

Curriculum Vitae

Name & Address

Karl Kuchler – *Professor of Molecular Genetics*

Medical University Vienna, Max F. Perutz Laboratories

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<http://www.mfpl.ac.at/index.php?cid=77> & <http://www.cdl.univie.ac.at/>



University Studies

October 1977 - March 1980, "Technical Chemistry" at the Technical University of Graz

May 1980 - December 1982, "Biochemistry and Food Biotechnology", Technical University of Graz

December 1982, "Dipl.-Ing." (MSc) Defense with "*First Class Honours*"

March 1983 - June 1986, PhD student of Prof. Friedrich Paltauf, Technical University of Graz.

1986, PhD Thesis "*Phospholipid Biosynthesis in Yeast*" PhD Defense with "*First Class Honours*"

Research & Professional Experience

July 1986 - September 1988, postdoctoral fellow with Prof. Günther Kreil at the Institute of Molecular Biology of the Austrian Academy of Sciences in Salzburg

October 1988 - March 1991, postdoctoral fellow with Prof. Jeremy Thorner in the Department of Molecular and Cell Biology at the University of California at Berkeley, USA

April 1991 - March 1992, senior research associate in the Lipid and Lipoprotein Research Group of the Department of Biochemistry at the University of Alberta in Edmonton, Canada

April 1992 - date, Faculty position in the Department of Molecular Genetics of at the Vienna Biocenter

August 1994 - date, Tenured *Associate Professor of Molecular Genetics* in Department of Medical Biochemistry of the Vienna Medical University at the Campus Vienna Biocenter

June 1996 - October 1996, Fulbright Sabbatical Fellow at the City of Hope National Cancer Center, USA

1999, Visiting Professor of the University of Kyoto supported by the Austrian Academic Exchange

May 2000 - November 2001, Cluster Manager for "*Biotechnology & Molecular Medicine*" at the Vienna Business Agency to coordinate the development of the Vienna Biotechnology Cluster

2008, Guest Professor and teaching at the Katholieke Universiteit Leuven, Belgium

2008, Guest Professor and teaching ("*Capita Selecta*") at the Comenius University Bratislava

March 2008 – July 2012, Director *Christian Doppler Laboratory for Infection Biology* Vienna Biocenter

Honors & Awards

1983 - 1986 "Österreichisches Begabtenstipendium" (for excellence in university studies)

September 1988 - March 1990, Postdoctoral Fellow of the Max Kade Foundation Inc.

October 1989 - March 1991, Postdoctoral Fellow of the Austrian Chamber of Commerce

April 1990 - March 1991, Erwin Schrödinger Postdoctoral Fellow of the Austrian Science Foundation

April 1991 - March 1992, Postdoctoral Fellow of the Alberta Heritage Foundation for Medical Research

1996, Novartis Prize (formerly Sandoz Prize) for Biology

2007, Life-Time Honorary Member of the Austrian Society of Biochemistry & Molecular Biology

2011 - Winner of the *ScienceSlam* Contest at the annual Open Day of the Medical University of Vienna

Experience in Management, Congress Organization & Professional Activities

1993, 1997 - 2000, Organizer of the annual "1st, 5th, 6th & 7th Vienna Biocenter Recess"

1995 - 2003, Officer in charge for biosafety and recombinant gene technology work at the Department of Molecular Genetics according to the Austrian Biosafety Law "GTG94"

1997, 1999, 2001 & 2003, Organizer and Chair of the international 1st, 2nd, 3rd & 4th **FEBS Advanced Lecture Courses on ABC Proteins** ("*ABC Transporters: From Multidrug Resistance to Genetic Disease*") with up to 250 participants in Gosau, Austria.

1997 - 1998, Planning and organization of the Austrian-wide exhibit "**gentechnik pro & contra**" for the information of the broad public on safety and risks of recombinant DNA technologies.

2000 – 2006, Board of directors and founding member of **dialog<>gentechnik** (formerly "*Gentechnik & Wir*") – a non-profit agency devoted to public understanding science & biotechnology.

May 2000 – October 2001, **Cluster Manager** for "**Biotechnology**" at the Vienna Business Agency to coordinate the development of the Vienna Region Biotechnology Cluster.

2001 – 2002, Co-Organizer of the international biotechnology business plan competition in life sciences "**Best of Biotech - BOB**" with the Vienna Business Agency and the Innovation Agency.

