



PERFORMANCE REPORT 2007

Department of Specific Prophylaxis and Tropical Medicine

at the

Center for Physiology, Pathophysiology & Immunology,

Medical University of Vienna

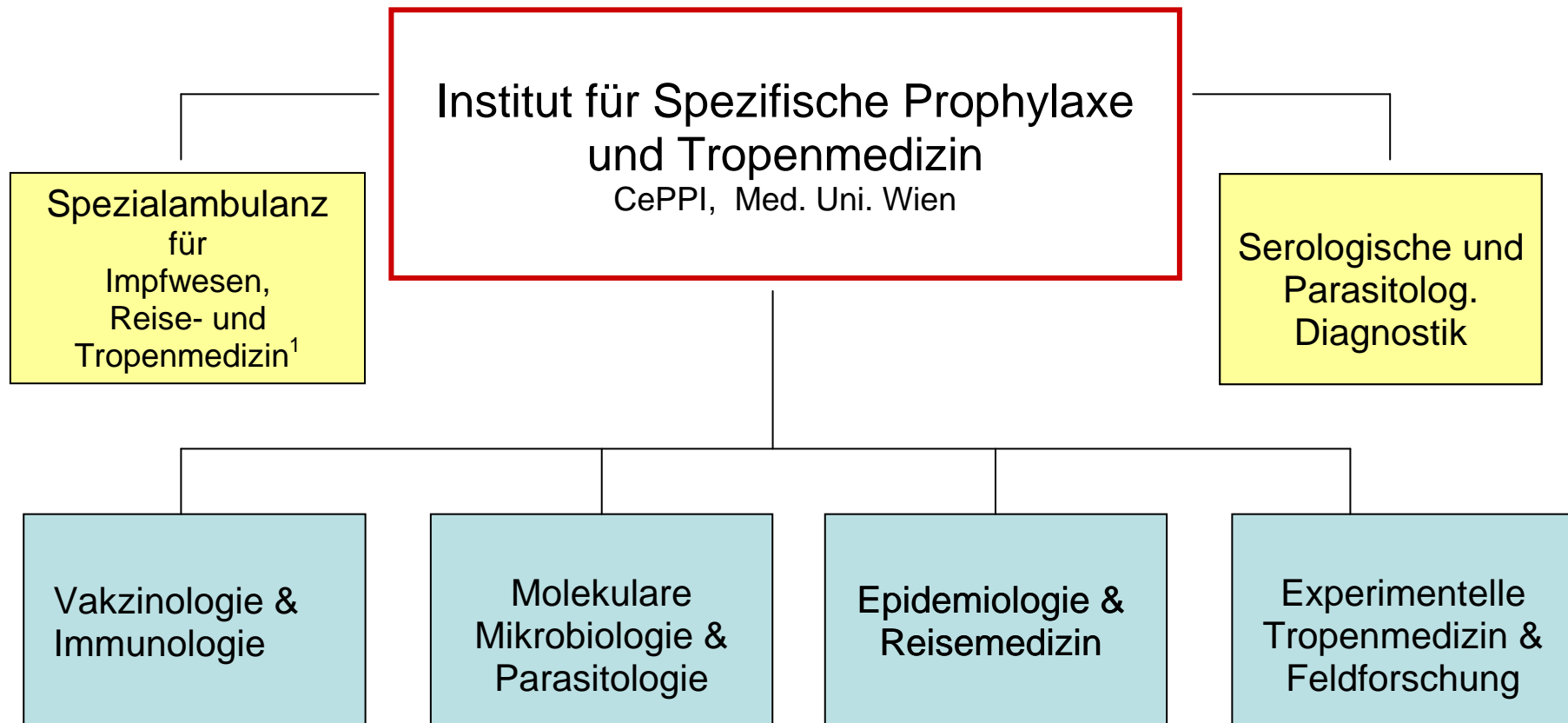
Head:

Univ. Prof. Ursula Wiedermann-Schmidt , MD, PhD

Overview of the Department

Profile, Mission-statement and Structure

Research programs and activities



¹Eröffnung 2008

Profile and Mission Statement

The Department is member of the Center for Physiology, Pathophysiology and Immunology (CePPI) of the Medical University Vienna and delivers and educates practical and theoretical view points of vaccinology and problems of infectious diseases in tropical and industrialized countries. Information and advices for national and international vaccinations, guidelines for vaccination schedules, and differential diagnosis of diseases from returning travellers are routinely performed.

The Department's research activities spotlight the following topics:

I. Vaccinology & Immunology:

This unit focuses on immunoprophylaxis and vaccination against infectious diseases, allergies and cancers, the development and validation of novel vaccine candidates and antigen delivery systems and the assessment of immediate and memory immune responses as well as vaccination failure after immunization. Vaccine development from bench to bedside in cooperation with clinical departments is performed with support of international vaccine companies.

II. Molecular Microbiology and Parasitology:

This unit uses biochemical and molecular biological methods to study open problems related to pathogenic microorganisms. Research aims to develop new chemotherapeutics and elucidate the mechanism of action of currently used ones, to study parasite antigens and host-parasite interactions. The implementation of PCR-based diagnostic methods for complicated cases is a new major focus.

III: Epidemiology and Travel Medicine:

This unit has established an Austrian-wide surveillance system for vaccine-preventable infectious diseases in children and adults. Epidemiological data from these studies impact on the Austrian recommendations for vaccination of the Austrian Supreme Board of Health. In cooperation with international vaccine companies vaccination trials (phase III/IV studies) in the field of infectiology and allergology are performed.

IV: Experimental Tropical Medicine and Field Research:

This unit operates field sites throughout South- and Southeast Asia focusing on new therapeutic options for treating tropical diseases, drug development, development of new diagnostic assays, and epidemiology of drug resistance and tropical diseases.

1. Structure:

The Department is structured into 4 research units and 1 patient-orientated unit (outpatient clinic – in progress - and diagnostic laboratory):

A. Vaccinology and Immunology:

(unit leader: Ursula Wiedermann-Schmidt, MD, PhD)

Establishment of new treatment strategies against vaccine preventable diseases (infectious diseases, allergies, tumors):

- New antigen-delivery systems for vaccination:
Lactic acid bacteria as edible vaccines; expression of recombinant allergens and protozoal antigens (e.g. SAG1 from *Toxoplasma gondii*)
Virosomes as adjuvants for systemic and mucosal vaccination with tumor antigens/peptides, allergen peptides etc.
- Use of mucosal adjuvants for enhanced immunogenicity, e.g. cholera B subunit, LTB from *E. coli*
- Development of a polyvalent allergy vaccine: development of novel allergen-chimers for nasal or oral vaccination against multisensitivities
- Development of a cancer vaccine against breast cancer and melanoma
- Immunological assessment of phase I clinical trial with cancer vaccines
- Characterization of cellular and humoral immune responses in responder versus non/low-responder vaccinees
- Immunological tolerance as vaccination strategy against immunological hyperresponsiveness (incl. allergy, autoimmunity)

B. Molecular Microbiology and Parasitology:

(unit leader: Michael Duchêne, PhD)

- Chemotherapy against *E. histolytica*: investigation of the mechanism of action of metronidazole on the molecular level
- Diagnosis of *E. histolytica* - *E. dispar*: differentiation of pathogenic and non-pathogenic forms of entamoeba in stool samples by means of PCR technology
- *Entamoeba histolytica*: Characterization of antigenic structures, use for vaccine development; mimotope technology

- *Acanthamoeba castellanii*: molecular processes during encystation and excystation
- *Bordetella pertussis*: examination of strain variation on the molecular biological level
- Antiprotozoal chemotherapy using substances derived from rainforest plants
- Immunomodulatory factors of *E. histolytica*: isolation and immunological characterization of factors with immunosuppressive or lytic capacities
- Moth allergens: characterization and isolation of allergens; recombinant production of the relevant allergens

C. Epidemiology and Travel Medicine:

(unit leader: Herwig Kollaritsch, MD)

