

2nd FEBS Advanced Lecture Course

**“ATP-Binding Cassette Transporters:
From Multidrug Resistance to Genetic Disease”**



Abstract Book

Supported by

Austrian Federal Ministry of Science and Transport

SmithKline Beecham

American Cystic Fibrosis Foundation

Dr. Josef Steiner Cancer Research Foundation

 **NOVARTIS**

Programme of 2nd FEBS Advanced Lecture Course in Gosau – ABC99

Programme Outline	February 20 Saturday	February 21 Sunday	February 22 Monday	February 23 Tuesday	February 24 Wednesday	February 25 Thursday	February 26 Friday	February 27 Saturday
Breakfast				7.00 am - 8.30 am				
Symposia	10.00 am to 7.30 pm Registration & Check-In	8.30 - 12.35 pm Symposium 1 ABC Proteins in Uptake & Efflux in Prokaryotes Speakers Holland Wandersman Staufacher Konings Rosen	8.30 - 12.35 pm Symposium 2 ABC Proteins from Fungi, Plants & Parasites Speakers Michaels Sanglard Rea Wirth Ouellette	8.30 - 12.35 pm Symposium 3 Mechanism & Substrates of Pgp & MRP Speakers Sarkadi Borst Sharom Clarke Shapiro	8.30 - 12.45 pm Symposium 4 Clin. & Pharmacol. Implications of Pgp, MRP & sPGP Speakers Keppeler Cole Oude-Efferink Fojo 11.50 am Keynote Lecture Higgins	8.30 - 12.35 pm Symposium 5 ABC Protein Genes in Human Genetic Disease I Speakers Riordan Welsh Gadsby Aguilar-Bryan Ueda	8.30 - 12.35 pm Symposium 6 ABC Protein Genes in Human Genetic Disease II Speakers Chimini Alikkets Smith Neefjes Elliott	7.00 - 11.00 am Check-Out Buses to Salzburg End of Course
Lunch & Break		12.35 - 4.30 pm	12.35 - 4.30 pm	12.35 - 4.30 pm	12.45 - 6.45 pm	12.35 - 4.30 pm	12.35 - 4.00 pm	
Workshop & Short Talks		4.30 - 7.25 pm Workshop (WS) & Short Talks (ST) Hung Dassa Schlösser Lanfermeijer Poole Smit Blight Kaur Van Veen	4.30 - 7.25 pm Workshop (WS) & Short Talks (ST) Martinoia Forestier Kuspa Pérez-Victoria Le Blancq Kuchler Kolaczowski Rogers Lomovskaya	4.30 - 7.25 pm Workshop (WS) & Short Talks (ST) Goda Druley Orr Hrycyna Dey Hooijberg Di Pietro Russel Evers Wijnholds	Visit to Salzburg 1.00 – 6.45 pm	4.30 - 7.00 pm Workshop (WS) & Short Talks (ST) Stutts Nagel Csanady Randak Linsdell Schwappach Hough Bryan	4.00 - 6.45 pm Workshop (WS) & Short Talks (ST) Lehner Neumann Ahn Sun Berger Glöckner Hamon Schmitz 6.45 pm Final Keynote Address Rominson	
Dinner		7.25 - 8.45 pm	7.25 - 8.45 pm	7.25 - 8.45 pm	6.45 - 8.00 pm	7.00 - 8.15 pm		
Posters & Talks & Discussions	8.00 pm Course Opening & Welcome Party	8.45 - 11.00 pm Poster Session 1 9.45-11.00 pm Hot Topic Discussion Topic to be announced	8.45 - 11.00 pm Poster Session 2 9.45-11.00 pm Hot Topic Discussion Topic to be announced	8.45 - 9.35 pm Workshop (WS) & Short Talks (ST) Arias Hofman Johnstone 9.45 - 11.00 pm Poster Session 3 9.45-11.00 pm Hot Topic Discussion Topic to be announced	8.00 - 11.10 pm Workshop (WS) & Short Talks (ST) Ling Stieger Strautnieks Jansen Kuwano Ishikawa Müller De Vree Wada Bates	8.15 - 11.00 pm Poster Session 4 9.45-11.00 pm Hot Topic Discussion Topic to be announced	8.15 pm Banquet & Gosau Young Investigator Award Farewell Party	

