

GENE THERAPY FOR NERVOUS SYSTEM (GT4CNS)

MIGUEL CHILLÓN



PROFILE

Dr. M. Chillon is an ICREA senior researcher and principal investigator of the UAB-VHIR Joint Unit at the Institute of Neuroscience (UAB) since 2017. Dr. Chillon obtained his PhD in Genetics at Hospital Duran i Reynals and Universitat de Barcelona in 1994 in Barcelona and received the Boehringer Mannheim Award in Human Genetics by the Spanish Association of Human Genetics in 1995, and was member of the research team awarded with the " Premio de Investigación Ciudad de Barcelona". Dr. M. Chillon became interested in neuromuscular and neurodegenerative diseases since his postdoctoral fellows with pionnering researchers in the field such as Dr. Michael Welsh at the Howard Hughes Medical Institute & Internal Medicine Department of the University of Iowa (US) a Howard Hughes investigator (1994-1997); and as Dr. Olivier Danos in Genethon II (France) as an EMBO postdoctoral researcher (1997-1999). After returning to Spain in 2000 and he obtained an ICREA position at the Biochemistry and Molecular Biology Dept at UAB and created his own research group in 2001, whose lines have focused from the beginning on four main objectives: (1) gene therapy strategies against cognitive decline in neurodegenerative diseases and aging; (2) gene therapy strategies for autoimmune

diseases; (3) gene therapy approaches for rare diseases affecting the nervous system, and (4) development of more efficient gene therapy vectors.

Besides, Dr. M Chillon is the founder and Director of the Vector Production Unit at UAB a technological platform to produce viral vectors (since 2004), Associated Professor at the Universitat Autònoma de Barcelona (since 2005), Group leader at Vall d'Hebron Hospital Research Institute (VHIR) (since 2017), the co-chair of the Advanced Therapies Platform of the European Organization EATRIS (European Infrastructure for Translational Medicine; <https://eatris.eu>), since 2016, and scientific advisor of different organizations and spin-off biotechs (Ninevah, Biointaxis, Klogene Therapeutics, Fundacion La Lucha de Abril, y la Asociación Española de Paraparesia Espástica Familiar (AEPEF)

Dr. Chillon (H-index: 27; 3470 citations, Scopus) has authored 78 peer-reviewed scientific articles, 3 reviews, 5 book chapters, is Editor of 1 book, and has directed 10 doctoral thesis. Also, Dr. M Chillon has generated 8 patents and founded 2 spin-off companies: NanoTherapix (2009) for the development of gene-cell therapeutic strategies with viral vectors and cells of the immune system, and Klogene (2016) for the development of gene therapy approaches for cognitive impairments. In addition, he has founded the Vector Production Unit (UPV) a vector Core to valorize the knowledge generated. Currently, the UPV is the first provider of Ad and AAV vectors to Spanish groups. Finally, it should be noted that as a recognition of his trajectory in knowledge transfer, the IP of the project received the “Transference Award” in 2018 granted by the Consejo Social of the UAB.

RESEARCH

RESEARCH INTERESTS/STRATEGIC OBJECTIVES

- 1) Molecular mechanisms involved in memory formation: Study of altered signaling pathways in CNS in aging and in Alzheimer's Disease
- 2) Gene Therapy Strategies for Neurodegenerative rare diseases: Spastic Paraplegia type 52 (SPG52); and GNB1 Encephalopathy
- 3) Generation and development of new AAV gene therapy vectors

MAIN RESEARCH LINES

Redes de Investigación Coopérativa en Salud (RICORS). Terapias Avanzadas. ISCIII-RD21/0017. (2021-2024)

A long-lasting anti-Covid-19 subcutaneous vaccine through a novel, industrially competitive and biologically safe nanomimetic concept (INVITA). Programa PANDEMIAS. (2021-2022)

Recombinant HEBE: A chimeric Chronokine to rejuvenate the Brain. Proof of Concept 2020. (2021-2022)

Personalized gene therapy for MECP2 using CRISPR/Cas9 technology together with AAV administration in 3D cell cultures and KI mice. European Joint Programme-Rare Diseases 2020. AC20/00051 (2021-2023)

Unidad de Producción de Vectores. Personal Técnico Apoyo. PTA2019-017896-I. (2020-2023)

Molecular and functional characterization of new recombinant chimeric chronokines. Implications for cognitive decline associated with aging. Proyectos I+D+i Retos Sociedad. PID2019-104034RB-I00. (2021-2023)

Desarrollo de nuevas terapias genéticas basadas en inteinas. Retos Colaboración. RTC2019006879-1. (2020-2022)

Una terapia innovadora contra el SARS-CoV-2 basada en ARN circulares (CIRCO-3). Fund. Santander. (2020-2021)

Desarrollo de una terapia génica para el tratamiento de las formas genéticas del Síndrome Nefrótico (AAV-Crb2). Convocatoria CERVERA 2020: IDI-20200258. (2020-2022)

Doctorado Industrial with Regi Jofre. AGAUR; 2018-DI-066.

