Development of Medicinal Chemistry and Chemical Biology Programs

Brief description

Our laboratory specializes in the development of drug candidates and chemical probes for the validation and identification of therapeutic targets, applying medicinal chemistry, chemical biology, and chemoproteomic strategies. These methodologies allow us to design and optimize molecules with therapeutic potential, as well as to discover new biological targets and evaluate their relevance in diseases. Their application is key in the pharmaceutical and biotechnological industries, as they accelerate the drug discovery process and facilitate the development of more effective and selective treatments for diseases that currently lack adequate treatment.

How does it work?

Based on the specific needs of the project, we have the capacity to develop the following activities:

(i) Identification of new molecular entities (hits) for therapeutic targets of interest using different methodologies, such as screening of compound libraries from our laboratory or commercial sources, fragment-based screening, or phenotypic screening.

(ii) Optimization programs for hits in terms of efficacy, selectivity, and pharmacokinetic properties, including synthesis, structural characterization (using ^{1}H and ^{13}C-NMR, IR, HPLC-MS, etc.), biological evaluation, and determination of ADME(T) properties).

Design and synthesis of PROTACs and functionalized chemical probes with specific tags (fluorophores, groups for bioorthogonal chemistry, affinity labeling, and photocrosslinking) for the visualization, identification, and validation of target proteins.

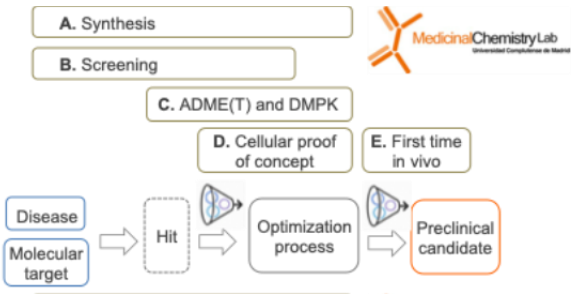

Figure 1. *Stages of the preclinical phase in a medicinal chemistry program for drug discovery.*

What problem does it solve?

The application of these methodologies allows for the identification of new therapeutic strategies and accelerates the development of innovative treatments in the pharmaceutical and biotechnological industries.

What future products will it develop?

Immediate product:

(i) Synthesis of new molecules (upon client request or developed by the laboratory), including the design of synthetic routes, optimization of reactions, preparation, and purification of the desired products.
(ii) Comprehensive characterization of molecules of interest, at the structural and purity levels.
(iii) In vitro screening of compounds: binding assays, enzymatic activity, ELISA, cellular cytotoxicity, calcium mobilization, protein expression levels.

Medicine Faculty. Entrepabellones building 7 y 8.
C/ Doctor Severo Ochoa, 7. 28040 Madrid.
comercia@ucm.es

(iv) Study of ADME(T) properties and pharmacokinetic (PK) profiling: solubility, chemical stability, serum and metabolic stability in liver microsomes of different species, binding to albumin (HSA) and plasma proteins (PPB), cellular permeability (PAMPA), plasma and brain levels (B/P), cytochrome (CYP) inhibition, cardiotoxicity (hERG).

(v) Proteomic selectivity profiling. The final products are bioactive molecules with therapeutic potential and chemical probes for target protein visualization and the validation of new pharmacological strategies.

These products have key applications in the pharmaceutical and biotechnological industries, as they can be used for:

(i) Prioritization and development of new candidate molecules for further drug advancement .

(ii) Identification of relevant disease targets .

(iii) Validation of therapeutic targets.

Ventajas competitivas frente a otras investigaciones

The work carried out in our group has led to the identification of new targets for bioactive molecules (*Chem. Eur. J.* **2016**, *22*, 1313; *Eur. J. Med. Chem.* **2025**, *283*, 117102) and the visualization of serotonin and cannabinoid receptors, as well as other proteins of interest (*Angew. Chem. Int. Ed.* **2012**, *51*, 6896; *J. Allergy Clin. Immunol.* **2014**, *133*, 926; *Bioconjugate Chem*. **2018**, *29*, 2021; *Bioconjugate Chem.* **2018**, *29*, 382; *Bioorg. Chem.* **2024**, *142*, 106967).

Additionally, our medicinal chemistry programs have enabled the validation of ICMT and NPM-1 proteins as new therapeutic targets for the treatment of the rare disease progeria and acute myeloid leukemia (AML), respectively (PCT/ES2014/070071, WO2014/118418; EP21382868.4, WO2018/234232; *J. Med. Chem.* **2019**, *62*, 6035; *ACS Cent. Sci.* **2021**, *7*, 1300; *JACS Au*, **2024**, *4*, 1786), as well as the development of novel bioisosteres for different indications (*Nat. Chem.* **2025**, doi: 10.1038/s41557-025-01746-7).

These representative results highlight the value of the methodologies available in our laboratory for the development of new drug candidates and the identification and validation of therapeutic targets.

¿Dónde se ha desarrollado?

This work is carried out at the MedChemLab (Laboratory of Medicinal Chemistry; www.quimicamedicaucm.es) in the Department of Organic Chemistry at the Faculty of Chemical Sciences, UCM.

Among the most relevant contributions in the last five years are: Validation of the ICMT enzyme in cancer and progeria; Validation of the NPM-1 protein in AML; Development, in collaboration with Vivia Biotech, of a potent allosteric modulator of the GLP-1 receptor for the treatment of type 2 diabetes; Ongoing research projects on PROTACs and RIBOTACs and on the validation of the nuclear receptor LRH-1 for the treatment of type 1 diabetes.

Y además...

We are looking for partners from public or private organizations related to the pharmaceutical industry who are interested in the development of new drugs.

Responsable de la investigación

Silvia Ortega Gutiérrez, siortega@ucm.es
Departament: **Organic Chemistry**
Faculty: **Chemical Sciences**