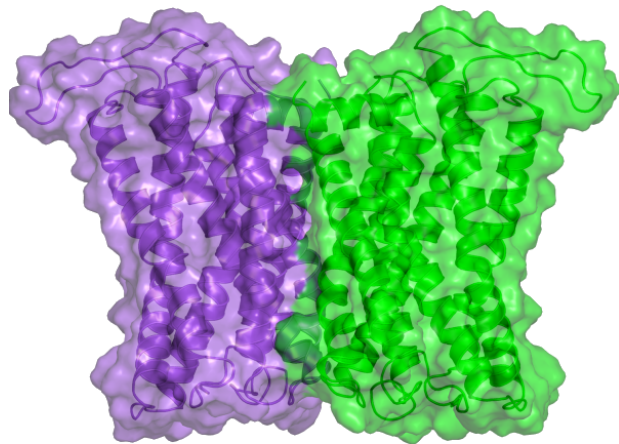
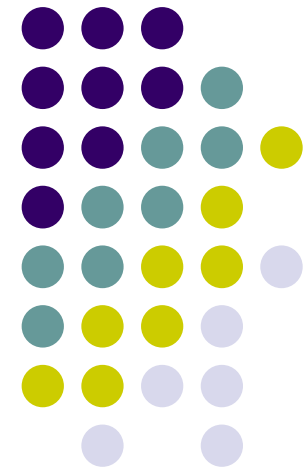


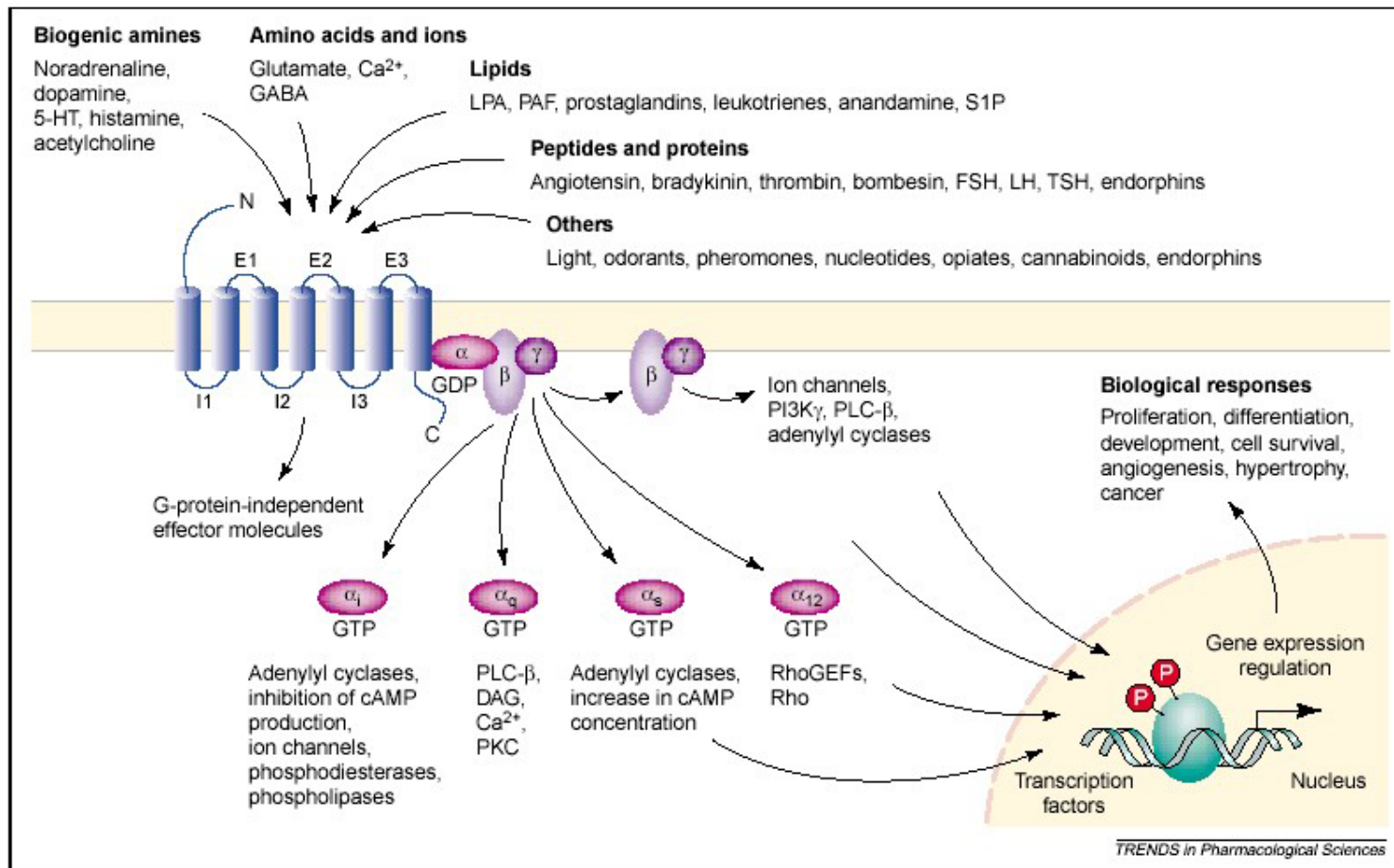
# Una nova visió de l'oligomerització de receptors acoblats a proteïna G