- Epidemiology of vaccine-preventable diseases and seroprotection studies
- FSME, hepatitis B, hepatitis A: evaluation of long-term efficacy of vaccination
- Long-term evaluation (until 2012) of immune responses and protection in former non-responders vaccinated with a new preS1/S2 hepatitis B vaccine
- Surveillance study of hospitalized invasive pneumococcus infections in Austria – influence of the national vaccination program for infants on the incidence of diseases
- Prospective study on antigen variance of *Bordetella pertussis* (Pertactin, Pertussistoxin)
- Immunogenicity and tolerability of an inactivated Japan B Encephalitis vaccine (multicenter phase III trial)

D. Experimental Tropical Medicine and Field Research:

(unit leader: Harald Noedl, MD, PhD)

- M A R I B (Malaria Research Initiative Bandarban) – tropical disease research center in Southeastern Bangladesh;
- Randomized, controlled, Phase II/III GCP clinical trials with novel combination therapies for the treatment of uncomplicated falciparum malaria in Thailand and Bangladesh;
- Artemisinin resistance in Cambodia, GCP clinical trial, collaboration with USAMC-AFRIMS, Bangkok;

- Antimalarial drug resistance monitoring throughout South- and Southeast Asia
- Development of novel ELISA-based assays for measuring *P. vivax* biomass as an indicator of parasite growth and its inhibition;
- Preclinical drug development and *in vitro* antimalarial activity of novel drugs; 2D and 3D quantitative structure activity relationship (QSAR) studies; identification of candidate drug targets in 2D-gels, collaboration with P. Chiba, Institute of Medical Chemistry
- Drug interaction studies with azithromycin, lumefantrine, and artemisinin derivatives;

E. Patient-orientated unit (head: U. Wiedermann-Schmidt, MD, PhD)

Outpatient Clinic for Vaccination, Travel and Tropical Medicine: (in progress)

An outpatient clinic for vaccination according to national and international guidelines and diseased returning travellers is currently established – in particular this clinic shall focus on vaccination in risk patients, such as immunocompromised-, oncological-, allergic patients, pregnant women, patients with autoimmunity or chronic diseases. Individual information, counselling and management of vaccination, as well diagnosis and therapy of diseased travellers returning from tropical countries will be performed. For in-patient treatment a cooperation with the Department of Internal Medicine I (Division of Infectious Diseases & Clinical Tropical Medicine) at the General Hospital Vienna (AKH) is established.

Diagnostic Laboratory for Serology and Tropical Diseases

Austrian Reference Center for Diphtheria-Tetanus and Pertussis-serology:

Measurement of antibody titers against Diphtheria, Tetanus and Pertussis according to WHO standards; management of serum sample archives and administration of databank.

Routine diagnostic of Malaria and *status febrilis* in returning travellers is performed.

Enlargement of the diagnostic profile with respect to bacteriologic and parasitologic diseases has been done (ELISA against Rabies, Bordetella pertussis PCR, Amoeba dispar, histolytica PCR, Dengue fever quick tests) and is being planned to continue for the future. Since April 2007 the diagnostic laboratory is certified according to ISO 9001 criteria.

2. Working profile of the Institute

Research/Diagnostics/Patients	65 %
Lectures	25 %
Administration	>10 %

3. Personnel of the Institute (see also page 55)

Personnel employed by the University (“Planstellen”)

1 University Professor (100%), 3 associate Professors (100 %)

2 administrative persons (50 %, 75 %)

2 technicians (100 %)

1 technician (50 %)

Personnel employed by grants or external sources

1 guest professor

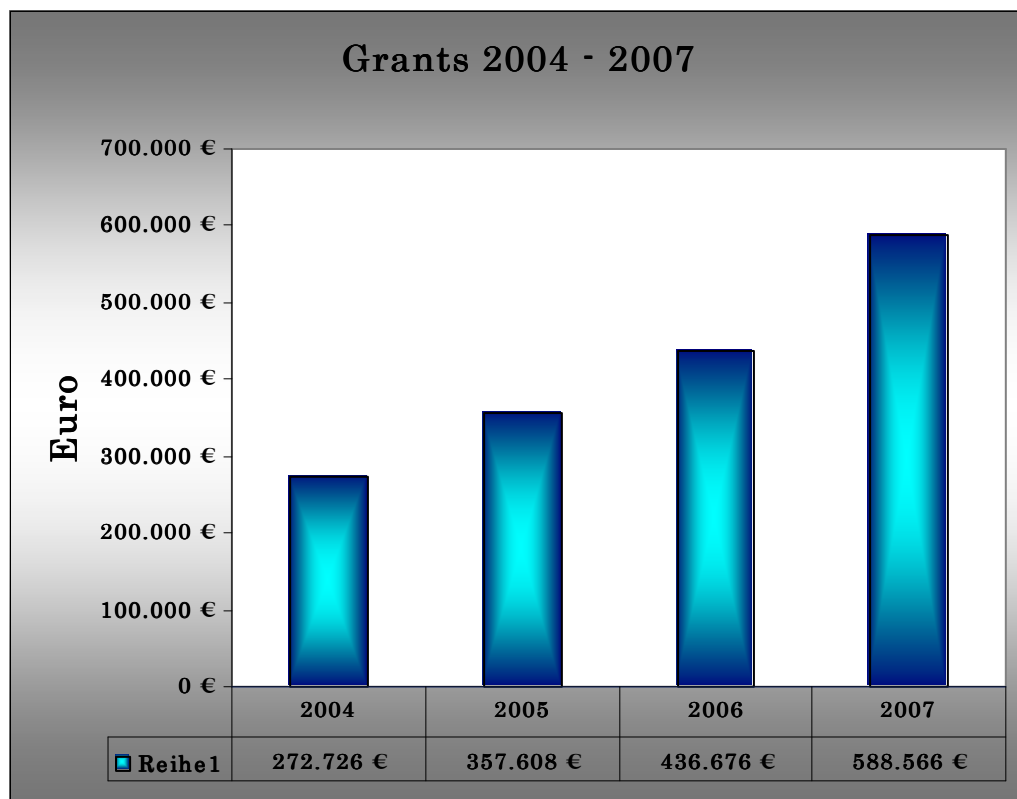
12 Post docs, 7 PhD students, 3 Diploma students

4. Grants and other sponsoring (2005-2009)

Identification and source of support	Title and head of project and cooperation partners	Duration of research project	Total sum of grant (€)	Aliquot for 2007 (€)
§ 27 62300001 (KV)	Diagnostik-Einnahmen	2007	41.171.90	41.171.90
§26 ÖNB – AP12226ONB	Genet. Typisierung d. Keuchhustenerregers Bordetella Pertussis bei österr. Patienten	2007 - 2009	45.000.00	30.000.00
§27 Nestlé – FA623A0203	Prenatal and perinatal intervention against allergic diseases	05.2007 – 04.2009	182.794.00	44.585.89
§26 Hochschuljubiläumsstiftung der Stadt Wien H1760/2006	The allergenic potential of the common household moth Plodia interpunctella	2007 -2008	5.000.00	3.863.00
§27 BioLife Science	Multi epitope vaccine against breast cancer	2006 -2008	158.480.00	64.795.36
§26 SFB-Project F01814	„ Mucosal tolerance induction: a strategy for prevention and therapy of type I allergy“.	02/2005-02/2012	732.080.00	20.216.85

§27 FFG Bridge 814280	Wirkprofil pflanzlicher Naturstoffe bei pathogenen Protozoen	2007 - 2010	47.000.00	-
§27 Baxter AG	Vero-cell influenza vaccine – H5N1 Studie	2007 - 2010	500.000.00	186.026.61
§26 FWF P18350-Bo2	New assays for <i>P. vivax</i> drug and vaccine development	2006-2007	156.302.00	78.151.00
§26 FWF P19044	Encystment and Excystment in <i>Acanthamoeba castellanii</i> : RNA and protein expression in differentiating cell	2006-2009	174.570.00	55.825.00
§26 Austrian Academy of Science P154-II	Building Research and Diagnostic Capacities at Bandarban Sadar Hospital, Bagladesh	2006-2008	25.000.00	17.000.00
§ 27 Parexel International	SPER JE-VAX vaccine for japenese enceph.	2005 - 2007	40.600,00	22.210.42
§26 BMWF	SEROPRÄV	2007 - 2008	49.440.00	24.720.00

Acquired financial support	2005-2009 (€)	Aliquot for 2007 (€)
TOTAL	2.157.437.90	588.566.03



5. Lectures and Education activities

Lectures

SSM3: Methodenseminar Impfwesen und Tropenmedizin/ 2 x 15 Std

Ringvorlesung International Health (Impfpräventable Erkrankungen)/2 Stunden

Seminar Funktionelle Pathologie/2 Stunden

Block 8: Abwehr von Infektionen: Wirt-Parasitinteraktion/ 2 Std.

