. German Society for Immunology. "Adaptive reconfiguration of the human NK-cell compartment in response to cytomegalovirus infection" (Hannover 2014)
 9. European Congress of Immunology (ECI). " Role of the CD94/NKG2C activating receptor in the adaptive-like human NK cell response to cytomegalovirus" (Vienna 2015)
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9. Ph.D Thesis Director

Number of thesis accomplished: 23 (9 in the last 10 years)

10. Honours and other professional activities

Management

- President of the Research Committee. University Hospital La Princesa. Madrid (1988-91). Coordination of the Research Unit development.
- Research and teaching coordinator. Responsible of the Research Unit. University Hospital La Princesa (December 1995- September 1996).
- President of the Research Committee. University Hospital La Princesa (1996-1998).
- Member of the National Immunology Committee (Ministry of Health) (designated by S.E.I. 1998-1999)

- Secretary of the Department of Experimental and Health Sciences (DCEXS-UPF) (September 2001- June 2002)
- Director of the Department of Experimental and Health Sciences (DCEXS-UPF) (June 2002-May 2004)
- Member of the Scientific Committee of the Barcelona Biomedical Research Park Foundation (PRBB) (2002-2004; 2007-)
- Coordinator of the Immunology Unit (DCEXS-UPF) (2000-)
- Committee for Research an Innovation in Health (Generalitat de Catalunya) (2011-2015)
- Director of Hospital del Mar Medical Research Institute (IMIM) (2006-2015)

Scientific Societies

- Member of: 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 of the Spanish Society for Immunology (1996-1999).
- President of the Spanish Society for Immunology (2004-2008).
- President of the Society for Natural Immunity (2005-2008)

Teaching:

- Immunology courses for undergraduate and PhD students. UAM (1987-1999)
- Immunology course for undergraduate students UPF (2000-)
- International Master and PhD Program. UPF (2003-)

Clinical duties: Staff responsible of diagnostic laboratories (Autoimmunity and Cellular Immunology). Immunology Service. University Hospital la Princesa. (1985-1999)

Project reviewer: FIS-ISCI (Ministry of Health), ANEP, MEC (Ministry of Education and Science), Wellcome Trust (UK), Medical Research Council (UK), Telethon (Italy), AIRC (Italy), INSERM (France), ANR (France).