



## International Meeting on Cholinesterases

20-25 September 2009, Šibenik, Croatia

### REPORT

The 10<sup>th</sup> International Meeting on Cholinesterases was organised jointly by the Institute for Medical Research and Occupational Health (IMI) and the Croatian Society of Biochemistry and Molecular Biology under the auspices of the Croatian Academy of Sciences and Arts. The meeting venue was in Šibenik, known for its scenic beauty and wealth of cultural and historical landmarks.

As the 10<sup>th</sup> meeting, it is a jubilee meeting on its own, but it was also a special jubilee for the organisers because Elsa Reiner and IMI organised the first meeting in the series. The past meetings took place in different countries and on different continents: Split, Croatia (1975), Bled, Slovenia (1983), La Grande Motte, France (1990), Eilat, Israel (1992), Madras, India (1994), La Jolla, USA (1998), Pucon, Chile (2002), Perugia, Italy (2004) and Suzhou, China (2007).

The meeting gathered about 200 participants from all continents and 28 countries including 25 participants from Croatia. It was sponsored by Croatian government, academia and companies, as well as foreign and international research institutions. The ISN as one of the main sponsors has been repeatedly pointed out throughout the meeting.

The scientific programme comprised two plenary lectures, oral presentations grouped under six sessions, and a 3D-session. The list of plenary and invited speakers (in order of speaking) is enclosed at the end of the report. Besides 44 lectures given by invited speakers, a novel feature of the programme were 42 short oral presentations given primarily by young researchers. A total of 102 posters were displayed throughout the meeting, and presented also during two poster sessions. The posters are reviewed by a four-member committee, and the best poster received an award from the *Biochemical Journal*.

There were no parallel sessions so that participants could attend all oral presentations. This is important because the field of cholinesterase research is widely multidisciplinary, from very fundamental (molecular structure, catalytic mechanism, genetics and evolution, cell biology) to more applied aspects (natural and synthetic cholinesterase inhibitors in Alzheimer's disease therapy, defense against anti-cholinesterase poisoning, pesticides and environment).

Every participant received the *Programme and Abstracts* book on registration. Proceedings comprising both oral and poster presentations will be published in the Elsevier journal *Chemico-Biological Interactions* (CBI) as full length papers or short communications.

More details about the meeting can be found at the meeting website – <http://10-che.imi.hr>.

The US\$ 6,000 allocated by the ISN were spent for the support of 12 young scientists as 500 US\$ fellowships to Jeremy Beck (USA), Vicky Ping Chen (China), Andrea Durrant (Israel), Eran Finkel (Israel), Ava Jiangyang Guo (China), Ondrej Holas (Czech Republic), Tuba Küçükılınç (Turkey/USA), Sofya Lushchekina (Russia), Emilio Marrero (Cuba/USA), Benoît Sanson (France), Jörg Steinfeld (Germany) and Shubham Vyas (India/USA).

Over more than three decades, the meeting participants have created “a family” that is continuously incorporating new members, thereby broadening and expanding worldwide contacts and collaboration. We very much hope that this trend will persist in the future. The 11<sup>th</sup> Meeting on Cholinesterases will be held in Russia.

Dr. Zrinka Kovarik  
on behalf of the Croatian Organising Board

Zagreb, 6.10.2009.



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## PLENARY SESSION

**Palmer Taylor** (La Jolla, USA): THE ROAD FROM SPLIT TO ŠIBENIK: A TORTUOUS PATH WITH GLOBAL COUSINS, CONNECTIONS AND COLLABORATIONS

**Joel L Sussman** (Rehovot, Israel) The EMBO Plenary Lecture: ACETYLCHOLINESTERASE: "CLASSICAL" AND "NON-CLASSICAL" FUNCTIONS DERIVED FROM 3D STRUCTURES

## SESSION 1: Structure of Cholinesterases and Related $\alpha/\beta$ Hydrolase-fold Proteins

**Doriano Lamba** (Trieste, Italy): THE YIN AND THE YANG OF *Torpedo californica* ACETYLCHOLINESTERASE REVERSIBLE AND PSEUDO IRREVERSIBLE INHIBITION: A STRUCTURAL AND MECHANISTIC OUTLOOK

**Florian Nachon** (La Tronche Cedex, France): CRYSTAL STRUCTURES OF HUMAN CHOLINESTERASES INHIBITED BY TABUN AND V-AGENTS

**Sergei Varfolomeev** (Moscow, Russia): BIOINFORMATICS AND QUANTUM/MOLECULAR MECHANICS IN ANALYSIS OF STRUCTURE, ELEMENTARY ACTS AND SPECIFICITY OF CHOLINESTERASES: HUMAN MOLECULAR POLYMORPHISM

