20th International Conference on Cytochrome P450:

Biochemistry, Biophysics and Biotechnology

August 27-31, 2017, Düsseldorf, Germany

Scientific program

Sunday, 27.08.2017

Registration open, Foyer, 13:00

Poster mounting, Foyer, 13:00 – 16:00

Evening session, LH 3A, 16:00 – 18:15

16:00 – 16:20

Vlada B. Urlacher *Opening remarks*

F. Peter Guengerich *Introduction to the history of the P450 meetings*

Opening lecture, 16:20– 17:20

Chair: Danièle Werck-Reichhart

Rita Bernhardt (*Saarland University,* Germany)

Steroid hormone biosynthesis meets biotechnology

Plenary lecture, 17:20 – 18:20

Chair: F. Peter Guengerich

Paul R. Ortiz de Montellano (*University of California, San Francisco,* USA)

The *Mycobacterium tuberculosis* cytochrome P450 system

Get together and poster viewing, Foyer, 18:20 – 20:00

Monday, 28.08.2017

Registration open, Foyer, 08:30 – 11:00

Morning sessions

LH 3A, 09:00 – 10:40

1. P450 Bioinformatics and Evolution

Chairs: Rebecca Wade and Jürgen Pleiss

09:00 – 09:30 **Danièle Werck-Reichhart** (*University of Strasbourg,* France)
Nature's strategies to evolve new P450 functions

09:30 – 09:50 **Michael C. Hutter** (*Saarland University*, Germany)
All around CYP106A2: The many faces of molecular modeling

09:50 – 10:20 **Elizabeth M. J. Gillam** (*University of Queensland,* Australia)
Ancestral sequence reconstruction of drug-metabolizing P450s: the "retro" approach to understanding drug metabolism

10:20 – 10:40 **Khajamohiddin Syed** (*Central University of Technology,* South Africa)
Two sides of the CYP53: *In silico* analysis of its role as a common alternative drug target and involvement in wood degradation

LH 3D, 09:00 – 10:30

2. P450 Biophysics

Chair: James J. De Voss

09:00 – 09:30 **Thomas C. Pochapsky** (*Brandeis University*, USA)
Some surprising implications of NMR-directed simulations of substrate recognition and binding by cytochromes P450

09:30 – 10:00 **Gianfranco Gilardi** (*University of Torino,* Italy)
Influence of inter-domain flexibility on the activity of 3A4-BMR chimeras in solution and on electrode surfaces

10:00 – 10:30 **Nitin Jain** (*University of Tennessee*, USA)
New insights into origins of thermostability and structural flexibility of the thermophilic P450, CYP119

Tea & Coffee, Foyer, 10:30 – 11:00

Morning sessions (continued)

LH 3A, 11:00 – 12:50

1. P450 Bioinformatics (continued)

Chairs: Danièle Werck-Reichhart and Elizabeth M. J. Gillam

11:00 – 11:30 **Rebecca Wade** (*HITS and Heidelberg University,* Germany)
Insights into the membrane and protein interactions of cytochrome P450 enzymes from molecular simulations

11:30 – 11:50 **Daan P. Geerke** (*Vrije Universiteit Amserdam,* Netherlands*)*
Modeling cytochrome P450s: Binding affinity prediction and insights into biocatalytic selectivity

11:50 – 12:20 **Jürgen Pleiss** (*University of Stuttgart*, Germany)
The sequence space of cytochrome P450 monooxygenases: hotspots, evolvability, and saturation

12:20 – 12:50 **Lars Olsen** (*University of Copenhagen,* Denmark)
Cytochrome P450 reactions studied with density functional theory

LH 3D, 11:00 – 12:50

2. P450 Biophysics (continued)

Chair: Gianfranco Gilardi and Victoria V. Shumyantseva

11:00 – 11:30 **Victoria V. Shumyantseva** (*Institute of Biomedical Chemistry, Moscow,* Russia)
Cytochrome P450 and electrochemistry: crosstalk with electrodes for metabolism modelling and screening substrate/inhibitor potency

11:30 – 11:50 **Nikos S. Hatzakis** (*University of Copenhagen*, Denmark)
Selective P450 activation by P450 oxidoreductase conformational sampling: A single molecule insight

11:50 – 12:20 **Hidehiko Hirakawa** (*University of Tokyo*, Japan)
Benefits from artificial assembly with redox partners

