Programa Cooperación Farma-Biotech

9º encuentro (4 de julio de 2013)

New Pharmacological Target for Fragile X Syndrome and Related Cognitive Disorders

Universitat Pompeu Fabra Barcelona

NeuroPhar

Barcelona, 4 de julio de 2013

GOBIERNO DE ESPAÑA MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

MEDICAMENTOS INNOVADORES Plataforma Tecnológica Española

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1. The Research Group

2. The Product

3. Partnering Opportunities

1. The Research Group

- *Name*: **Laboratory of Neuropharmacology**-NeuroPhar, Dpt. Health&Experimental Sciences, **Universitat Pompeu Fabra**, Barcelona

- *Director*: **Rafael MALDONADO** (>**230 papers** in international journals, including ***Nature***, ***Science***, ***Nature Medicine***, ***Nature Neuroscience***, ***Nature Genetics***, among others)

- *Collaborating companies*: Pharmaceutical (e.g. Esteve, Ferrer) and biotech (e.g. Panlab, Pharmaleads, BrainCo, Janus Developments)

- Funding sources: 72% (1 M€) PUBLIC – 28 (0.4 M€) % PRIVATE (2012)

- *Mission*: Our main interest is the development of research lines aimed at the identification of **new therapeutic targets at the nervous system level**, with a particular focus on cognitive and affective (depression and anxiety) disorders, chronic pain, eating disorders and drug addiction

1. The Research Group

1. Pain models in rodents

- 1.1. Nociceptive models
- 1.2. Inflammatory, neuropathic and osteoarthritic models
- 1.3. Operant models (80 operant cages for rodents)

2. Anxiety models in rodents

- 2.1. Non-operant models
- 2.2. Operant models

3. Depression models in rodents

- 3.1. Acute models
- 3.2. Chronic Unpredictable Mild Stress Paradigm

4. **Dependence models in rodents**

- 4.1. Non-operant models
- 4.2. Operant models

5. Cognitive models in rodents

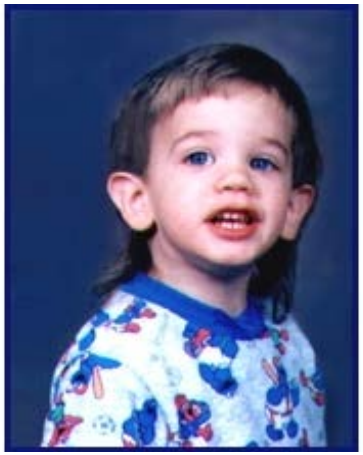
- 5.1. Non-operant models
- 5.2. Operant models

7. Neurochemical models and *in vivo* microdialysis in rodents

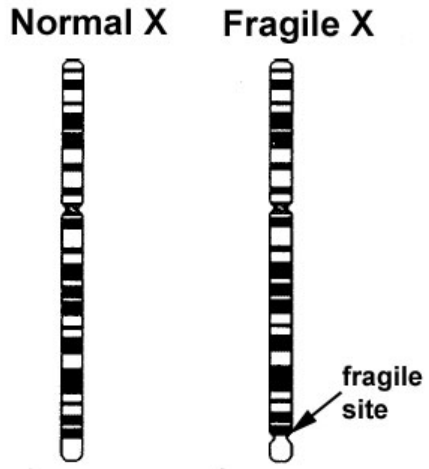
8. Microsurgery techniques in rodents

2. The Product: Target Indications

- **Cognitive deficits: we have reached a proof of concept for the Fragile X Syndrome** (Busquets-Garcia et al., ***Nature Medicine*** 19:603, 2013)



- **Physical changes** (long faces, muscular hipotony)
- **Learning and memory impairments**
- **Social and anxiety-like problems**
- **Impaired dendritic spines and synaptic plasticity**
- **Incidence: 1:4,000 males and 1:6,000 females**



2. The Product: Innovative mechanisms of action

Rescuing the cognitive deficit in Fragile X Syndrome mouse model

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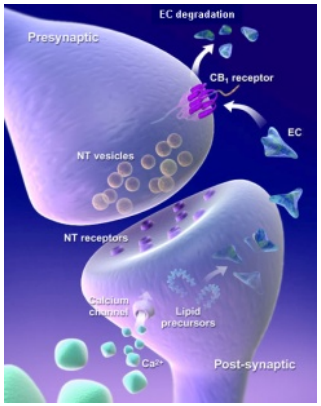

