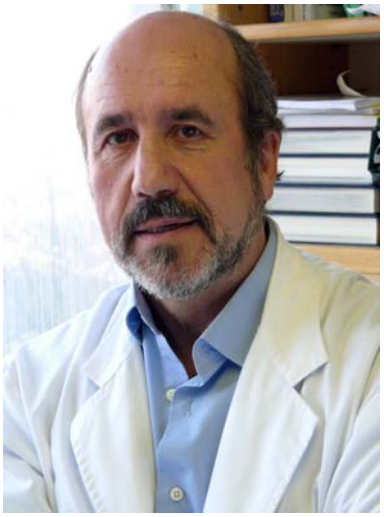

Curriculum vitae

Mariano Esteban Rodríguez

Date: September 11th 2009

NAME: MARIANO ESTEBAN RODRÍGUEZ

Prof. Esteban come back to Spain in 1992 after a 22 years of stay abroad in research and academic centres, to direct the newly created National Center for Biotechnology (CNB) of CSIC in Madrid. Within a short time, he recruited excellent Group Leaders and the Center won international credibility, as a place of excellence for basic science in the areas of health, agriculture and environment. In addition, the Centre became an attraction for industries by establishing models of collaboration with national and international companies. The Centre was subject to a recent peer evaluation review by an International Committee and was highly appraised as " centre of excellence in biotechnology".

Prof. Esteban is a well-recognised scientist with a long experience in molecular basis of pathogenesis by infectious agents. In particular, his group in Spain has made major contributions on the biology of vaccinia virus, the mechanism of action of interferons and development of vaccines against major diseases like Aids, malaria and leishmaniasis. His current work is supported by grants from national (MEyC; FIS; FIPSE, Foundation Botín), international agencies (NIH, USA; Bill y Melinda Gates, European Union) and industries.

Prof. Esteban has published over 250 papers in prestigious journals presented over 240 communications to international meetings and has given many seminars worldwide. He is a Member of a number of prestigious scientific international societies, Member of Editorial Boards and peer-review in major journals. He is also a Member of European and Spanish organizations He has organized international scientific meetings: President of XI International Poxvirus and Iridovirus Meeting, Toledo, 1996; President of the Fifth European Conference on Experimental AIDS Research (ECEAR-2000), Madrid, and Vice-president of the European Virology meeting in Madrid, in 2004. He participates in academic activities at the Autonomous University of Madrid and is member of the Royal Society of Pharmacy of Spain.

Education and degrees:

University of Santiago (Spain), M.S. (School of Pharmacy) 1967
University of Santiago (Spain), M.S. (Biological Sciences) 1972
University of Santiago (Spain), Ph.D. (Microbiology) 1970

Professional experience:

2003-present. Head of the Poxvirus and Vaccine group, CNB, CSIC
1992-2003. Director, Centro Nacional de Biotecnologia, CSIC, Madrid
1987-88. Sabbatical, Virology Division, National Institute for Medical Research, London. UK
1985 –1992. Professor, Departments of Biochemistry, Microbiology and Immunology. State University of New York, Health Science Center at Brooklyn, New York.
1982-1985. Associate Professor of Biochemistry, Microbiology and Immunology. State University of New York, Health Science Center at Brooklyn, New York.
1979-1982. Assistant Professor, Departments of Biochemistry, Microbiology and Immunology. State University of New York, Downstate Medical Center, Brooklyn, NY.
1978. Visiting Professor, Laboratory of Molecular Biology, University of Gent, Belgium.
1974-1977. Instructor, Department of Microbiology, Rutgers Medical School, New Jersey.

1970-1974. Research Associate, Virology Division, National Institute for Medical Research, Mill Hill, London, UK.

Teaching experience:

In the USA (Health Science Center, Brooklyn, NY)

l. Medical School Courses:

(a) General Biochemistry
(b) Nine-week selective course in General Biochemistry
(c) Microbiology and Immunology

2. School of Graduate Studies

(a) Molecular Genetics, GI l02, 4 credits
(b) Animal Virology, G l03, 6 credits
(c) Biochemistry, G l03, 8 credits
(d) Microbial Genetics, G l02, 6 credits
(e) Techniques in Molecular Cloning, G-507, 4 credits

Member of President's Advisory Committee on Research Allocation, l984-l987.
Member of Search Committee for Chairman of Microbiology and Immunology, 1981
Member of Search Committee for Chairman of Anatomy and Cell Biology, 1982-1984
Committee of the Graduate School Faculty, 1980
Co-Director of Molecular Genetics Course 1980-1986
Chairman, Recombinant Biohazards Committee, 1990-1992
Group Leader, AIDS Research, 1990-1993

In Spain-Universidad Autónoma, Madrid:
Immune System and Infectious Agents. 4 credits course 1996-present

Supervision and Direction of PhD Thesis:

1. Cabrera, Carlos V. (1978). Studies on the structure and genetic expression of poxvirus. Departments of Microbiology, Rutgers Medical School, CMDNJ, Piscataway, New Jersey and School of Pharmacy, Universidad de Santiago de Compostela, España.

2. Dallo, Shatha (1986). Isolation and characterization of spontaneous deletion mutants of vaccinia virus. Department of Microbiology and Immunology, SUNY Health Science Center at Brooklyn, NY. Premio extraordinario.

