NEUROCIENCIAS

NEUROLOGÍA

ÁREA: NEUROCIENCIAS

└ GRUPO: NEUROLOGÍA

COMPOSICIÓN DEL GRUPO

Responsable: José M. Serratosa Fernández (Profesor Asociado de la UAM/Jefe de Unidad 744 CIBERER)

EPILEPSIA

José M Serratosa
Marina Sánchez
Beatriz G Giráldez
Laura Olivié
Daniel Fernández
Pedro Martínez Ulloa
María Machío
Marta Oses
Teresa Montojo
Gema Sánchez

MOVIMIENTOS ANORMALES

Pedro García Ruiz-Espiga
Javier del Val
Marta Ruiz
Cici Féliz
Teresa Montojo
Asunción Martínez

DEMENCIAS

Estrella Gómez Tortosa
Pablo Agüero
Maria José Sainz

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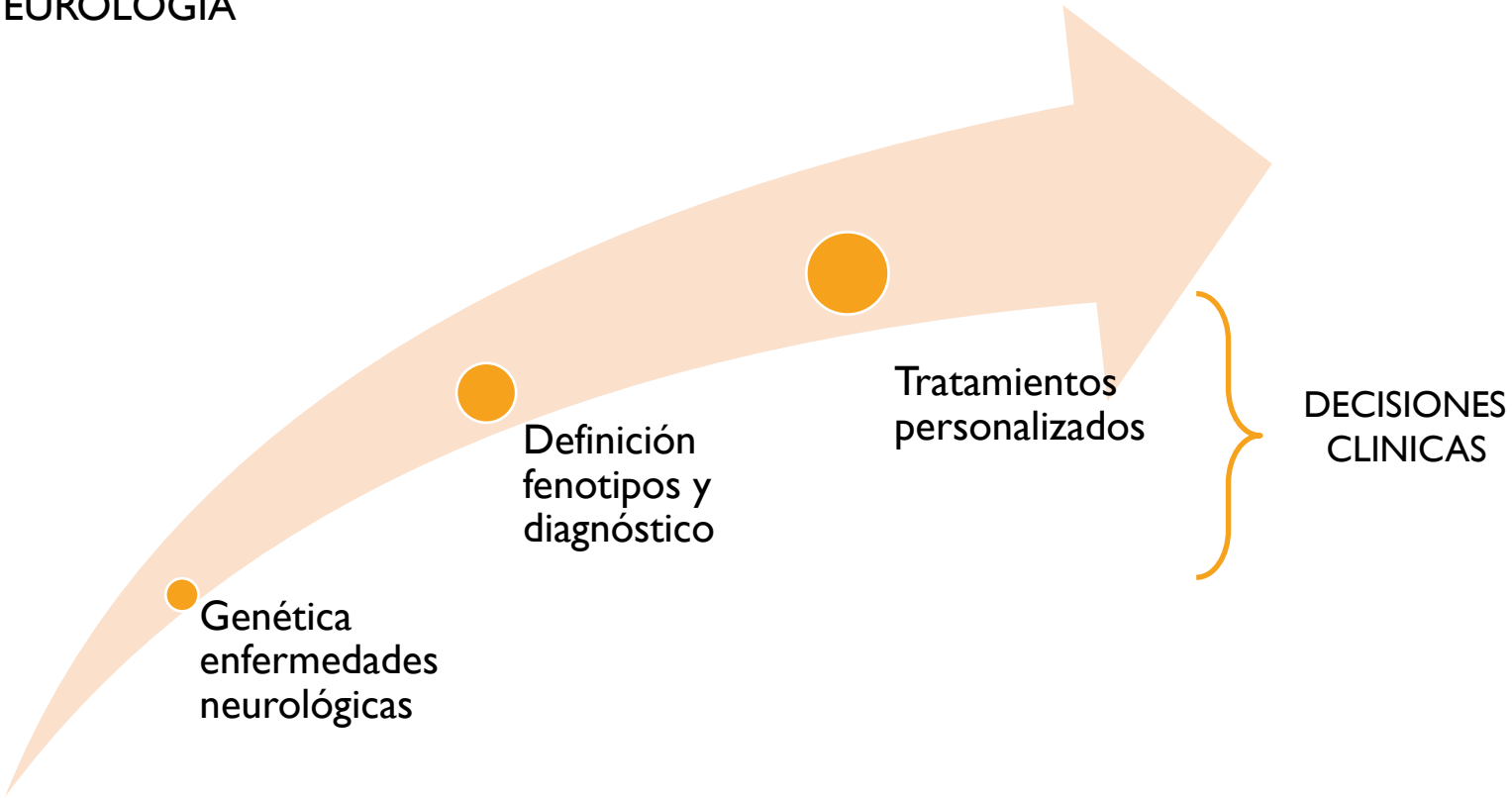
└→ GRUPO: NEUROLOGÍA