Block 8: Grundlagen des Impfwesens/ 1 Std

Block 21: Grundlagen der Reisemedizin/1 Stunde

In training for Specialist in Specific Prophylaxis and Tropical Medicine

Maria Paulke-Korinek; MD

Kamela Thriemer; MD

Angelika Wagner, MD

Diploma Thesis and Doctoral Thesis- Students:

Margit Tazreiter, PhD Student

Elisabeth Hoflehner, PhD Student

Benedikt Ley, Dissertation Dr. rer. nat.

Maria Paulke-Korinek, PhD-Student

Oumaporn Tasanor, PhD Student

Angelika Wagner, PhD Student

Mariella Jung, Diploma student (Medicine)

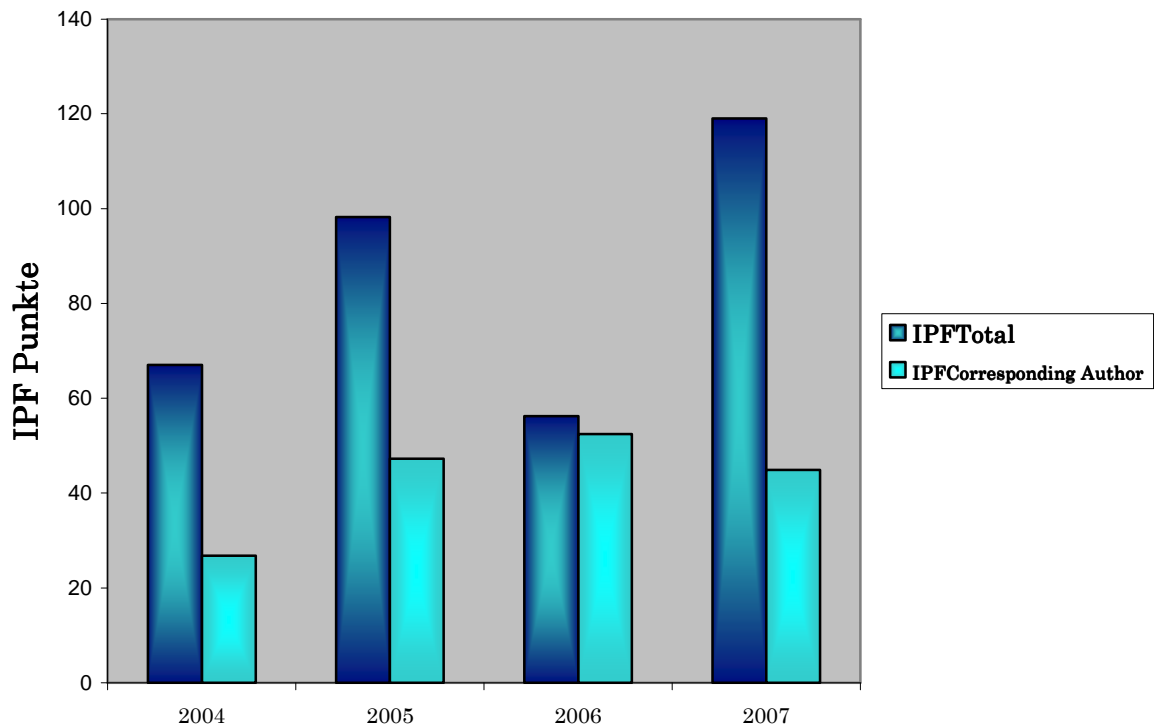
Paul Swoboda, Diploma student (Medicine)

Matthias Vossen, Diploma student (medicine)

6. Publications (peer reviewed) 2007:

Total number 2007	Total IP	IP correspondence
	119.024	44.887
IP/Acad. Pos.	29.756	11.221

IPF 2004 - 2007



Publication list of the Department 2007

1. Originalarbeiten

Coldren, R.L., K. Jongsakul, S. Vayakornvichit, H. Noedl, M.M. Fukuda.
 2007. Apparent Relapse of Imported Plasmodium ovale Malaria in a
 Pregnant Woman. *Am. J. Trop. Med. Hyg.* 77(5): 992-994.
 IPF: **2.546**

Haque, R., K. Thriemer, Z. Wang, K. Sato, Y. Wagatsuma, M.A. Salam, S. Akther, J. Akter, M. Fukuda, R.S. Miller, H. Noedl. 2007. Therapeutic efficacy of artemether-lumefantrine for the treatment of uncomplicated *Plasmodium falciparum* malaria in Bangladesh. *Am. J. Trop. Med. Hyg.* 76(1):39-41.
 IPF: **2.546**

Köhler, M., D. Leitsch, U. Fürnkranz, M. Duchêne, H. Aspöck, J. Walochnik. 2008. *Acanthamoeba* strains lose their abilities to encyst synchronously upon prolonged axenic culture. *Parasitol. Res.*, in press.
 IPF: **1.140**

Kollaritsch, H., C. Wensch, C. Hatz, G. Laer, B. Bauer, U. Hollenstein, M. Haditsch, G. Diridl, W. Malinowski, E. Jeschko, G. Payer-Neundlinger, N. Speiser-Remp, H.E. Pichler, H. Rumpold, H. Stemberger, G. Eder, G. Wiedermann, U. Wiedermann. 2007. [Medical clearance for missions abroad (EEU): definitions, recommendations for use and performance.] *Wien Klin Wochenschr.* 119 Suppl 3:13-25. German.
 IPF: **0.804**

Kollaritsch, H., U. Wiedermann. 2007. [Examples for vaccines against diarrheal diseases--rotavirus and traveller's diarrhea] *Wien Med Wochenschr.* 157(5-6):102-106.
 IPF: 0.00

Leitsch, D., D. Kollarich, I. B. H. Wilson, F. Altmann, M. Duchêne. 2007. Nitroimidazole action in *Entamoeba histolytica*: a central role for thioredoxin reductase. *PLoS Biology* 5: e211.
 IPF: **14.101**

Noedl H., S. Krudsood, W. Leowattana, N. Tangpukdee, W. Thanachartwet, S. Looareesuwan, R.S. Miller, M. Fukuda, K. Jongsakul, Y. Kritsanai, S. Sriwichai, C. Ohrt, C. Knirsch. 2007. In vitro antimalarial activity of azithromycin, artesunate, and quinine in combination and correlation with clinical outcome. *Antimicrob. Agents Chemother.* 51(2):651-656
 IPF: **4.153**

Nothdurft HD, Dahlgren AL, Gallagher EA, Kollaritsch H, Overbosch D, Rummukainen ML, Rendi-Wagner P, Steffen R, Van Damme P. 2007. Ad hoc Travel Medicine Expert Panel for ESENEM. The risk of acquiring hepatitis A and B among travelers in selected Eastern and Southern Europe and non-European Mediterranean countries: review and consensus statement on hepatitis A and B vaccination. *J Travel Med* 14(3):181-187.
 IPF: **1.333**

Rendi-Wagner, P., M. Paulke-Korinek, G. Stanek, G. Khanakah, H. Kollaritsch. 2007. Impact of a pertussis booster vaccination program in adolescents and adults on the epidemiology of pertussis in Austria. *Pediatr Infect Dis J* 26(9):806-810.
 IPF: **3.215**

Rendi-Wagner, P., M. Korinek, A. Mikolasek, A. Vécsei, H. Kollaritsch. 2007. Epidemiology of travel-associated and autochthonous hepatitis A in Austrian children, 1998 to 2005. *J Travel Med* 14(4):248-253.