PROGRAMME of 2nd FEBS ADVANCED LECTURE COURSE

SATURDAY	February 20
COURSE REGISTRATION & HOTEL CHECK-IN	9.00 am - 7.30 pm
Official Course Opening	8.15 pm - 8.30 pm
Dinner Buffet & Welcome Party	8.30 pm - open end
SUNDAY	February 21
<i>Breakfast</i>	7.00 - 8.30 am
SYMPOSIUM 1 <i>Chairman: Barry Holland</i> ABC Proteins in Uptake & Efflux in Prokaryotes	8.30 am - 12.35 pm
Barry Holland Structural and functional analysis of the oligomeric <i>E. coli</i> haemolysin transporter	8.30 - 9.15
Cecile Wandersman Hemophore structure, function and secretion	9.15 - 10.00
Cynthia Stauffacher Powering the ABC transporter: The crystallographic structure of the ATP-binding cassette, RbsA	10.00 - 10.45
<i>Coffee & Refreshment Break</i>	10.45 - 11.05
Wil Konings Expression and study of multidrug transporters in <i>Lactococcus lactis</i>	11.05 - 11.50
Barry Rosen Pathways of arsenic detoxification in <i>Saccharomyces cerevisiae</i>	11.50 - 12.35
LUNCH & AFTERNOON BREAK	12.35 - 4.30 pm
WORKSHOP (WS) & SHORT TALKS (ST)	4.30 - 7.25 pm
<i>Chairwoman: Cynthia Stauffacher</i>	
Li-Wei Hung (WS) Crystal structure of the ATP-binding subunit of an ABC transporter, the histidine permease of <i>Salmonella thyphimurium</i> , at 1.5 Å resolution	4.30 - 4.50
Elie Dassa (WS) Subunit interactions in ABC transporters	4.50 - 5.10
Andreas Schlösser (ST) The cellobiose ABC transporter of <i>Streptomyces reticuli</i>	5.10 - 5.25
Frank Lanfermeijer (ST) The Opp system of <i>Lactococcus lactis</i> binds and transports unusually large peptides	5.25 - 5.40
Philip Poole (WS) The general L-amino acid permease of <i>Rhizobium leguminosarum</i> is an ABC uptake system that also influences efflux of solutes	5.40 - 6.00

<i>Coffee & Refreshment Break</i>	6.00 - 6.20
John Smit (WS) Adapting the S-layer protein secretion apparatus of the bacterium <i>Caulobacter</i> to secrete recombinant proteins	6.20 - 6.40
Mark Blight (ST) Over-production, purification and preliminary characterisation of full-length <i>E. coli</i> HlyB expressed in <i>Lactococcus lactis</i>	6.40 - 6.55
Parjit Kaur (ST) The DrrA and DrrB proteins of the doxorubicin efflux pump of <i>Streptomyces peucetius</i> form a novel ABC transporter	6.55 - 7.10
Hendrik Van Veen (ST) Towards the drug transport and catalytic cycle of <i>LmrA</i> , the bacterial homologue of the human multidrug resistance P-glycoprotein	7.10 - 7.25
DINNER	7.25 - 8.45 pm
POSTER SESSION	8.45 - 11.00 pm
HOT TOPIC DISCUSSION (Topic to be announced)	9.45 - 11.00 pm