1999 - date, Member of the Austrian "**Gene Technology Commission**" - the national advisory board for the federal government for all scientific questions related to the Gene Technology Law GTG94.

2004 – date, Co-Chair & Co-Organizer of 1st, 2nd, 3rd & 4th **FEBS Advanced Lecture Courses on Systems Biology** ("*Systems Biology: From Molecules to Life*") with 200 participants in Gosau in March 2005 & 2007 in Gosau, 2009 in Alpbach, and 2011 in Innsbruck.

2003 - 2004, Co-Organizer & Member of the Organizing Committee of the "**International Conference on Systems Biology ICSB2004**" in October 2004 in Heidelberg.

2005, Co-Founder CIBIV - "**Center Integrative Bioinformatics Vienna**" Campus Vienna Biocenter

2005 – date, Organizer & Chair of 1st, 2nd, 3rd & 4th **FEBS Special Meetings on ABC Proteins** ("*ABC Transporters, From Multidrug Resistance to Genetic Disease*") – ABC2006, ABC2008 % ABC2010 - with 320 participants in Innsbruck, Austria.

2009, Co-Organizer of 1st and 2nd **Joint OeGMM / ÖGACH Workshop MedMy2009 / MedMyc2011: Medical Mycology – From Basic Science to Clinical Needs**. Campus Vienna Biocenter, Vienna, December 4-5, 2009

2009 - date, Co-Organizer of the **MYK2010 Congress** in Vienna

2005 - 2007, Organizer & Chair of the **32nd Annual FEBS Congress FEBS2007** ("*Molecular Machines*") with 2300 participants from July 7-12, 2007 in Vienna, Austria

2005 – 2008, Member Executive Committee of *Austrian Society Biochemistry & Molecular Biology*

2003 – date, Member Executive Committee of *Austrian Society for Medical Mycology*

2003 – date, Vice-President *Max Kade Alumni Section* of the Academy of Sciences Alumni Club

2003 – date, Board of Directors & Treasurer "*Friends of the Austrian Academy of Sciences Association*"

2012– date, President of the *Alumni Association of the Austrian Academy of Sciences*

International Activities as Peer-Reviewer for Scientific Journals

Ongoing and continuous peer-reviewing activities for scientific journals, including *Cell*, *Nature*, *Mol. Cell*, *PLoS Genetics*, *PLoS Pathogens*, *PLoS Biology*, *PLoS One*, *EMBO J.*, *EMBO Rep.*, *Proc. Natl. Acad. Sci. (USA)*, *J. Biol. Chem.*, *Cancer Res.*, *Mol. Microbiol.*, *Mol. Cell. Biol.*, *Mol. Biol. Cell*, *Yeast*, *Biochim. Biophys. Acta*, *FEBS Lett.*, *Mol. Gen. Genetics*, *Eukaryotic Cell*, *Exp. Cell Res.*, *J. Cell Science*, *Microbiology*, *Cell. Mol. Life Sci.*, *App. Env. Microbiol.*, *Biol. Chem. J. Pharmacol. Exp. Therap.*, *Int. J. Antimicrobial Agents*, *Microbiology*, *Vaccine*, *Fungal Genet. Biol.*, *Infection & Immunity*, *Frontier Science*

1999 - 2003, Member of the Advisory Board "*Cellular and Molecular Life Sciences*".

2004 - 2007, Member of the Editorial Board "*Molecular Microbiology*"

2005 - 2010, Executive Board & Trustee "*Federation of European Biochemical Societies - FEBS*"

2005 - 2010, Elected Chair of the "*FEBS Advanced Courses Committee*"

2005 – date, Associate Editor & Editorial Board "*Current Genetics*"

2008 – date, Associate Editor & Editorial Board "*Microbiology*"

2010 – date, Associate Editor & Editorial Board “*Frontiers in Microbiology*“

2012 – on, Associate Editor & Editorial Board “*Systems Biomedicine*“

2013 – on, Editorial Board “*Pathogens & Disease*“ (formerly *FEMS Immunology & Medical Microbiology*)

Experience in International Science Funding & Policy-Making & Advisory Boards

Review of both grant and fellowship applications for the *Wellcome Trust Foundation*, *German Science Foundation DFG*, *Human Frontiers of Science HFS*, *BBSRC United Kingdom*, *Suisse National Foundation*, *Genome Canada*, *Austrian National Bank*, *Leuven University Foundation*, *Slovenian Science Foundation*, *Grant Agency of the Czech Republic*, *Italian Science Foundation MUIR-CINECA*; *Hungarian Ministry of Science*, *CNR Italy*, *FWO Holland*, *EC DGXII panels during FP5, FP6 and FP7*.