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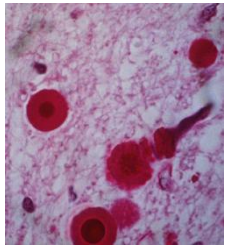
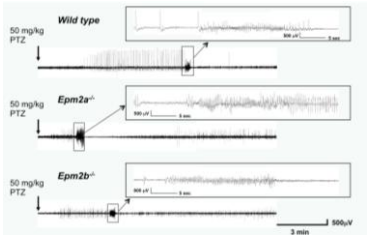
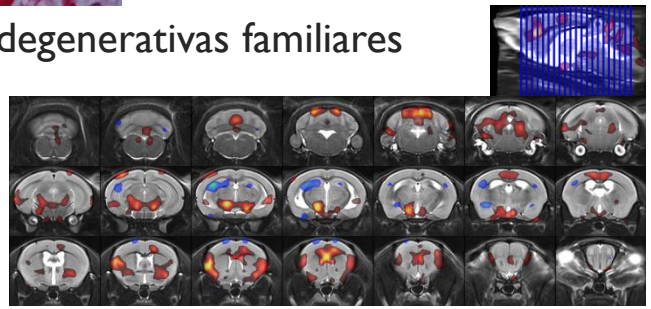
OBJETIVOS

- Profundizar en el conocimiento de la fisiopatología de enfermedades neurológicas
  - Movimientos anormales
    - Enfermedad de Parkinson
    - Enfermedad de Huntington





  - Demencias
    - Nuevos marcadores genéticos y biológicos en demencia degenerativas familiares



  - Epilepsias de base genética
    - Encefalopatías epilépticas de la infancia (+ en adultos)
    - Enfermedad de Lafora

- Generar herramientas diagnósticas y terapéuticas que mejoren la asistencia a los pacientes afectados

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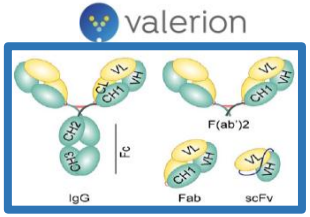
LÍNEAS DE INVESTIGACIÓN
PROYECTOS QUE LAS SUSTENTAN

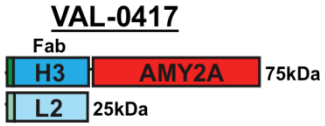
- Estudio Generation HD (terapia genica en enfermedad de Huntington)
- Estudio Enroll (seguimiento de EH a lo largo del tiempo)
- Correlaciones clínico-genéticas en demencias hereditarias y en nonagenarios cognitivamente preservados (PI14/00099, FIS 2016-2019)
- Estudio de un nuevo gen asociado a enf de Alzheimer y de una plataforma para el estudio genético ágil de demencia hereditarias (SAF2010-18277, MINC 2010-2014)
- Lafora epilepsy: Basic mechanisms to therapy (1P01NS097197-01, NIH, 2016-2021)
- LAF-NHS. Prospective, Longitudinal, observational study of the natural history and functional status of patients with Lafora disease (Ionis, Valerion)
- Genética de las Epilepsias Humanas. Identificación de nuevos genes, diagnóstico precoz y su utilidad clínica (SAF2014-59594-R, MINC 2015-2018)

