



CURRICULUM VITAE OF ESTEBAN DOMINGO

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Present position: Ad Honorem (Emeritus) Professor of Research at the Spanish Research Council (CSIC).

Education: B.Sc. in Chemistry at the University of Barcelona (1965). Ph.D. in Biochemistry, University of Barcelona (1969). Maximum grades: "Premio Extraordinario" for B.Sc. (1965) and for Ph.D. (1969).

Postdoctoral experience:

- Oct. 1969-Dec. 1973: With Prof. Robert C. Warner, Department of Molecular Biology and Biochemistry, University of California at Irvine, California (USA). *In vitro* transcription.
- Jan. 1974-July 1976: With Prof. Charles Weissmann, Institut für Molekularbiologie I, Universität Zürich, 8093 Zürich (Switzerland). Genetics of phage Q β .

Visits to other laboratories and sabbaticals:

- 1980-81: BIOGEN S.A. (Switzerland). Molecular cloning and gene expression.
- August 1983: National Institute for Medical Research, Mill Hill, London (UK), with Dr. J. Skehel. Dideoxy sequencing of influenza virus genes.
- August 1988 - August 1989: Sabbatical year at the Univ. of California, San Diego (USA), with Dr. J. Holland. RNA virus heterogeneity.
- Jan. 1991 - April 1991: Additional visit at UCSD, with Dr. J. Holland. RNA virus heterogeneity.
- Oct. 1999 – Nov. 1999: Scripps Research Institute, with Drs. M.B.A. Oldstone and J.C. de la Torre. Genetics of lymphocytic choriomeningitis virus.

Membership:

- Editorial board of: *Microbiologia S.E.M.* (since 1985) / *Virus Research* (since 1987) / *J. Gen. Virology* (1988-1993; and since 2003) / *J. Virol.* (since 1995) / *Viral Immunology* (1994-1999) / *Archives in Virology* (since 1997) / *Virologie* (France) (since 1997) / *AIDS Reviews* (1999-2003) / *Virology* (since 2002) / Associate editor, *PLoS Pathogens* (since 2008).
- Editor of *J.Gen.Virol.* (1998-2002).
- Spanish representative in the Standing Technical Committee of FAO on FMD research (1986-1992).
- Member of the Advisory Committee of the Division of Virology of the International Union of Microbiological Societies (IUMS) (1999-2005).

- Founder member and scientific board member of Institute Para Limes, The Netherlands (since 2006).
- President of the Spanish Society for Virology (since 2007).
- Editor of Virus Research (since 2012).

Teaching: At the Univ. Calif. Irvine (1971-73) and Univ. Autónoma de Madrid (Spain) 1978-1992 / Director of "Master in Biotechnology" given at the CBMSO (1992-1993), and coordinator (1994-1995). Professor at the "Cours de Virologie Fondamentale", Institut Pasteur, Paris, France (since 1993). Professor at the course "Genetics and Evolution of Viruses"(since 2003), Univ. of Helsinki, Finland. Organizer: Dr. A. Plyusnin.

Director or co-director of 22 Doctoral Theses.

Publications: 360 papers in international journals and books; H index=69 (December 2013).
Author or editor of 5 books.

Main scientific achievements: Demonstration of high mutation rates and quasispecies dynamics of RNA viruses. Establishment of cell lines persistently infected with foot-and-mouth disease virus. Lethal mutagenesis as a new antiviral strategy.

Main scientific interests: Biological implications of quasispecies dynamics. Molecular basis of virus extinction by enhanced mutagenesis. Antiviral activity of nucleoside analogues.

Main scientific distinctions:

- Member of the EMBO (since 1991).
- Honorary Member of the European Society for Veterinary Virology (since 1997).
- Member of the European Academy (since 1998).
- Doctor *Honoris causa* from the Université de Liège, Belgium (1999).
- Doctor *Honoris causa* from the University of Bern, Switzerland (2004).
- Premio Cultura Viva (2010).
- Member of Real Academia de Ciencias Exactas, Físicas y Naturales, from the Natural Sciences Section (since 2012).

Ten most important publications until 2000:

Domingo, E., Flavell, R.A. and Weissmann, C. (1976). *In vitro* site-directed mutagenesis: Generation and properties of an infectious extracistronic mutant of bacteriophage Q β . *Gene* 1, 3-25.

[First construction of a viable virus mutant by site-directed mutagenesis]

Batschelet, E., Domingo, E. and Weissmann, C. (1976). The proportion of revertant and mutant phage in a growing population, as a function of mutation and growth rate. *Gene* 1, 27-32.

