Pharmacology of ion channels and vascular and gastrointestinal smooth muscle

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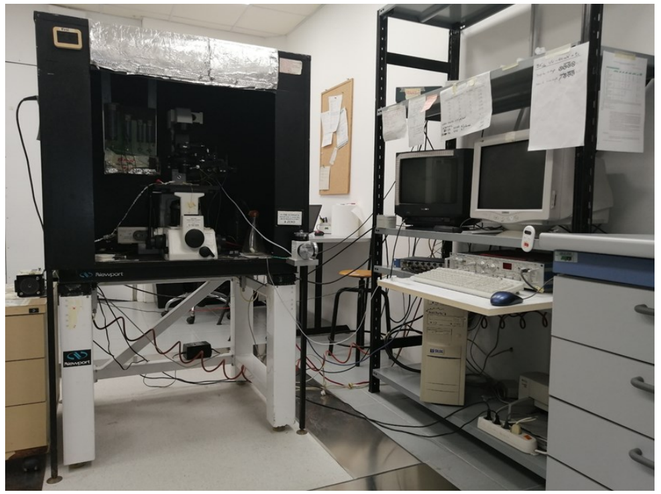
- **LABORATORY OF ION CHANNEL PHARMACOLOGY**
- **LABORATORY OF ISOLATED ORGAN PHARMACOLOGY**

Research activity

- **Vascular effects of flavonoids and other compounds of natural origin**, widely distributed in the Mediterranean diet. The data obtained highlighted, for the first time, the modulatory activity of a series of flavonoids structurally related to quercetin and myricetin on the ionic currents through Ca^{2+} and K^{+} channels. The studies were conducted using the patch-clamp technique in cells isolated from the vascular smooth muscle of laboratory animals. The effects on the currents were then validated on the mechanical activity of isolated organs *in vitro*. A close correlation between the structure of the flavonoids studied and the modulatory activity itself was also demonstrated via molecular modeling analysis.
- **Valorization of food extracts and waste from agricultural production.** The data obtained highlighted the nutraceutical (cardiovascular protective) potential of local products such as olive oil and garlic and waste obtained during wine and citrus fruit processing.
- **Cardiovascular toxic effects of new anticancer and multidrug resistance reverting agents.** Identification, in the early development phase, of the cardiovascular toxic effects of new anticancer and multidrug resistance reverting agents, through *in vitro/ex vivo* experiments, carried out both at cellular level and on tissue-organs, for the optimization or selection phases of the candidate drug development. The effects on Ca^{2+} and K^{+} currents, including hERG, in freshly isolated and cultured cell lines, using the patch-clamp technique, and the vasodilatory/vasoconstrictor activity in isolated vessels in vitro are evaluated.
- **New modulators of vascular ion channels.** Characterization of the effects of new synthetic molecules, antioxidant food additives and the rat-selective toxin norbormide, as well as their derivatives, on vascular mechanical function and on the activity of ion channels, such as Ca^{2+} and K^{+}, involved in its regulation. The aim is to identify new potential drugs, safe diagnostic tools, or better pest-control agents.

Images

Laboratory of ion channel pharmacology: one of the two patch-clamp rigs available in the laboratory.



Laboratory of isolated organ pharmacology : set-up for the analysis of conductance vessels (left) and resistance vessels (right).

Technologies and services

Laboratory of Isolated Organ Pharmacology: one Unit can measure the mechanical function of six conductance vessels (large caliber), one Unit can measure the mechanical function of three resistance vessels (small caliber), and one Unit can measure the mechanical function of two gastrointestinal preparations.

Laboratory of Ion channel pharmacology: two patch-clamp rigs can record ionic currents in single cells.

“hERG channel facility“: for studying the effects of new molecules on the I_{Kr} current recorded in HEK293 cells expressing the human $K_V11.1$ channel (hERG). This service, provided for a fee, can be used both by colleagues at the University of Siena and by external parties (private or public).

The two laboratories allow the analysis of potential vascular and/or gastrointestinal effects and the definition of the mechanism of action of extracts and single natural and synthetic compounds, to enhance their **pharmaceutical and nutraceutical potential**. Furthermore, it is possible, at an early stage of development, to determine the toxic potential of new molecules.

Applications and collaborations

Activities already carried out for businesses

Contract for scientific research activities with **Rottapharm** S.p.A. Title: “Effects of Andolast on $K_{Ca}3.1$ currents in RBL-2H3 cells”.

Projects and collaborations already started

Contracts for scientific research activities with **Landcare Research New Zealand Limited**. Title: “From fruit fly to pest control” and “Precision Pest Eradication – pest-selective control tools”. The objective of the project is to achieve the commercialization of substances capable of eradicating pest species such as rats and mice in a highly selective manner, without being toxic to humans or polluting the environment.

For more information

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