12:20 – 12:50 **Lionel Cheruzel** (*San Jose State University*, USA)
Hybrid P450 enzymes for selective light-driven C-H functionalization

Lunch, Foyer, 12:50 – 14:00

Afternoon sessions

LH 3A, 14:00 – 15:30

3. P450 and Drug Metabolism

Chair: Nico P. E. Vermeulen

14:00 – 14:30 **Hiroshi Yamazaki** (*Showa Pharmaceutical University,* Japan)
Human drug metabolism in humanized-liver mice and non-human primate models

14:30 – 14:50 **Mery Giantin** (*University of Padua*, Italy)
Functional impact of cytochrome P450 3A (CYP3A) exonic polymorphisms in cattle

14:50 – 15:30 **Steven P. Hanlon** (*F. Hoffmann-La Roche Ltd, Switzerland)*
and **Matthias Kittelmann** (*Novartis Pharma AG, Switzerland)*
25 Years of P450 and other oxidizing enzymes at Roche and Novartis: Applications in biocatalysis

Tea & Coffee, Foyer, 15:30 – 16:00

LH 3D, 14:00 – 15:30

4. Catalytic Mechanisms of P450

Chair: Paul R. Ortiz de Montellano

14:00 – 14:30 **Michael T. Green** (*University of California Irvine,* USA)
Selenocysteine-ligated P450 compound I is more reactive than wild type: A direct link between electron donation and the rate of C-H bond activation

14:30 – 15:00 **John C. Hackett** (*Virginia Commonwealth University*, USA)
Unconstrained molecular dynamics simulations of substrate binding to cytochrome P450 3A4

15:00 – 15:30 **William M. Atkins** (*University of Washington,* USA)
Protein and ligand dynamics of Cytochrome P4503A4 in lipid nanodiscs

Evening sessions

LH 3A, 16:00 – 17:20

3. P450 and Drug Metabolism (continued)

Chair: Hiroshi Yamazaki

16:00 – 16:30 **Nico P. E. Vermeulen** (*Vrije Universiteit Amsterdam*, Netherlands)
Bioactivation to and protection against chemically reactive drug metabolites: Emphasis on human cytochrome P450s and GSTs

16:30 – 16:50 **Laura N. Jeffreys** (*University of Manchester*, UK)
Novel FDA-approved drug compounds capable of binding to P450 BM3 'gatekeeper' mutations

16:50 – 17:20 **Ilia G. Denisov** (*University of Illinois Urbana-Champaign,* USA)
The allosteric mechanism of CYP3A4 in the membrane

LH 3D, 16:00 – 17:20

4. Catalytic Mechanisms of P450 (continued)

Chair: William M. Atkins

16:00 – 16:30 **James J. De Voss** (*University of Queensland*, Australia)
The mechanism of CYP199A4 catalysed dehydrogenation

16:30 – 16:50 **Lucy A. Waskell** (*University of Michigan Medical School*, USA)
Cytochrome b5 stimulates catalysis by rapidly protonating the hydroperoxo intermediate $(Fe^{3+}OOH)^{-}$ of cytochrome P450 2B4

16:50 – 17:20 **Donghak Kim** (*Konkuk University,* South Korea)
Kinetic analysis of human cytochrome P450 4A11 and its allelic variants

Poster session I, Foyer, 17:20 – 19:00

Presenting authors of posters with an uneven number (e.g. P01, P03, etc.) are requested to be present at their posters for questions and discussion.

Tuesday, 29.08.2017

Registration open, Foyer, 08:30 – 11:00

Morning sessions

LH 3A, 09:00 – 10:20

5. Structure of P450

Chair: John H. Dawson

09:00 – 09:30 **Stephen G. Sligar** (*University of Illinois Urbana-Champaign*, USA)
Multiple pathways of catalysis by cytochrome P450

09:30 – 09:50 **P. Ross Wilderman** (*University of Connecticut*, USA)
Structural and functional characterization of mammalian CYP2B enzymes from the desert woodrat (*Neotoma lepida)*

09:50 – 10:20 **Emily E. Scott** (*University of Michigan*, USA)
Interactions of cytochrome P450 enzymes with cytochrome b_5