[First calculation of a mutation rate for an RNA virus]

Domingo, E., Sabo, D.L., Taniguchi, T. and Weissmann, C. (1978). Nucleotide sequence heterogeneity of an RNA phage population. *Cell* 13, 735-744.

[First evidence of quasispecies dynamics in an RNA virus]

Domingo, E., Dávila, M. and Ortín J. (1980). Nucleotide sequence heterogeneity of the RNA from a natural population of foot-and-mouth disease virus. *Gene* 11, 333-346.

[First calculation of population heterogeneity of an animal RNA virus *in vivo*]

Sobrino, F., Dávila, M., Ortín, J. and Domingo, E. (1983). Multiple genetic variants arise in the course of replication of foot-and-mouth disease virus in cell culture. *Virology* 128, 310-318.

[Demonstration of population dynamics in an animal virus]

Mateu, M.G., Martínez, M.A., Rocha, E., Andreu, D., Parejo, J., Giralt, E., Sobrino, F. and Domingo, E. (1989). Implications of a quasispecies genome structure: effect of frequent, naturally occurring amino acid substitutions on the antigenicity of foot-and-mouth disease virus. *Proc. Natl. Acad. Sci. USA* 86, 5883-5887.

[Demonstration of the implication of quasispecies dynamics in antigenic variation]

Holland, J.J., Domingo, E., de la Torre, J.C. and Steinhauer, D.A. (1990). Mutation frequencies at defined single codon sites in vesicular stomatitis virus and poliovirus can be increased only slightly by chemical mutagenesis. *J. Virol.* 64, 3960-3962.

[Initial study that documented the feasibility of an error catastrophe-lethal mutagenesis approach for an RNA virus]

Verdaguer, N., Mateu, M.G., Andreu, D., Giralt, E., Domingo, E. and Fita, I. (1995). Structure of the major antigenic loop of foot-and-mouth disease virus complexed with a neutralizing antibody: direct involvement of the Arg-Gly-Asp motif in the interaction. *EMBO J.* 14, 1690-1696.

[First evidence that a receptor recognition site overlapped with an antigenic site in a virus]

Escarmís, C., Dávila, M., Charpentier, N., Bracho, A., Moya, A. and Domingo, E. (1996). Genetic lesions associated with Muller's ratchet in an RNA virus. *J. Mol. Biol.* 264, 255-267.

[First molecular characterization of the genetic changes in a virus as a result of Muller's ratchet]

Ruiz-Jarabo, C.M., Arias, A., Baranowski, E., Escarmís, C. and Domingo, E. (2000). Memory in viral quasispecies. *J. Virol.* 74, 3543-3547.

[First evidence of the presence of a molecular memory in a viral quasispecies]

Selected publications since 2001 (peer-reviewed research articles, and international review articles and books):

Domingo, E., Biebricher, C., Eigen, M. and Holland, J.J. (2001). *Quasispecies and RNA Virus Evolution: Principles and Consequences*. Landes Bioscience, Austin.

Fares, M.A., Moya, A., Escarmís, C., Baranowski, E., Domingo, E. and Barrio, E. (2001). Evidence of positive selection in the capsid-protein coding region of the foot-and-mouth disease virus (FMDV) subjected to experimental passage regimens. *Mol. Biol. Evol.* 18, 10-21.

Arias, A., Lázaro, E., Escarmís, C. and Domingo, E. (2001). Molecular intermediates of fitness gain of an RNA virus: characterization of a mutant spectrum by biological and molecular cloning. *J. Gen. Virol.*, 82, 1049-1060.