**Pascale Marchot** (Marseille, France): STRUCTURE-FUNCTION RELATIONSHIPS OF NEUROLIGIN AND ITS  $\beta$ -NEUREXIN COMPLEX

## SESSION 2: Molecular Biology and Cell Biology of Cholinesterases and Alternative Functions of Cholinesterases

**Hermona Soreq** (Jerusalem, Israel): DIVERSE FEATURES AND MICRO-RNA REGULATION OF ALTERNATIVE AChE VARIANTS

**Shelly Camp** (La Jolla, USA): CONTRIBUTIONS OF TRANSGENIC STUDIES TO UNDERSTANDING CHOLINESTERASE DISPOSITION AND FUNCTION

**Eric Krejci** (Paris, France): CONTROL OF MUSCLE CONTRACTION BY ACETYLCHOLINESTERASE

**Karl WK Tsim** (Hong Kong, China): PRIMA DIRECTS THE LOCALIZATION OF TETRAMERIC AChE: PROBING THE POSSIBLE FUNCTIONS OF THIS ENZYME IN MUSCLES, NEURONS AND OSTEOBLASTS

**Richard L Rotundo** (Miami, USA): TRANSLATIONAL AND POST-TRANSLATIONAL REGULATION OF ACETYLCHOLINESTERASE EXPRESSION AND ASSEMBLY *in vitro* AND *in vivo*

**Susan A Greenfield** (Oxford, UK): ROLE OF AChE-DERIVED C TERMINAL PEPTIDES IN BRAIN FUNCTION AND DYSFUNCTION

**Claire Legay** (Paris, France): ColQ DOES MORE THAN ANCHORING CHOLINESTERASES AT THE NEUROMUSCULAR JUNCTION

**Janez Sketelj** (Ljubljana, Slovenia): MOTOR NERVES REGULATE THE EXPRESSION OF AChE-ASSOCIATED COLLAGEN Q IN RAT MUSCLES

**Alexander G Karczmar** (Maywood, USA): CHOLINESTERASES AND THE CHOLINERGIC SYSTEM IN ONTOGENESIS, AND THEIR NON-SYNAPTIC ROLE

## SESSION 3: Interaction of Cholinesterases with Substrates, Inhibitors and Reactivators

**Daniel M Quinn** (Iowa City, USA): ACCUMULATION OF TETRAHEDRAL INTERMEDIATES IN CHOLINESTERASE CATALYSIS: A SECONDARY ISOTOPE EFFECT STUDY

**Jure Stojan** (Ljubljana, Slovenia): EVIDENCE FOR NON-PRODUCTIVE SUBSTRATE BINDING INTO THE ACTIVE SITE OF VERTEBRATE ACETYLCHOLINESTERASE

**Terrone L Rosenberry** (Jacksonville, USA): SELECTIVE INTRODUCTION OF EQUILIBRIUM ASSUMPTIONS PROVIDES AN ALGEBRAIC FORMULATION OF COMPETITIVE INHIBITION CONSTANTS FOR ACETYLCHOLINESTERASE

**William Stephen Brimijoin** (Rochester, USA): CYSTEINE-REACTIVE AGENTS TARGET INSECT ACETYLCHOLINESTERASE – POTENTIAL FOR SPECIES-SELECTIVE PESTICIDES

**Chang-Guo Zhan** (Lexington, USA): STRUCTURE-AND-MECHANISM-BASED DESIGN OF SUBSTRATE-SELECTIVE HIGH-ACTIVITY MUTANTS OF CHOLINESTERASES

**Serge N Moralev** (St Petersburg, Russia): INVESTIGATION OF STRUCTURE-ACTIVITY RELATIONSHIPS IN ORGANOPHOSPHATES – CHOLINESTERASE INTERACTION USING DOCKING ANALYSIS

**Patrick Masson** (La Tronche Cedex, France): STRUCTURAL APPROACH TO THE AGING OF PHOSPHORYLATED CHOLINESTERASES

**Zoran Radić** (La Jolla, CA): INTERACTION KINETICS OF OXIMES WITH NATIVE, PHOSPHORYLATED AND AGED HUMAN ACETYLCHOLINESTERASE AND BUTYRYLCHOLINESTERASE

**Zrinka Kovarik** (Zagreb, Croatia): OXIME-ASSISTED REACTIVATION OF PHOSPHORYLATED BUTYRYLCHOLINESTERASE



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### SESSION 4: Anticholinesterases: Mechanisms of Toxicity, Detoxication and Therapy, and Counter-Terrorism Strategies