3. Maa, Juehn-Shin (1988). Biochemical and genetic characterization of immunodominant proteins of vaccinia virus. Department of Biochemistry, SUNY Health Science Center at Brooklyn, NY.

4. Kahn, Jeffrey S. (1990). Structural and functional studies of the vaccinia virus nucleic acid-dependent ATPase. Department of Microbiology and Immunology, SUNY Health Science Center at Brooklyn, NY.

5. Gong, Shiaoching (1990). Genetic variability of the 14 KDa envelope protein of vaccinia virus and involvement of this protein in virus-induced cell fusion. Department of Biochemistry, SUNY Health Science Center at Brooklyn, NY.

6. Chingfeng Lai (1990). Structural and functional characterization of the vaccinia virus 14 KDa envelope protein synthesized in Escherichia coli. Department of Biochemistry, SUNY Health Science Center at Brooklyn, NY.

7. Walter E. Demkowicz (1991). Identification and immunologic characterization of two antigenic core proteins of vaccinia virus. Department of Microbiology and Immunology, SUNY Health Science Center at Brooklyn, NY.

8. Rodriguez, J-R (1992). Characterization of attenuated variants of vaccinia virus as safe recombinant vaccines: application as a vaccine against AIDS. Department of Biochemistry, SUNY Health Science Center at Brooklyn, NY. Universidad Autónoma de Madrid. Premio extraordinario.

9. Irvine, Martin (1993). Identification and characterization of mutants of vaccinia virus with increased sensitivity to interferon. Department of Microbiology and Immunology. SUNY, Health Science Center at Brooklyn, N.Y.

10. Lee, S.B (1994). Structure and function of the interferon-induced double-stranded RNA-dependent protein kinase. Department of Microbiology, SUNY Health Science Center at Brooklyn, N.Y. Premio extraordinario.

11. Melková, Zora (1995). Macrophage antiviral activity: Role of Interferon-gamma and nitric oxide in the inhibition of vaccinia virus growth in macrophages. State University of New York, Health Science Center at Brooklyn, N.Y. USA.

12. Pavón, Miguel (1997). La proteina kinasa humana inducida por interferón y sensible a dsRNA (PKR): caracterización preliminar, proteinas de unión y algunas propiedades nuevas. Centro Nacional de Biotecnologia. Universidad Autónoma de Madrid

13. Collado, Manuel (1997). Modulación de la respuesta inmunitaria frente a la proteina env del VIH-1, mediante su fusión a antígenos del virus vaccinia. Centro Nacional de Biotecnologia. Universidad Autónoma de Madrid.

14. Vazquez, Isabel (1998). Caracterización de los dominios funcionales de la proteina de 14 kDa del virus vaccinia que juega un papél importante en la interacción virus-célula. Centro Nacional de Biotecnologia y Facultad de Farmacia de la Universidad de Santiago de Compostela.

15. Gonzalo, Rosa (1999). Desarrollo de estrategias de inmunización frente a Leishmania basadas en virus vaccinia recombinantes en el modelo murino. Centro Nacional de Biotecnologia, Universidad Autónoma de Madrid.

16. Moratilla, Marta (1999). Análisis estructurales y funcionales del genoma del virus Molluscum

contagiosum. Centro Nacional de Biotecnología. Universidad Autónoma de Madrid

17. Gil, Jesús (2000). Mecanismo de inducción de apoptosis y activación de NF-kB por la proteina quinasa dependiente de dsRNA, PKR. Centro Nacional de Biotecnología, Universidad Autónoma de Madrid. Premio extraordinario

18. Abaitúa, Fernando (2001). Potenciación de la respuesta inmune frente al antígeno de la envuelta del virus de la inmunodeficiencia humana (VIH-1) por recombinantes atenuados del virus vaccinia que expressan citoquinas I tipo Th1 (FN-gamma e IL-12). Universidad Autónoma de Madrid. Sobresaliente cum laude.

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19. Juan Carlos Gallego Gómez (2003). Biología celular de la infección y morfogénesis de mutantes atenuados del virus vaccinia. Universidad Autónoma de Madrid. Sobresaliente cum laude.

20. Carmen E. Gómez (2003). Respuesta inmune generada por sistemas combinados de vacunación frente a péptidos de la envuelta del VIH-1 incluidos en la proteína multiepitópica TAB-13. Universidad Autónoma de Madrid. Sobresaliente cum laude

21. Maria Angel García Chaves (2004). Mecanismo de acción y regulación de la proteína quinasa inducida por interferon, PKR. Universidad Autónoma de Madrid. 30 Abril de 2004. Sobresaliente cum laude. Premio Extraordinario de la UAM.

22. Soledad Blanco Chapinal (2005). Estrategias de modulación de la respuesta inmune frente a malaria en el modelo murino de Plasmodium yoelii. Universidad Autónoma de Madrid. 16 Diciembre de 2005. Sobresaliente Cum Laude.

23. Andrea Vandermeeren (2006).Study of the HCV polyprotein expresión from an inducible vaccinia virus recombinant and its implication in the host-cell responses. Universidad Autónoma de Madrid. 30 de Marzo de 2006. Sobresaliente cum laude.

24. Eva Pérez Jiménez (2006). Desarrollo de una vacuna frente a leishmaniasis. Universidad Autónoma de Madrid. 29 Mayo. Sobresaliente cum laude.