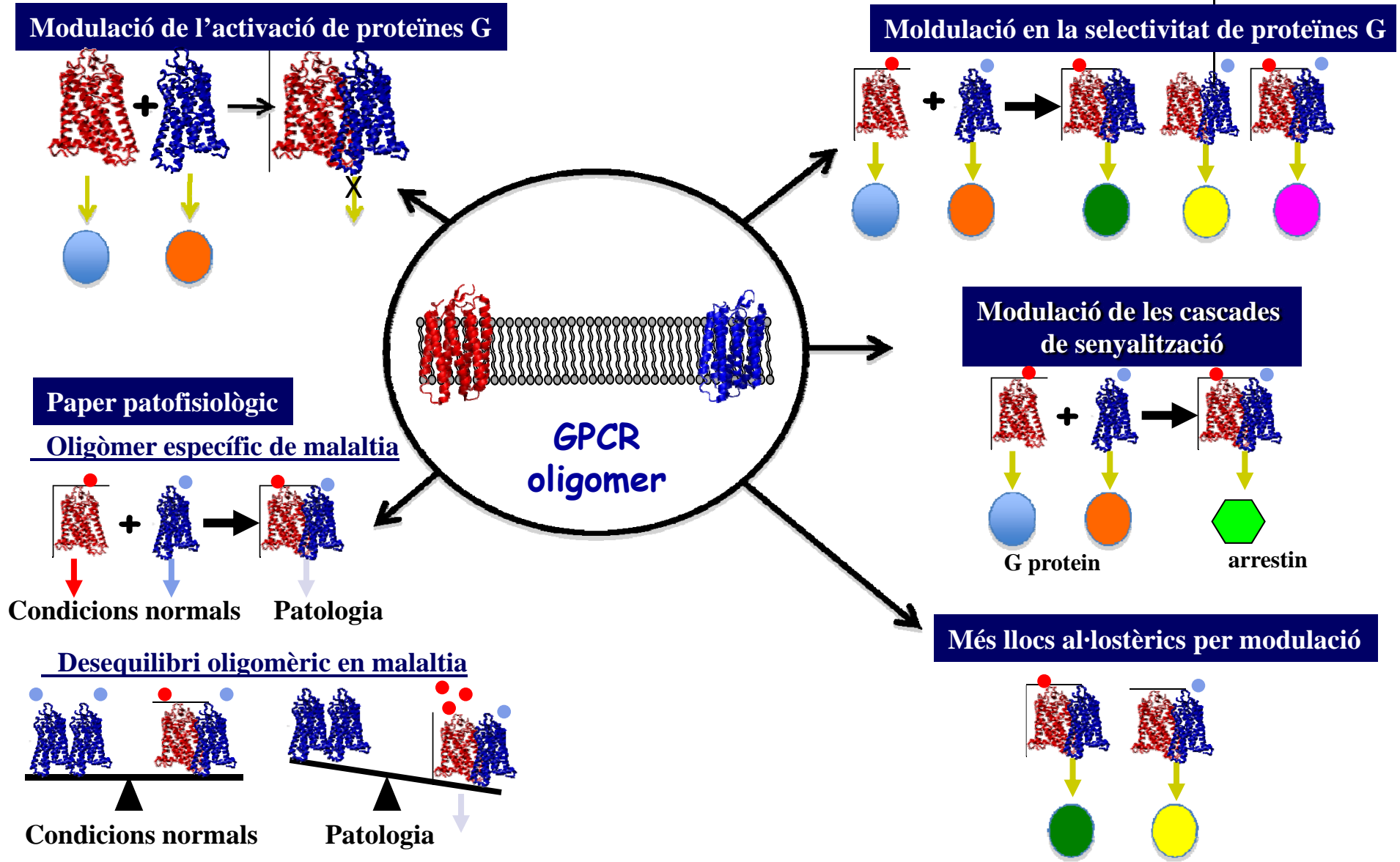
Jorge Gandía  
Grup de Neurofarmacologia i Dolor  
Facultat de Medicina-Bellvitge  
Universitat de Barcelona



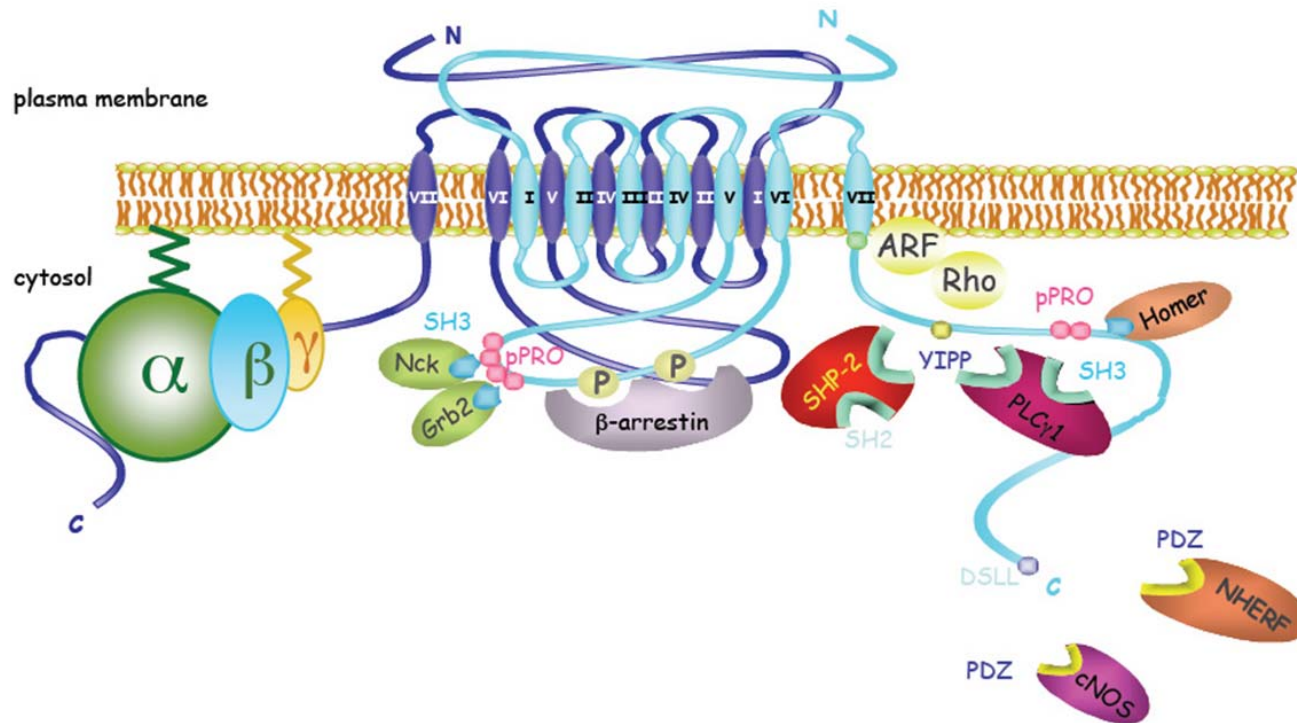
# GPCRs



# Els GPCR oligomeritzen



# Els oligòmers de GPCR formen una gran xarxa de proteïnes



- Sorgeix un nou repte: identificar nous oligòmers de GPCR i altres proteïnes que hi interactuin