IPF: **1.333**

Rendi-Wagner, P., M. Korinek, B. Winkler, M. Kundi, H. Kollaritsch, U. Wiedermann. 2007. Persistence of seroprotection 10 years after primary hepatitis A vaccination in an unselected study population. *Vaccine* 25(5):927-931.

IPF: **3.159**

Rendi-Wagner P., M. Paulke-Korinek, M. Kundi, U. Wiedermann, B. Laaber, H. Kollaritsch. 2007. Antibody persistence following booster vaccination against tick-borne encephalitis: 3-year post-booster follow-up. *Vaccine* 25(27):5097-5101.

IPF: **3.159**

Repa, A., H. Kozakova, T. Hudocovic, R. Stepankova, T. Hrcir, H. Tlaskalova, A. Pollak, U. Wiedermann. 2007. Susceptibility to nasal and oral tolerance induction to the major birch pollen allergen Bet v 1 is not dependent on the presence of the microflora.

Immunology Letters, in press

IPF: **2.352**

Tasanor, O. B., D. Brem, M. Leitsch, M. Binder, M. Duchêne, H. Greger, W. Wernsdorfer. 2007. Development of a pharmacodynamic screening model with *Entamoeba histolytica*.

Wien. Klin. Wochenschr. 119: 88-95.

IPF: **0.804**

Tasanor O., M. Ernst, K. Thriemer, G.F. Ecker, H. Noedl, P. Chiba. 2007. Characterization of a novel class of antimalarials and its applicability to plasmodial target identification. *Wien. Klin. Wochenschr.* 119 Suppl 3:83-87.

IPF: **0.804**

Tauber, E., H. Kollaritsch, M. Korinek, P. Rendi-Wagner, B. Jilma, C. Firbas, S. Schranz, E. Jong, A. Klingler, S. Dewasthaly, C.S. Klade. 2007. Safety and immunogenicity of a Vero-cell-derived, inactivated Japanese encephalitis vaccine: a non-inferiority, phase III, randomised controlled trial. *Lancet* 370(9602):1847-1853.

IPF: **25.800**

Thriemer K., W.A. Khan, P. Starzengruber, R. Haque, M.G. Vossen, A.S.P. Marma, S. Akther, M. Fukuda, H. Noedl. 2007. In vitro interaction of dihydroartemisinin and lumefantrine in clinical field isolates from Bangladesh. *Wien. Klin. Wochenschr.* 119 Suppl 3:67-70.

IPF: **0.804**

Vossen M.G., R. Haque, P. Starzengruber, W. Ali Khan, K. Thriemer, A.S. Marma, S. Akther, M. Fukuda, H. Noedl. 2007. In vitro interaction studies of azithromycin and dihydroartemisinin in Plasmodium falciparum isolates from Bangladesh. *Wien. Klin. Wochenschr.* 119 Suppl 3:71-75.
IPF: **0.804**

Wagner, S., J. Jasinska, H. Breiteneder, M. Kundi, H. Pehamberger, O. Scheiner, C. Zielinsky, U. Wiedermann. 2007. Delayed tumor onset and reduced tumor growth progression after immunization with a Her-2/neu multi-peptide vaccine and IL-12 in c-neu transgenic mice.
Breast Cancer Research and Treatment 106 (1) 29:38
IPF: **4.671**

Wiedermann, U., A. Mercenier. 2007. New allergy intervention strategies: hitting the mucosal road.
Clin Exp. Allergy 37 (4) 473:475
IPF: **3.668**

Wild, Carmen., M. Wallner, K. Hufnagl, H. Fuchs, K. Hoffmann-Sommergruber, H. Breiteneder, O. Scheiner, F. Ferreira, U. Wiedermann-Schmidt. 2007. A recombinant allergen chimera as novel mucosal vaccine candidate for prevention of multi-sensitivities. *Eur J of Allergy & Clin. Imm* 62/1: 33-41
IPF: **5.334**

Bublin, M.; D. Allwarth, H. Breiteneder. 2007, E. Hoflehner, K. Hufnagl, C. Radauer, O. Scheiner, B. Wagner, S. Wagner, U. Wiedermann*,. Use of a genetic Cholera toxin B subunit/allergen-fusion molecule as mucosal delivery system with immunosuppressive activity against Th2 immune responses. *Vaccine*, 2007 Dec 5;25(50):8395-404..IPF: **3.159**

2. Review artikel :

Chretien J.P., M. Fukuda, H. Noedl. 2007. Improving surveillance for antimalarial drug resistance. *JAMA*. 23;297(20):2278-2281.
IPF: **23.175**

Clark, C. G., U. C. Alsmark, M. Tazreiter, Y. Saito-Nakano, V. Ali, S. Marion, C. Weber, C. Mukherjee, I. Bruchhaus, E. Tannich, M. Leippe, T. Sicheritz-Ponten, P. G. Foster, J. Samuelson, C. J. Noël, R. P. Hirt, T. M. Embley, C. A. Gilchrist, B. J. Mann, U. Singh, J. P. Ackers, S. Bhattacharya, A. Bhattacharya, A. Lohia, N. Guillén, M. Duchêne, T. Nozaki, and N. Hall. 2007. Structure and content of the Entamoeba histolytica genome. *Adv. Parasitol.* 65: 51-190.
Impact: **4.826**

Daniel, C., A. Repa, A. Mercenier, U. Wiedermann-Schmidt, J. M. Wells. 2007. The European LABDEL project and its relevance to the prevention and treatment of allergies. *Eur J of Allergy & Clin. Imm* 62/11: 1237-1242
IPF: **5.334**

SUMME IPF: 119.024

Individual working reports

I. Vaccinology and Immunology

Unit Leader: Univ. Prof. Ursula Wiedermann-Schmidt, MD, PhD

Co-workers

Erika Garner-Spitzer, Tech.

Mag. Elisabeth Hoflehner, PhD-student

Dr. Karin Hufnagl, Senior Post Doc

Dipl. Ing. Joanna Jasinska

Dr. Irma Schabussova, PhD

Dr. Angelika Wagner, MD (Arzt in Ausbildung)

Dr. Andreas Repa (associated member in cooperation with Department of Pediatrics, Vienna)

1. Research interests

- Animal models for infectious diseases, allergy and tumorbiology
- Mucosal vaccines: oral and nasal vaccines for prophylaxis and therapy of allergy, infectious diseases and cancer (breast cancer, melanoma)
- Delivery systems/adjuvants for vaccines, new forms of vaccination for prophylaxis and therapy
- Immunological tolerance induction: A concept for treatment of immunological disorders
- Immunological mechanisms underlying tolerance induction

2. Research programs

A. Ongoing projects

Animal models

Mouse models of allergy/asthma:

Mucosal polyvalent vaccine against allergic multisensitivities

Hepatitis A vaccination in mice

(Hepatitis A vaccination and its influence on atopy)

Model of Toxoplasma gondii infection

(Cooperation with Prof. E. Förster-Waldl; Prof. Pollak/Kinderklinik)

Mouse models for breast cancer and melanoma

(Cooperation with the Department of Internal Medicine, Prof. Zielinski; Department of Dermatology, Prof. Pehamberger; Institute of Pathophysiology/Div.IV Prof. Scheiner/Prof. Breiteneder).

Mucosal vaccination and delivery of vaccines

Use of lactic acid bacteria (LAB) for immunomodulation

Characterization of cytokine profile of spleen cells after *in vitro* stimulation with different lactic acid bacteria for evaluation of the immunomodulating capacity of different lactic acid bacteria

- Mucosal application of different LAB prior and after sensitization with an allergen or hypoallergenic molecules (prophylaxis, therapy)
- Use of LAB as expression system for production of allergens or hypoallergenic variants and use as a mucosal antigen delivery system. Use of selected lactic acid bacteria for expression of polypeptides or novel chimeric allergens for treatment of multisensitization.
- Use of LABs for expression of tachyzoite antigens of *Toxoplasma gondii* – development of a mucosal vaccine against toxoplasmosis
- Use of LABs for expression of tumor antigens , i.e. peptides of the tumor antigen Her-2/neu. The expression of antigen in LAB is performed in cooperation with the Institute Pasteur in Lille, France (Prof. Bruno Pot).