Unitat Producció de Vectors (UPV). Ajuts TECNIO. (2018)

Ajuts per definir i potenciar els plans d'actuació en transferència tecnològica dels desenvolupadors de tecnologia

Validation of the capacity of sKL in bloodstream to cross BBB and its therapeutic use in neurodegenerative and demyelinating diseases. AGAUR (#2016LLAV00033) (2017-2018).

ELI-KLAD:Non-invasive sensitive diagnostic for early stages of Alzheimer's Disease. Universitat Autònoma Barcelona. Program SmartMoney (T2014/34) (2017-2018).

Combined Gene Therapy to correct oxidative stress in type 2 diabetic neuropathy. Marato TV3. 201607.10. (2017-19)

LAB FEATURED PUBLICATIONS

Ángel Edo, Laura Calvo-Barreiro, Herena Eixarch, Assumpció Bosch, Miguel Chillón, and Carmen Espejo. Therapeutic effect of IL21 blockage by gene therapy in Experimental Autoimmune Encephalomyelitis. Neurotherapeutics (in press) (2022)

J. Roig-Soriano, C. Griñán-Ferré, J.F. Espinosa-Parrilla, C. R. Abraham, A. Bosch, M. Pallàs, M. Chillon. AAV-mediated expression of α Klotho isoforms rescues relevant aging hallmarks in senescent SAMP8 mice. Aging Cell. (in press) (2022)

Marc Leal-Julià, Jorge J. Vilches, Andrea Onieva, Sergi Verdés, Ángela Sánchez, Miguel Chillón, Xavier Navarro, Assumpció Bosch. Proteomic quantitative study of dorsal root ganglia and sciatic nerve in type 2 diabetic mice. Molecular Metabolism. : Jan;55:101408. (2022)

T.A. Rubinstein, I. Reuveni, A. Hesin, A.K.Goldberg, H. Olauson, T.E. Larsson, C.R. Abraham, E. Zeldich, A. Bosch, M. Chillón, K.S. Hollander, A.Y. Orbach, G.W. Vainer, I. Wolf , and T. Rubinek. A Transgenic Model Reveals the Role of Klotho in Pancreatic Cancer Development and Paves the Way for New Klotho-Based Therapy. Cancers. Dec 15;13(24):6297. (2021)

E. Aubets , M. Chillon , C. J Ciudad , V. Noé. PolyPurine Reverse Hoogsteen Hairpins work as RNA species for gene silencing. International Journal of Molecular Sciences. 16;22(18):10025 (2021)

Mòdol-Caballero G, García-Lareu B, Herrando-Grabulosa M, Verdés S, López-Vales R, Pagès G, Chillon M, Navarro X, Bosch A. Specific expression of Glial-Derived Neurotrophic Factor in muscles as gene therapy strategy for Amyotrophic Lateral Sclerosis. *Neurotherapeutics*. 18:1113-1126. (2021)

C. Griñán-Ferré, V. Izquierdo, A. Bellver-Sanchis, R. Corpás, J. Roig-Soriano, M. Chillón, C. Andres-Lacueva, M. Somogyvári, Csaba Sötti, C. Sanfeliu and M. Pallàs. The pleiotropic neuroprotective effects of resveratrol: from antioxidant to epigenetic nheritance modulator. *Ageing Research Reviews*. (67):101271: 1-24. (2021)

M Vogel-González, M Talló-Parra, V Herrera-Fernández, G Pérez-Vilaró, M Chillón, X Nogués-Solan, S Gómez-Zorrilla, I López-Montesinos, I Arnau-Barrés, M Luisa Sorli, J Pablo Horcajada, N García-Giralt, J Pascual, J Díez, R Vicente, R Güerri-Fernández. Low zinc levels at admission associates with poor clinical outcomes in SARS-CoV-2 infection. *Nutrients*. 13(2):562: 1-13. (2021)

A. Sánchez, B. García-Lareu, M. Puig, E. Prat, J. Ruberte, M. Chillón, V. Nunes, R. Estévez, A. Bosch. Cerebellar Astrocyte Transduction as Gene Therapy for Megalencephalic Leukoencephalopathy. *Neurotherapeutics*. 17:2041-2053. (2020)

A. Bosch, M. Chillón. Gene Therapy Approaches in CNS Regenerative Medicine. *Handbook of Innovations in Central Nervous System Regenerative Medicine*. USA. Elsevier. 8th June 2020. pages 375-399. ISBN: 9780128180846

G. Pagès, L. Giménez-Llort, B. García-Lareu, L. Ariza, M. Navarro, J. Ruberte, C. Casas, M. Chillón, A. Bosch. Intrathecal AAVrh10 corrects Biochemical and Histological Hallmarks of Mucopolysaccharidosis VII Mice and Improves Behavior and Survival. *Human Molecular Genetics*. 1;28(21):3610-3624. (2019)

A. Massó, A. Sánchez, A. Bosch, L. Gimenez-Llort, M. Chillón. Secreted-Klotho isoform protects against age-dependent memory deficits . *Molecular Psychiatry*. Sep;23(9):1-11. (2018)