25. José Luis Nájera (2007). Caraterización “in vitro” e “in vivo” de los vectores atenuados de poxvirus MVA y NYVAC como candidatos vacunales frente al VIH/SIDA. Universidad Autónoma de Madrid. 23 de Noviembre. Sobresaliente “cum laude”

26. Elena Domingo Gil (2008). Caracterización de la apoptosis inducida por el sistema 2-5A/RNasa L. Universidad Autónoma de Madrid. 15 Febrero. Sobresaliente “cum laude”

Fellowships and Memberships:

1967-fellow of CSIC
1970- 1971- British Council fellow
1972-1974- EMBO fellow
1978- EMBO visiting Professor fellow

Honorary member of the following Societies:
American Society of Microbiology
American Society of Virology
British Society of Microbiology
Spanish Society of Microbiology
Harvey Society
The Society of Sigma Xi
New York Academy of Sciences
American Association for the Advancement of Science

Participation in Congresses and Scientific Conferences:
More than 240.

Since 2000:

1. Risco C., Rodriguez D., Lechaire J.P., Rodriguez J.R., Gaill F., Esteban M. and Carrascosa J.L. (2000). New insights on the structure and morphogenesis of vaccinia virus. XII European Congress on Electron Microscopy (Brno, Czech Republic, July 9-14).

2. Navarro, J., Abad, M.L., Resino, S., Jimenez, J.L., Canto, C., Rodriguez, D., Lopez, F., Esteban, M., Muñoz-Fernandez, M.A, and Fernandez-Cruz, E (2000). Effect of a gp120-depleted inactivatyed HIV-1 immunogen (Remunetm) on the control of nuclear factor kappa-B activation, cytokine production and augmentation of HIV-specific cytotoxic T lymphocytes. V European Conference on Experimental Aids Research (ECEAR). Madrid, June 16-19.

3. Ramirez, J.C., Gherardi, M. M, and Esteban, M (2000). IL-2 actions on the specific anti-env cell mediated immune response when delivered from vaccinia virus and bimodal DNA prime/boost vaccination regimen. . V European Conference on Experimental Aids Research (ECEAR). Madrid, June 16-19.

4. Gomez, C. E., Rodriguez, D., Rodriguez, J.R., Abaitua, F., Duarte, C, and Esteban, M (2000). A V3 loop multiepitope polypeptide of HIV-1 Env (TAB13) expressed from DNA, vaccinia virus WR and modified virus Ankara vectors induces peptide specific CD8+ T cell response in mice. V European Conference on Experimental Aids Research (ECEAR). Madrid, June 16-19.

5. Yang, W.Y.,Chang, L-Y., Gil, J., Esteban, M, and Roth, D (2000). The effect of specific phosphorylation of plant eIF-2a on plant translational control. Translational Control. Cold Spring Harbor . New York. August

6. Risco, C., Rodriguez, D., Rodriguez, J.R., Esteban, M and Carrascosa, J.L (2000). New insights on the structure and morphogenesis of vaccinia virus. XIII International poxvirus and Iridovirus symposium. Montpellier, France, September 2-6, p79.

7. Abaitua, F., Rodriguez, J.R., Rodriguez, D, and Esteban, M (2000). Coadministration of two vaccinia virus recombinants expressing HIV-env and interferon gamma results in a decreased in viral replication but favours a strong anti-env immune response. XIII International poxvirus and Iridovirus symposium. Montpellier, France, September 2-6, p138.

8. Gil, J, and Esteban, M (2000). Inhibition of vaccinia virus replication by the interferon-induced protein kinase PKR: mechanism of action. XIII International poxvirus and Iridovirus symposium. Montpellier, France, September 2-6, p154.

9. Ramirez, J.C., Gherardi, M, and Esteban, M (2000). IL-18 and IL-12 synergize in protection against vaccinia virus infection in mice and enhance the cellular immune response against the virus. XIII International poxvirus and Iridovirus symposium. Montpellier, France, September 2-6, p158.

10. Rodriguez, J.R., Gherardi, M., Rueda, G.G., Nussenzweig, R., Casal, I., Esteban, M, and Rodriguez, D (2000). Immunogenicity of parvovirus VLPs bearing a CD8+ T cell epitope of the CS protein of P. yoelii: enhanced CD8+ T cell response by boosting with vaccinia virus recombinant. XIII International poxvirus and Iridovirus symposium. Montpellier, France, September 2-6, p188.

11. Navarro, J., Abad, M.L., Resino, R., Jimenez, J.L., Cantó, C., Diaz, L., Rodriguez, D., Esteban, M, Muñoz-Fernandez, M.A and Fernandez-Cruz, E (2000). Effect of a Gp 120-depleted inactivated HIV-1 immunogen (Remune TM) on the control of nuclear factor Kappa-B activation, cytokine production and augmentation of HIV-1 specific cytotoxic T lymphocytes. Fifth. Eur. Conf. Exp. AIDS Res (ECEAR) 16-19 June, Madrid, Spain.

12. Ramirez, J.C., Gherardi, M.M., Rodriguez, D., Rodriguez, J.R and Esteban, M (2000). IL-12 actions on the specific anti-env cell mediated immune response when delivered from vaccinia virus in bimodal DNAprime /VV boost vaccination regimen. Fifth. Eur. Conf. Exp. AIDS Res (ECEAR) 16-19 June, Madrid, Spain.

