



CSIC
CONSEJO SUPERIOR DE INVESTIGACIONES CIENTÍFICAS

 **UNIVERSITAS**
*Miguel
Hernández*

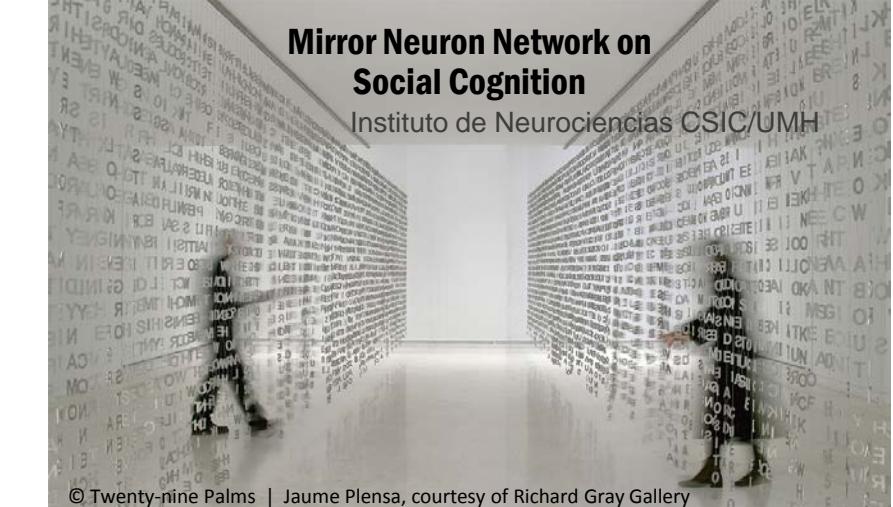
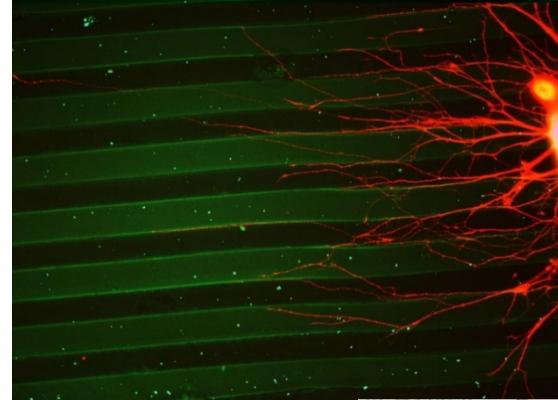
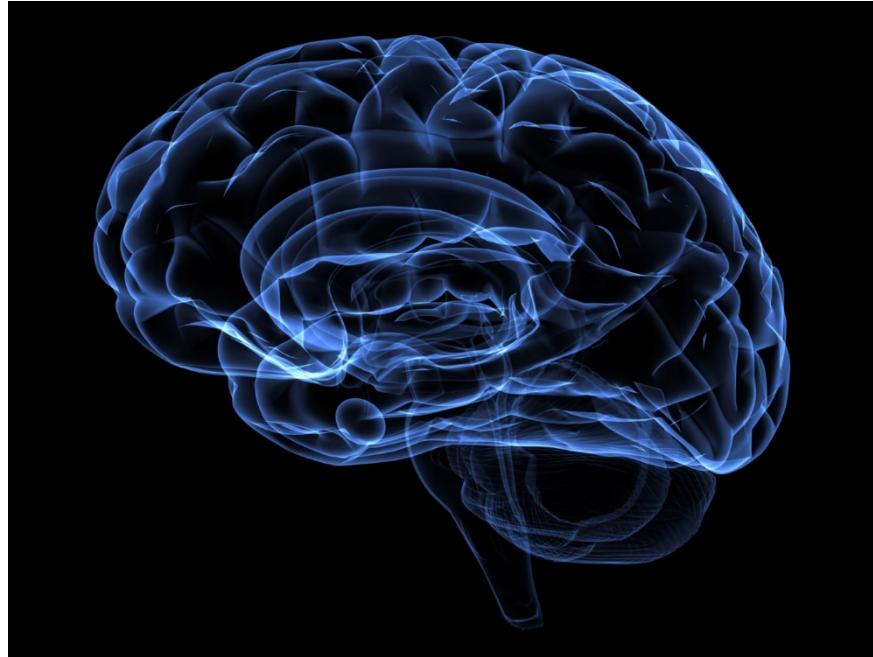