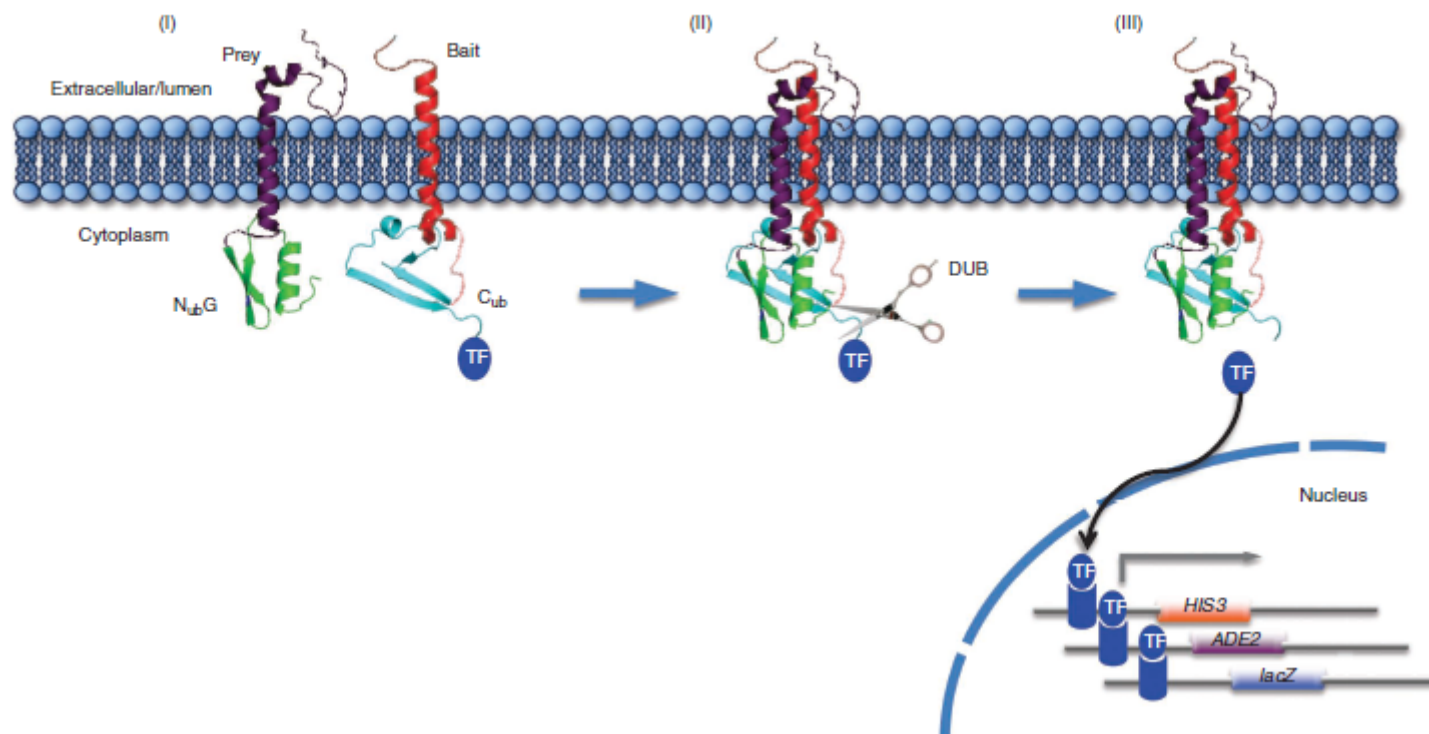
# MYTH



## Detecting interactions with membrane proteins using a membrane two-hybrid assay in yeast

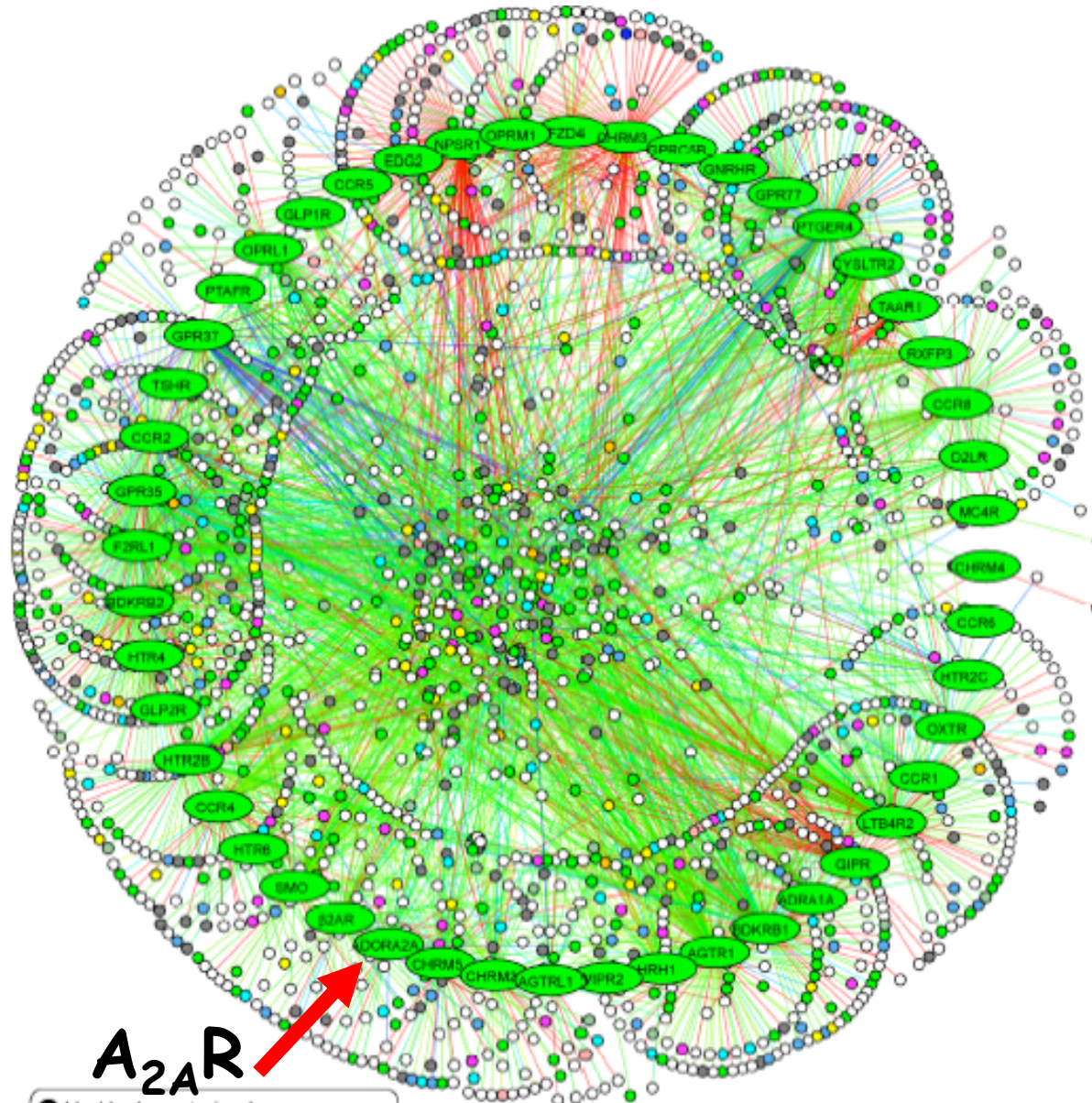
Jamie Snider, Saranya Kittanakom, Dunja Damjanovic, Jasna Curak, Victoria Wong & Igor Stagljar

Department of Biochemistry and Department of Molecular Genetics, Terrence Donnelly Centre for Cellular and Biomolecular Research, University of Toronto, Toronto, Ontario, Canada. Correspondence should be addressed to I.S. (igor.stagljar@utoronto.ca).





# The Receptorsome Project



# GPR37

- GPCR orfe, pertany a la família I

The neuropeptide head activator is a high-affinity ligand for the orphan G-protein-coupled receptor GPR37

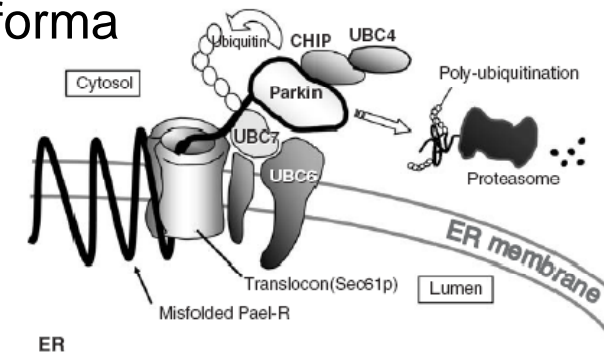
Meriem Rezgaoui<sup>1</sup>, Ute Süsens<sup>1</sup>, Atanas Ignatov<sup>1</sup>, Mathias Gelderblom<sup>2</sup>, Günter Glassmeier<sup>3</sup>, Inga Franke<sup>1</sup>, Jens Urny<sup>1</sup>, Yuzuru Imai<sup>4</sup>, Ryosuke Takahashi<sup>3</sup> and H. Chica Schaller<sup>1,\*</sup>