13. García, M.A., Gil, J., Jimenez, V y Esteban, M (2001). La expresión de la proteina E3L del virus vaccinia en células 3T3 inhibe la apoptosis mediada por PKR. . VII Congreso Nacional de Virología. Valencia, 16-19 Sept. p94

14. Gil, J., García, M.A., Rullás, J., Alcamí, J y Esteban, M (2001). Inducción de la apoptosis y activación del factor de transcripción NF-kB por la enzima PKR. . VII Congreso Nacional de Virología. Valencia, 16-19 Sept. p79

15. Abaitua, F., Rodriguez, J.R., Rodriguez, D y Esteban, M (2001). La respuesta inmune frente a la proteina env del VIH se incrementa por la coexpresión de la proteina de choque térmico Hsp70. . VII Congreso Nacional de Virología. Valencia, 16-19 Sept. p74.

16. Gallego, J.C., Rodriguez, D., Risco, C., Cabezas, P., Carrascosa, J.L., Rodriguez, J.R y Esteban, M (2001). Morfogénesis de un mutante (M65) del virus vaccinia: caracterización estructural y funcional. VII Congreso Nacional de Virología. Valencia, 16-19 Sept. p162

17. Blanco, S., Rodriguez, J.R., Abaitua, F., Zavala, F., Esteban, M y Rodriguez, D (2001). Modulación por citoquinas de la respuesta inmune frente al antígeno CS de Plasmodium. . VII Congreso Nacional de Virología. Valencia, 16-19 Sept. p165

18. C.Gómez, C.E., Rodriguez, D., Rodriguez, J.R., Abaitua, F., Duarte, C y Esteban, M (2001). VII Congreso Nacional de Virología. Valencia, 16-19 Sept. p166.

19. López-Fuertes, L., Pérez-Jimenez, E., Moreno, S., Vila-Coro, A., Wittig, B., Junghans, C., Konig, S.A., Simon, M and Esteban, M (2001). DNA immunization of susceptible mice with minimalistic expression constructs expressing the LACK protein of Leishmania major. VII Congreso Nacional de Virología. Valencia, 16-19 Sept. p166

20. Tapia, E., Pérez-Jimenez, E., López-Fuertes, L., Gonzalo, R y Esteban, M (2001). Inducción de una respuesta inmune protectiva frente a la Leishmaniasis cutánea mediante la utilización de vectores de DNA y virus vaccinia recombinantes que expresan la proteina LACK de Leishmania infantum. . VII Congreso Nacional de Virología. Valencia, 16-19 Sept. p167.

21. Sánchez, A.B., Rodriguez, D., Garzón, A., Amorena, B., Esteban, M y Rodriguez, J.R (2001). La proteina env del virus Maedi-Visna expresada por un recombinante del virus vaccinia induce fusión en células de distintos orígenes. . VII Congreso Nacional de Virología. Valencia, 16-19 Sept. p169.

22. Gallego, J.C., Rodriguez, D., Cabezas, P., Risco, C., Rodriguez, J.C., Carrascosa, J.L and Esteban, M (2001). Vaccinia Virus Morphogenesis: Characterization of the Attenuated Mutant M65. EMBO Workshop "Cell Biology of Virus infection". Heidelberg. Sept. 22-25..

23. Gherardi, M.M., Ramírez, J.C, and Esteban, M. (2001). IL-18 and IL-12 induce a synergistic effect in the protection against Vaccinia virus infection in mice.10thEuropean Congress on Biotechnology, Madrid (Spain), July.

24. López-Fuertes, L, Pérez-Jiménez,E., Moreno, S., Vila-Coro, A., Wittig, B., Junghans, C., Konig, S.-A., Timon, M, and Esteban, M (2001). DNA immunization of susceptible mice with minimalistic expression constructs expressing the LACK protein of Leishmania major. 11TH International. Congress of Immunology, Stockholm, July 22-27.

25. Didierlaurent A., Ramirez J. C., Finke D., M. Esteban, JC. Sirard and J. P. Kraehenbuhl. (2001). Portal of entry of HIV at mucosal sites and strategies to prevent infection. Proceedings of the 6th European Conference on Experimental AIDS Research - ECEAR 2001 (Edinburgh, UK, June 23-26, 2001).

26. Gherardi, M.M., Pérez-Jimenez, E., Nájera, J.L., D. Rodríguez., García-Sastre, A., Palese, P and Esteban, M (2002). Prime/Boost immunization schedules based on influenza and vaccinia virus (VV) vectors (MVA and WR) potentiate cellular immune responses agasinst HIV-env protein systemically and in the genito-rectal drainig lymph nodesXIV International AIDS conference, Barcelona (Spain), July 7-12.

27. Gallego-Gómez, J.C., Risco, C., Rodriguez, D., Cabezas, P., Carrascosa, J.L, and Esteban,

M. (2002). Vaccinia virus and attenuated mutants induces epithelial to mesenchimal transitions. XIV International Poxvirus Symposium. Lake Placid, New York, July, p138.

28. Esteban, M. (2002). Recombinant poxviruses as efficient inducers of primed CD8+T cells: role of cytokines. Juan March Workshop on "Molecular Mechanisms of immune modulation: Lessons from viruses. Madrid, February 25-27.

29. Esteban, M. (2003). Cell signalling in apoptosis and role of PKR. International Symposium on "Triggering and modulation of natural and acquired immunity to pathogens". Würzburg, Germany, April 3-5.