**Instituto
de
Neurociencias**

<http://in.umh.es/>

*Julio Barbas
20 de julio de 2016*

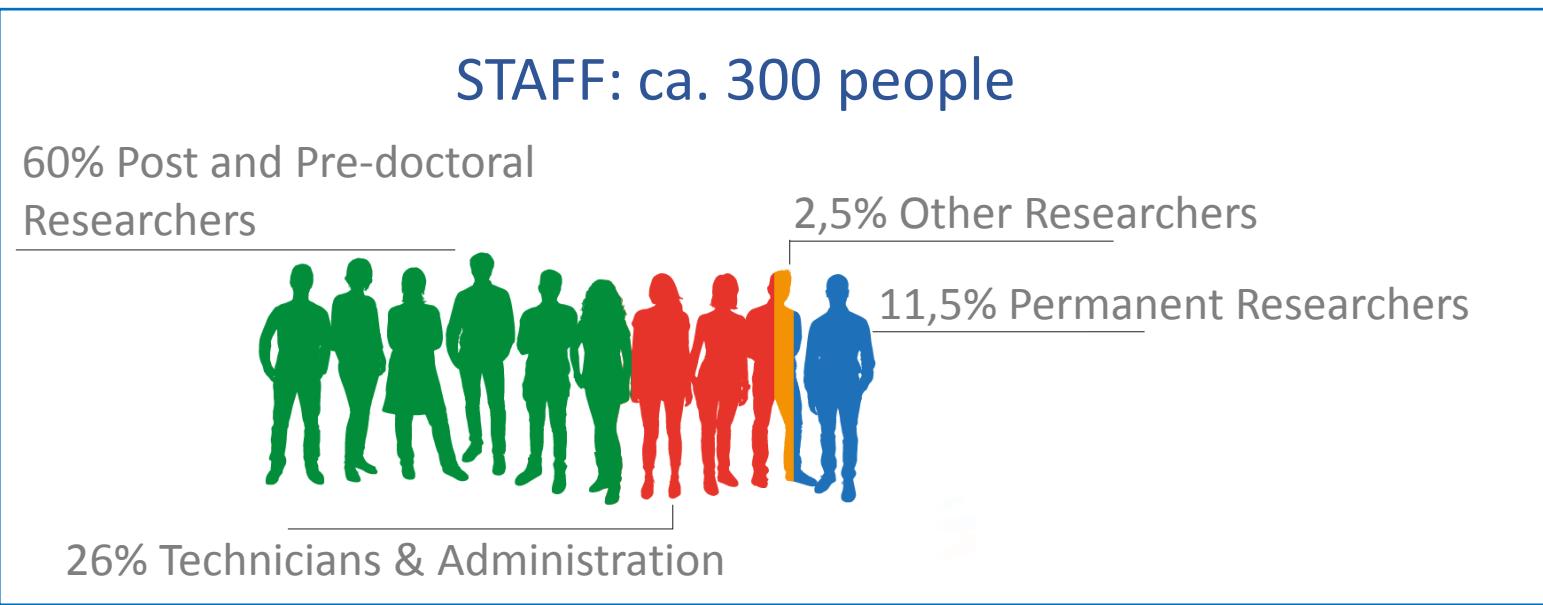
Our mission:



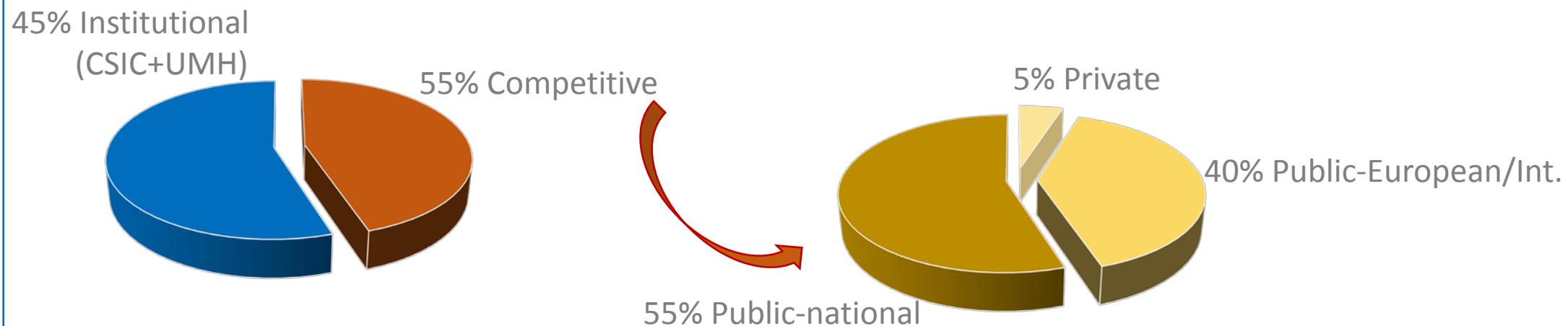
Scientific Departments:

- **Developmental Neurobiology**
- **Molecular Neurobiology**
- **Cellular & Systems Neurobiology**

Some figures:



BUDGET: ca. 10 M€/y (ave.2013-15)



1. AVIZOREX PHARMA, S.L. AND ITS LEAD COMPOUND AVX-012 FOR DRY EYE SYNDROME



Ocular surface wetness is regulated by TRPM8-dependent cold thermoreceptors of the cornea

2010

Andrés Parra¹, Rodolfo Madrid^{1,2}, Diego Echevarría¹, Susana del Olmo³, Cruz Morenilla-Palao¹, M Carmen Acosta¹, Juana Gallar¹, Ajay Dhaka⁴, Félix Viana¹ & Carlos Belmonte^{1,3}



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NATURE CELL BIOLOGY | ARTICLE



Direct inhibition of the cold-activated TRPM8 ion channel by G_α_q

2013

Xuming Zhang, Stephanie Mak, Lin Li, Andres Parra, Bristol Denlinger, Carlos Belmonte & Peter A. McNaughton



ARTICLE

Received 14 Nov 2014 | Accepted 13 Apr 2015 | Published 22 May 2015

DOI: 10.1038/ncomms8150

OPEN

TRPM8 is a neuronal osmosensor that regulates eye blinking in mice

2015

Talisia Quallo^{1,*}, Nisha Vastani^{1,*}, Elisabeth Horridge^{1,*}, Clive Gentry¹, Andres Parra², Sian Moss¹, Felix Viana², Carlos Belmonte², David A. Andersson¹ & Stuart Bevan¹



Abnormal activity of corneal cold thermoreceptors underlies the unpleasant sensations in dry eye disease

Illés Kovács^{a,b}, Carolina Luna^a, Susana Quirce^a, Kamila Mizerska^a, Gerard Callejo^{c,d}, Ana Riestra^b, Laura Fernández-Sánchez^f, Victor M. Meseguer^a, Nicolás Cuenca^a, Jesús Merayo-Lloves^e, M. Carmen Acosta^a, Xavier Gasull^{c,d}, Carlos Belmonte^{a,e}, Juana Gallar^{a,*}

2016



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Ophthalmology biotech focused on developing **novel therapies for Dry Eye Syndrome (DES)** based on the research of Prof. Carlos Belmonte on the **role of eye surface temperature-sensitive nerve fibers in tear film regulation**

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INVENTION (2010)



PATENT APPLICATION (2010)

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PUBLICATION (2010 after P.A. priority date)

 **nature
medicine**



Ocular surface wetness is regulated
by TRPM8-dependent cold
thermoreceptors of the cornea

Andrés Parra¹, Rodolfo Madrid^{1,2}, Diego Echevarría¹, Susana del Olmo³,
Cruz Morenilla-Palao¹, M Carmen Acosta¹, Juana Gallar¹, Ajay Dhaka⁴,
Félix Viana¹ & Carlos Belmonte^{1,3}

“Phase I/II, double-blind, placebo-controlled study assessing the safety and efficacy of **AVX-012** Ophthalmic Solution in subjects with mild-to-moderate Dry Eye Syndrome”

AVIZOREX PHARMA, S.L. inception as UMH spin-off obtaining exclusive license from UMH/CSIC (2013)