MONDAY	February 22
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<i>Breakfast</i>	7.00 - 8.30 am
SYMPOSIUM 2 <i>Chairwoman: Susan Michaelis</i> ABC Proteins from Fungi, Plants & Parasites	8.30 am - 12.35 pm
Susan Michaelis Trafficking and activity of Ste6p, the α -factor mating pheromone transporter in yeast	8.30 - 9.15
Dominique Sanglard The role of multidrug transporters in the resistance of yeast clinical isolates to antifungal agents	9.15 - 10.00
Philip Rea MRP subclass ABC transporters from plants and yeast	10.00 - 10.45
<i>Coffee & Refreshment Break</i>	10.45 - 11.05
Dyann Wirth ABC transporters in <i>Leishmania</i> and <i>Plasmodium</i>	11.05 - 11.50
Marc Ouellette The role of the ABC transporter PgpA in metal resistance in <i>Leishmania</i>	11.50 - 12.35
LUNCH & AFTERNOON BREAK	12.35 - 4.30 pm
WORKSHOP (WS) & SHORT TALKS (ST)	4.30 - 7.25 pm
<i>Chairman: Karl Kuchler</i>	
Enrico Martinoia (WS) AtMRP3 and AtMRP5: Comparison of two closely related <i>Arabidopsis</i> ABC transporters	4.30 - 4.50

Cyrille Forestier (WS) Modulation of plant ion channels by ABC proteins	4.50 - 5.10
Adam Kuspa (WS) Cell-type specific ABC transporters implicated in the control of <i>Dictyostelium</i> development	5.10 - 5.30
José Pérez-Victoria (ST) High-affinity binding of flavones to cytosolic domain of <i>Leishmania tropica</i> multidrug transporter, and reversal of resistance to daunomycin	5.30 - 5.45
Sylvie Le Blanq (ST) A <i>Cryptosporidium parvum</i> ABC protein at the host-parasite interface	5.45 - 6.00
<i>Coffee & Refreshment Break</i>	6.00 - 6.20
Karl Kuchler (WS) Modulation of inhibitor susceptibility and drug transport by point mutations in the yeast Pdr5 ABC drug efflux pump	6.20 - 6.40
Marcin Kolaczowski (ST) <i>In vitro</i> and <i>in vivo</i> characterization of the substrate specificity of yeast multidrug ABC transporters - in search for function	6.40 - 6.55
Bruce Rogers (ST) Generation of gene-knockout mutants deficient in multidrug pumps: Sensitive tools for drug discovery	6.55 - 7.10
Olga Lomovskaya (ST) Inhibiting efflux pumps	7.10 - 7.25
<i>DINNER</i>	7.25 - 8.45 pm
POSTER SESSION	8.45 - 11.00 pm
HOT TOPIC DISCUSSION (Topic to be announced)	9.45 - 11.00 pm

TUESDAY	February 23
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<i>Breakfast</i>	7.00 - 8.30 am
SYMPOSIUM 3 <i>Chairman: Balazs Sarkadi</i> <i>Mechanism & Substrates of P-glycoprotein & MRP</i>	8.30 am - 12.35 pm
Balázs Sarkadi Molecular mechanism and transport-related ATPase cycle of the multidrug transporters	8.30 - 9.15
Piet Borst The MRP family	9.15 - 10.00
Frances Sharom Fluorescence spectroscopic approaches to understanding the structure and function of the P-glycoprotein multidrug transporter	10.00 - 10.45
<i>Coffee & Refreshment Break</i>	10.45 - 11.05
David Clarke Probing the drug-binding site of the human multidrug resistance P-glycoprotein using cysteine-scanning mutagenesis and disulfide crosslinking	11.05 - 11.50