30. Gherardi, M., Perez-Jimenez, E., Nájera, J.L, and Esteban, M (2003). Modified vaccinia Ankara virus can be used as a mucosal vector for HIV antigens: its immunogenicity can be improved with a mucosal adjuvant or after applying a DNA/MVA scheme. Modern Vaccines Adjuvants and Delivery Systems. Dublin, 4-6 June.

31. Pérez-Jimenez, E., Gherardi, M., Kochan, G, and Esteban, M. (2003). Recombinant modified vaccinia virus Ankara expressing the leishmania infantum p36/Lack (MVAp36) antigen triggered a pronounced Th1 immune response against the antigen. Modern Vaccines Adjuvants and Delivery Systems. Dublin, 4-6 June.

32. A. Mörner, A. Aubertin, V. Erfle, M. Esteban, H. Fredlund, M-JFrachette, K. Karlén, P. Liljeström, C. Nilsson, E. Olausson-Hansson, G.Sutter, R. Wagner, B. Wahren, M. Widfeldt, R. Thorstensson, G. Biberfeld. (2003). Comparison of different heterologous prime-boost HIV-1/SIV vaccine regimens including recombinant DNA, SFV, MVA and proteins; immune responsesand viral load in cynomolgus macaques after intrarectal challenge with SHIV-BX08". The 2nd IAS Conference on HIV Pathogenesis and Treatment. Paris, France,13-16 July.

33. Guerra, S., López, L., Conde, R., Pascual-Montano, A., Esteban, M, (2003). Alteración de la expresión génica de células humanas tras la infección con el virus Vaccinia empleando microchips de cDNA. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept.: p. 178.

34. Muñoz-Fontela, C., Arroyo, J., Nombela, C., Esteban, M., Rivas, C. (2003). Actividad transformante de la proteína latente LANA2 del virus del sarcoma de Kaposi (KSHV) en células B. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept.: p. 29.

35. Guerra, S., Aracil, M., Conde, R., Bernard, A., Esteban, M. (2003). La proteína celular Wasp regula la salida del virus Vaccinia de la célula mediante la formación de colas de actina. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept.: p. 33.

36. García, M. A., Gil, J., Gómez-Puertas, P., Guerra, S., Rullas, J., Alcamí, J., Moscat, M., Esteban, M. (2003). Los factores de asociación a receptores de la familia TNF (TRAF) median la activación del factor de transcripción NFKB mediante la proteína quinasa PKR, dependiente de RNA bicatenario. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept.: p. 34.

37. Blanco, S., Abaitua, Esteban, M., F., Rodríguez, J. R., Zavala, F., Rodríguez, D. (2003). Mantenimiento de la respuesta inmune celular frente al antígeno CS de *P. yoelii* mediante la administración de IL-15. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept.: p. 147.

38. Pérez-Jiménez, E., Gherardi, M. M., Kochan, G., Esteban, M. (2003). La inmunización con un virus MVA recombinante que expresa la proteína LACK de *Leishmania infantum* induce una potente respuesta TH1. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept.: p. 148.

39. Ventoso, I., Berlanga, J. J., De Haro, C., Esteban, M. (2003). Papel de las eIF2 proteína quinasas en la respuesta antiviral de la célula. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept.: p. 103.

40. Garzón, A., Schleich, S., Rodríguez, J. R., Esteban, M., Griffiths, G., Krinjse-Locker, J., Rodríguez, D. (2003). Caracterización fenotípica de formas mutantes de la proteína A14L del virus Vaccinia. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept.: p. 132.

41. Esteban, M. (2003). Análisis genómico de la respuesta celular a la infección con el virus Vaccinia. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept.: p. 10.

42. Domingo-Gil, E., García, M. A., Rivas, C., Esteban, M. (2003). La apoptosis mediada por el sistema 2-5A/RNasaL inducida por los interferones no implica la actividad de las caspasas 3, 8 y 9. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept. p. 173.

43. Vandermeeren, A. M., Gómez, C. E., Patiño, C., Esteban, M. (2003). Expresión regulada de la poliproteína de HCV por recombinante del virus Vaccinia: análisis de las alteraciones celulares mediante microscopía electrónica. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept. p. 153.

44. Nájera, J. L., Gherardi, M. M., Esteban, M. (2003). Estudio comparativo de vectores atenuados del virus Vaccinia (MVA y NYVAC) que expresan antígenos del virus de la inmunodeficiencia humana (VIH-1). VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept. p. 204.

45. Gherardi, M. M., Pérez-Jiménez, E., Nájera, J. L., Esteban, M. (2003). El virus atenuado de Vaccinia (MVA) puede ser utilizado como vector de antígenos de HIV para impactar mucosas: aumento de su inmunogenicidad mediante un adyuvante de mucosas y la aplicación de esquemas de inmunización ADN/MVA. VIII Congreso Nacional de Virología, Barcelona 2003, 12-15 Sept. p. 206.

46. Esteban, M (2004). Vaccinia virus: its usefulnees as a vector for a wide range of vaccination purposes. Spanish-Belgian Symposium on Perspectives and Applications of Biotechnology within the European Unión framework. Madrid. Feb 2-3.