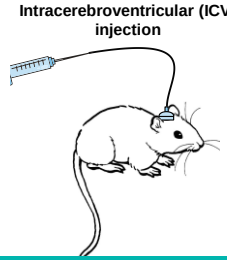
RESULTADOS OBTENIDOS

- Publicaciones 2013-2017: 126
- Tesis: 5
- Guías: SEN, SEEP
- Proyectos públicos: 4
- Ensayos clínicos nuevas terapias
  - Huntington
  - Lafora
- Registros: Lafora, EE *KCNQ2*, *KCNA2*, Landau-Kleffner, S. Lennox-Gastaut, status, primera crisis

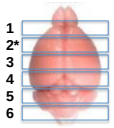
VAL-0417 reduces glycogen load *in vivo* - brain



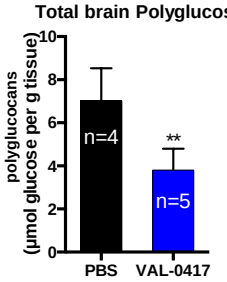




Continuous infusion of VAL-0417 (0.08mg/day) or PBS for 28 days via ICV catheter

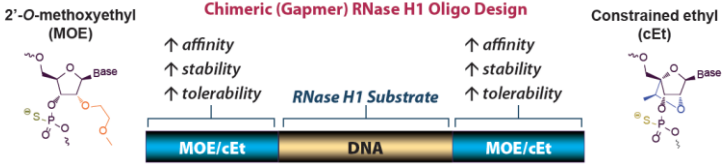


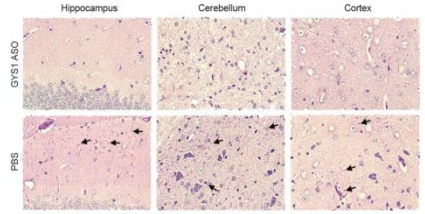
Polyglucosan content

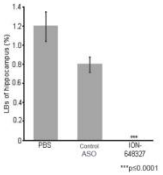


Reducing glycogen synthase activity with an ASO

IONIS PHARMACEUTICALS

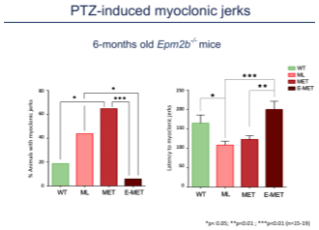


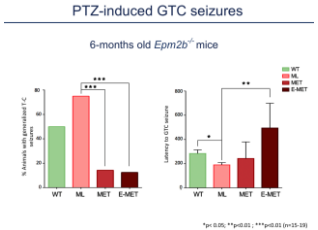


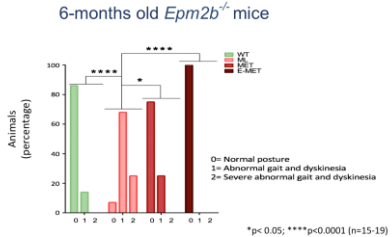


Protocol:
One month old EPM2A (-/-) mice (n=6 per group). Injected twice with 300µg of PBS, GYS1 or Control mismatch ASO by ICV bolus injection at age 1m and 2m of age and sacrificed at 4m.

Metformin reduces seizure susceptibility in Lafora mice







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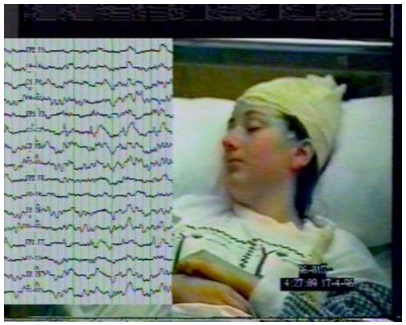