- Núñez, J.I., Baranowski, E., Molina, N., Ruiz-Jarabo, C.M., Sánchez, C., Domingo, E. and Sobrino, F. (2001). A single amino acid substitution in nonstructural protein 3A can mediate adaptation of foot-and-mouth disease virus to guinea-pig. *J. Virol.*, 75, 3977-3983.
- Sobrino, F. and Domingo, E. (2001). Foot-and-mouth disease in Europe. *EMBO Reports* 2, 459-461.
- Baranowski, E., Ruiz-Jarabo, C. M. and Domingo, E. (2001). Evolution of cell recognition by viruses. *Science* 292, 1102-1105.
- Baranowski, E., Ruiz-Jarabo, C. M., Lim, M. and Domingo, E. (2001). Foot-and-mouth disease virus lacking the G-H loop: the mutant spectrum uncovers interactions among antigenic sites for fitness gain. *Virology* 288, 192-202.
- Quer, J., Hershey, C.L., Domingo, E., Holland, J.J. and Novella, I.S. (2001). Contingent neutrality in competing viral populations. *J. Virol.*, 75, 7315-7320.
- Domingo, E., Mas, A., Yuste, E., Pariente, N., Sierra, S., Gutiérrez-Rivas, M. and Menéndez-Arias, L. (2001). Virus population dynamics, fitness variations and the control of viral disease: an update. *Prog. Drug Res.* 57, 79-115.
- Pariente, N., Sierra, S., Loweinstein, P.R. and Domingo, E. (2001). Efficient virus extinction by combinations of a mutagen and antiviral inhibitors. *J. Virol.* 75, 9723-9730.
- Briones, C., Mas, A., Pérez-Olmeda, M., Altisent, C., Domingo, E. and Soriano, V. (2001). Prevalence and genetic heterogeneity of the reverse transcriptase T69S-S-X insertion in pre-treated HIV-infected patients. *Intervirology* 44, 339-343.
- Domingo, E., Ruiz-Jarabo, C.M., Sierra, S., Arias, A., Pariente, N., Baranowski, E. and Escarmís, C. (2002). Emergence and selection of RNA virus variants: memory and extinction. *Virus Res.* 82, 39-44
- Villén, J., Borrás, E., Shaaper, W.M.M., Meloen, R.H., Dávila, M., Domingo, E., Giralt, E. and Andreu, D. (2002). Functional mimicry of a discontinuous antigenic site by a designed synthetic peptide. *Chem. BioChem.* 3, 175-182.
- Ruiz-Jarabo, C.M., Arias, A., Molina-París, C. Briones, C., Baranowski, E., Escarmís, C. and Domingo, E. (2002). Duration and fitness dependence of quasispecies memory. *J. Mol. Biol.* 315, 285-296.
- Escarmís, C., Gómez-Mariano, G., Dávila, M., Lázaro, E. and Domingo, E. (2002). Resistance to extinction of low fitness virus subjected to plaque-to-plaque transfers: diversification by mutation clustering. *J. Mol. Biol.* 315, 647-661.
- Domingo, E. (2002). Quasispecies theory in virology. *J. Virol.* 76, 463-465.
- Sevilla, N., Domingo, E. and de la Torre, J. C. (2002). Contribution of LCMV towards deciphering biology of quasispecies in vivo. *Curr. Top. Microbiol. Immunol.* 263, 197-220.
- Lazaro, E., Escarmis, C., Domingo, E. and Manrubia, S.C. (2002) modeling viral genome fitness evolution associated with serial bottleneck events: evidence of stationary states of fitness. *J. Virol* 76, 8675-8681.
- Domingo, E., Baranoswki, E., Escarmís, C., Sobrino, F. and Holland, J.J. (2002). Error frequencies of picornavirus RNA polymerases: evolutionary implications for virus

- populations. In: *Molecular Biology of Picornaviruses*. B.L. Semler and E. Wimmer, eds. pp. 285-298. ASM, Washington, DC.
- Quiñones-Mateu, M.E., Tadele, M., Mas, A., Weber, J., Rangel, H.R., Chakraborty, B., Clotet, B., Domingo, E., Menendez-Arias, L. and Martinez, M.A. (2002). Insertions in the reverse transcriptase increase both drug resistance and viral fitness in a human immunodeficiency virus type 1 harboring the multi-NRT I resistance 69 insertion complex mutation. *J. Virol.*, 76 (20), 10546-52.
- Domingo, E., Baranowski, E., Escarmis, C. and Sobrino, F. (2002). Foot-and-mouth disease virus. *Comp. Immunol. Microbiol. and Infections Diseases* 25, 297-308.
- Grande-Perez, A., Sierra, S., Castro, M.G., Domingo, E. and Lowenstein, P. (2002). Molecular intertermination in the transition to error catastrophe. Systematic elimination of lymphocytic choriomeningitis virus through mutant spectrum complexity. *Proc. Natl. Acad. Sci. USA*, 99 (20), 12938-43.
- Mas, A., Vázquez-Alvarez, B., Domingo, E. and Menéndez-Arias, L. (2002). Multidrug-resistant HIV-1 reverse transcriptase: involvement of ribonucleotide-dependent phosphorylation in cross-resistance to nucleoside analogue inhibitors. *J. Mol. Biol.* 18, 181-197.
- Woolhouse, M.E.J., Webster, J.P., Domingo, E., Charlesworth, B. and Levin, B.R. (2002). Biological and biomedical implications of the coevolution of pathogens and their hosts. *Nature Genetics* 32, 569-577.
- Ruiz-Jarabo, C.M., Ly, C., Domingo, E. and de la Torre, J.C. (2003). Lethal mutagenesis of the prototypic arenavirus lymphocytic choriomeningitis virus (LCMV). *Virology* 308, 37-47.
- Baranowski, E., Ruiz-Jarabo, C.M., Pariente, N., Verdaguer, N. and Domingo, E. (2003). Evolution of cell recognition by viruses: a source of biological novelty with medical implications. *Advances in Virus Res.*, 62, 19-111.
- Domingo, E., Escarmis, C., Baranowski, E., Ruiz-Jarabo, C.M., Carrillo, E., Nuñez, J.I. and Sobrino, F. (2003). Evolution of foot-and-mouth disease virus. *Virus Research*, 91, 47-63.
- Tami, C., Taboga, O., Berinstein, A., Nuñez, J. I., Palma, E. L., Domingo, E., Sobrino, F. and Carrillo, E. (2003). Evidence of the coevolution of antigenicity and host cell tropism of foot-and-mouth disease virus in vivo. *J. Virol.*, 77, 1219-1226.
- Domingo, E., Ruíz-Jarabo, C.M., Arias, A., Molina-París, C., Briones, C., Baranowski, E. and Escarmis, C. (2003). Detection and biological implications of genetic memory in viral quasispecies, pp. 259-276. *In* A. Matsumori (ed.), *Cardiomyopathies and Heart Failure: Biomolecular, Infectious and Immune Mechanisms*. Kluwer Academic Publishers, London, UK.
- Pariente, N., Airaksinen, A. and Domingo, E. (2003). Mutagenesis versus inhibition in the efficiency of extinction of foot-and-mouth disease virus. *J. Virol.*, 77, 7131-7138.