Use of virosomes as antigen delivery systems for vaccination

Development of a virosome-based peptide vaccine against allergy and cancer – cooperation with Pevion Biotech/Berna, Switzerland:

A virosome based peptide vaccine against breast cancer has been developed and tested in a preclinical trial (mouse experiments). A phase I clinical trial has been initiated in Sept. 2006.

Virosomes are also used for the development of a combined vaccine against allergic multisensitivities.

Use of cholera toxin B subunit for mucoal delivery of an allergy vaccine

In previous studies we demonstrated that antigens chemically coupled to the B subunit of cholera toxin (CTB) elicit different immunomodulatory properties when applied via the mucosal route. In order to improve the immunomodulatory properties of CTB a fusion molecule of CTB and the allergen Bet v 1 was produced. Intranasal application of this fusion molecule prior to allergic sensitization led to successful suppression of allergic immune responses. In coming experiments fusionmolecules of CTB and peptides of different allergens are planned in order to develop a mucosal poly-valent allergy.

Mucosal tolerance induction

Establishment of a model of polysensitization (immunization with several antigens) and tolerance induction by co-administration of several antigens (“poly-tolerization”): Aim: polyvalent mucosal allergy vaccine: Hybrid allergens, containing several antigens were constructed and were mucosally applied to polysensitized mice, leading to significant reduction of allergic immune responses to all antigens. (Hufnagl et al JACI 2005). This project is part of a Special Research Program (SFB F018), entitled “Molecular and immunological strategies for prevention, diagnosis and treatment of type I allergies”.

Production of chimeric molecules for development of a polyvalent vaccine

In order to be able to treat patients with multiple sensitivities to different allergens, novel molecules that include more than two non-cross reactive allergens were created. These allergen chimeras were done by cDNA cloning of several immunodominant epitopes into one complete molecule and expressed in E.coli. The allergen chimeras were tested for their capacity to act as tolerogens in a mouse model of polysensitization (Wild et al, Allergy 2006). In cooperation with the Nestlé Research Center Lausanne selected lactic acid bacteria are tested for their immunomodulating capacity in conjunction with or without the allergen chimeras (preventive allergy vaccine).

Development of a peptide/mimotop based vaccine against breast cancer and melanoma

A mouse model of breast cancer was established using transgenic mice expressing the tumor antigen Her2/neu in the mammary glands. SCID mice are used to induce melanoma by injecting a human melanoma cell line. These models are used for vaccination with tumor antigen-specific peptides, in order to induce an active immunity against the tumor antigens, leading to reduction of tumor cell growth *in vivo*. (J. Jasinksa et al Int. J. Cancer 2003; Wagner et al J. Immunol. 2005, Wagner et al Breast Cancer Res. Therapy 2007).

In cooperation with Pevion Biotech/Crucell a virosome-peptide Her-2/neu vaccine against breast cancer was developed. The first clinical trial (Phase I/II) was started in September 2006 in cooperation with the Department of Internal Medicine I (Division of Oncology; Prof. Zielinski; Prof. Wiltschke) at the General Hospital Vienna and BioLife Science.

Characterization of immunological responsiveness and non-responsiveness following vaccination in a healthy study population

Evaluation of antibody titers 10 years after hepatitis A vaccination. Measurement of cellular immune responses and immunological memory in "non-responder versus high responder vaccinees" (Rendi-Wagner et al Vaccine 2006). 52 patients were tested for antibody titers and cellular immune responses prior and after booster vaccination. Lymphocyte proliferation and cytokine production pattern after antigen-specific stimulation was measured and changes in T cell surface antigen- and hepatitis A receptor expression after booster vaccination evaluated. The study aims at defining immunological characteristics of low-responsiveness after vaccination and examine whether these are general or antigen-specific phenomena within a defined collective of vaccinees. This study is the basis for further studies on hyporesponsiveness following vaccination with hepatitis B, or tick borne encephalitis etc.

Garner- Spitzer E; M. Kundi, P. Rendi-Wagner, B. Winkler, G. Wiedermann, H. Holzmann, Ch. Herzog, H. Kollaritsch, U. Wiedermann. Characterization of low/no and high responsiveness after hepatitis A vaccination by defined cellular markers. Submitted 2008.

B. Newly initiated projects

Recombinant bacterial-based mucosal vaccine against protozoal infections.

Toxoplasma gondii is an ubiquitous intracellular parasite, which infects all mammals; In Middle Europe approx. 40 % are sero-positive. In healthy people the infection usually is asymptomatic but may develop into heavy disease if the immune system is not fully developed or suppressed with ocular or cerebral toxoplasmosis being the most frequent manifestations. Although screening programs have been internationally introduced with good results, Toxoplasmosis still is one of the most pronounced opportunistic infections world-wide. The aim of the project is the development of a vaccine on the basis of protective surface antigens, expressed during the acute and chronic phase of infection. The ultimate goal is an oral vaccine. The project is performed in cooperation with the Institute Pasteur de Lille, the Department of Pediatrics at the MUW, the VetMed Vienna and the Department of Microbiology in Gdansk, Poland.

Immunomodulation by *Toxoplasma gondii* – characterization of regulatory mechanisms induced by the parasite:

According to the hygiene hypothesis, postulating that a reduction of microbial exposure (Hepatitis A, helminth infections, *Toxoplasma* infection) leads to an increase in allergic diseases, we have recently shown in a mouse model that infection with *Toxoplasma gondii* prevents the development of allergy and reduces already ongoing allergic symptoms. Our data indicate that immunoregulation of the parasite depends on distinct mechanisms in the acute and the chronic stage of disease. In cooperation with the lab of Prof. Rick Maizels we are now trying to characterize the immunoregulation during infection in more detail.

Polymorphism of the Austrian *Bordetella pertussis* population: molecular typing of patients' isolates

The project aims to determine the spectrum of *B. pertussis* strains in Austria and how this spectrum is related to those of other European countries; furthermore possible genetic variation of the bacterial sequences shall be evaluated and compared with the bacterial sequences within common vaccines. During the project a standard PCR diagnostic for *B. pertussis* infections shall be established and correlations between positive isolates and specific antibody titers performed. This project is done in cooperation with the research units "Molecular Microbiology and Parasitology" and "Epidemiology and Travel Medicine".

3. Publications

Rendi-Wagner, P.; M. Korinek, B. Winkler, M. Kundi, H. Kollaritsch, and U. Wiedermann*. 2007. Persistence of seroprotection 10 years after primary hepatitis A vaccination in an unselected study population. *Vaccine*, 25:927.

Rendi-Wagner, P.*; M. Paulke-Korinek, M. Kundi, U. Wiedermann, B. Laaber, and H. Kollaritsch. 2007. Antibody persistence following booster vaccination against tick-borne encephalitis: 3-year post-booster follow-up. *Vaccine*, 25:5097.

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Bublin, M.; E. Hoflehner, B. Wagner, C. Radauer, S. Wagner, K. Hufnagl, D. Allwarth, O. Scheiner, U. Wiedermann*, H. Breiteneder. 2007. Use of a genetic cholera toxin B subunit/allergen-fusion molecule as mucosal delivery system with immunosuppressive activity against Th2 immune responses. *Vaccine*, 2007 Dec 5;25(50):8395-404..

Kollaritsch, H*.; and U. Wiedermann. 2007. Examples for vaccines against diarrheal diseases- rotavirus and traveller's diarrhea. *Wien Med Wochenschr*, 157:102.

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Daniel, C.; A. Repa, A. Mercenier, U. Wiedermann*, J. Wells. 2007. The European LABDEL project and its relevance to the prevention and treatment of allergies *Allergy*, 62(11):1237-42.