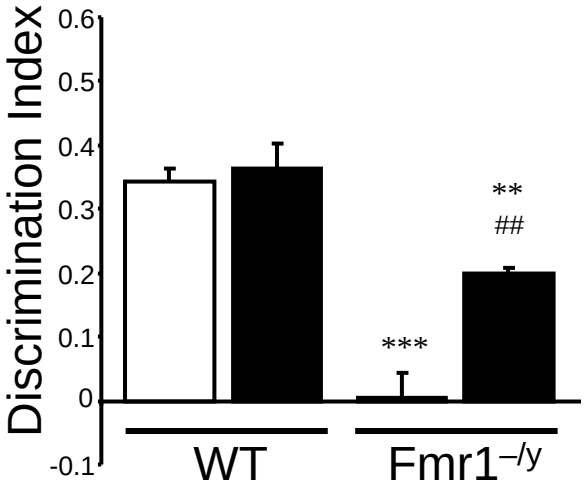

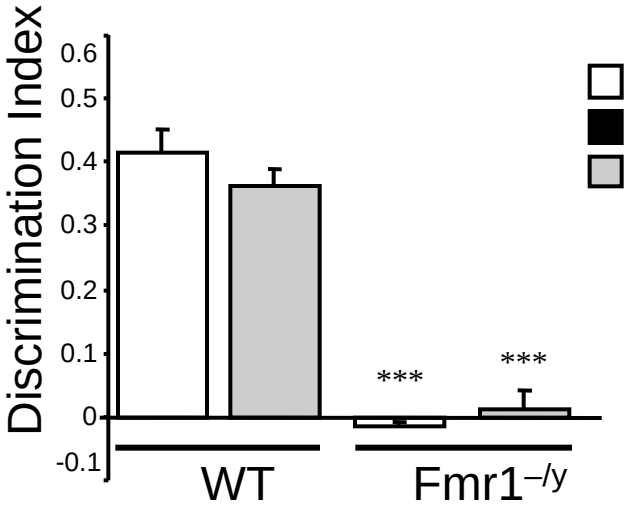

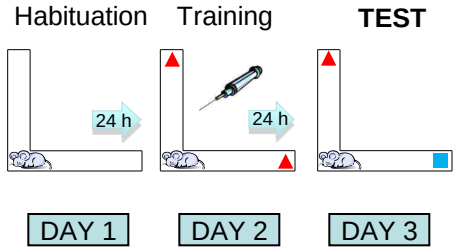

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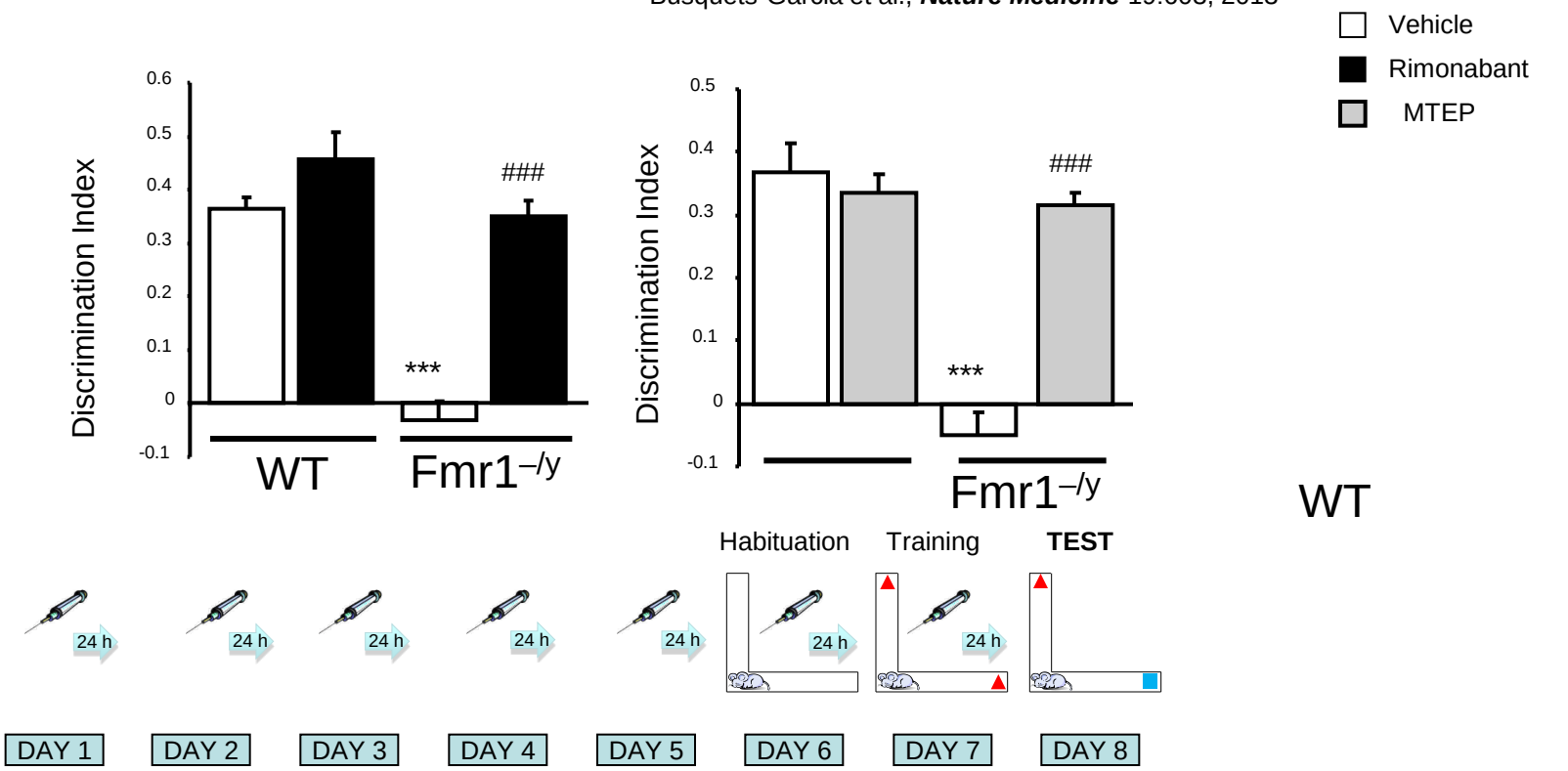