2003 - 2005, member of the **Steering Committee** for “*HepatosSys - Systems Biology of the Hepatocyte*“

2003 – date, participation in international review panels **NGFNII-Proteomics**, **NGFNII-Exploratory Grants**, & **QuantPro** (German Ministry for Education and Science, **bmb+f**)

2004 - 2005, member **Steering Committee** for **ESF Forward Look** on “*Systems Biology*“

2001 - 2003; Panel member of the **bmb+f “Bio-Chance”** scheme for biotech start-up companies

2003 - date, Member of the Jury for the **Biotechnica Award** for biotech companies (Deutsche Messe)

2007 - date, Chair Scientific Advisory Board of CIBIV “*Center Integrative Bioinformatics Vienna*“

2009 – 2010, Member international expert panel (*CNR Institutes*) in the **Italian CNR Evaluation**

2010 – 2013, Member expert review panel (*Bio2 – Functional Biology*) in the Dutch **FWO Agency**

2012 – date, Member Scientific Advisory Board, BBSRC Programme Grant CRISP (Chair Alistair Brown)

Public Understanding of Science – Activities in Science in & for Society

Numerous **lectures** for the **public** and **in high schools**, as well as in primary schools on basic biology, science, gene technology, and on the role of today’s biotechnology in day-to-day life in a modern society.

Regular participation in annual educational programmes offering teaching for the public and schools (“**University Meets Public**“). Basic scientific lectures in the area *Infection Biology & Drug Resistance* for the interested broad public audience in public school facilities.

Initiator and Organizer if the „**Kids Congress**“ in collaboration with the *Childrens University Vienna* with some 800 school children age 7-12 attending two scientific lectures during the FEBS2007 Congress in Vienna.

Co-founder of **dialog<>gentechnik** (<http://www.dialog-gentechnik.at/index.php>), a public body dedicated to public outreach activities in biosciences. Numerous interviews, commentaries in the **daily / weekly print media**, including interviews on TV and radio on public perception of science and biotechnology.

Co-Initiator and co-founder of the **Vienna Open Lab** (<http://www.viennaopenlab.at/>) to train and educate pupils and teachers basic methods in modern molecular biology through hands-on activities.

Membership in Professional Societies

Austrian Society for Biochemistry Molecular Biology & Max Kade Alumni Club

Austrian Society of Genetics and Gene Technology & Austrian Society for Medical Mycology

Genetics Society of America & American Society of Microbiology

American Society of Cell Biology & American Society for Biochemistry & Molecular Biology

Selection of Scientific Publications

Overall, more than **130 publications**, including papers in peer-reviewed journals, reviews, book chapters; editor of several text books and special journal issues. The cumulative impact factor of all publications is currently about **600**. More than **130 invited seminars** or plenary **lectures** at international meetings, conferences, and university institutions. Based on *ISI Web of Knowledge*, publications have been cited more than **4200** times, with a current life-time **Hirsch Index** of **h36**. Publication activities started in 1986, the year when the PhD was obtained.

Tscherner, M., E. Stappler, D. Hnisz & K. Kuchler (2012). The histone acetyltransferase Hat1 facilitates DNA damage repair and morphogenesis in *C. albicans*. **Mol. Microbiol.** In press doi 10.1111/mmi.12051

Hnisz, D., A. Bardet, C. Nobile, U. Schoeck, A. Petryshin, W. Glaser, A. Johnson, A. Stark, & K. Kuchler (2012). Histone deacetylation at coding sequences adjusts transcription kinetics during *Candida albicans* morphogenesis. **PLoS Genetics**, in press

Majer, O., Bourgeois, C., F. Zwolanek, M. Mack, C. Lassing, D. Kerjaschki, M. Müller & K. Kuchler (2012). Type I interferon signaling promotes fatal immunopathology through the recruitment of inflammatory monocytes and neutrophils. **PLoS Pathogens** 8: e1002811

