Selected centres:

- Institute of Molecular and Translational Medicine, Palacky University, Olomouc, Czech Republic.
- Mario Negri Institute for Pharmacological Research, Milan, Italy
- Institute of Biomedicine and Translational Medicine, Tartu University, Tartu, Estonia
- Fondazione IRCCS Fondazione Pascale, Napels, Italy
- Institute of Chemical Technologies Prague, Czech Republic
- Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences, Czech Republic
- Neuratris-French Alternative Energies and Atomic Energy Commission (CEA), France
- CNCCS - IRBM Science Park, Rome, Italy
- Istituti Fisioterapici Ospitalieri - Regina Elena Tumor research, Italy
- Vall d'Hebron Research Institute (VHIR), Barcelona, Spain
- University of Oslo (UiO), Norway

Literature

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- **Morosi L, Zucchetti M, D'Incalci M, Davoli E.** Imaging mass spectrometry: challenges in visualization of drug distribution in solid tumors. Curr Opin Pharmacol. 2013, 13(5):807-12.

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Access leading academic expertise In vitro **ADME profiling** in drug development

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ADME PROFILING OF NEW DRUG CANDIDATES:

COST EFFECTIVE ENABLING TECHNOLOGIES IN DRUG DESIGN AND DEVELOPMENT

SELECTING THE MOST PROMISING COMPOUNDS TO REDUCE LATE STAGE ATTRITION

One of the major causes of drug failure is still the poor PK/PD profile in addition to a lack of safety and efficacy. Studies to determine the drug candidate´s absorption, distribution, metabolism and excretion (ADME) from the body in translational models are therefore key to reducing attrition in the later stages of development. For early detection of viable drug candidates, it is necessary to get information on chemical stability, rate of metabolism, absorption from the small intestine or active efflux mediated by transporter proteins. Cost-efficient, predictive and reproducable compound screens with access to state-of-the art techniques can greatly improve research outcomes in the early translational phases of drug development and enable better decision making points. The EATRIS consortium can provide the right information, expertise and infrastructure to help your academic or start-up drug discovery program become more efficient, by eliminating candidates with unfavourable ADME characteristics and avoiding unnecessary fails in clinical trials.

> *"Unfavourable absorption, distribution, metabolism and excretion (ADME) properties can be prevented as a cause of drug candidate failure"*

The EATRIS ADME profiling Network

EATRIS is an expanding European network of qualified translational centres that offers high-end infrastructure for preclinical and clinical studies to support development. Contact EATRIS to find an institution with the relevant expertise to match with your research request.

In vitro ADME profiling

- Determination of chemical stability of compounds in aqueous solution (non-enzymatic degradation)
- Determination of chemical stability of compounds in biological fluids (saliva, gastric juice) and tissue homogenates
- Assessment of passive absorption (PAMPA permeability)
- Assessment of GIT permeability (Caco-2 permeability)
- Identification of P-glycoprotein substrates (MDR1-MDCK cell permeability)
- Prediction of blood brain barrier permeability (MDR1-MDCK cell permeability)
- Determination of the stability of drug candidates (plasma stability assay)
- Prediction of in vitro intrinsic clearance of drug candidates (microsomal stability assay)
- Determination of drug plasma protein binding (plasma protein binding assay with incorporation of rapid equilibrium dialysis)
- Advanced mass spectrometry methods (MALDI, DESI, SIMS, LAESI) for detailed analysis of drugs and metabolites
- In silico prediction and PK/PD modeling of human ADME profile to support anticipated clinical dose calculation
- Advanced bioanalysis, including radiochemical profiling
- Robust technologies, like RapidFire high-throughput mass spectrometry with high compatibility for various biological matrices.

In vivo ADME profiling

- Quantitative determination of the distribution of compounds in organs and tissues of small rodents (mouse, rat) by LC-MS
- Qualitative determination of the distribution of compounds in organs and tissues of small rodents (mouse, rat) by Matrix Assisted Laser Desorption Ionization- Time of Flight Imaging (MALDI-TOF)

Technical and Regulatory (QA/QC) aspects of ADME profiling

- Optimised experimental setup in preclinical biodistribution studies supports the design of safety studies for clinical authorization.
- Robust high-throughput mass spectroscopy platforms provide reliable results ready for submission of clinical candidates

"Optimal pharmacokinetics is as important as biological activity"