AVIZOREX
PHARMA
ENVISIONING THERAPEUTICS

2. UNBIASED DRUG SCREENS IN DROSOPHILA FOR TARGETING RESISTANT CANCER

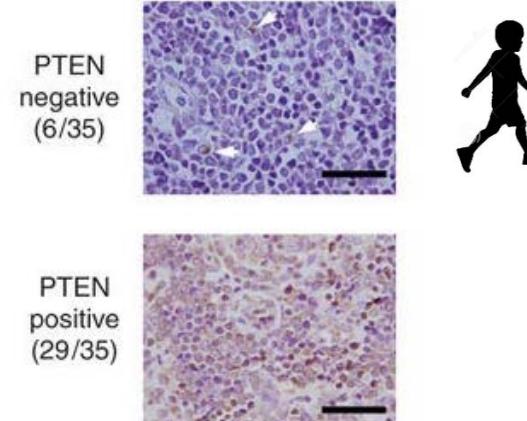


Epigenetic silencers and Notch collaborate to promote malignant tumours by *Rb* silencing

Dolors Ferres-Marco, Irene Gutierrez-Garcia, Diana M. Vallejo, Jorge Bolivar, Francisco J. Gutierrez-Aviño & Maria Dominguez

2016

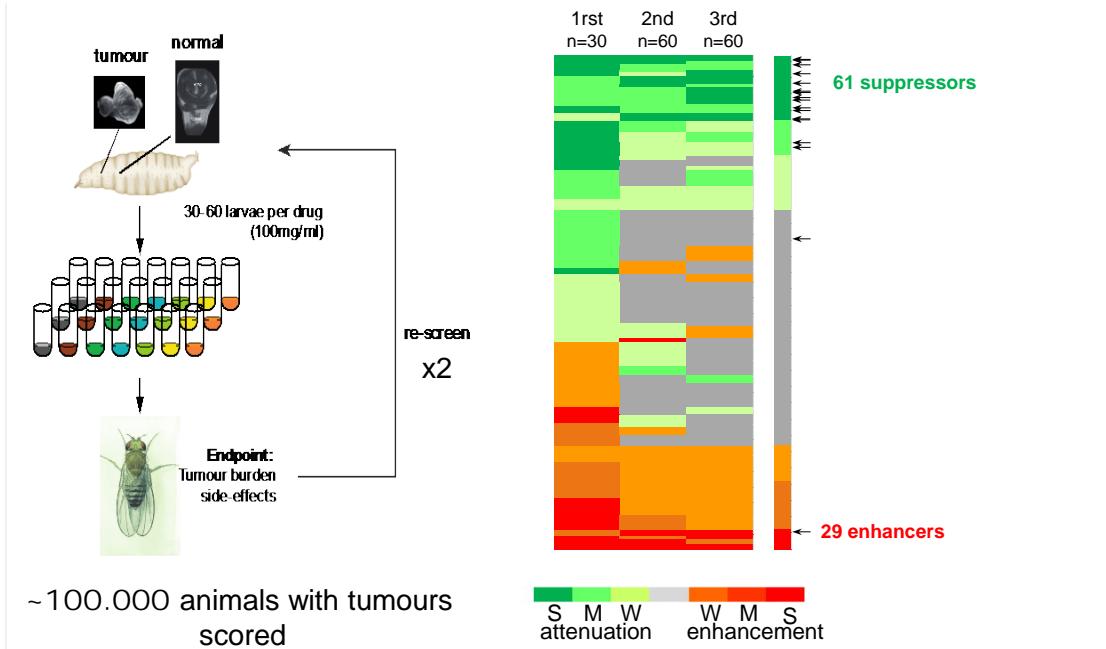
validation in resistant human leukemic cells



unbiased high-throughput screens
uncovering the uncharacterized, and the unexpected

Akt Notch cooperation

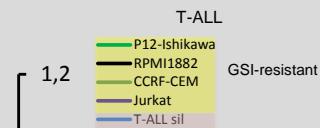
childhood T-ALL, pancreatic cancer, breast, lung, GI, prostate cancers etc



fly-based screen, LOPAC¹²⁸⁰ library, blinded test

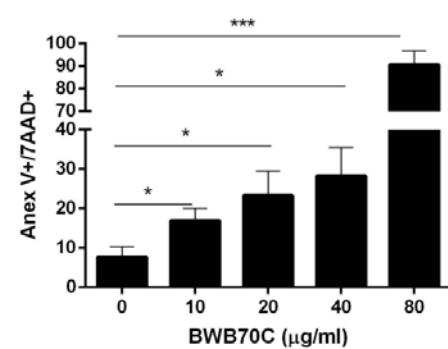
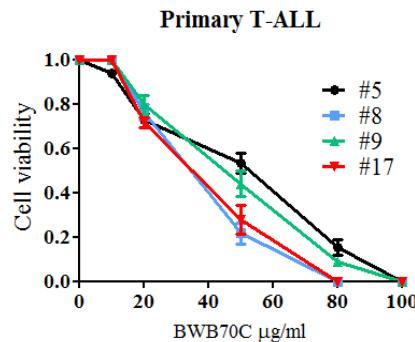
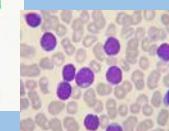
Both GSI-resistant and sensitive T-ALLs are sensitive to BW B70C