- També conegut com Pael-R (Parkin associated endothelin-like receptor): relacionat amb una forma juvenil de la malaltia de Parkinson

Pael receptor induces death of dopaminergic neurons in the substantia nigra via endoplasmic reticulum stress and dopamine toxicity, which is enhanced under condition of parkin inactivation

Yasuko Kitao<sup>1,\*†</sup>, Yuzuru Imai<sup>2,†</sup>, Kentaro Ozawa<sup>1</sup>, Ayane Kataoka<sup>2</sup>, Toshio Ikeda<sup>3</sup>, Mariko Soda<sup>2</sup>, Kazuhiko Nakimawa<sup>4</sup>, Hiroshi Kiyama<sup>4</sup>, David M. Stern<sup>7</sup>, Osamu Hori<sup>1</sup>, Kazumasa Wakamatsu<sup>6</sup>, Shosuke Ito<sup>6</sup>, Shigeyoshi Itoharu<sup>3</sup>, Ryosuke Takahashi<sup>2,5,†</sup> and Satoshi Ogawa<sup>1,†</sup>



- Involucrat en el metabolisme de la dopamina:

GPR37 associates with the dopamine transporter to modulate dopamine uptake and behavioral responses to dopaminergic drugs

Daniela Marazziti, Silvia Mandillo, Chiara Di Pietro, Elisabetta Golini, Raffaele Matteoni, and Glauco P. Tocchini-Valentini\*