Ryan, O., RS. Shapiro, CF. Kurat, D. Mayhew, A. Baryshnikova, B. Chin, Z-Y. Lin, M.J. Cox, F. Vizeacoumar, D. Cheung, S. Bahr, K. Tsui, F. Tebbji, A. Sellam, F. Istel, T. Schwarzmüller, T.B. Reynolds, K. Kuchler, D.K. Gifford, M. Whitway, G. Giaever, C. Nislow, M. Costanzo, A-C. Gingras, R.D. Mitra, B. Andrews, G.R. Fink, L.E. Cowen & C. Boone; (2012). Global gene deletion analysis exploring yeast filamentous growth. **Science** 337: 1353-1356 doi: 10.1126

Tierney, L., L. Rizzetto, D. Cavaliere* & K. Kuchler* (2012). Systems biology of host-fungus interactions: turning complexity into simplicity? **Curr Opin Microbiol.** 15: 440-446

Tierney, L., J. Linde, S. Müller, S. Brunke, B. Hube, R. Guthke & K. Kuchler (2012). Parallel RNA-seq reveals novel interspecies gene regulatory networks of *C. albicans* invading innate immune cells. **Frontiers Microbiol** 3: Epub 2012 Mar 12

Relloso, M., L. Aragonese-Fenoll, C. Bourgeois, G. Romera, K. Kuchler, A.L. Corbí, MA. Muñoz-Fernandez, J.L. Rodríguez-Fernández & Rosalia Diez-Orejas (2012). Estrus impairs the trigger of Th17 immune response by altering dendritic cell function. **J. Leukocyte Biol** 91:159-165

Bourgeois, C., O. Majer, I.E. Frohner, I. Lesiak.-Markowicz, K-S. Hildering, W. Glaser, S. Stockinger, T. Decker, M. Müller, S. Akira, & K. Kuchler (2011). Conventional dendritic cells mount a type I IFN response against *Candida* spp. requiring novel phagosomal TLR7-mediated IFN-beta signaling. **J. Immunol.** 186: 3104-3112

Frohner, I.F., C. Bourgeois, K. Yatsyk, O. Majer & K. Kuchler (2009). The *Candida albicans* *Sod5* cell surface superoxide dismutase degrades host-derived reactive oxygen species (ROS) to escape immune surveillance. **Mol. Microbiol.** 71: 240-252

Hnisz, D., T. Schwarzmüller, & K. Kuchler (2009). Transcriptional loops meet chromatin – a dual layer network controls white-opaque switching in *Candida albicans*. **Mol. Microbiol.** 74: 1-15

Hnisz, D., O. Majer, I.E. Frohner, V. Komnenovic, & K. Kuchler (2010). The Set3/Hos2 histone deacetylase complex attenuates cAMP/PKA signaling to regulate morphogenesis and virulence of *Candida albicans*. **PLoS Pathogens**, 13:6(5): e1000889 doi:10.1371

Gregori, C, C. Schüller, Ingrid, E. Frohner, G. Ammerer & K. Kuchler (2008). Weak organic acids trigger conformational changes of the yeast transcription factor War1 *in vivo* to elicit stress adaptation. **J. Biol. Chem.** 283:25752-764

Schüller C., Y.M. Mamnun, H. Wolfger, N. Rockwell, J. Thorner & K. Kuchler (2007). Membrane-active compounds activate yeast ABC efflux transporters through PDR- and STRE-dependent mechanisms. **Mol. Biol. Cell.** 18: 4932-4944

Wolfger, H., Y. M. Mamnun & K. Kuchler (2004). The ABC protein Pdr15 is a general stress response factor implicated in cellular detoxification. **J. Biol. Chem.** 279: 11593-11599

Schüller, C., Y. M. Mamnun, M. Mollapour, G. Krapf, P. Piper & K. Kuchler (2004). The global weak acid stress response in the yeast *Saccharomyces cerevisiae* requires activation of a dedicated transcriptional regulator. **Mol. Biol Cell** 15: 706-720

Kren, A., Y.M. Mamnun, B. Bauer, C. Schüller, H. Wolfger, C. Gregori, K Hatzixanthis, M. Mollapour, P. Piper & K. Kuchler (2003). War1p, a novel transcription factor controlling weak acid stress response in yeast. **Mol. Cell Biol.** 23: 1775-1785