**David Lenz** (Aberdeen Proving Ground, USA): BUTYRYLCHOLINESTERASE AS A DRUG FOR PROTECTION AGAINST ORGANOPHOSPHORUS POISONS: SUCCESSES AND CHALLENGES

**Avigdor Shafferman** (Ness Ziona, Israel): NEXT GENERATION OF OP-BIOSCAVENGERS

**Franz Worek** (Munich, Germany): EVALUATION OF MEDICAL COUNTERMEASURES AGAINST ORGANOPHOSPHORUS COMPOUNDS: THE VALUE OF EXPERIMENTAL DATA AND COMPUTER SIMULATIONS

**Zoran Grubič** (Ljubljana, Slovenia): THE EFFECTS OF DFP ON THE PRECURSORS OF HUMAN MUSCLE REGENERATION

**Peter Eyer** (Munich, Germany): PARADOX FINDINGS MAY CHALLENGE ORTHODOX REASONING IN ACUTE ORGANOPHOSPHORUS POISONING

**Michael Eddleston** (Newcastle, UK): A GOTTINGEN MINIPIG MODEL OF DIMETHOATE ORGANOPHOSPHORUS PESTICIDE POISONING

### SESSION 5: Enzymes Other than Cholinesterases Reacting with Anticholinesterase Agents

**Marcello Lotti** (Padova, Italy): SOLUBLE PHENYL-VALERATE ESTERASES OF HEN SCIATIC NERVE AND THE PROMOTION OF ORGANOPHOSPHATE INDUCED DELAYED POLYNEUROPATHY

**Gabi Amitai** (Ness Ziona, Israel): ENZYMATIC DETOXIFICATION OF NERVE AGENTS AT HIGH BULK AND SURFACE CONCENTRATIONS

**Yacov Ashani** (Rehovot, Israel): STEREOSPECIFIC SYNTHESIS OF ANALOGS OF NERVE AGENTS AND THEIR USE FOR SELECTION AND CHARACTERIZATION OF PARAOXONASE CATALYTIC SCAVENGERS

**Oksana Lockridge** (Omaha, USA): A NEW MOTIF FOR ORGANOPHOSPHORUS AGENT BINDING TO PROTEINS THAT HAVE NO ACTIVE SITE SERINE

**Dragomir Draganov** (Ashland, USA): LACTONASES WITH ORAGNOPHOSPHATASE ACTIVITY: STRUCTURAL AND EVOLUTIONARY PERSPECTIVES

**Ashima Saxena** (Silver Spring, USA): DEVELOPING CATALYTIC BIOSCAVENGERS FOR THE PROPHYLAXIS OF CHEMICAL WARFARE AGENT TOXICITY

**Clement E Furlong** (Seattle, USA): HUMAN PON1 – A BIOMARKER FOR RISK OF DISEASE AND EXPOSURE

### 3D SESSION

**Martin Weik** (Grenoble, France): STRUCTURAL DYNAMICS OF ACETYLCHOLINESTERASE

**Fredrik Ekström** (Umeå, Sweden) (*crystallography*) and **Yuan-Ping Pang** (Rochester, USA) (*simulation*): STRUCTURE OF HI-6-SARIN-ACETYLCHOLINESTERASE DETERMINED BY X-RAY CRYSTALLOGRAPHY AND MICROSECOND MOLECULAR DYNAMICS SIMULATION: REACTIVATOR MECHANISM AND DESIGN

**Yves Bourne** (Marseille, France): COMPARATIVE OVERVIEW OF NEUROLIGIN VERSUS ACETYLCHOLINESTERASE AND THEIR RESPECTIVE NEUREXIN AND FASCICULIN COMPLEXES

### SESSION 6: Diseases Related to Cholinesterases and Therapy with Cholinesterase Inhibitors

**Giancarlo Pepeu** (Florence, Italy): CHOLINESTERASE INHIBITORS AND COGNITIVE PROCESSES

**Ezio Giacobini** (Geneva, Switzerland): CHOLINESTERASE INHIBITORS ROLE IN THE THERAPY OF ALZHEIMER DISEASE

**Taher Darreh-Shori** (Stockholm, Sweden): APOLIPOPROTEIN E AND A $\beta$  MAY AFFECT THE CHOLINERGIC NEUROTRANSMISSION BY BOOSTING THE ACTIVITY AND STABILITY OF CHOLINESTERASES IN THE BRAIN

**Ninoslav Mimica** (Zagreb, Croatia): THE CHOLINESTERASE INHIBITORS – CURRENT CLINICAL VIEW AND CROATIAN REALITY