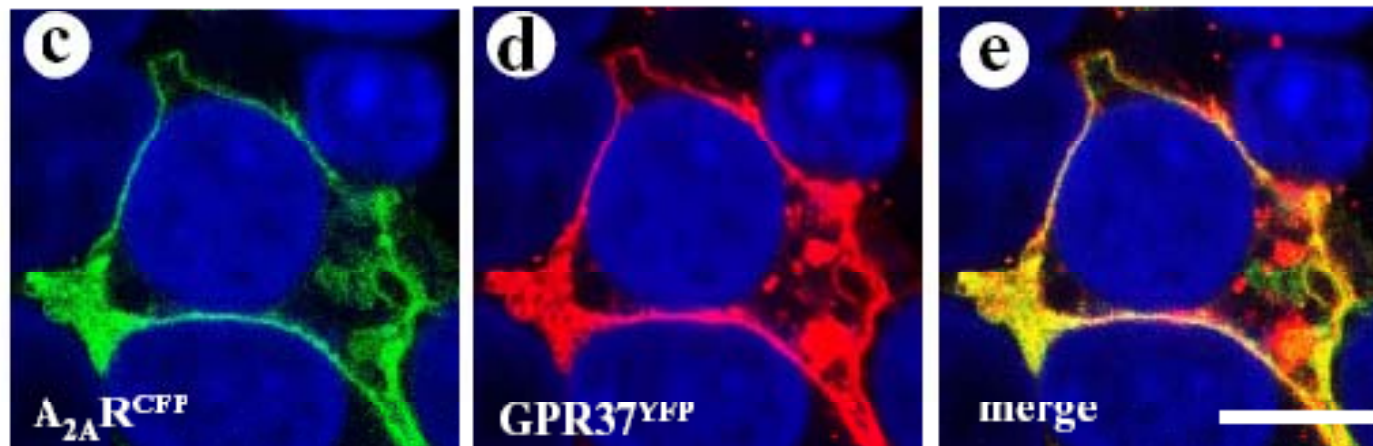
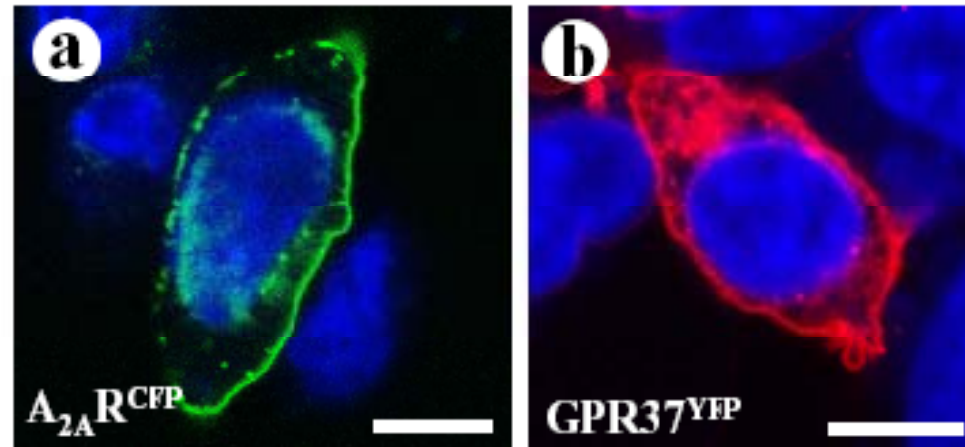
Istituto di Biologia Cellulare-Consiglio Nazionale delle Ricerche, Campus "A. Buzzati-Traverso," Via E. Ramerini 32, Monterotondo Scalo, I-00015 Rome, Italy

Communicated by Robert Haselkorn, University of Chicago, Chicago, IL, and approved April 19, 2007 (received for review April 2, 2007)

# L'oligòmer $A_{2A}R$ /GPR37



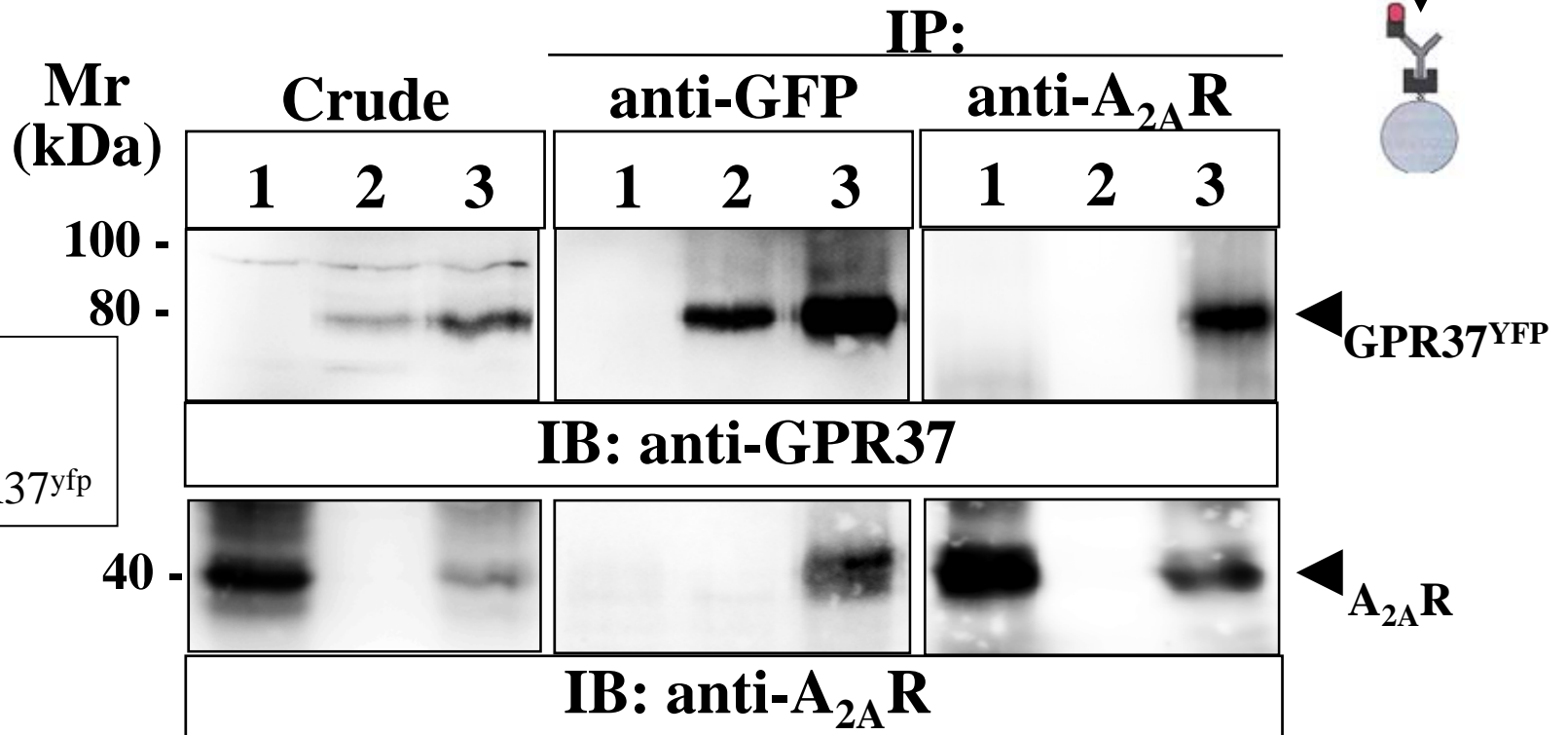
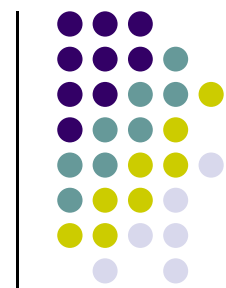
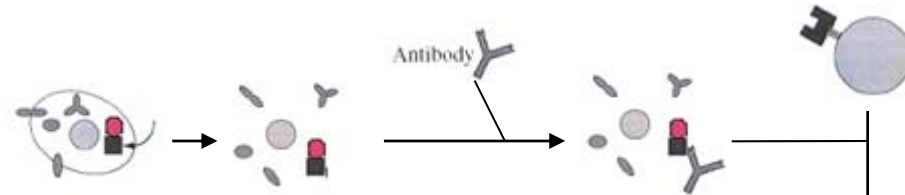
- Co-distribució