Relative cell viability (MTT)



primary PTEN⁻— T-ALL cells and BWB70C

primary T-ALL
From patients with
relapse disease



relapse/refractory primary T-ALL #17
(N1^{ICD} and PTEN^{loss})

Multiple drugs (23/47) pre-selected in flies inhibit GSI-resistant T-ALL

Notch i

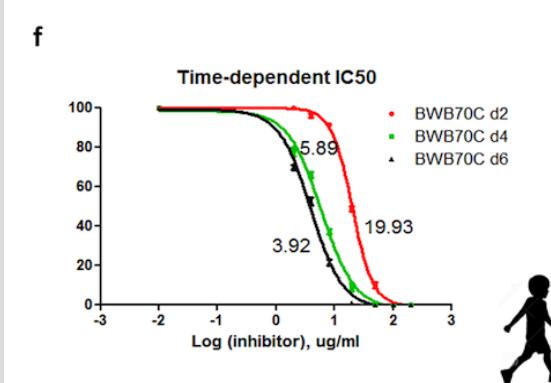
Cell viability of GSI-resistant RPMI882 T-ALL

Six compounds has no or low citotoxicity in PBMCs from healthy individuals



The six drugs with high 'therapeutic index'

Clemizole hydrochloride
Progesterone
Calcimycin



dials)

IC50, dose-and time- response, etc

3. FUNCTIONAL REORGANIZATION OF BRAIN NETWORKS FOR PROGNOSIS OF MENTAL/NEUROLOGICAL DISORDERS AND THERAPY EVALUATION



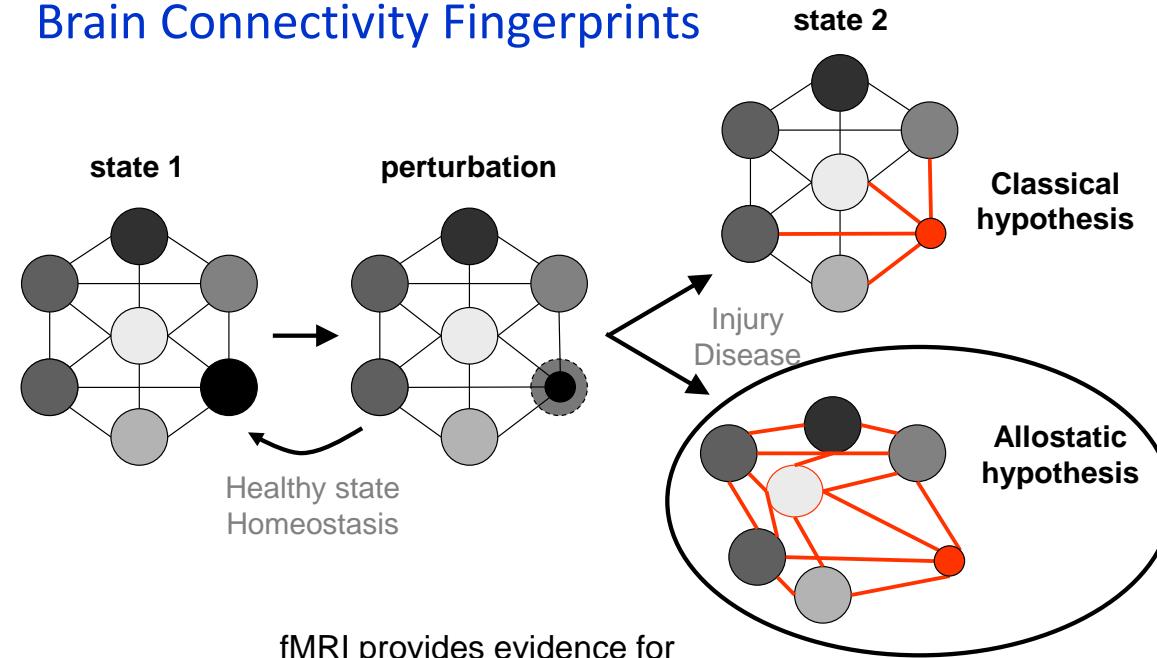
Avoiding catastrophic failure in correlated networks of networks