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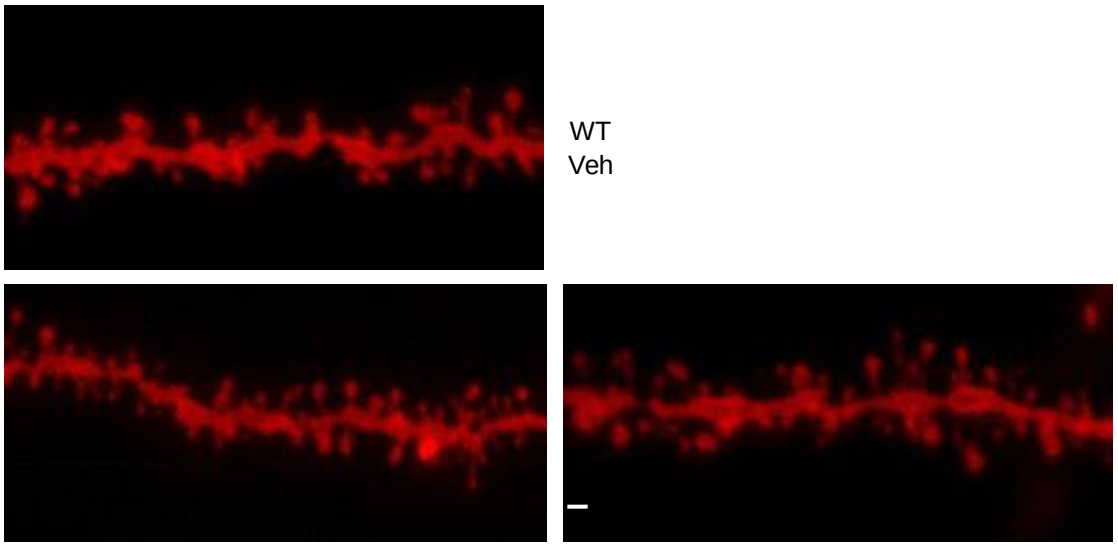