47. Guerra, S., López-Fernández, L., Pascual-Montano, A and Esteban, M (2004). Identification

of human genes during MVA infection. XVth International Poxvirus and Iridovirus meeting. Oxford, UK. September 3-8

48. Guerra, S., Aracil, M., Conde, R., Bernard, A and Esteban, M (2004). Involvement of Wiskott-Aldrich syndrome protein (WASP) in vaccinia virus pathogenesis. XVth International Poxvirus and Iridovirus meeting. Oxford, UK. September 3-8

49. Gherardi, M.M, Pérez-Jiménez, E., Nájera, J.L and Esteban, M (2004). Enhancement of HIV immunity in the genital tract after a DNA prime-MVA boost by the mucosal adjuvant cholera toxin. XVth International Poxvirus and Iridovirus meeting. Oxford, UK. September 3-8.

50. Risco, C., Fernández, J.J., Esteban, M., Carrascosa, J.L., Cyrklaff, M, and Baumeister, W (2004). Tomographic reconstruction of vaccinia virus. II European Virology Meeting (EuroVirology) (2004). Madrid, September 5-9.

51. Pérez-Jimenez, E., Kochan, G., Gherarrdi, M, and Esteban, M (2004). Patterns of immune response elicited by prime/boost vaccination with DNA and the attenuated modified vaccinia virus Ankara recombinants expressing LACK of Leishmania infantum. II European Virology Meeting (EuroVirology) (2004). Madrid, September 5-9.

52. Kochan, G., Pérez-Jimenez, E., Gómez, C.E., MacMahon-Pratt, D, and Esteban, M (2004). Comparison of protective efficacy of recombinant vaccinia virus expressing Leishmania p36/LACK, nuclease P-4 or methalloprotease gp63 in mice challenged with leishmania major. II European Virology Meeting (EuroVirology) (2004). Madrid, September 5-9.

53. Muñoz, C., García, M-A., García-Cao, I., Matheu, A., Arroyo, J., Collado, M., Esteban, M., Serrano, M, and Rivas, C (2004). Antiviral activity of tumor suppressors. II European Virology Meeting (EuroVirology) (2004). Madrid, September 5-9.

54. Ventoso, I., Sanz, M. A., Molina, S., Berlanga, J., Carrasco, L, and Esteban, M (2004). Translation control and antiviral response of the cell. II European Virology Meeting (EuroVirology) (2004). Madrid, September 5-9.

55. García, M-A., Muñoz, C., Matheu, A., Collado, M., Serrano, M., Esteban, M, and Rivas, C (2004). Antiviral activity of the tumor suppressor INK4a/ARF locus. II European Virology Meeting (EuroVirology) (2004). Madrid, September 5-9.

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PATENTS

-VECTORES RECOMBINANTES BASADOS EN EL VIRUS MODIFICADO DE ANKARA (MVA) COMO VACUNAS CONTRA LEISHMANIASIS. Solicitud de invención Nº 200501886, 30 Julio 2005; PCT/ES2006/070122. Concedido Título de Patente de Invención, Oficina Española de Patentes y Marcas, 16 Febrero, 2009. Nº publicación 2281252. Eva Pérez-Jiménez y Mariano Esteban

-VECTORES RECOMBINANTES BASADOS EN EL VIRUS MODIFICADO DE ANKARA (MVA) COMO VACUNAS PREVENTIVAS Y TERAPEUTICAS CONTRA EL SIDA. Título de invención Nº 200501841, 16 febrero 2009 (solicitud 27 julio 2005). Carmen E. Gómez, José L. Nájera, Victoria Jiménez y Mariano Esteban

-MEJORAS INTRODUCIDAS EN EL OBJETO DE LA PATENTE PRINCIPAL Nº ES200501841 PARA VECTORES RECOMBINANTES BASADOS EN EL VIRUS MODIFICADO DE ANKARA (MVA) COMO VACUNAS PREVENTIVAS Y TERAPÉUTICAS CONTRA EL SIDA. Solicitud P200600762. 24 Marzo, 2006; PCT/ES2006/070114. Carmen E. Gómez, José L. Nájera, Victoria Jiménez y Mariano Esteban

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-MODIFIED POXVIRUSES. US Provisional Patent Application No. 61/102,401. November 11, 2008. Michael Way, Antonio Postigo, Yoshiki Arakawa, Mariano Esteban, Susana Guerra.

-MODIFIED IMMUNIZATION VECTORS. US Provisional Patent Application, April 2009. Mariano Esteban, Bertram Jacobs, Giuseppe Pantaleo, Cornelius Melief, Rafick Sekaly, James Tartaglia.

Projects funded (in the last ten years)

Título del proyecto: Molecular and cellular principles of membrane virus biosynthesis and infection
Entidad financiadora: European Union, FMRX-CT98-0225

Duración, desde: 1998 hasta: 2001
Investigador responsable: Mariano Esteban

Título del proyecto: Malaria vaccine: attenuated influenza and vaccinia vectors
Entidad financiadora: NIH (USA). AI36526.05
Duración, desde: 1998 hasta: 2003
Investigador responsable: Mariano Esteban

Título del proyecto: Estrategias de terapia génica en las infecciones por VIH
Entidad financiadora: Comunidad de Madrid. 08.6/0020/1997
Duración, desde: 1998 hasta: 2001
Investigador responsable: Mariano Esteban

Título del proyecto: Mecanismo de inducción de apoptosis por los interferones: papél de las enzimas proteina quinasa (PKR) y sistema 2-5A sintetasa/RnasaL.
Entidad financiadora: Ministerio de Educación y Cultura, PM-98-0112
Duración, desde: 1999 hasta:2002
Investigador responsable: Mariano Esteban