# L'oligòmer A<sub>2A</sub>R/GPR37

- Co-immunoprecipitació

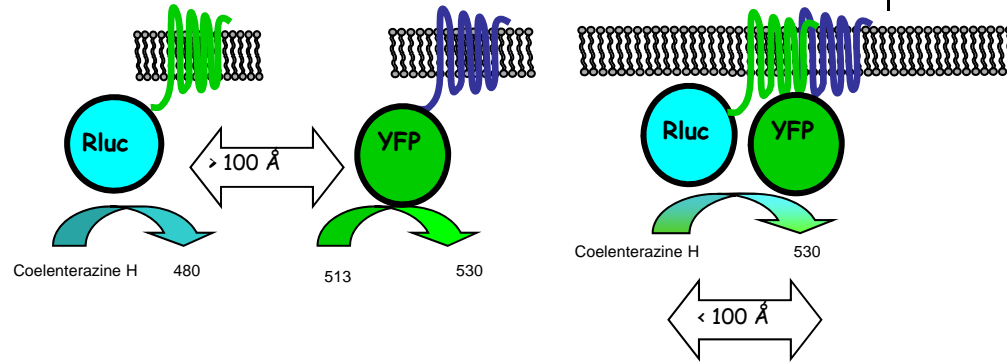


1: A<sub>2A</sub>  
 2: GPR37<sup>yfp</sup>  
 3: A<sub>2A</sub> + GPR37<sup>yfp</sup>