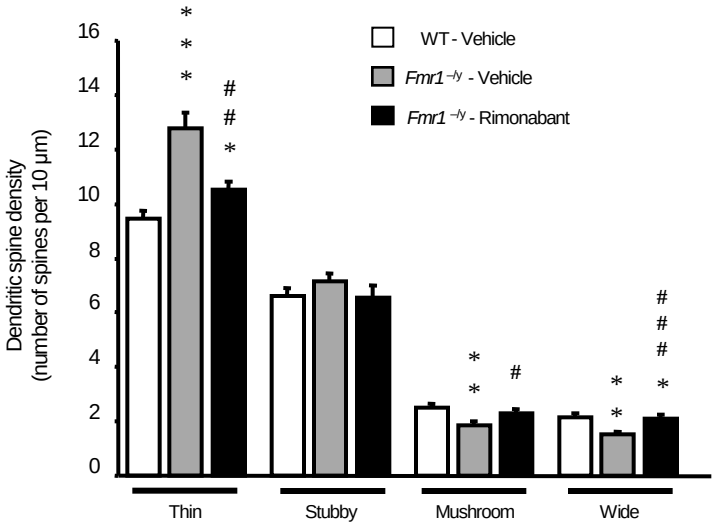

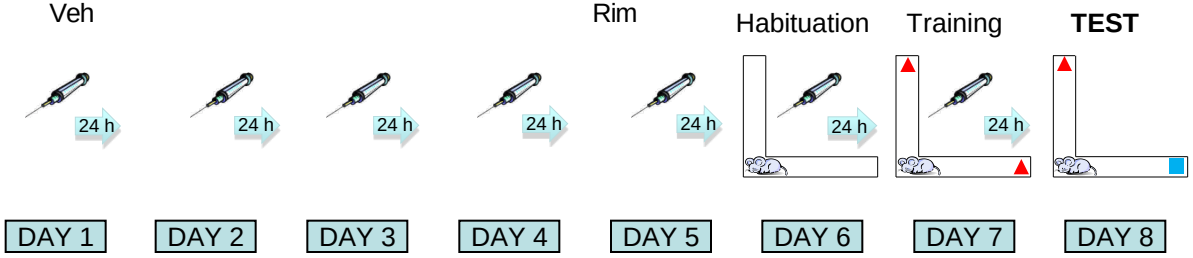

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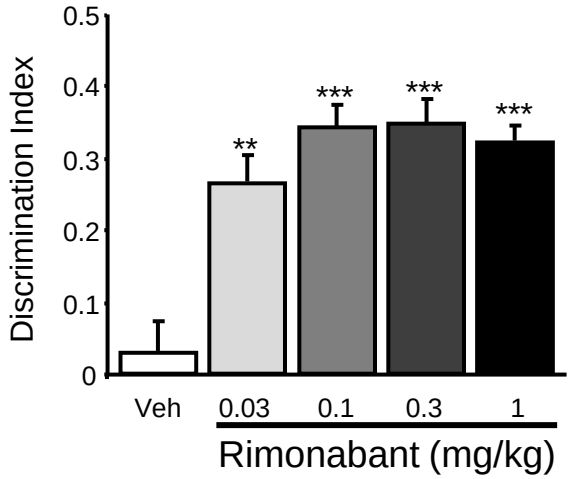
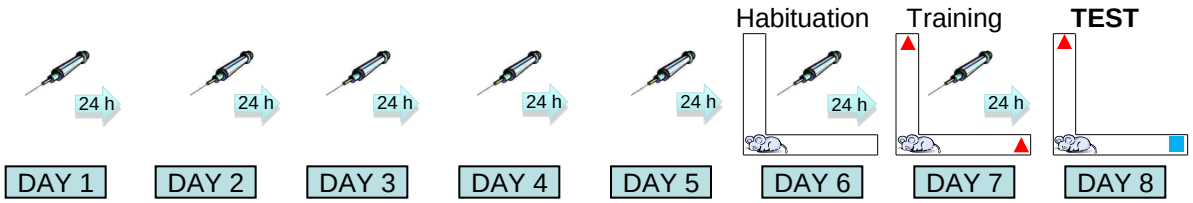


Rimonabant

	HUMAN	MOUSE	
	20 mg/day ACOMPLIA Metabolic Effectiveness In humans	4 mg/kg Metabolic effectiveness in rodents	Serious secondary adverse effects
	5 mg/day	1 mg/kg	Few adverse effects detected
	0.5 mg/day	0.1 mg/kg	



2. The Product: Innovative mechanisms of action

- The partial **blockade of the endocannabinoid system** has not been used yet as a pharmacological target for treating **cognitive deficits involving dendritic spines alterations**

- Using a **low dose** of a CB1 cannabinoid receptor antagonist has beneficial effects on the cognitive deficits in these genetic models: a 20 mg pill (Acomplia) would be **reduced to around 0.5 mg pill**

2. The Product: Differential features facing the market

1. Possibility of treatment of **orphan diseases** with already available and/or new drugs
2. **Low drug doses devoid of side-effects**
3. **Clinically well characterized pharmacological target**

- Present pharmacological drugs under **clinical trials** are:
  - mGluR5 antagonist AFQ056 (*Novartis*)
  - mGluR5 antagonist RO4917523 (*Roche*)
  - GABAb agonist STX209 (*Seaside*)
- **No treatment** available so far

2. The Product: Current status of development

- **Dose-response curve** for the different manifestations of the cognitive impairment (doses from 0.03 to 1 mg/kg in mice show a significant improvement in memory)

- **Proof of concept in other murine disease models** with cognitive impairment

2. The Product: IPR protection

- **#PCT/EP2013/055728, Priority date: 19/03/2013**

2. The Product: Pitfalls & Risks to be considered

- **Transfer from mouse to human**
- **Treatment of infants**
- **Putative secondary effects** (dose-related)

3. Partnering Opportunities

- We are now performing further preclinical assays to complement the results obtained so far (**proof-of-concept**), including other disease models sharing common features with FXS.
- The main outcome will be the **validation of the new target** for the **reprofiling** of existing drugs or for the **development** of new drugs for FXS and related diseases.
- To validate the target identification and the technology employed we would need **co-funding** from investors or possible **licensees**.

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