LH 3D, 09:00 – 10:20

6. P450 -Redox Partner Interaction

Chair: Thomas L. Poulos

09:00 – 09:30 **Shengying Li** (*Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Sciences,* China)
Functional modulation of microbial P450 enzymes by alternative redox partner proteins

09:30 – 09:50 **Diana Campelo** (*Nova University of Lisbon,* Portugal)
The hinge region of human NADPH-cytochrome P450 reductase in conformational switching: the critical role of ionic strength

09:50 – 10:20 **Stephen G. Bell** (*University of Adelaide*, Australia)
Exploring the diversity of bacterial P450 electron transfer systems

Tea & Coffee, Foyer, 10:20 – 10:50

Morning Sessions (continued)

LH 3A, 10:50 – 12:10

5. Structure of P450 (continued)

Chair: Stephen G. Sligar

10:50 – 11:20 **Eric F. Johnson** (*The Scripps Research Institute*, USA)
X-ray crystal structures of rabbit P450 4B1 reveal structural adaptations for ω-hydroxylation

11:20 – 11:50 **Michal Otyepka** (*Palacky University Olomouc,* Czech Republic)
Membrane attached cytochrome P450; from structure to mechanism of drug binding

11:50 – 12:10 **Ammar Abdulmughni** (*Saarland University, Germany*)
Novel Cytochrome P450 enzymes from *Bacillus megaterium*: Characterization, 3D structures and engineering

LH 3D, 10:50 – 12:10

6. P450 - Redox Partner Interaction (continued)

Chair: Thomas C. Pochapsky

10:50 – 11:20 **Thomas L. Poulos** (*University of California Irvine*, USA)
Interplay between redox partner binding and the P450 O_2 activation machinery

11:20 – 11:50 **Marcellus Ubbink** (*Leiden University*, Netherlands)
Structure and dynamics of the complex of cytochrome P450cam and putidaredoxin

11:50 – 12:10 **Samuel L. Freeman** (*University of Leicester,* UK)
Orchestrated domain movement in catalysis by NADPH-cytochrome P450 reductase

Packed lunch provided in Foyer, 12:10

Conference excursions, 13:00 – 20:00

Wednesday, 30.08.2017

Morning sessions

LH 3A, 09:00 – 10:20

7. P450 and Drug Design

Chair: Eric F. Jonson

09:00 – 09:30 **F. Peter Guengerich** (*Vanderbilt University School of Medicine*, USA)
Cytochrome P450 enzymes as drug targets and issues with multi-step reaction sequences

09:30 – 09:50 **Aditi Das** (*University of Illinois Urbana-Champaign*, USA)
Cardioprotective and cardiotoxic role of CYP2J2, the primary CYP in human cardiomyocytes

09:50 – 10:20 **Galina I. Lepesheva** (*Vanderbilt University School of Medicine*, USA)
Sterol 14α-demethylases: phylum-specific structural features and structure-based design of antiprotozoan, antifungal and anticancer drugs

LH 3D, 09:00 – 10:20

8. Non-heme Oxygenases

Chair: Martin Hofrichter

09:00 – 09:30 **Sheila J. Sadeghi** (*University of Torino,* Italy)
Polymorphism of flavin-containing monooxygenase 3 in the era of personalized medicine

09:30 – 09:50 **Shingo Nagano** (*Tottori University,* Japan)
Crystal structure of F6'H, a 2-oxoglutarate-dependent dioxygenase and a key enzyme in coumarin biosynthesis

09:50 – 10:20 **Marco W. Fraaije** (*University of Groningen*, Netherlands)
Redesign and biocatalytic exploration of flavin-containing monooxygenases

Tea & Coffee, Foyer, 10:20 – 10:50

Morning sessions (continued)

LH 3A, 10:50 – 11:50

7. P450 and Drug Design (continued)

Chair: F. Peter Guengerich

10:50 – 11:20 **Irina A. Pikuleva** (*Case Western Reserve University*, USA)
CYP46A1: from biochemistry to the clinical trial

11:20 – 11:50 **Kirsty J. McLean** (*University of Manchester,* UK)
Structures and drug targeting of *M. tuberculosis* cytochrome P450 enzymes: screening for function and inhibition

LH 3D, 10:50 – 11:50

8. Non-heme Oxygenases (continued)

Chair: Marco Fraaije

10:50 – 11:20 **Pimchai Chaiyen** (*Vidyasirimedhi Institute of Science and Technology*, Thailand)
Beyond monooxygenation by flavin-dependent enzymes