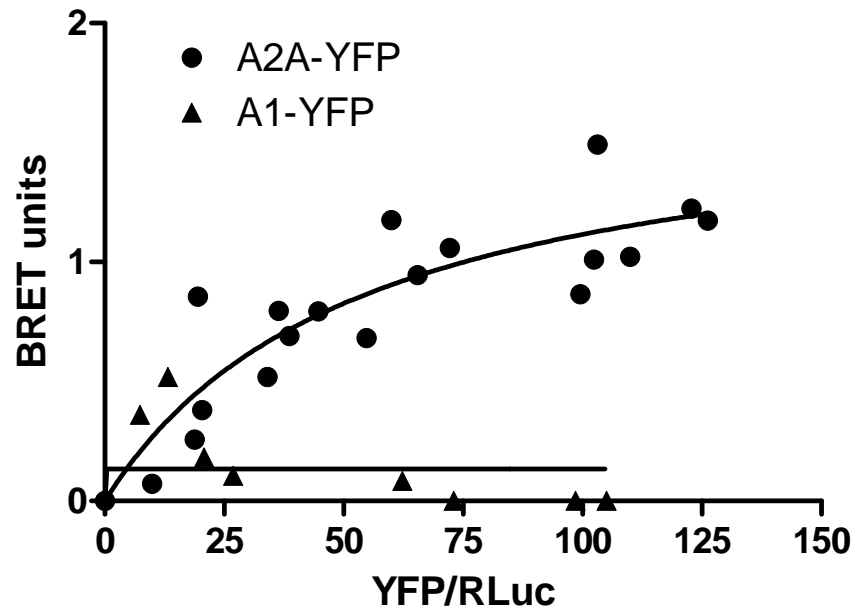
# L'oligòmer A<sub>2A</sub>R/GPR37



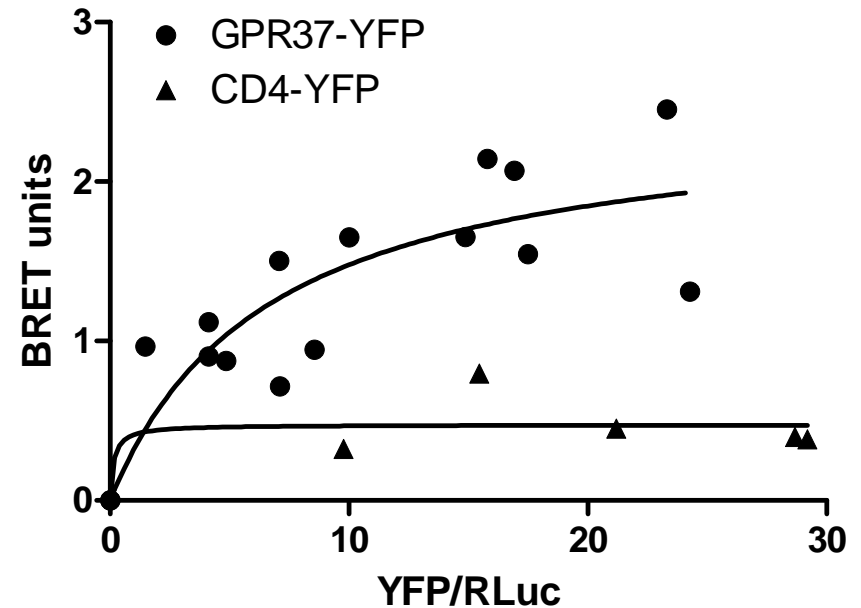
- Interacció *in vivo*:  
BRET



**GPR37-Rluc**



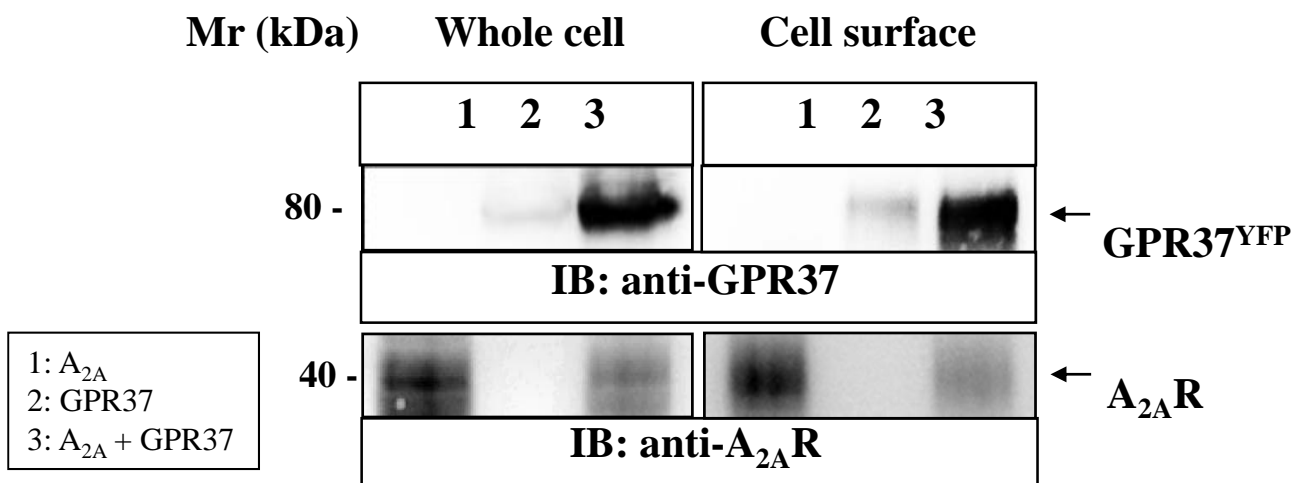
**A2A-RLuc**





# L'oligòmer $A_{2A}R/GPR37$

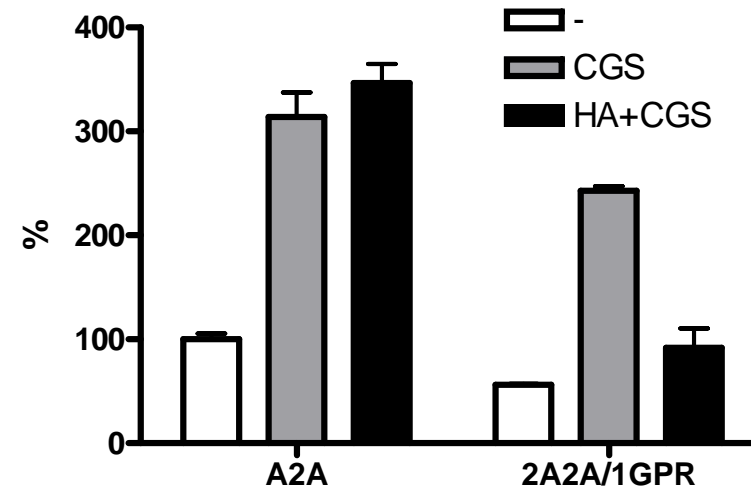
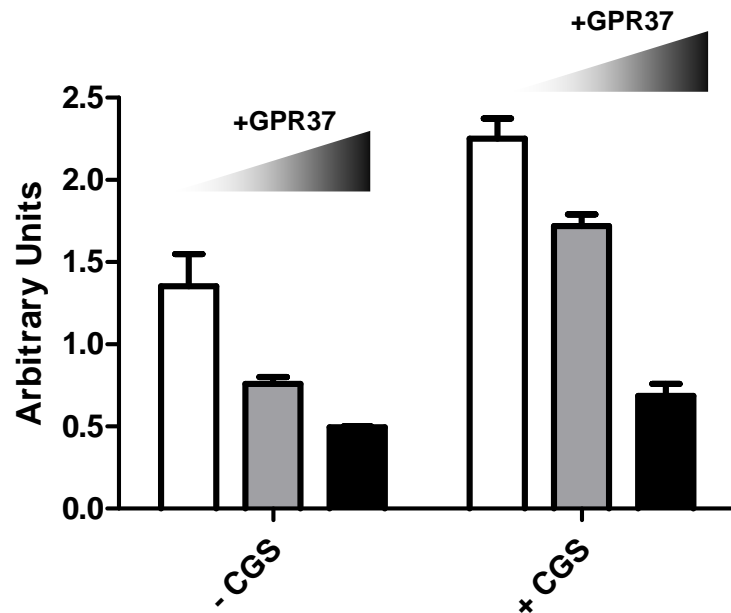
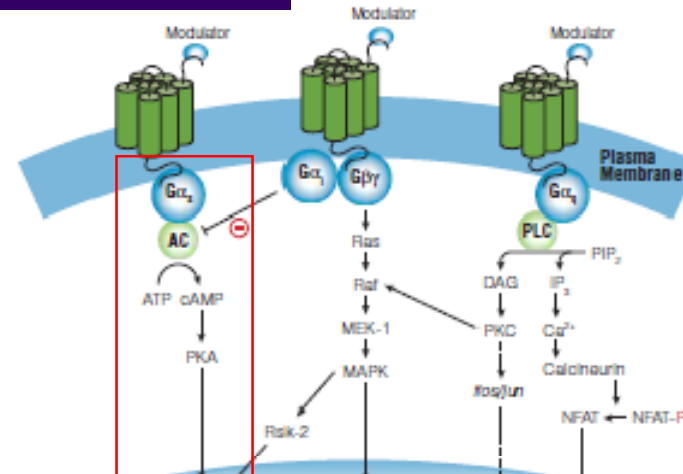
- Rellevància funcional (I)
  - Expressió en superfície



