



*Oficina de Transferencia de Resultados de Investigación (OTRI)*

## Laboratory of Cellular Neuroscience and Plasticity

### **Brief description**

The Laboratory of Cellular Neuroscience and Plasticity (LCNP) at Pablo de Olavide University (UPO) is focused on the **basic and applied study of cellular and molecular mechanisms** underlying normal and altered physiology of the nervous system in mammals.

LCNP's experts work on the study of the **processes and plastic changes in the brain after certain types of lesions, in response to learning and emotions, as well as the changes observed in the formation of cortical maps during development**. The study and understanding of synaptic plasticity processes is crucial to understand brain physiology, the mechanisms involved in plastic processes and the ways to manipulate it for healing purposes.

The LCNP also work in the **identification of potential therapeutic targets for a variety of disorders of the nervous system, the validation of substances that induce neuronal death and in the development and testing of new materials and techniques in neurobiology**. For instance we have collaborated in the synthesis and testing of a new caged compound (which becomes active in response to light stimulation only) that has been used at subcellular level.

To perform these studies, the laboratory team uses a wide range of techniques: **electrophysiology techniques** (electrical activity recordings in in vitro and in vivo models); **imaging techniques** (photolysis, light induced channel activation); **hystology/morphological techniques** and **biochemical techniques** (neurotransmitter release study in synaptosomes preparations).

### **Scientific and technological services offered.**

- Determination of potential therapeutic targets for the treatment of nervous system disorders.
- Validation of substances that induce neuronal death.
- Design and testing of new materials and techniques in neurobiology. For instance we have participated in the design and synthesis of a new molecule which becomes active under light stimulation (caged compounds) in a localized compartment (subcellular level) of the cell under study. These molecules are of a great value in the study of synaptic plasticity.
- Pharmacological studies, analysis of different substances with potential pharmacological use, determination of the dose-response relationship (in vitro and in vivo) in different cell types: glia, cardiomyocytes, tumoral cells and others.
- Determination of the cellular and molecular mechanisms of action for different substances in the nervous system and analysis of the cellular signalling pathways involved.
- Determination of the toxic effects and excitotoxicity induced by different substances. Direct measures of parameters related with cellular death (slices and cellular cultures).
- Determination of physiological changes in brain slices using patch clamp technique.



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- Determination of the role of ion channels in physiological processes.
- Analysis of the changes in electrical activity patterns in control animals and in different animal models of nervous system disorders (in brain slices as well in *in vivo*, awake and anesthetized animals).
- Determination of neurotransmitter release in brain synaptosomes.
- Characterization of animal models of different nervous system disorders and conditions.

### **Innovative aspects / Competitive Advantages**

#### ***Possible therapeutic target determinations for different nervous system alterations.***

- We are **specialists in the use of the patch-clamp technique**, which allows high resolution studies at cellular and subcellular level.
- We use the patch-clamp technique in cellular culture and brain slices. We also **characterize animal models of some nervous system disorders (Alzheimer, Autism and Epilepsy)** and identify the effect of different substances in the nervous system and its effective dose in *in vivo* and *in vitro* models.
- We are specialists in the **discrimination/determination of pre- and postsynaptic mechanisms underlying synaptic plasticity, drugs effects and other cellular processes. For this purpose we perform paired recordings** in which we record two connected neurons at the same time.

[Rodríguez-Moreno, A., Upton, A.L., Banerjee, A., González-Rueda, A., Craig, M., Paulsen, O. \(2013\). Presynaptic self-depression at developing neocortical synapses. Neuron 77:35-42. Portada.](#)

[Rodríguez-Moreno, A. & Paulsen, O. \(2008\). Spike timing-dependent long-term depression requires presynaptic NMDA receptors. Nat. Neurosci. 11\(7\):744-745.](#)

#### ***Validation of substances that induce neuronal death.***

- We are **trained/qualified to determine and quantify** in a simple and direct way, the **type and number of cells that die** by the action of specific substances. This type of study has important implications for the study of diseases such as Alzheimer's (AD), Parkinson's (PD) and Amyotrophic Lateral Sclerosis (ALS). (**Anatomically**).
- We can **obtain electric records from damaged or dead cells** and characterize them from a functional point of view. (**Functionally**).

#### ***Design of new materials and application techniques to neurobiology.***

- **Design and synthesis of new molecules** which becomes active under light stimulation (**caged compounds**) in a localized compartment of the cell which has been stimulated.

In this regard it is noteworthy that scientists themselves manufactured a new caged compound susceptible to ultraviolet light to characterize the localization of receptors



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involved in processes such as learning or emotions. In particular it has established axonal location of NMDA type receptors responsible for t-LTD, a form of plasticity responsible for learning and neuronal maturation in the cortex. To make this possible, the researchers surrounded a molecule (called MK801) with a cage which makes the molecule inactive when it has the cover. MK801 blocks NMDA-type receptors (both extra- and intracellularly). This new molecule is called Caged-MK801 and allows the study of the involvement of NMDA receptors in specific localized areas and only when applying the ultraviolet light. See paper: [Rodríguez-Moreno A, Kohl, MM, Reeve, J et al., \(2011\) Presynaptic induction and expression of timing-dependent long-term depression demonstrated by compartment-specific photorelease of a use-dependent NMDA receptor antagonist. J. Neurosci. 31, 8564-8569.](#)

- We **design sensitive equipment** for recording electrical currents obtaining **better signals with less background**.
- We **design specific software** set to the specific experimental needs for the obtention of electrical cerebral activity.
- We **design new molecules** useful in the study of synaptic plasticity, which is a qualitative improvement in their study.
- We **design glass pipettes with different shapes, size and tip adjustment**. It allows the recording of neural and cellular activity in any configuration and with maximal quality.
- We **design cannulas and electrodes** that allow acting in a very specific way at localized cerebral parts, even at cellular levels.
- Above mentioned techniques allow us to observe, monitor and record the **effects of certain drugs at tissues and individual cell levels** – with a patch clamp technique– and **at a subcellular level** – by the use of “caged molecule” activation in different and specific cellular compartments.

#### Scientific and technical equipment available

- 4 setups for patch-clamp *in vitro* (for extra and intracellular recordings)
- 1 setup for *in vivo* recordings.
- 1 glass puller with high quality allowing the obtention of pipettes with the desired features.
- Fluorescent microscopy.
- Cell cultures.

#### Types of companies / entities interested

- Research centres focused on nervous system disorders.



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- Pharmaceutical Industry, for the performance of preclinical tests in the development of new therapeutic agents.
- Pharmaceutical Industry: Use of new molecules which becomes active under light stimulation (caged compounds). Functionality test for molecules with some chemical modification and its physiological effects
- Public Administration entities interested in the determination of toxicological influence of some substances in humans as well in animals.

**Research team responsibility:**

Laboratory of Cellular Neuroscience and Plasticity (BIO 330)

<http://www.upo.es/investiga/labneurocienciacelularyplasticidad/index.jsp>