11:20 – 11:50 **Martin Hofrichter** (*Technical University Dresden*, Germany)
Fungal peroxygenases: a hidden treasure to discover

Lunch, Foyer, 11:50 – 13:00

Afternoon sessions

LH 3A, 13:00 – 14:50

9. P450 Gene Regulation

Chairs: Ulrich M. Zanger and David J. Waxman

13:00 – 13:30 **David J. Waxman** (*Boston University*, USA)
CAR regulation of mouse liver chromatin accessibility, histone modifications and early gene responses

13:30 – 13:50 **Albert Braeuning** (*German Federal Institute for Risk Assessment,* Germany)
Convergence of β-catenin- and hepatocyte nuclear factor 1α-dependent signaling at the *Cyp2e1* promoter

13:50 – 14:20 **Miki Nakajima** (*Kanazawa University*, Japan)
Post-transcriptional regulation of PK/PD-associated genes by A-to-I RNA editing

14:20 – 14:50 **Ulrich M. Zanger** (*Dr. Margarete Fischer-Bosch Institute of Clinical Pharmacology*, Germany)
Regulation of human drug metabolizing cytochromes P450 – new basic and clinical aspects

LH 3D, 13:00 – 14:50

10. P450 and Steroid Metabolism

Chairs: Damjana Rozman and Amit V. Pandey

13:00 – 13:30 **Bon-chu Chung** (*Institute of Molecular Biology, Academia Sinica,* Taiwan)
Steroidogenic enzyme CYP11A1 remodels mitochondrial cristae

13:30 – 13:50 **Giovanna Di Nardo** (*University of Torino,* Italy)
Effect of R264C and R264H polymorphisms on human aromatase function: implications for breast cancer risk

13:50 – 14:20 **Toshiyuki Sakaki** (*Toyama Prefectural University*, Japan)
Characterization of CYP27B1 or CYP24A1 knockout rats generated by CRISPR/Cas9 system

14:20 – 14:50 **Edward T. Morgan** (*Emory University,* USA)
Nitric oxide stimulates proteolytic degradation of human CYP51A1

Tea & Coffee, Foyer, 14:50 – 15:20

Evening sessions

LH 3A, 15:20 – 16:40

11. P450 Biotechnology

Chair: Luet Lok Wong

15:20 – 15:50 **Manfred T. Reetz** (*Philipps-University Marburg and Max-Planck-Institut für Kohlenforschung*, Germany)
Recent progress in the directed evolution of selective P450 enzymes

15:50 – 16:10 **Alexander Dennig** (*Graz University of Technology,* Austria)
The CYP152 family - Promising catalysts for valorization of fatty acids into chemical building blocks

16:10 – 16:40 **Sabine L. Flitsch** (*University of Manchester*, UK)
Cytochrome P450 monooxygenases in *de novo* enzyme cascades

LH 3D, 15:20 – 16:40

10. P450 and Steroid Metabolism (continued)

Chair: Toshiyuki Sakaki

15:20 – 15:50 **Damjana Rozman** (*University of Ljubljana, Slovenia*)
Blocking hepatic *Cyp51* from cholesterol synthesis promotes hepatocarcinogenesis

15:50 – 16:10 **Maki Tsujita** (*Nagoya City University*, Japan)
Probucol increased adrenal CYP11A1, HMGCoAR and VKORC1 expression and rescued LCAT null male mice propagation

16:10 – 16:40 **Amit V. Pandey** (*University Children's Hospital, Bern*, Switzerland)
Androgen biosynthesis in humans by cytochrome P450s: Regulation, and targeting in diseases

Poster session II, Foyer, 16:40 – 18:00

Presenting authors of posters with an even number (e.g. P02, P04, etc.) are requested to be present at their posters for questions and discussion.