Saulo D. S. Reis, Yanqing Hu, Andrés Babino, José S. Andrade Jr, Santiago Canals, Mariano Sigman & Hernán A. Makse

2014



Brain Connectivity Fingerprints

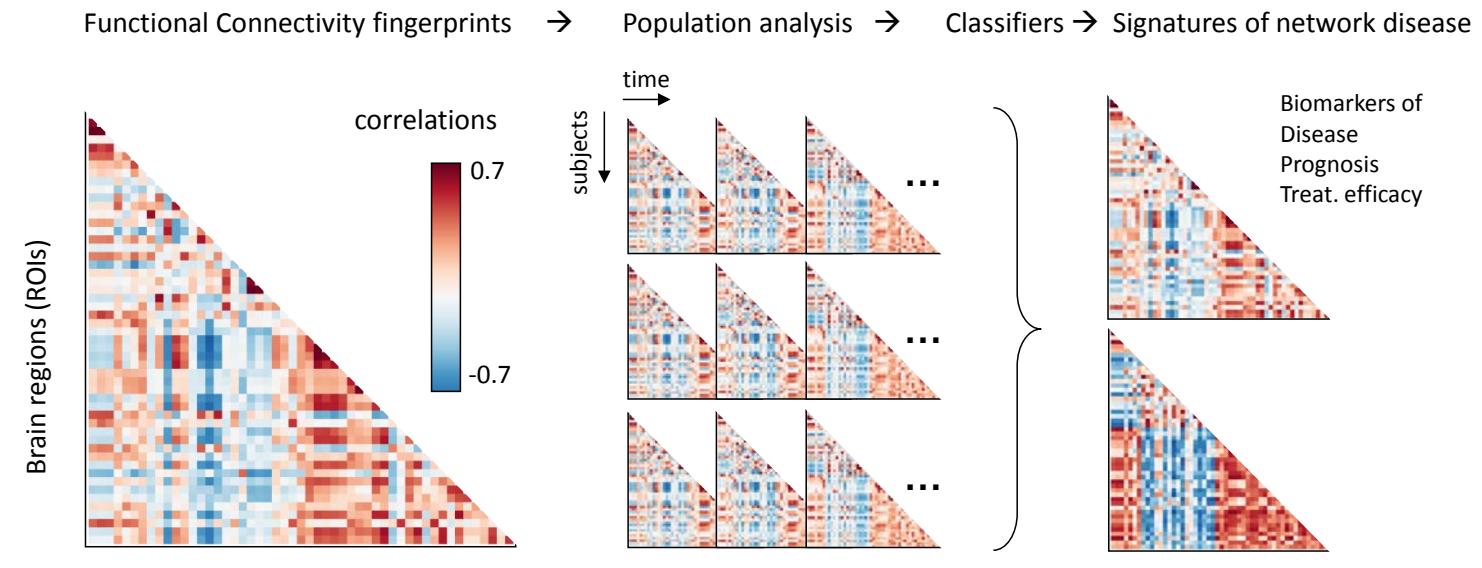
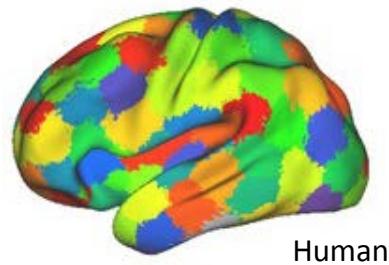
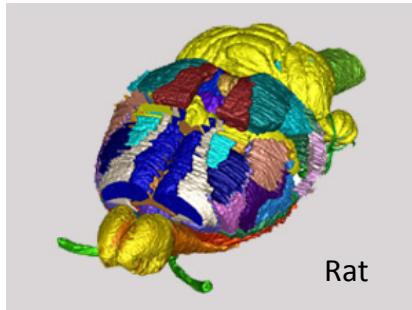