Adam Shapiro		11.50 - 12.35
Three cooperative sites of P-glycoprotein for drug binding and transport		
<i>LUNCH & AFTERNOON BREAK</i>		12.35 - 4.30 pm
WORKSHOP (WS) & SHORT TALKS (ST)		4.30 - 7.25 pm
<i>Chairman: David Clarke</i>		
Katalin Goda	(ST)	4.30 - 4.45
Complex drug binding interactions and extensive conformational changes in Pgp-mediated drug pumping		
Todd Druley	(ST)	4.45 - 5.00
Analysis of conformation changes of the <i>MDR1</i> P-glycoprotein detectable by altered immunoreactivity		
George Orr	(ST)	5.00 - 5.15
Characterization of the binding site(s) for Taxol in P-glycoprotein		
Christine Hrycyna	(ST)	5.15 - 5.30
Both ATP sites of human P-glycoprotein are essential but not equivalent		
Saibal Dey	(ST)	5.30 - 5.45
Stereospecific modulation of the human multidrug transporter (P-glycoprotein) by <i>cis</i> and <i>trans</i> isomers of the dopamine receptor antagonist flupentixol: Evidence for an allosteric modulator site		
<i>Coffee & Refreshment Break</i>		5.45 – 6.05
Jan Hooijberg	(ST)	6.05 - 6.20
Comparison of flavopiridol and other (iso)flavonoids in their interaction with the multidrug resistance protein 1		
Attilio Di Pietro	(ST)	6.20 - 6.35
A modulator-interacting region on cytosolic nucleotide-binding domains of P-glycoprotein: bifunctional interactions with flavonoids		
Frans Russel	(WS)	6.35 - 6.55
Role and substrate specificity of Mrp2 in the renal excretion of anionic xenobiotics and conjugates		
Evers Raymond	(ST)	6.55 - 7.10
Functional characterization of the multidrug resistance proteins MRP1 and <i>cMOAT(MRP2)</i> in polarized MDCKII cells		
Jan Wijnholds	(ST)	7.10 - 7.25
Multidrug Resistance Protein 1 protects the oropharyngeal mucosal layer and the testicular and kidney tubules against drug-induced damage		
<i>DINNER</i>		7.25 - 8.45 pm
WORKSHOP (WS) & SHORT TALKS (ST)		8.45 - 9.35 pm
Irwin Arias	(WS)	8.45 - 9.05
Hepatocellular ABC proteins: regulation of function and intracellular trafficking by PI 3-kinase and its products		
Johann Hofmann	(ST)	9.05 - 9.20
Protein kinase C inhibitors and P-glycoprotein		
Ricky Johnstone	(ST)	9.20 - 9.35
The drug efflux protein P-glycoprotein can protect tumor cells from multiple forms of caspase-dependent apoptosis		

<i>Short Coffee & Refreshment Break</i>	9.35 - 9.45
POSTER SESSION	9.45 - 11.00 pm
HOT TOPIC DISCUSSION (Topic to be announced)	9.45 - 11.00 pm

WEDNESDAY	February 24
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<i>Breakfast</i>		7.00 - 8.30 am
SYMPOSIUM 4	<i>Chairman: Dietrich Keppler</i>	8.30 am - 12.45 pm
<i>Clinical & Pharmacological Implications of Pgp, MRP & sPGP</i>		
Dietrich Keppler		8.30 - 9.15
ATP-dependent conjugate export pumps of the MRP family		
Susan Cole		9.15 - 10.00
Mechanistic and structural features of Multidrug Resistance Protein, MRP		
Ronald Oude-Elferink		10.00 - 10.45
Defects in biliary lipid transport		
<i>Coffee & Refreshment Break</i>		10.45 - 11.05
Antonio Fojo		11.05 - 11.50
ABC Transporters: role in clinical drug resistance and evaluation of the potential to impact therapeutic outcome by modulating their activity		
KEYNOTE PLENARY LECTURE		
Chris Higgins		11.50 - 12.45 pm
ABC transporters and multidrug resistance: From microbes to man (<i>Special Lecture supported by the Austrian Ministry of Science and Transport</i>)		
LUNCH & AFTERNOON BREAK		12.45 - 6.45 pm
VISIT TO SALZBURG		
Buses leave Hotel at		13.00 pm
Return from Salzburg to the venue		6.45 pm
DINNER		6.45 - 8.00 pm
WORKSHOP (WS) & SHORT TALKS (ST)		8.00 - 11.10 pm
<i>Chairman: Victor Ling</i>		
Victor Ling	(WS)	8.00 - 8.20
Sister of P-glycoprotein (sPgp)		
Bruno Stieger	(ST)	8.20 - 8.35
The interaction of the canalicular bile salt export pump with xenobiotics		
Sandra Strautnieks	(ST)	8.35 - 8.50
A gene encoding a liver-specific ABC transporter is mutated in progressive familial intrahepatic cholestasis		
Peter Jansen	(ST)	8.50 - 9.05
The bile salt export pump BSEP/SPGP is not expressed in patients with progressive familial cholestasis type 2		