- Airaksinen, A., Pariente, N., Menéndez-Arias, L. and Domingo, E. (2003). Curing of foot-and-mouth disease virus from persistently infected cells by ribavirin involves enhanced mutagenesis. *Virology*, 311, 339-349.
- Manrubia, S.C., Lázaro, E., Pérez-Mercader, J., Escarmís, C. and Domingo, E. (2003). Fitness distributions in exponentially growing asexual populations. *Phys. Rev. Lett.*, 90, 188101-188104.
- Lázaro, E., Escarmís, C., Pérez-Mercader, J., Manrubia, S.C. and Domingo, E. (2003). Resistance of virus to extinction on bottleneck passages: Study of a decaying and fluctuating pattern of fitness loss. *Proc. Natl. Acad. Sci. USA*, 100, 10830-10835.
- Sánchez, G., Bosch, A., Gómez-Mariano, G., Domingo, E. and Pinto, R.M. (2003). Evidence for quasispecies distributions in the human hepatitis A virus genome. *Virology*, 315, 34-42.
- Briones, C., Domingo, E. and Molina-París, C. (2003). Memory in retroviral quasispecies: experimental evidence and theoretical model for human immunodeficiency virus. *J. Mol. Biol.*, 331, 213-29.
- Domingo, E. (2003). Quasispecies and the development of new antiviral strategies. *Prog. Drug. Res.*, 60, 134-158.
- Ruiz-Jarabo, C.M., Miller, E., Gómez-Mariano, G. And Domingo, E. (2003). Synchronous loss of quasispecies memory in parallel viral lineages: a deterministic feature of viral quasispecies. *J. Mol. Biol.*, 333, 553-563.
- Domingo, E. (2003). Complexities of virus-cell interactions. *Current Opinion in Microbiology*, 6, 383-385 [In addition, E.D. is the editor of the volume entitled “Host-Microbe interactions: viruses”].
- Gonzalez-Lopez, C., Arias, A., Pariente, N., Gomez-Mariano, G. and Domingo, E. (2004). Preextinction viral RNA can interfere with infectivity. *J. Virol.*, 78, 3319-3324.
- Pariente, N., Pernas, M., de la Rosa, R., Gómez-Mariano, G., Fernández, G., Rubio, A., Lopez, M., Benito, J.M., Lopez-Galíndez, C., Leal, M., Domingo, E., Martínez, M.A. and Mas, A. (2004). Long term suppression of plasma viremia with highly active antiretroviral therapy despite virus evolution and very limited selection of drug-resistant genotypes. *J. Med. Virol.*, 73, 350-361.
- Arias, A., Ruiz-Jarabo, C.M., Escarmís, C. and Domingo, E. (2004). Fitness increase of memory genomes in a viral quasispecies. *J. Mol. Biol.*, 339, 405-42.
- Arnedo-Valero, M., Plana, M., Mas, A., Guilà, M., Gil, C., Castro, P., García, F., Domingo, E., Gatell, J.M. and Pumarola, T. (2004). Similar HIV-1 evolution and immunological responses at 10 years despite several therapeutics strategies and host HLA types. *J. Med. Virol.*, 73, 495-501.
- Ruiz-Jarabo, C.M., Pariente, N., Baranowski, E., Dávila, M., Gómez-Mariano, G. and Domingo, E. (2004). Expansion of host cell tropism of foot-and-mouth disease virus despite replication in a constant environment. *J. Gen. Virol.*, 85, 2289-2297.