fMRI provides evidence for
NETWORK allostasis in pathology

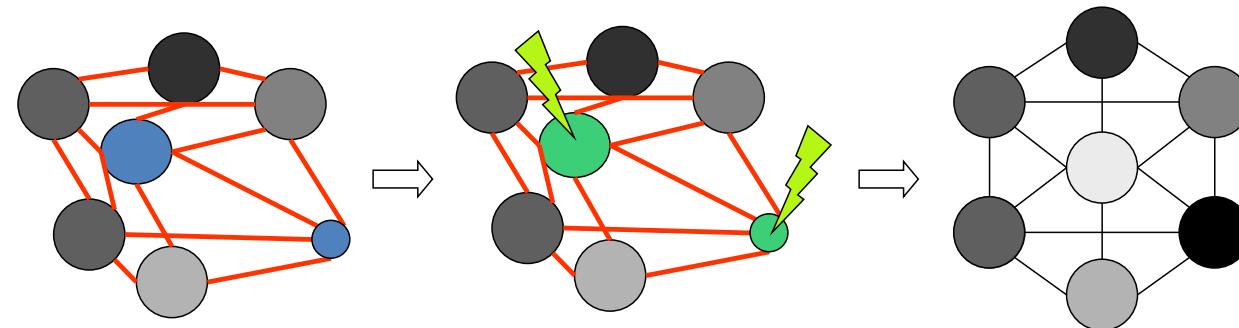


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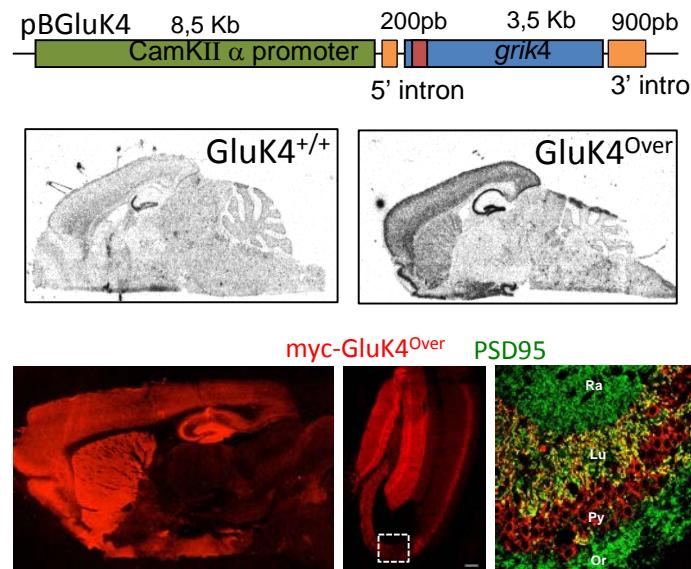
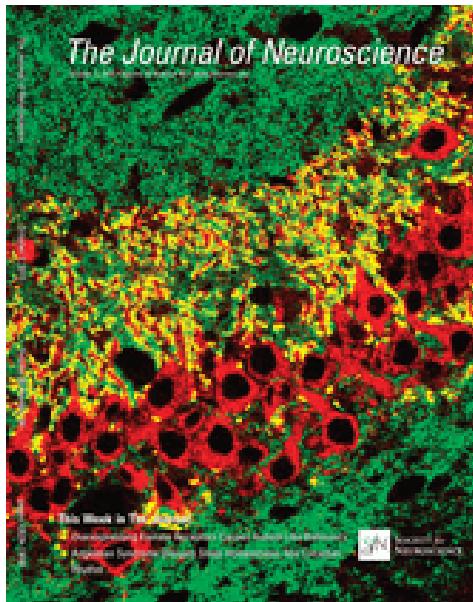
Functional maps (fMRI)



Network analysis identifies critical nodes → Targeted interventions → Network retuning (re-homeostasis)



