



**Charles University in Prague**

**Expression of interest for cooperation in FP7 project/s**

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Faculty/institute: Faculty of Pharmacy in Hradec Králové

Department: Dept. Biochemical Sciences

Collaboration form: Project partner

Size of the research group: small

Specific programme: Cooperation – Health

Activity area: HEALTH-2007-1.3-1 Novel alternative testing strategies for use in pharmaceutical discovery and development

(Biotransformation of medicaments and other xenobiotics, molecular mechanisms of drug action including undesirable effects, modification of protein molecules by drugs and pathological conditions)

Cooperation interest: The proposed project would be focused on disclosure of molecular mechanisms of adverse drug effects and possible ways of their elimination in view of long-time pharmacotherapy during ageing and civilization diseases (cardiovascular, tumor).

Annotation: Every medical drug possesses more or less undesirable effects. In the ageing European population, the consumption of drugs dramatically increases. Drugs are often used long time and in various combinations increasing adverse drug effects (ADE) and the risk of negative actions. The aim of this project is to study molecular mechanisms of undesirable effects of long-term used drugs. Many mechanisms of ADE are connected with drug biotransformation and interactions with metabolic pathways. The project is focused on negative effects of drugs and their products, their modulation effects on enzymes of biotransformation and of endogenous metabolism, including formation of ROS and modification of protein molecules. Biochemical, molecular-biological and analytical methods and in vitro model systems of all levels (purified and recombinant proteins, cell lines, isolated hepatocytes and kardiomyocytes, tissue slices) will be used for these purposes. Disclosure of mechanisms of negative drug effects looks towards possible ways of safer pharmacotherapy.

Expertise offered for the FP7 project:

In vitro studies of drug metabolism, disclosure of molecular mechanisms of undesirable effects connected with biotransformation, and interactions of drugs and their metabolites with metabolic pathways, their modulation effects on enzymes of biotransformation and of endogenous metabolism, including formation of ROS and modification of protein molecules.

Number of Ph.D. students: 9



Major international publications:

Wsól V., Skálová L., Szotáková B. Chiral Inversion of Drugs: Coincidence or Principle? *Current Drug Metab.* 5 (2004) 517-533

Skálová, L., Nobilis, M., Szotáková, B., Kondrová, E., Šavlík, M., Wsól, V., Pichard-Garcia, L., Maser, E. Carbonyl reduction of the potential cytostatic drugs benfluron and 3,9-dimethoxybenfluron in human in vitro. *Biochem. Pharmacol.* 64 (2002) 297-305

Dršata J., Beránek M., Palička V.: Inhibition of aspartate aminotransferase by glycation in vitro under various conditions. *J. Enz. Inhibition Med. Chem.* 17, 2002, 31-36

Previous participation in international research projects: The individual members of the group participated in research of host research institutes during their stay abroad: University Medical School Schleswig-Holstein, Inst. Toxicol. Pharmacol. for Natural Scientists, Kiel, Germany (Prof. Wsól, Dr. Szotáková), University of Helsinki Faculty of Pharmacy, Drug Discovery and Development Technol. Center, Helsinki, Finland (Doc. Skálová), Istituto di Ricerche Farmacologiche Mario Negri Bergamo, Italy (Prof. Dršata)

Available research infrastructure: The Department of Biochemical Sciences consists of two working groups: General and Pharmaceutical Biochemistry, and Pathological Biochemistry, six members of each.

The department co-operates in research with the Czech Academy of Sciences (Inst. of Organic Chemistry and Biochemistry), Veterinary Res. Inst. In Brno, Medical Faculty Palacký Univ. Olomouc (Dept. Medical Biochem.)

Major research interest/focus: The research of the group is focus on biotransformation of xenobiotics and their effect on proteins at molecular level. The investigation concerns substances with pharmacotherapeutical activity. The research is carried out in relation to new ways of biotransformation and drug-protein interactions with pathological models and situations in which the interactions occur – diabetes, cardiovascular diseases, cancer. Purification of proteins, recombinant proteins, and bioanalytical methods (HPLC, enzyme assays, spectroscopic methods) are used in the investigations

Www pages: [http://www.faf.cuni.cz/eng\\_default.asp](http://www.faf.cuni.cz/eng_default.asp)

Existing international collaboration partners:

1. University Medical School Schleswig-Holstein, Inst. Toxicol. Pharmacol. for Natural Scientists, Kiel, Germany

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