- García-Arriaza, J., Manrubia, S.C., Toja, M., Domingo, E. and Escarmís, C. (2004). An evolutionary transition towards defective RNAs that are infectious by complementation. *J. Virol.*, 78, 11678-11685.
- Ferrer-Orta, C., Arias, A., Perez-Luque, R., Escarmís, C., Domingo, E. and Verdaguer, N. (2004). Crystal structure of foot-and-mouth disease virus RNA-dependent RNA polymerase and its complex with a template-primer RNA. *J. Biol. Chem.*, 279, 47212-47221.
- Domingo, E., Pariente, N., Airaksinen, A., González, C., Sierra, S., Herrera, M., Grande-Perez, A., Lowenstein, P.R., Manrubia, S.C., Lázaro, E. and Escarmís, C. (2004). Foot-and-mouth disease virus evolution: exploring pathways towards virus extinction. *Curr. Top. in Microbiol. and Immunol.*, 288, 149-173.
- Domingo, E., Gonzalez-López, C., Pariente, N., Airaksinen, A. and Escarmís, C. (2005). Population dynamics of RNA viruses: the essential contribution of mutant spectra. *Arch. Virol.*, 19 [SUPP.]: 59-71.
- Domingo, E., Escarmís, C., Lázaro, E. and Manrubia, S.C. (2005). Quasispecies dynamics and RNA virus extinction. *Virus Res.* 107, 129-139.
- Domingo, E. (2005). Antiviral strategy on the horizon. *Virus Research* 107, 115-116. Preface written as guest editor of the Special Issue of *Virus Res.* on "Virus entry into error catastrophe as a new antiviral strategy", vol. 107 n° 2.
- Domingo, E., Ed. (2005). "Virus entry into error catastrophe as a new antiviral strategy." *Virus Res.* 107: 115-228.
- Domingo, E. and Holland, J.J. (2005). The origin and evolution of viruses. In: B.W.J. Mahy and V. ter Meulen, eds. *Topley and Wilson's Microbiology and Microbial Infections*. Volume 1. Virology. Hodder Arnold, ASM Press Washington, D.C. pp. 11-23.
- Perales, C., Martín, V., Ruiz-Jarabo, C.M., and Domingo, E. (2005). Monitoring sequence space as a test for the target of selection in viruses. *J. Mol. Biol.*, 345, 451-459.
- Domingo, E. (2005). Microbial evolution and emerging diseases. In: C. Power and R.T. Johnson, eds. *Emerging Neurological infections*. Taylor & Francis, Boca Raton FL., pp. 1-34.
- Novella, I.S., Gibertson, D.L., Borrego, B., Domingo, E. and Holland, J.J. (2005). Adaptability costs in immune escape variants of vesicular stomatitis virus. *Virus Res.*, 107, 27-34.
- Manrubia, S.C., Escarmís, C., Domingo, E. and Lázaro, E. (2005). High mutation rates, bottlenecks, and robustness of RNA viral quasispecies. *Gene*, 347, 273-282.
- Yuste, E., Borderia, A.V., Domingo, E. and López-Galindez, C. (2005). Few mutations in the 5' leader region mediante fitness recovery of debilitated human immunodeficiency type 1 viruses. *J. Virol.*, 79, 5421-5427.
- Grande-Pérez A, Lazaro E, Lowenstein P, Domingo E and Manrubia SC (2005) Suppression of viral infectivity through lethal defection. *Proc. Natl. Acad. Sci. USA* 102, 4448-4452.

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- González-López C, Gómez-Mariano G, Escarmís C y Domingo E (2005) Invariant aphthovirus consensus nucleotide sequence in the transition to error catastrophe. *Infection Genetics and Evolution*, 5, 366-374.
- Grande-Pérez A, Gómez-Mariano G, Lowenstein PR y Domingo E (2005) Mutagenesis-induced, large fitness variations with an invariant arenavirus consensus genomic nucleotide sequence. *J. Virol.* 79, 10451-10459.
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