<i>Coffee & Refreshment Break</i>		9.05 – 9.25
Michihiko Kuwano	(WS)	9.25 - 9.45
Molecular mechanisms for specific expression of <i>MDR1</i> gene in human tumors: YB-1, DNA methylation and gene rearrangements		
Toshihisa Ishikawa	(WS)	9.45 - 10.05
Biological significance of coordinated expression of MRP1 and gamma-glutamylcysteine synthetase in cell cycle arrest caused by anticancer prostaglandins		
Michael Müller	(WS)	10.05 - 10.25
Regulation of hepatic ATP-binding cassette proteins during cell cycle and cytokine-induced stress response		
Marleen De Vree	(ST)	10.25 - 10.40
Correction of <i>Mdr2</i> deficiency by transplantation of <i>MDR3</i> transgenic hepatocytes		
Morimasa Wada	(ST)	10.40 - 10.55
Genomic structure, mutations and functional role of the canalicular multispecific organic anion transporter (<i>cMOAT</i>) gene in Dubin-Johnson syndrome and cancer cells		
Susan Bates	(ST)	10.55 - 11.10
Molecular cloning of cDNAs which are highly overexpressed in mitoxantrone-resistant cells. Demonstration of homology to novel ABC half-transporter genes		

THURSDAY	February 25
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<i>Breakfast</i>		7.00 - 8.30 am
SYMPOSIUM 5	<i>Chairman: John Riordan</i>	8.30 am - 12.35 pm
<i>ABC Protein Genes in Human Genetic Disease I</i>		
John Riordan		8.30 - 9.15
Influence of phosphorylation by protein kinase A on CFTR at the cell surface and at the endoplasmic reticulum		
Michael Welsh		9.15 - 10.00
Probing the function of the CFTR Cl ⁻ channel		
David Gadsby		10.00 - 10.45
What controls opening and closing of CFTR Cl ⁻ ion channels?		
<i>Coffee & Refreshment Break</i>		10.45 - 11.05
Lydia Aguilar-Bryan		11.05 - 11.50
Familial hyperinsulinemic hypoglycemia of infancy and beta-cell K _{ATP} channels		
Kazumitsu Ueda		11.50 - 12.35
Cooperative interaction of two nucleotide binding folds of ABC proteins-SUR1 and MDR1		
LUNCH & AFTERNOON BREAK		12.35 - 4.30 pm
WORKSHOP (WS)& SHORT TALKS (ST)		4.30 - 7.00 pm
<i>Chairman: David Gadsby</i>		

Jackson Stutts	(WS)	4.30 - 4.50
AKAP-mediated regulation of CFTR by cAMP		
Georg Nagel	(ST)	4.50 - 5.05
Gating by nucleotide binding to two different binding sites on CFTR investigated by rapid concentration changes		
Laszlo Csanady	(ST)	5.05 - 5.20
Can CFTR work as a "conventional" ABC-transporter? Coexpression of two halves of CFTR lacking the R domain results in fully functional channels		
Christoph Randak	(ST)	5.20 - 5.35
The second nucleotide binding fold of CFTR combines activities of an ATPase, a GTPase and an adenylate kinase that are inhibited by genistein		
Paul Linsdell	(ST)	5.35 - 5.50
Functional similarities between CFTR and MRP: Implications for cystic fibrosis		
<i>Coffee & Refreshment Break</i>		5.50 - 6.10
Blanche Schwappach	(WS)	6.10 - 6.30
A novel ER retention sequence regulates the assembly and stoichiometry of plasma membrane K_{ATP} channels		
Emma Hough	(ST)	6.30 - 6.45
Identification of regions that regulate the sulphonylurea receptor mediated surface expression of $K_{IR}6.2$		
Joseph Bryan	(ST)	6.45 - 7.00
$K_{IR}6.2$ and sulphonylurea receptors share determinants of functional expression, intrinsic gating, and ATP-inhibition of K_{ATP} channels		
<i>DINNER</i>		7.00 - 8.15 pm
POSTER SESSION		8.15 - 11.00 pm
HOT TOPIC DISCUSSION (Topic to be announced)		9.45 - 11.00 pm