Schabussova, I., A. Hasam, I. van Die, P. Kosma, and R.M Maizels. 2007. O-Methylated glycans from *Toxocara* are specific targets for antibody binding in human and animal infections. *Int J Parasitol.* 37: 97-109

Gerstmayr, M., N. Ilk, I. Schabussova, B. Jahn-Schmid, E.M. Egelseer, U.B. Sleytr, C. Ebner, and B. Bohle. 2007. A novel approach to specific allergy treatment: the recombinant allergen-S-layer fusion protein rSbsC-Bet v 1 matures dendritic cells that prime Th0/Th1 and IL-10-producing regulatory T cells. *J Immunol* 179: 7270-5

TOTAL Impactfactor: IP corresp: 115.865

4. Cooperations

National cooperations within the MUW:

Department of Spezifische Prophylaxe & Tropenmedizin:

Unit: Prof. Kollaritsch: Vaccination studies in cooperation with the outpatient clinic for travel medicine; immunological memory and cellular immune responses after vaccination

Unit: Prof. Duchêne: Immunological characterization of protozoal and bacterial (*Bordetella pertussis*) antigens

Unit: Prof. Wernsdorfer: cytotoxicity of plant derived extracts with anti-protozoal effects

Cooperation within the Special Research Program for Allergy (SFB F018): Institute of Pathophysiologie: Prof. Scheiner, Prof. Breiteneder, Prof. Bohle, Prof. Valenta
Dermatology: Prof. D. Maurer, Prof. Adelheide Elbe

Department of Pediatrics: Prof. A. Pollak, Dr. E. Förster-Waldl,

Department of Internal Medicine I: Prof. C. Zielinski

Department of Dermatology: Prof. H. Pehamberger

National Cooperations outside MUW

Prof. F. Ferreira, Institut f. Genetik und allg. Biologie, University of Salzburg

Prof. S. Thalhamer, Institut f. Genetik, University of Salzburg

BioLife Science (peptid/mimotop vaccine against breast cancer and melanoma)

Austrian Wirtschaftsservice, Fa TECMA: DI Dr. Behnoosh Amirmani (Lizenzrechtvergabe von Patent „Polyvalente Allergievakzine“ Patentinhaber: U. Wiedermann)

International cooperations

Prof. Rick Maizels, Institute of Immunology and Infectious Diseases, University of Edinburgh, UK

Dr. Hermeljin Smitts, Medical Center of Parasitology, Cellular Immunology of Helminths, Univ. Leiden, Netherlands

Prof. Harald Renz, Institut f. Klin. Chemie u. Molekulare Diagnostik d. Philipps Universität, Marburg, Germany.

Dr. Annick Mercenier; Head of Bioscience Department, Nestlé Research Center, CH-Lausanne

Dr. Adrian Zürcher, Nestlé Research Center Lausanne

Dr. Bruno Pot; Head of the Institute for Bacteriology and Ecosystems; Institute Pasteur de Lille, France

Dr. Rinaldo Zurbriggen, Pevion Biotech/Berna/Crucell

Prof. Helena Tlaskalova, Dr. Hanka Kozakova; Institute for Immunology and Gnotobiotics; Prague, Tchech Republic

Prof. Jozef Kur, Institute of Microbiology, University of technology, Chemical Faculty, Gdansk, Poland

5. Grants and third party funds

- 1) **§ 26 Austrian Science Fund.** Sonderforschungsbereich (SFB, F01814)
 „Molecular and immunological strategies for prevention, diagnosis and treatment of type I allergy“ (period 2002-2010)
 Start. Febr 2002-2008. PI: U. Wiedermann-Schmidt; coordinator: R. Valenta
 In February the project was prolonged for 3 years: **293.430 €**
20.216.85 € for 2007
- 2) **§ 26 ÖNB Jubiläumsfonds** AP12226ONB “ Genetische Typisierung d. Keuchhustenerregers Bordetella Pertussis bei österr. Patienten“ (period 2007 – 2009), total sum of grant **45.000 €, 15.000 €** for 2007
- 3) **§ 27 Nestlé Research Center FA623A0203** „Prenatal and perinatal intervention against allergic diseases“, (period 2007 – 2009) total sum of grant **300.000 CHF, 73.318.26** for 2007
- 4) **§ 27 Biolife Science** (Multiepitope vaccine against breast cancer) (2006 -)
64.795.36 € for 2007

TOTAL for 2007: € 173.330.47

6. Diploma, PhD-thesis, Lectures

Mag. Elisabeth Hoflehner (Biology/Genetics)

“Production and Characterization of allergen chimers for mucosal treatment of allergic diseases”

(PhD student since Sept 2005)

Lectures

Impfpraktikum (Praktikum f. Mediziner im Abschnitt II) (2,5 Std)

Kombinationswahlfach für Funktionelle Pathologie für Mediziner (1,5 Std)

Wahlfach „Tropenmedizin“ (3 Std)

Krankheit, Krankheitsursachen, Krankheitsbilder (MCW, Block 8) (1 Std)

Methodenseminar „Impfungen und Tropenmedizin“ (SSM3, MCW); 15 Std.

7. Awards, Functions, Patents

Functions

Member of the Austrian Council for Immunization Practice (ACIP) of the Austrian Supreme Board of Health.

Awards and Travel Grants

Junior Award 2007, 3. Preis, der ÖGTP, Wien, Österreich, 22. – 24.11.2007

A. Wagner, L. Holec, J. Kur, E. Förster-Waldl, A. Joachim, A. Pollak, O. Scheiner, U. Wiedermann

Evaluation of recombinant Toxoplasma antigens as potential vaccine candidates for protection against Toxoplasmosis (oral presentation)

Travel grant for the 5th EAACI-Gallen Davos Meeting, Switzerland 01. – 04.

February 2007

ÖGAI Reisestipendium 26th Congress of the European Academy of Allergology and Clinical Immunology

Göteborg, Schweden, 09. -13.June 2007

E. Hoflehner, K. Hufnagl, M. Bublin, B. Wagner, O. Scheiner, H. Breiteneder, and U. Wiedermann

“Intranasal treatment with a cholera toxin B subunit/allergen-fusion molecule leads to suppression of Th2 immune responses in a murine model of birch pollen allergy “
(poster)

Patents

European patent application. "Multiepitope vaccine against Her-2 over expressing breast cancer" (Wiedermann, Breitender, Scheiner, Pehamberger, Zielinski).

8. International Exchange

Student exchange with the Institute of Gnotobiology and Immunology, Prag and Nove Hradec, Czech Republic

9. Referee activity, Editor

Immunology letters

Int. Arch. Allergy Immunol

Vaccine

Clinical and Experimental Immunol

Clinical and Experimental Allergy

Allergy

J. of Travel Medicine

10. Congresses and Presentations

Invited lectures (UW)

Vaccination Schedules: Empiricism or Evidence based Medicine. 40th Pediatric Symposium, Oberurgl, Tyrol, Jan 2007.

Humoral and Cellular Immune responses 10 years after hepatitis A primary vaccination. 16th Annual Austrian Symposium of Vaccination, Salzburg, 23-24 March 2007.

Vaccines against Diarrhoeal Diseases: Past, Present and Future. 10th Conference of the International Society of Travel Medicine. Vancouver Canada. 20-24 May 2007.

Mucosal tolerance – a treatment strategy against allergies. XXVI EAACI, Göteborg, Sweden, 9.- 13.6.2007.

Mucosal Tolerance; Seminarreihe "Immunologie, Allergologie, Pneumologie" an der Uni-Klinik Giessen und Marburg, Prof. H. Renz; Marburg, Deutschland; 25.-26. Juni 2007.

Vaccine against Her-2/neu overexpressing breast cancer - from bench to clinical testing. Austrian Symposium of Vaccination, Gmunden, 27th- 28th Sept. 2007.

Mucosal tolerance for treatment of allergies. Scientific Seminar, Institute of Immunology and Infectious diseases; Univ. Edinburgh, 25-26th Oct. 2007

New vaccine developments; new adjuvant systems. 41th Austrian Society of Tropical Medicine and Parasitology; Vienna, 22-24th Nov. 2007.