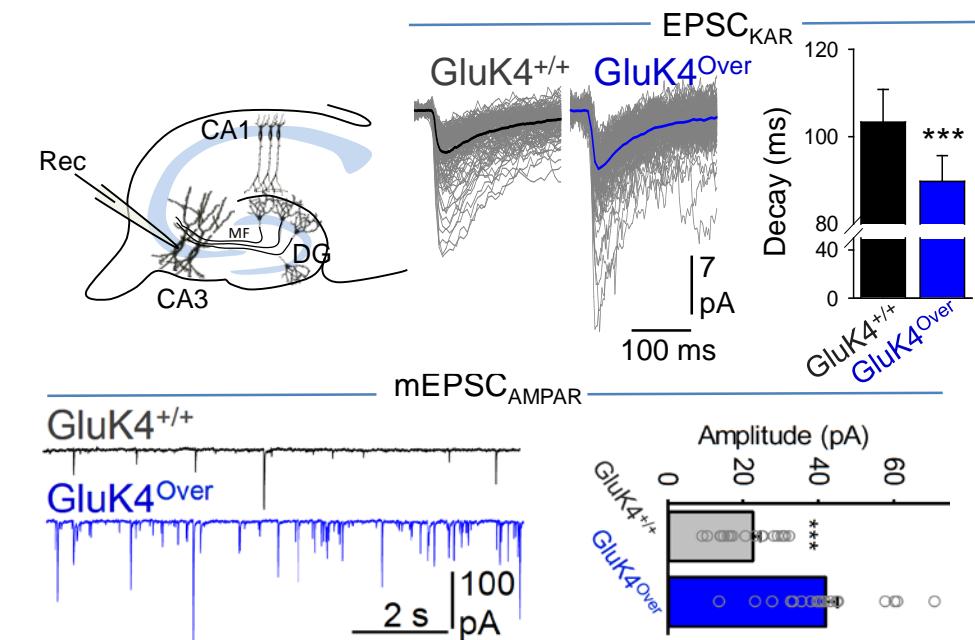
4. NEW ANIMAL MODEL FOR THE STUDY OF AUTISM, ANXIETY AND DEPRESSION



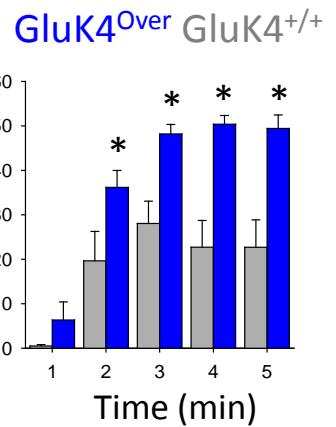
Increased Dosage of High-Affinity Kainate Receptor Gene *grik4* Alters Synaptic Transmission and Reproduces Autism Spectrum Disorders Features

M. Isabel Aller, Valeria Pecoraro, Ana V. Paternain, Santiago Canals, and Juan Lerma

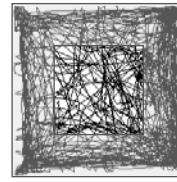
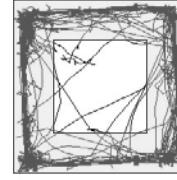
2015



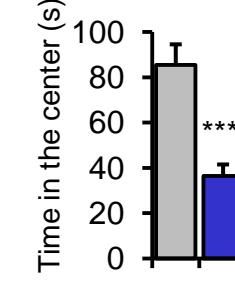
Forced Swimming test



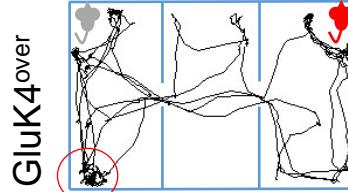
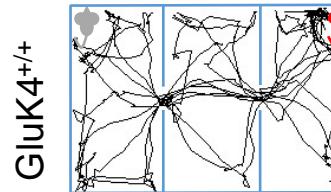
Open Field

GluK4^{+/+}GluK4^{Over}

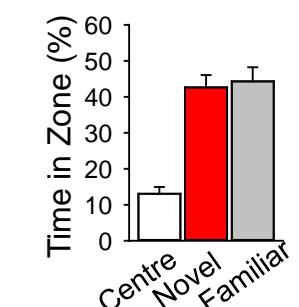
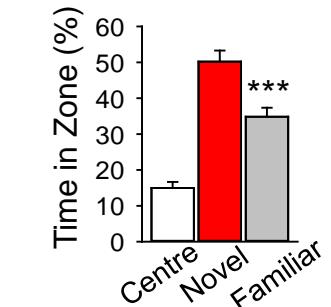
■ GluK4^{+/+}
■ GluK4^{Over}



Social Interaction test

GluK4^{+/+}GluK4^{Over}

Immobility (s)

Tianeptine but not Fluoxetine normalizes Anhedonia in GluK4^{Over} mice