FRIDAY	February 26
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<i>Breakfast</i>	7.00 - 8.30 am
SYMPOSIUM 6	<i>Chairwoman: Giovanna Chimini</i>
ABC Protein Genes in Human Genetic Disease II	8.30 am - 12.35 pm
Giovanna Chimini	8.30 - 9.15
ABC1 and the engulfment of apoptotic cells : a question of lipid scrambling?	
Rando Allikmets	9.15 - 10.00
Human ABC transporter superfamily and the <i>ABCR</i> gene, involved in five eye diseases	
Kirby Smith	10.00 - 10.45
Mammalian peroxisomal ABC half transporters in health, disease & therapy	
<i>Coffee & Refreshment Break</i>	
Jaques Neefjes	11.05 - 11.50
Substrate capture and translocation by the peptide transporter TAP	

Tim Elliot Role of the Transporter Associated with Antigen Presentation and associated cofactors in antigen presentation to T lymphocytes	11.50 - 12.35
<i>LUNCH & AFTERNOON BREAK</i>	12.35 - 4.00 pm
WORKSHOP (WS)& SHORT TALKS (ST)	4.00 - 6.40 pm
<i>Chairman: Robert Tampé</i>	
Paul Lehner (WS) Tapasin stabilizes the TAP transporter and is essential for MHC Class I antigen presentation	4.00 - 4.20
Lars Neumann (ST) Mechanistic and kinetical studies of the peptide transporter TAP	4.20 - 4.35
Jinhi Ahn (ST) ATPase activity of the purified rod photoreceptor ABCR protein is stimulated by retinal	4.35 - 4.50
Hui Sun (ST) Retinal stimulates the ATP hydrolysis by reconstituted ABCR: Synergism with non-retinoid compounds	4.50 - 5.05
<i>Coffee & Refreshment Break</i>	5.05 - 5.25
Johannes Berger (ST) Novel therapeutic strategies for X-linked adrenoleukodystrophy	5.25 - 5.40
Johannes Gloeckner (ST) The human adrenoleukodystrophy protein and related ABC transporters interact with the farnesylated peroxisomal assembly protein PEX19	5.40 - 5.55
Yannick Hamon (ST) Subcellular localization of the mammalian ABC transporter ABC1	5.55 - 6.10
Gerd Schmitz (WS) The human ATP-binding cassette transporter 8 (ABC8) is a cholesterol sensitive gene which is involved in macrophage cholesterol transport	6.10 - 6.30
<i>Coffee & Refreshment Break</i>	6.30 - 6-45
FINAL KEYNOTE ADDRESS Igor Roninson <i>(Special Lecture supported by the Austrian Ministry of Science and Transport)</i>	6. 45 - 7.30 pm
CONCLUDING REMARKS Piet Borst, Karl Kuchler, John Riordan	7.30 - 7.45
Banquet and Farewell Party	8.15 pm - open
“GOSAU YOUNG INVESTIGATOR AWARD”	

SATURDAY	February 27
<i>Breakfast</i>	7.00 - 8.30 am
HOTEL CHECK OUT	8.15 - 11.00 am
OFFICIAL END OF THE COURSE	11.00 am
Shuttle Buses to Salzburg (detailed schedule to be announced)	