# L'oligòmer A<sub>2A</sub>R/GPR37



- Rellevància funcional (II)
  - Producció d'AMPC

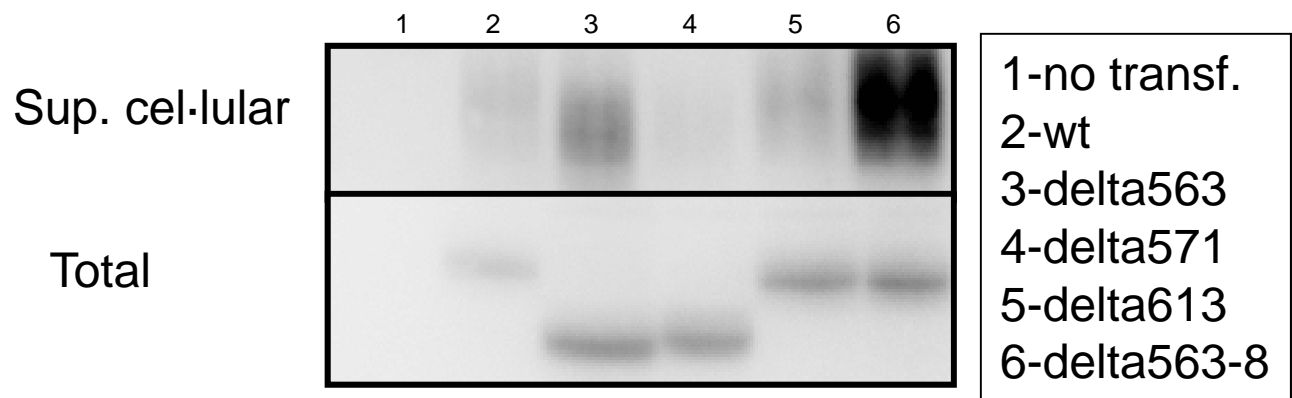




# L'oligòmer A<sub>2A</sub>R/GPR37



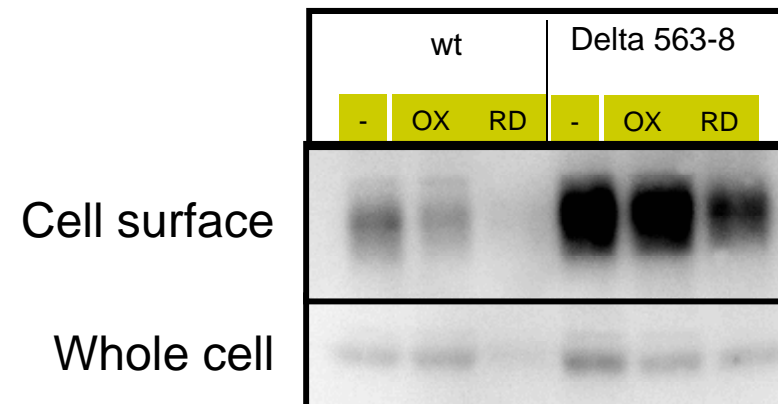
- Anàlisi estructural de GPR37



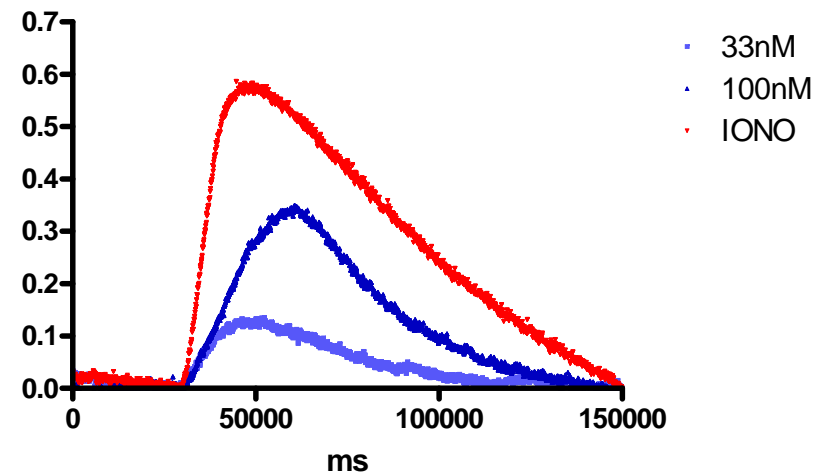
# L'oligòmer A<sub>2A</sub>R/GPR37



- Condicions oxidatives/reductores



- Activació de canals de calci (FLUO4)
  - Bateria de pèptids anàlegs a HA



# L'oligòmer A<sub>2A</sub>R/GPR37



- Generació de ratolins *gpr37* -/-
  - Animals hemiparkinsonians vs individus control en presència/absència d'un antagonista del receptor A<sub>2A</sub>



# Una nova visió de l'oligomerització de receptors acoblats a proteïna G

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