Optopharmacological compounds targeting mGlu5 receptors

CSIC, IBEC, UAB and CNRS have developed the first light-regulated mGluR5 negative allosteric modulators. Control of drug action is obtained by means of light irradiation, being these drugs capable of reversible switching between inactive and active states for controlled application in treatment of pain or Parkinson among other diseases.

An offer for Patent Licensing and/or R+D collaboration

Light induction of allosteric modulation of mGluR5

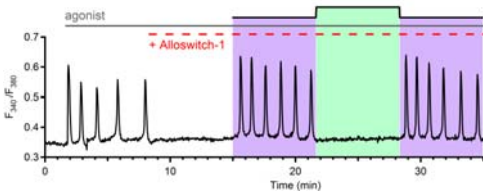
Drugs that target G protein-coupled receptors (GPCRs) account for the majority of best-selling medicines on the market and nearly half of the prescription pharmaceuticals. However, some challenges remain unsolved such as that these drugs are applied systemically and it's not possible regulate their spatial effects in order to target to a specific organ of interest.

We have developed the first light-regulated negative allosteric modulators (NAM) of the metabotropic glutamate receptor 5 (mGluR5) with potential pharmacological activity on important therapeutic targets.

Administration of these light-regulated drugs in combination with light specifically in certain time and region would provide a qualitatively new degree of control and regulation of drug action.

High potency of these compounds has been proved both *in vitro*, in cultured HEK cells overexpressing mGluR5 and rat cortical astrocytes, showing an IC50 between 30-500 nM and *in vivo in a Xenopus tropicalis* tadpoles model.

Due to the roles of mGlu5 receptors in synaptic transmission, these light regulated compounds may have application for pain, Parkinson, epilepsy or anxiety treatments, with local controlled application.



Intracellular calcium signals in HEK cells expressing mGlu5. Activation at 390nm (violet) and deactivation at 490 nm (green) after compound administration at 100 nM.

Main advantages and applications

- The first drug-like optopharmacological ligands to target allosterically an endogenous GPCR (mGluR5).
- These compounds are non-competitive antagonists acting only on glutamate activated receptors avoiding desensitization side effects.
- Show high selectivity over other mGlu receptors both in dark and at 380nm or 490 nm irradiation.
- Higher activity than other known mGluR5 NAM such as Fenobam, which are no light dependent.
- Potential application for local controlled treatment in a specific target region.
- Absence of toxicity both in vitro and in vivo.
- Ongoing efficacy demonstration in Parkinson and pain animal models.

Patent Status

Priority patent application filed

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CSIC Consejo Superior de Investigaciones Científicas

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cnrs