Reinoso-Martín, C., C. Schüller, M. Schuetzer-Muehlbauer & K. Kuchler (2003). The yeast protein kinase C cell integrity pathway mediates tolerance to the antifungal drug caspofungin through activation of Sit2p MAP kinase signaling. **Eukaryotic Cell.** 2: 1200-1210

Schützer-Mühlbauer, M., B. Willinger, G. Krapf, S. Enzinger, E. Presterl & K. Kuchler. (2003). The *Candida albicans* Cdr2p ATP-binding cassette transporter confers resistance to caspofungin. **Mol. Microbiol.** 48: 225-235

Mamnun, Y., Pandjaitan, R., Y. Mahé, A. Delahodde & K. Kuchler. (2002). The yeast zinc finger regulators Pdr3p and Pdr1p regulate the pleiotropic drug resistance (PDR) as homo- and heterodimers *in vivo*. **Mol. Microbiol.** 46: 1429-1440

Gaedeke, N., M. Klein, U. Kolukisaouglu, C. Forestier, A. Müller, M. Ansorge, D. Becker, Y. Mamnun, K. Kuchler, B. Schulz & E. Martinoia (2001). The *Arabidopsis thaliana* transporter AtMRP5 controls root development and stomata movement. **EMBO J.** 20: 1875-1887

Egner, R. B. E. Bauer, & K. Kuchler (2000). The transmembrane domain 10 of the yeast Pdr5p ABC antifungal efflux pump determines both substrate specificity and inhibitor susceptibility. **Mol Microbiol** 1461: 1255-1263

Egner, R., F. E. Rosenthal, N. Kralli, D. Sanglard & K. Kuchler (1998). Genetic separation of FK506 susceptibility and drug transport in the yeast Sts1/Pdr5 ABC multidrug resistance transporter. **Mol. Biol. Cell.** 9: 523-543

Plemper, R. K, R. Egner, K. Kuchler & D.H. Wolf (1998). Endoplasmic reticulum degradation of a mutated ATP-binding cassette transporter Pdr5 proceeds in a concerted action of Sec61 & the proteasome. **J. Biol. Chem.** 273: 32848-32856 (DHW & KK equal senior authors)

Piper, P., Y. Mahé, S. Thompson, R. Pandjaitan, C. Holyoak, R. Egner, M. Mühlbauer, P. Coote, & K. Kuchler (1998). The Pdr12 ABC transporter is required for the development of weak organic acid resistance in yeast. **EMBO J.** 17: 4257-4265

Bartl, S., Taplick, J., Lagger, G., Khier, H., K. Kuchler, & C. Seiser (1997). Identification of histone deacetylase1 as a growth factor-inducible gene. **Mol. Cell. Biol.** 17: 5033-5043

Kean, L. S., Grant, A. M., Angeletti, C., Mahé, Y., Kuchler, K., Fuller, R. S., & W. J. Nichols. (1997). Plasma membrane translocation of fluorescent-labeled phosphatidylethanolamine is controlled by the transcription regulators *PDR1* and *PDR3*. **J. Cell. Biol.** 138: 255-270

Mahé Y., Y. Lemoine, & K. Kuchler (1996). The ATP-binding cassette multidrug transporters Pdr5 and Snq2 of *Saccharomyces cerevisiae* can mediate transport of steroids *in vivo*. **J. Biol. Chem.** 271: 25167-25173

Egner, R., Mahé Y., Pandjaitan, R., & K. Kuchler (1995). Endocytosis and vacuolar degradation of the plasma membrane localized yeast Pdr5 ATP-binding cassette multidrug transporter. **Mol. Cell. Biol.** 15: 5879-5887

Sanglard, D., Kuchler, K., Ischer, F., Pagani, J.-L., Monod, M. K., & J. Bille (1995). The mechanisms of azole antifungals resistance in *Candida albicans* isolates from AIDS patients involve specific multidrug transporters. **Antimicrob. Agents Chemoth.** 39: 2378-2386

Bissinger, P. & K. Kuchler (1994). Molecular cloning and expression of the *S. cerevisiae* *STS1* gene: A yeast ABC-transporter conferring mycotoxin resistance. **J. Biol. Chem.** 269: 4180-4187

Kuchler, K., H. Dohlman, & J. Thorner (1993). The *a*-factor transporter (*STE6* gene product) from *Saccharomyces cerevisiae* and cell polarity. **J. Cell Biol.** 120:1203-1215