Mucosal antigen delivery systems. Seminar at the Department of Cell Biology and Histology, Academic Medical center, Univ. Amsterdam, 4-5th Dec. 2007

Vaccines against Pneumococcal diseases. Medical Dialog – Pneumococcal Diseases, Vienna, 13th Dec. 2007

Congress presentations

5th EAACI-Ga'len Davos Meeting

Davos, Switzerland, 01.-04. February 2007

E. Hoflehner¹, K. Hufnagl, M. Bublin, B. Wagner, O. Scheiner, H. Breiteneder, and U. Wiedermann

“Transmucosal antigen delivery system as immunomodulatory tool: suppression of Th2 immune responses by a cholera toxin B subunit/allergen-fusion molecule “(oral)

5th EAACI-Gallen Davos Meeting

Davos, Schweiz vom 1.2. – 4.2.2007

A. Wagner, E. Förster-Waldl, E. Garner-Spitzer, A. Pollak, A. Joachim, U. Wiedermann

Influence of *Toxoplasma gondii* infection on allergic sensitization – experimental implications on the hygiene hypothesis. (poster)

5th EAACI-Ga'len Davos Meeting

Davos, Switzerland, February 01-04, 2007

Schabussova, I., M., Gerstmayr, A. Radakovics, N. Ilk, M. Sara, U. B. Sleytr, and B. Bohle. “Bacterial cell surface protein (SbsC) activates human immune cells via Toll-like receptors (TLR) 2, 4, LPS binding protein (LBP) and CD14” (poster)

1st International Symposium on Allergooncology Vienna, Austria 16.Apr.2007

J. Jasinska, S. Wagner, R. Zurbriggen, M. Amacker, H. Breiteneder, H.

Pehamberger, O. Scheiner, C. Wiltschke, C. C. Zielinski, U. Wiedermann

Development of a novel vaccine against breast cancer based on Her-2/neu peptides coupled to immunopotentiating reconstituted influenza virosomes (poster)

26th Congress of the European Academy of Allergology and Clinical Immunology (EAACI)

Göteborg, Schweden, 09. -13. June 2007

E. Hoflehner, K. Hufnagl, M. Bublin, B. Wagner, O. Scheiner, H. Breiteneder, and U. Wiedermann

“Intranasal treatment with a cholera toxin B subunit/allergen-fusion molecule leads to suppression of Th2 immune responses in a murine model of birch pollen allergy “ (poster)

EAACI, Göteborg, Sweden, 9.-13.6.2007

A. Wagner, E. Förster-Waldl, E. Garner-Spitzer, O. Scheiner, A. Pollak, A. Joachim, U. Wiedermann

Toxoplasma gondii infection reduces allergic responses in a mouse model of birch pollen sensitization – experimental evidence for the hygiene hypothesis (oral presentation and poster)

FWF Universitätsvorlesung 2007

Vienna, Austria, 22. June 2007

K. Hufnagl, E. Hoflehner, B. Bohle, E. Garner-Spitzer, O. Scheiner and U. Wiedermann

“Mucosal tolerance induction with birch pollen related food allergens as a prevention strategy for the oral allergy syndrome” (poster)

FWF Universitätsvorlesung 2007

Vienna, Austria, 22. June 2007

Erika Garner-Spitzer, Pamela Rendi-Wagner, Birgit Winkler, Michael Kundi, Christian Herzog, Herwig Kollaritsch, and Ursula Wiedermann

„Investigation of humoral and cellular immune responses 10 years after hepatitis A vaccination” (poster)

Jahrestagung ÖGLMKC 2007 / Biomed Austria (Berufsverband Biomed. Analytiker)

Vienna, Austria, 19. September 2007

Erika Garner-Spitzer, Pamela Rendi-Wagner, Birgit Winkler, Michael Kundi, Christian Herzog, Herwig Kollaritsch, and Ursula Wiedermann

„Investigation of humoral and cellular immune responses 10 years after hepatitis A vaccination” (oral)

ÖGTP, Wien, Österreich, 22. – 24.11.2007

A. Wagner, L. Holec, J. Kur, E. Förster-Waldl, A. Joachim, A. Pollak, O. Scheiner, U. Wiedermann

Evaluation of recombinant Toxoplasma antigens as potential vaccine candidates for protection against Toxoplasmosis (oral presentation)

Jahrestagung der ÖGTP

Wien, Austria, November 22 – 24, 2007

Schabussova, I., H. Amer, P., Kosma, B., Bohle, R. M., Maizels, and U.

Wiedermann. “Worms and their gadgets: sweet manipulation” (oral presentation)

Jahrestagung der ÖGAI 2007

Alpbach, Austria, 13.-15.December 2007

E. Hoflehner, K. Hufnagl, B. Wagner, K. Hoffmann-Sommergruber, B. Bohle, O. Scheiner and U. Wiedermann

“Mucosal poly-tolerance induction with birch pollen related food allergens or genetically engineered allergen chimers for prevention of the oral allergy syndrome.” (poster)

Jahrestagung der ÖGAI 2007

Alpbach, Austria, 13.-15.December 2007

K. Hufnagl, C. Wild, I. Schabussova, A. Zuercher, A. Mercenier, O. Scheiner and U. Wiedermann

“Mucosal co-application of probiotics and allergen chimers at the time of polysensitization prevents allergic Th2 immune responses and airway inflammation in mice”

(oral presentation)

ÖGAI, Alpbach, Österreich, 12. – 14.12.2007

A. Wagner, E. Förster-Waldl, E. Garner-Spitzer, O. Scheiner, A. Pollak, A. Joachim, U. Wiedermann

Induction of regulatory cells may protect from allergy development in a mouse model of toxoplasmosis

(oral presentation)

Vaccine Congress, Amsterdam, The Netherlands 9-11 Dec 2007

J. Jasinska, U. Wiedermann

Virosome-based multi-epitope vaccine against Her-2/neu overexpressing tumors:
from bench to clinic (oral)

II. Molekulare Mikrobiologie und Parasitologie

Unit leader: A.o. Univ. Prof. Michael Duchêne, PhD

Co-workers

1. Ing. Marina Binder, technician
2. Dr. David Leitsch, postdoc (FWF grant P19044, from September 1, 2006)
3. Dr. Birgit Wagner, postdoc (Jubiläumsfonds der Österreichischen Nationalbank, from February 1, 2007) in collaboration with the units "Epidemiology and Travel Medicine", and "Vaccination and Immunology"
4. Mag. Margit Tazreiter (maiden name Margit Hofer), PhD student (preparation of thesis)

1. Major research topics

The main focus of the group remains the human intestinal parasite *Entamoeba histolytica*. We are associated with the *E. histolytica* genome project, and our main goal is to understand the molecular mechanisms of the interaction of chemotherapeutic agents with the amoebae on the proteome and genome levels. Other important projects are the characterization of the major proteophosphoglycan surface antigen and the differentiation between pathogenic *E. histolytica* and nonpathogenic *E. dispar*. In addition, we are involved in an insect allergy project on the Indianmeal moth *Plodia interpunctella*. Further collaborative projects are described below.

2. Current projects

New routes to chemotherapy of *E. histolytica* and other protist parasites.

Alkylphosphocholines developed by Prof. Dr. Hansjörg Eibl in Göttingen are used for the treatment of visceral leishmaniasis. Dr. Karin Seifert in our lab and Doz. Dr. Julia Walochnik (Department of Medical Parasitology) showed that these substances are also active against *E. histolytica* (Seifert *et al.*, 2001) and *Acanthamoeba* spp. (Walochnik *et al.*, 2002), as well as *Trichomonas vaginalis* (Blaha *et al.*, 2006). A new interesting agent is N-chlorotaurine studied by Mag. Ursula Fürnkranz in the laboratory of Doz. Dr. Walochnik. An important collaboration that has led to a new FFG project is described below.

Mechanism of action of metronidazole in *E. histolytica* and *T. vaginalis*

Metronidazole is one of the most successful antibiotic agents. It has been used for more than 40 years to treat *E. histolytica* infections, up to date with no significant signs of developing drug resistance. It is also the gold standard for the treatment of *T. vaginalis* and *Giardia intestinalis* infections, and it is active against many anaerobic and microaerophilic bacteria such as *Helicobacter pylori* or *Bacteroides* spp. In spite of all this success, there are large gaps in our knowledge of the molecular mechanism of action of metronidazole, and the parasites' response to the drug.