1996

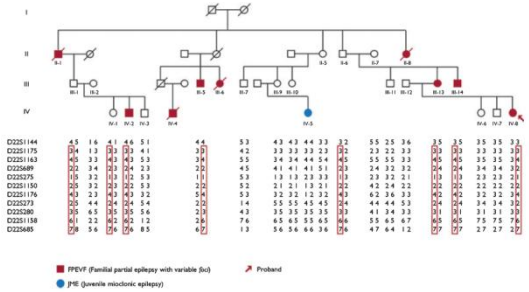
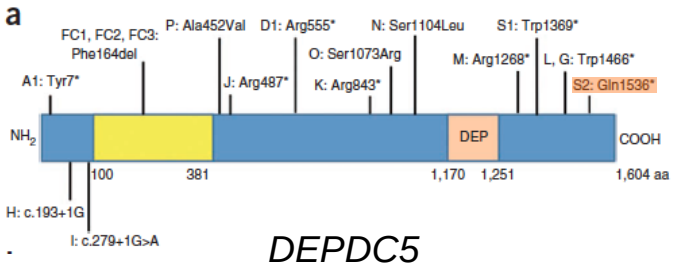
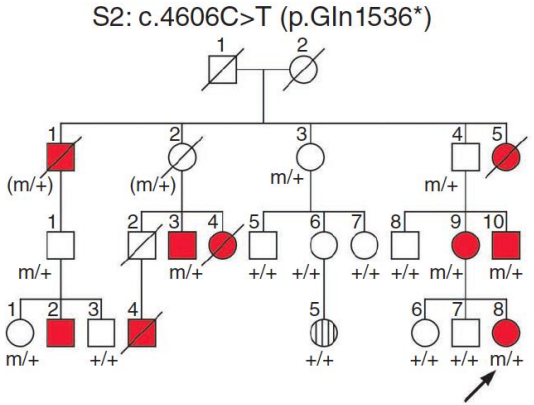


Figure 1.
FPEVF pedigree. Individuals marked with red symbols were considered as affected with partial epilepsy. The individual marked with a blue symbol had JME. The disease-associated haplotype is boxed.
Epilepsia © ILAE

2005



DEPDC5



2013

Dibbens et al, Nat Genet 2013;45:546-51

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Variant Intestinal-Cell Kinase in Juvenile Myoclonic Epilepsy

J.N. Bailey, L. de Nijs, D. Bai, T. Suzuki, H. Miyamoto, M. Tanaka, C. Patterson, Y.-C. Lin, M.T. Medina, M.E. Alonso, J.M. Serratosa, R.M. Durón, V.H. Nguyen, J.E. Wight, I.E. Martínez-Juárez, A. Ochoa, A. Jara-Prado, L. Guilhoto, Y. Molina, E.M. Yacubian, M. López-Ruiz, Y. Inoue, S. Kaneko, S. Hirose, M. Osawa, H. Oguni, S. Fujimoto, T.M. Grisar, J.M. Stern, K. Yamakawa, B. Lakaye, and A.V. Delgado-Escueta

The American Journal of Human Genetics *93*, 1–9, November 7, 2013 1

De Novo Loss-of-Function Mutations in *CHD2* Cause a Fever-Sensitive Myoclonic Epileptic Encephalopathy Sharing Features with Dravet Syndrome

Arvid Suls,[1,2,38] Johanna A. Jaehn,[3,38] Angela Kecskés,[4,38] Yvonne Weber,[5,38] Sarah Weckhuysen,[1,2] Dana C. Craiu,[6,7] Aleksandra Siekierska,[4] Tania Djémié,[1,2] Tatiana Afrikanova,[4] Padhraig Gormley,[8] Sarah von Spiczak,[3] Gerhard Kluger,[9] Catrinel M. Iliescu,[6,7] Tiina Talvik,[10,11] Inga Talvik,[10,11] Cihan Meral,[12] Hande S. Caglayan,[13] Beatriz G. Giraldez,[14] José Serratosa,[14] Johannes R. Lemke,[15] Dorota Hoffman-Zacharska,[16] Elzbieta Szczepanik,[17] Nina Barisic,[18] Vladimir Komarek,[19] Helle Hjalgrim,[20,21] Rikke S. Møller,[20] Tarja Linnankivi,[22] Petia Dimova,[23] Pasquale Striano,[24] Federico Zara,[25] Carla Marini,[26] Renzo Guerrini,[26] Christel Depienne,[27,28,30] Stéphanie Baulac,[27,28,29] Gregor Kuhlenbäumer,[31] Alexander D. Crawford,[4,32] Anna-Elina Lehesjoki,[33,34,35] Peter A.M. de Witte,[4] Aarno Palotie,[8,36,37] Holger Lerche,[5] Camila V. Esguerra,[4,39] Peter De Jonghe,[1,2,39,*] Ingo Helbig,[3,39] and the EuroEPINOMICS RES Consortium