Kuchler, K., & J. Thorner (1992). Functional expression of human *mdr1* in the yeast *Saccharomyces cerevisiae*. **PNAS (USA)** 89: 2302-2306

Kuchler, K., K. Richter, J. Trnovsky, R. Egger, & G. Kreil (1990). Two precursors of thyrotropin releasing hormone from Skin of *Xenopus laevis*. Each contains seven copies of the end product. **J. Biol. Chem.** 265:11731-11735

Kuchler, K., R. Sterne, & J. Thorner (1989). *Saccharomyces cerevisiae* *STE6* gene product: A novel pathway for protein export in eukaryotic cells. **EMBO J.** 8: 3973-3985

Kuchler, K., M. Gmachl, M.J. Sippl, & G. Kreil (1989). Analysis of the cDNA for phospholipase A₂ from honeybee venom glands: The deduced amino acid sequence reveals homology to the corresponding vertebrate enzymes. **Eur. J. Biochem.** 184: 249-254

Kuchler, K., G. Daum, & F. Paltauf (1986). Subcellular and submitochondrial localization of phospholipid-synthesizing enzymes in *S. cerevisiae*. **J. Bacteriology** 165: 501-510

National / International Teaching Experience

Technical University of Graz

1983 - 1986: Department of Biochemistry at the Technical University of Graz (chair Prof. Dr. F. Paltauf). As a graduate student, responsible for independent teaching of sections in the major classes: "**Biochemistry**" (cell fractionation, phospholipids, metabolites); "**Advanced Biochemistry**" (protein purification, phospholipid biosynthesis, advanced cell fractionation); "**Methods in Biochemistry**" (chromatography methods).

1985 - 1986: Department of Biochemistry at the Technical University of Graz. Organization, planning and teaching of the *laboratory course* and seminar: "**Methods in yeast genetics**" (yeast cloning, complementation analysis, random spore analysis, strain construction, micromanipulation).

University of Salzburg

1987 - 1988: Teaching affiliation with the Department of Biochemistry at University of Salzburg while affiliated with the Austrian Academy of Sciences; teaching and organization of a *laboratory course* and seminar ("**Methods in DNA sequence analysis**") held at the Institute of Molecular Biology of the Austrian Academy of Sciences in Salzburg.

University of Graz

1996 - 2000: Teaching affiliation as **Guest Professor** at the in the Department of Microbiology & Genetics of the University of Graz to teach the main classes "**Genetics**" and "**Recombinant DNA Technology**" for 80-100 *Microbiology* undergraduate students per year.

Medical University of Vienna & University of Vienna

1992 - date: Continuous teaching of lab courses and several classes at the **Medical Faculty** of the **University of Vienna**, to become the Medical University Vienna later on. ("**Medicinal Chemistry**" and "**Biochemistry**"), as well as **speciality classes** (i.e. "*ABC Proteins in anticancer and microbial multidrug resistance*") in several Blocks of the new curriculum of the Medical University of Vienna. A copy of selected online evaluations from one *MCW Block (BL7)* from *WS2005* and *WS2007* is included.

1993, 1995, 1998, 2001: Teaching the main class at **Medical Faculty** of the **University of Vienna**. "*Introduction to Medicinal Chemistry*" for some 300 first year medical students in each year.

Foreign Universities & International Teaching at Lecture Courses

2008: **Guest Professorship** with the **Katholieke University of Leuven**, Belgium teaching several seminars in the area of *Infection Biology* (Host – "*Molecular basis of host immune response against fungal pathogens*", Pathogens – "*The molecular basis of fungal virulence and host invasion - virulence genes*", as well as classes on multidrug resistance such as "*Molecular mechanism of drug resistance in microbial pathogens and cancer cells*"). Furthermore, teaching of **soft-skills** such as **grant-writing** ("*How to write and NOT to write grant applications*").

2009: **Guest Lectureship Series** at the **Comenius University Bratislava** in Slovakia (*Capita Selecta Programme*) – teaching seminars in the area of *Infection Biology* (Host – "*Molecular basis of host immune response against fungal pathogens*", Pathogens – "*The molecular basis of fungal virulence and host invasion - virulence genes*").