Título del proyecto: Modulación de la respuesta inmune frente a antígenos del virus de la inmunodeficiencia humana (VIH)
Entidad financiadora: Comisión Interministerial de Ciencia y Tecnologia (CICYT), SAF98-0056,
Duración, desde: 1998 hasta: 2001
Investigador responsable: Mariano Esteban

Título del proyecto: Development of immunogenic and safe vaccinia virus vaccines.
Entidad financiadora: European Union. BIOTECH Program . PL970456
Duración, desde: 1998 hasta: 2001
Investigador responsable: Mariano Esteban

Título del proyecto: . Effector and memory anti-malaria CD8+ cell responses.
Entidad financiadora: National Institutes of Health (NIH), 1 RO1 AI44375-01
Duración, desde: 1999 hasta: 2003
Investigador responsable: Mariano Esteban

Título del proyecto: Project Leader of the EuroVac Cluster, European Vaccine Effort Against HIV/AIDS
Entidad financiadora: Fifth Framework Programme, QLRT-PL1999-01321
Duración, desde:2000 hasta: 2003
Investigador responsable: Mariano Esteban

Título del proyecto: European Vaccine against AIDS
Entidad financiadora: Programme EVA CFAR, QLRT-PL1999-00609
Duración, desde: 2000 hasta: 2003
Investigador responsable: Mariano Esteban

Título del proyecto: Visceral Leishmaniasis Vaccine-Murine Model Studies

Entidad financiadora: National Institutes of Health (NIH), 5R01AI45044-02
Duración, desde: 1999 hasta: 2003
Investigador responsable: Mariano Esteban

Título del proyecto: Desarrollo de una vacuna contra Leishmaniasis
Entidad financiadora: Comunidad Autonoma de Madrid (CAM), 08.2/0057/2000
Duración, desde: 2001 hasta: 2003
Investigador responsible: Mariano Esteban

Título del proyecto: Desarrollo de una vacuna contra Leishmaniasis
Entidad financiadora: Comunidad Autonoma de Madrid (CAM), 08.2/0057/2000
Duración, desde: 2001 hasta: 2003
Investigador responsible: Mariano Esteban

Principal investigator. Desarrollo de una vacuna contra leishmaniasis. Comunidad Autónoma de Madrid (CAM) 08.2/0057/2000-2001.

Project Leader of the EuroVac Cluster, European Vaccine Effort Against HIV/AIDS, Fifth Framework Programme, QLRT-PL1999-01321, Euros 500.000, 2000-2005

Concerted Action, Fifth Framework Programme, European Vaccine against Aids (EVA) CFAR, QLRT-PL1999-00609, 2000-2003.

Principal investigator. Contract with MOLOGEN, Germany, 2000-2001

Principal investigator. Contract with ITALFARMACO, Spain, 2001

Principal investigator. Premio IBERDROLA Ciencia y Tecnología, Profesores Visitantes, 2000-2003

Principal Investigator. Desarrollo de nuevas herramientas moleculares para el estudio del virus de la hepatitis C y su aplicación a morfogénesis, estructura, resistencia del virus a interferon y caracterización de la respuesta inmune al virus. BIO2000-0340-P4, 2001-2003. 171.649 Euros.

Principal investigator. Diseño y utilización del virus vaccinia como vacuna contra distintas enfermedades: análisis de la interacción virus-célula y modulación de la respuesta inmune. BIO2001-2269, 2001-2003, 170.000 Euros

Principal investigator. Desarrollo de nuevas herramientas moleculares para el estudio del virus de la hepatitis C y su aplicación a morfogénesis, estructura, resistencia del virus a interferon y caracterización de la respuesta inmune al virus. BIO2000-0340-P4. 2000-2003, 171.649 Euros.

Principal investigator. Analysis of the molecular mechanism of hepatitis C virus (HCV) resistance to antiviral therapy. EU QLK2-CT-2002-00954. 2002-2005, 124.313 Euros

Coordinator. Increasing the potency of vaccinia MVA vaccines. EU QLK2-CT-2002-01867. 2002-2006. 220.000 Euros

Principal investigator. European vaccine effort against HIV/AIDS (EuroVac III). QLK2-CT-2002-01431. 2002-2007. 50.000 euros

Principal investigator. Potenciación de la respuesta inmune (sistémica y de mucosas) frente al virus de la inmunodeficiencia humana (VIH-1). FIPSE, 2002-2006, 209.365 Euros

Principal Investigator. Vaccine strategies for combined targeting of innate and adaptive immune pathways (VaccTIP). EU-2004-012161. 2005-2007. 177.000 euros

Principal Investigator. Host immune activation optimised vaccinia virus vectors for vaccine development (MVACTOR). LSHP-CT-2006-037536. 2006-2009. 175.000 euros

Principal investigator. Diseño de nuevas vacunas tanto preventivas como terapéuticas para las enfermedades de mayor prevalencia: sida, hepatitis C y cáncer de próstata. BIO2004-03954. 2004-2007. 180.000 euros.

Principal Investigator. Desarrollo de vacunas contra enfermedades prevalentes. Fundación Botín 2005-2010. 1.000.000 euros.

Principal Investigator. Caracterización funcional y utilización de la proteína quinasa (PKR) inducida por los interferones como mediador de apoptosis e inhibidor tumoral. 2005-2008. 150.000 euros.

Principal Investigator. Pox T cell vaccine Discovery Consortium. Fundation Bill and Melinda Gates. $1.037.000. 2006-2011.