nature genetics

Mutations in *GRIN2A* cause idiopathic focal epilepsy with rolandic spikes

Johannes R Lemke[1,2,50], Dennis Lal[2–5,50], Eva M Reinthaler[2,6,50], Isabelle Steiner[7], Michael Nothnagel[3], Michael Alber[8], Kirsten Geider[9], Bodo Laube[9], Michael Schwake[10], Katrin Finsterwalder[11], Andre Franke[12], Markus Schilhabel[12], Johanna A Jähn[2,11], Hiltrud Muhle[2,11], Rainer Boor[11,13], Wim Van Paesschen[14], Roberto Caraballo[15], Natalio Fejerman[15], Sarah Weckhuysen[2,16–18], Peter De Jonghe[2,16,17,19], Jan Larsen[2,20], Rikke S Møller[2,20], Helle Hjalgrim[2,20], Laura Addis[21], Shan Tang[21], Elaine Hughes[22], Deb K Pal[2,21], Kadi Veri[2,23], Ulvi Vaher[2,23], Tiina Talvik[2,23], Petia Dimova[24], Rosa Guerrero López[2,25], José M Serratosa[2,25], Tarja Linnankivi[2,26], Anna-Elina Lehesjoki[2,27], Susanne Ruf[8], Markus Wolff[8], Sarah Buerki[28], Gabriele Wohlrab[29], Judith Kroell[30], Alexandre N Datta[31], Barbara Fiedler[32], Gerhard Kurlemann[32], Gerhard Kluger[33], Andreas Hahn[2,5], D Edda Haberlandt[34], Christina Kutzer[35], Jürgen Sperner[36], Felicitas Becker[2,37], Yvonne G Weber[2,37], Martha Feucht[38], Hannelore Steinböck[39], Birgit Neophythou[40], Gabriel M Ronen[41], Ursula Gruber-Sedlmayr[42], Julia Geldner[43], Robert J Harvey[44], Per Hoffmann[45,46], Stefan Herms[45,46], Janine Altmüller[2,3], Mohammad R Toliat[2,3], Holger Thiele[2,3], Peter Nürnberg[2–4,47], Christian Wilhelm[7], Ulrich Stephani[2,11,13], Ingo Helbig[2,11], Holger Lerche[2,37], Fritz Zimprich[2,6,51], Bernd A Neubauer[2,5,51], Saskia Biskup[7,48,49,51] & Sarah von Spiczak[2,11,51]

ARTICLE

De Novo Mutations in Synaptic Transmission Genes Including *DNM1* Cause Epileptic Encephalopathies

EuroEPINOMICS-RES Consortium,* Epilepsy Phenome/Genome Project, and Epi4K Consortium

The American Journal of Human Genetics *95*, 360–370, October 2, 2014

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

6 January 2017
EMA/741007/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Metformin for the treatment of progressive myoclonic epilepsy type 2 (Lafora disease)

On 12 December 2016, orphan designation (EU/3/16/1803) was granted by the European Commission to Centro de Investigación Biomédica en Red (CIBER), Spain, for metformin for the treatment of progressive myoclonic epilepsy type 2 (Lafora disease).

Search Orphan Drug Designations and Approvals

Generic Name:	metformin
Trade Name:	N/A
Date Designated:	12/14/2017
Orphan Designation:	Treatment of progressive myoclonus epilepsy type 2 (Lafora disease)
Orphan Designation Status:	Designated
FDA Orphan Approval Status:	Not FDA Approved for Orphan Indication
Marketing Approval Date:	N/A
Approved Labeled Indication:	
Exclusivity End Date:	N/A
Sponsor:	Consorcio Centro de Investigación Biomédica en Red, M.P. (CIBER) Monforte de Lemos 3-5 Pabellon 11 Madrid Spain *The sponsor address listed is the last reported by the sponsor to OOPD.*

PERSPECTIVAS FUTURAS

- Terapias personalizadas en epilepsia
  - Reposicionamiento de fármacos
  - Conjugados Ac-enzima
  - ASOs
- Terapias personalizadas en Parkinson y Huntington
  - ASOs
  - Combinaciones de fármacos a bajas dosis
- Diagnóstico preciso de demencias genéticas