1997, 1999, 2001 & 2003: Organizer and Chair of the international **1st, 2nd, 3rd and 4th FEBS Advanced Lecture Courses** on **ABC Proteins** ("*ABC Transporters: From Multidrug Resistance to Genetic Disease*") with 120 student participants.

2005, 2007, 2009, & 2011: Co-Organizer & Co-Chair of **1st, 2nd, 3rd and 4th FEBS Advanced Lecture Courses** on **Systems Biology** ("*Systems Biology: From Molecules to Life*") with 120 young scientists

Main Research Interests

Fungal infections constitute a growing medical problem causing an enormous economical burden due to astronomical healthcare costs exceeding billions just in the western world. In developing countries, high costs associated with invasive fungal diseases often impede therapies. The major fungi infecting humans on both continents include *Candida* spp (*C. albicans*, *glabrata* and especially *C. tropicalis* in India) accounting for 80% of all infections, and representing the 4th-most leading cause of nosocomial diseases. The attributable mortalities of about 40% just for candidemias exceeds that of all *Gram*-negative bacterial septicemias, emphasizing their medical importance. In addition to classical risk factors such as immune suppression, hematological malignancies, transplantation and neutropenia, infections are increasingly observed in non-neutropenic intensive care unit patients. Recent changes in the epidemiology of fungal infections complicate the scenario, as the challenge of rapid, reliable and accurate clinical diagnosis remains unsolved. Finally, clinical antifungal therapy is confronted with problems such as inherent antifungal tolerance in case of *C. glabrata*, high-cost antifungals such as candins, or narrow-spectrum and even toxicity of drugs.

Hence, our research interests focus on host-microbe interplays, since this work has translational potential in infection biology. Hence, my group uses **genomics** methodologies and technologies necessary for studies aimed at a better understanding of **host-pathogen interactions** and **drug resistance** in prevalent **human fungal pathogens** such as ***Candida* spp**. The aim is to improve our understanding of the molecular mechanisms underlying fungal pathogenicity.

Most if not all host-pathogen interactions are characterized by highly dynamic and interdependent relationships due to alternating attack and defense mechanisms exerted by each partner. Thus, we have set out to decipher fungal virulence by studying the simultaneous molecular processes occurring both in the pathogen and in its host. We are now among few groups able to study the dynamics of infectious processes in both **mammalian host cells** and **pathogens**. Iterative systems biology approaches enable us to study the dynamics of reciprocal attack and defense events during fungal infections. Our work stretches from functional and mechanistic studies on single genes and signaling pathways to **genome-wide** approaches through quantitative transcriptomics, functional genomics and/or reverse-genetics. Finally, we use **interdisciplinary** theoretical approaches to better understand and infer interdependent **genetic regulatory networks** that control the molecular cross-talk of **signaling** during host-pathogen interactions. The major goal is therefore to unravel the complexity of **molecular signaling processes** that determine fungal virulence and shape the host immune response. We are also particularly interested in delineating adaptive genetic, as well as tolerogenic mechanisms in the host, which enable microbial pathogens to evade immune surveillance, thereby leading to dissemination and invasive diseases or other mechanisms that enable colonization in the case of host tolerance, respectively. As for **fungal pathogens**, we use reverse-genetics as well as forward-genetics to:

- i) identify fungal virulence and genes implicated in antifungal drug resistance,
- ii) decipher the role of histone-modifying enzymes such as histone deacetylases / histone acetyl transferases (HDAC/HAT) in morphogenetic switching or cell fate determination,
- iii) study the genetic and genomic adaptation processes occurring in fungal pathogens during specific host niche colonization, and
- iv) decipher the structure-function relationships of ABC transporters conferring antifungal drug resistance in relevant *Candida* spp.

On the **host immune response aspect**, we are delineating:

- (i) the signaling response in primary *ex vivo* innate immune cells, as well as in mouse models infected with fungal pathogens, including the function of novel microbial pathogen receptors
- (ii) the signaling cross-talk of adaptive and innate immunity during immune surveillance,
- (iii) the role of type I interferons (i.e. IFN- β) in fungal virulence and host dissemination, and which mechanism IFN- β signaling exploits to stimulate migration of inflammatory phagocytes
- (iv) the signaling mechanisms by which innate phagocytes provide instructions for the adaptive immune response, but also how signaling drives the recruitment of inflammatory phagocytes and controls the outcome of fungal infections.