Principal Investigator. Red de SIDA, ISCIII-RETIC-RD06/006. 2007-2010. 248.000 euros.

Principal Investigator. Modificación genetica y optimización inmunológica de una vacuna (MVA-B) contra el VIH-1 subtipo B. Fundación para la Investigación y la Prevención del Sida (FIPSE). 2007-2010. 172.374 euros

Principal Investigator. Biología del virus vaccinia y su aplicación como vacuna contra enfermedades prevalentes. SAF2008-020362008-2013. 500.000 euros

Member of European Comités.

- Member of the European Action Progamme Against AIDS. 1994-present

- Member of the COST /STD Initiative for a European Vaccine Program.
  1994-97.

- Member of the European Concerted Action Against Malaria, 1996-98

- Member of External Advisory Group (EAG) of the European Commission, key action 2, Control of

Infectious Diseases, Fifth Framework Programme.1998-2002

- Member of WHO Advisory Committee on Variola Virus Reseach, 1998-present

- Member of Strategic Advisory Group of Experts (SAGE) for Immunization, Vaccines and Biologicals, WHO, 2002-2007

- Member of Advisory Group for the Sciende Foundation of Ireland, 2000-present

- Member of European Science Foundation (ESF) Group for Research Infraestructures on Biomedical Sciences, 2003-present

- Member of Scientific Advisory Group, Novartis, Spain. 2002-present

-Founder and Board Member of the European Foundation Against AIDS (EuroVacc) 2002-present

Peer reviewer :

1) Journals: Science; EMBO J.; J. Virol. ; Virology. ; J. Gen. Virol. ; Arch. Virology; Virus Research; J. Biol. Chem.; J. Interferon and Cytokine Research; ONCOGENE; Molecular Therapy; Vaccine. FEBS Lett. Cell Host & Microbe.

2) Projects: National Science Foundation (NSF), USA; American Cancer Society, USA; Natural Sciences and Engineering Research Council of Canada (NSERC); Human Frontiers, EU; Austrian Science Fund; National Science Foundation of Ireland; Research Grants Council, Hong Kong; Medical Research Council of South Africa; Israel Science Foundation; Agencia Nacional de Evaluación y Prospectiva (ANEP); Fondo de Investigaciones Sanitarias (FIS); Comunidad Autónoma de Madrid (UAM); Fundación para la Investigación sobre el Sida (FIPSE) .

3) Research centers: Miembro del Comité Externo de Evaluacion de los centros: Centro Nacional de Ingeniería y de Industria Tecnológica (INETI) del Ministerio de Ciencia y Tecnología de Portugal; Instituto de Investigaciones Bioquímicas, Fundación Campoamor, Buenos Aires, Argentina (para Abril, 2001) .Molecular Virology Institut, Munich (2002).

Research:

The main objectives of our laboratory are geared to understand the molecular basis in the pathogenesis of infectious agents and their interaction with the host, as well as to use this knowledge in the development of vaccines that might be effective against diseases like AIDS, malaria and leishmaniasis. As a model system of infectious agent and as a delivery vector for expression of genes of interest, we used vaccinia virus (VV) a member of the poxvirus family. The research areas of our lab are.

1. *Vaccinia virus (VV) assembly*.

VV assembly is a complex process in which more than 100 proteins participate, and by studying this process we might also provide important insights in cell biology. Our objectives are to understand, at the molecular and cellular

levels, how viral membranes and cores are formed, and what are the viral proteins involved in these events that lead to virion assembly

2. *Mechanism of antiviral and anticellular action of interferons.*

For years, our laboratory has been investigating the mechanism of action of interferons (IFN), since these molecules play major roles as a first-line host defense against viral infections, tumor cell growth and regulation of the immune system. We have provided important insights into the mechanism of apoptosis action by the IFN-induced ds-RNA dependent protein kinase (PKR), and we have identified the inhibitory effects exerted over PKR by some viral genes. The role of these proteins in defense, particularly on innate immune responses is being investigated.

3. *Virus-host cell interactions*

How poxviruses alter host cell responses following virus infection is a poorly characterized process. Our objective was to know the impact of vaccinia virus on host cell gene expression profiling in order to identify cellular genes relevant for VV replication as well as for host cell defense, and to develop cell culture and animal models for functional gene studies. To this aim, we used microarrays to identify cellular genes specifically induced in the course of virus infection using virulent and attenuated VV strains with potential as human vaccines. A number of host genes have been identified and their role in virus pathogenesis is being investigated using animal model systems.

5. *Development of vaccines against Aids, malaria and leishmaniasis*.

Our laboratory has been developing immunization strategies against HIV, malaria and leishmania based on the use of VV recombinants. We have pioneered the development of protocols based on heterologous immunization approaches (prime/booster) with vectors that induced enhanced cellular immune responses, leading to protection in murine models against malaria (*Plasmodium yoelii*) and leishmania (*L. major and L. infantum)*. These studies have defined immunological parameters to expand CD8+ T cells during primary and secondary immunizations, with significance in the development of prophylactic and therapeutic strategies against infectious agents and tumor diseases. We have engineered potential vaccines against HIV/AIDS and clinical studies are underway. Novel vaccines with enhanced immunogenicity against HIV are being developed in our lab for testing in non-human primate models, as well as we are producing new vaccines against hepatitis C, leishmania and cancer.

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