Conference dinner, Deichgraf, Siegburger Str. 161, Düsseldorf, 19:00

Thursday, 31.08.2017

Morning sessions

LH 3A, 09:00 – 10:50

11. P450 Biotechnology (continued)

Chairs: Luet Lok Wong and Sabine L. Flitsch

09:00 – 09:30 **Martha S. Smit** (*University of the Free State,* South Africa)
Regiospecific P450 catalysed in-chain hydroxylation for lactone synthesis

09:30 – 09:50 **Marco Girhard** (*Heinrich-Heine University*, Germany)
P450 enzymes in reaction cascades for oxy-functionalization of natural products

09:50 – 10:20 **Ulrich Schwaneberg** (*RWTH Aachen University*, Germany)
Eighteen years of directed P450 BM3 evolution: lessons and success stories

10:20 – 10:50 **Monika Müller** (*InnoSyn B.V.*, Netherlands)
Biocatalytic pilot scale processes using P450 monooxygenases *in vitro*

LH 3D, 09:00 – 10:50

12. Novel P450 Functions and Reactions

Chairs: Allan Rettie and Max Cryle

09:00 – 09:30 **Frank J. Gonzalez** (*National Cancer Institute, Bethesda,* USA)
Can xenobiotic-metabolizing CYPs be targeted for the treatment of metabolic disease?

09:30 – 09:50 **Matthew E. Albertolle** (*Vanderbilt University School of Medicine*, USA)
Oxidative inhibition of cytochrome P450 4A11 by heme-thiolate cysteine sulfenylation

09:50 – 10:20 **Rudi Fasan** (*University of Rochester*, USA)
P450-catalyzed nitrene transfer reactions: reaction scope and mechanistic investigations

10:20 – 10:50 **Andrew W. Munro** (*University of Manchester*, UK)
Novel structural and catalytic properties of P450 peroxygenase enzymes

Tea & Coffee, Foyer, 10:50 – 11:10

Morning sessions (continued)

LH 3A, 11:10 – 13:10

11. P450 Biotechnology (continued)

Chairs: Martha Smit and Ulrich Schwaneberg

11:10 – 11:40 **Luet Lok Wong** (*University of Oxford*, UK)
Developing CYP102A1 mutants as general oxidation catalysts

11:40 – 12:00 **Shyamalava Mazumdar** (*Tata Institute of Fundamental Research*, India)
Role of substituents on the reactions of polyaromatics catalysed by CYP175A1

12:00 – 12:30 **Erika Plettner** (*Simon Fraser University,* Canada)
Vinylic chloride removal by cytochrome P450cam (CYP101A1)

12:30 – 12:50 **Kim Thoa Nguyen** (*Institute of Biotechnology, Vietnam Academy of Science and Technology*, Vietnam)
Potential exploitation of novel thermostable cytochrome P450s from hotspring in Vietnam

12:50 –13:10 **Nao Katsuyama** (*Osaka Prefecture University,* Japan)
Identification of novel microbial P450s capable of intermolecular C-C coupling reactions

LH 3D, 11:10 – 13:00

12. Novel P450 Functions and Reactions (continued)

Chairs: Andrew W. Munro and Rudi Fasan

11:10 – 11:40 **Max J. Cryle** (*Monash University and EMBL Australia,* Australia)
Completing the glycopeptide antibiotic cyclisation cascade

11:40 – 12:00 **Svetlana Gorina** (*Kazan Institute of Biochemistry and Biophysics*, *Russian Academy of Sciences,* Russia)
The CYP74 enzymes: Structural and functional characteristics, evolution

12:00 – 12:30 **Allan E. Rettie** (*University of Washington,* USA)
Potential cancer application of CYP4 enzymes: From B to Z

12:30 – 13:00 **Matthias Bureik** (*Tianjin University*, PR China)
Human CYP4Z1 and breast cancer

Lunch, Foyer, 13:10 – 14:15

Afternoon sessions

LH 3A, 14:15 – 16:00

Young Researchers' Session

Chair: Vlada B. Urlacher

14:15 – 14:30 **Ksenia Juravel** (*Hebrew University of Jerusalem*, Israel)
Is evolution of polyphagia in *Bemisia tabaci* complex relating to positive selection in cytochrome P450 enzymes?

14:30 – 14:45 **Stella Child** (*University of Adelaide,* Australia*)*
The CYPome of *Mycobacterium marinum* and the associated electron transfer partners

14:45 – 15:00 **Best poster presentation**

Closing Lecture 15:00 – 15:30

Chair: Rita Bernhardt

Tsuneo Omura (*Kyushu University,* Japan) **Future perception in P450 research**

Poster award and Closing ceremony 15:30 – 16:00