In our previous FWF project we studied this response in *E. histolytica*. To cut a long story short, there was only a very modest response both on the mRNA level studied by microarray hybridization analysis (Tazreiter *et al.*, accepted providing modifications) and on the protein level as studied by two-dimensional gel electrophoresis (Leitsch *et al.*, 2005; 2007). There was only a slight but significant up-regulation of mRNAs encoding enzymes of oxidative stress response such as superoxide dismutase and peroxiredoxin, and enzymes of the glycolytic pathway, and a modest down-regulation of mRNA encoding actin and an enzyme involved in lipid biosynthesis.

It is well-established that metronidazole by itself is not toxic to host or parasite cells. Only in the parasite, the nitro group in metronidazole is reduced and activated to a nitroradical anion and to further reduction products. These activated metabolites are known to be chemically very reactive and it was assumed they were unspecifically reacting with DNA and proteins leading to indiscriminate destruction. Surprisingly, our proteome work revealed that a small number of proteins (thioredoxin reductase, thioredoxin, superoxide dismutase, purine nucleoside phosphorylase, and a small protein of unknown function which we named MTP1) are reproducibly modified by activated metronidazole. The reaction of cysteine residues in the protein with the reduced metronidazole leads to proteins with attached aminoimidazoles which migrate at the similar molecular weight but shifted to a basic isoelectric point in two-dimensional electrophoreses. In some cases this modification was shown to inhibit the enzyme activity. In addition, the activated metronidazole also reacts with free thiol molecules such as cysteine in the cells and significantly diminishes these protective molecules. In accordance with these findings, added cysteine rescued *E. histolytica* from metronidazole poisoning. Finally we discovered that thioredoxin reductase, one of the modified proteins, was able to reduce metronidazole and therefore it is not surprising that components of the redox-protective network are the first victims of metronidazole modification. The results of these studies were published recently (Leitsch *et al.*, 2007).

Taken together, our work showed that the thiol-based redox network of *E. histolytica* is a major target of metronidazole and other nitroimidazoles, but we do not understand this network well. In addition, we do not know exactly which small thiol molecules are attacked, and if this or the damage to cysteine-containing proteins is more relevant for the killing of the amoebae, and which are the further processes leading ultimately to cell death. Ultimately the studies can give us new targets and new handles for treating *E. histolytica* infections.

In the past year Dr. Leitsch and Ing. Binder have extended our work to *T. vaginalis* (manuscript submitted). Here again, thioredoxin reductase is able to reduce metronidazole, and this enzyme and functionally associated other proteins are then modified by the activated metabolites. These results will highlight the similarities and differences between the thiol-based redox networks of the two parasites, and they show that the mechanisms we have discovered for *E. histolytica* are not limited to one parasite.

Anti-protozoal chemotherapy using substances isolated from rainforest plants

In a collaboration with Prof. Dr. Harald Greger* and Dr. Brigitte Brem (Faculty Center of Botany, University of Vienna, *Project Head), Dr. Andreas Obwaller, Orphanidis, Vienna, Doz. Dr. Julia Walochnik, and Prof. Dr. Walther Wernsdorfer experiments were initiated investigating isolated plant substances - in particular flavaglines from *Aglaia* spp. as possible cytotoxic agents against protist parasites and fungi. This year we obtained a grant from the FFG to extend this work to a number of parasites and to perform initial toxicological studies to evaluate the isolated substances for their potential for further development. Some preliminary data on *E. histolytica* generated by Ms. Oumaporn Tasanor and Prof. Dr. Walther Wernsdorfer have been published this year (Tasanor *et al.*, 2007).

PCR differentiation of *Entamoeba histolytica* from *Entamoeba dispar* in stool samples for diagnosis

Whereas *E. histolytica* is the pathogenic amoeba species able to cause life-threatening dysentery and liver abscess, *E. dispar* is a harmless gut commensal. As unfortunately the two cannot be differentiated reliably microscopically, Ing. Binder adapted a real-time PCR assay developed in the Bernhard Nocht Institute for Tropical Medicine in Hamburg (Blessmann *et al.*, 2002) for our laboratory. The test was trained with a number of patients' samples that had been differentiated by starch gel electrophoresis and is now used as an in-house assay for the support of stool diagnosis.

The *E. histolytica* genome project

The *E. histolytica* genome project has been carried out as a collaboration involving 16 laboratories in many countries of the world, mainly the Sanger Institute in the UK and the Institute for Genomic Research in the USA (Loftus *et al.*, 2005). Mag. Hofer in our group established three databases of genes encoding enzymes, cytoskeletal proteins, and stress proteins (Hofer and Duchêne, 2005) which were the basis for our oligonucleotide microarray, and were also used in the genome annotation (Loftus *et al.*, 2005). After many final corrections, the large review on the content of the *E. histolytica* genome was finally published in *Advances in Parasitology* (Clark *et al.*, 2007).

Characterization of a major proteophosphoglycan surface antigen

In our group, a protective monoclonal antibody EH5 directed against a proteophosphoglycan antigen (PPG) from *E. histolytica* had been raised (Marinets *et al.*, 1997). The PPGs are highly complex molecules consisting of a GPI-anchored polypeptide carrying a large number of glycan side chains attached via serine-linked phosphodiester bonds. So it is not possible to produce the whole molecules as a possible vaccine. In her PhD thesis Dr. H. Melzer identified peptide sequences mimicking the epitope of antibody EH5 from a phage display library (Melzer *et al.*, 2002, 2003). The mimotope consensus sequence represents a sequential epitope and allowed Ing. Marina Binder to use the genome data to identify and clone a gene potentially coding for the EH5 core polypeptide. The protein encoded by this gene has similarity to the CD68 antigen expressed by phagocytic cells of the human immune system. In a collaboration with Prof. Dr. Andreas Spittler and Dr. Kambis Sadeghi we gathered evidence to support the hypothesis that the PPG / CD68 relationship may be associated with phagocytic function, pointing to a very ancient functional relationship between amoebae and phagocytic immune cells. So far the final answer is missing whether the protein containing the mimotope sequence and the PPG core polypeptide are identical. In a collaboration with Prof. Dr. Iain Wilson (Department für Chemie, Universität für Bodenkultur) we hope to obtain this answer in the close future.

Proteomics of cyst formation in the free-living amoeba *Acanthamoeba castellanii*

In contrast to the situation in *E. histolytica*, there are well-established methods for cyst formation in *Acanthamoeba castellanii*. In a cooperation with Doz. Dr. Walochnik and Dr. Martina Köhler (Department of Medical Parasitology), Mag. Andrea Deutsch, Dr. Martina Marchetti, and Prof. Dr. Günter Allmaier (Institute of Chemical Technologies and Analytics, Vienna University of Technology), Dr. Leitsch examined the protein changes during the process of encystation in *A. castellanii*. In contrast to the minimal response in *E. histolytica* to chemotherapeutics, the conditions inducing cyst formation in *A. castellanii* induced the synthesis of numerous proteins as shown by two-dimensional electrophoresis. Many changes can be observed as early as after 4 hours. In contrast to the situation in *E. histolytica*, the lack of a completed genome project led to delays in the identification of protein spots. Careful comparison of *Acanthamoeba* strains showed that those that were freshly isolated more readily encysted compared to the strains that had been in the laboratory for a long time. There is good evidence that the cause of these changes is epigenetic regulation. These results were published recently (Koehsler *et al.*, in press).

Allergens from the moth pests *Plodia interpunctella* and *Ephesia kuehniella*: characterization, recombinant production and evaluation of the allergens

Moth pests feeding on kitchen supplies are highly prevalent in many households of the industrialized countries. Ing. M. Binder had shown that a high proportion of indoor allergic patients had IgE against moth extracts. The *P. interpunctella* arginine kinase (Plo i 1) was characterized as a major novel allergen (Binder *et al.*, 2001). During the

following project supported by the "Jubiläumsfonds der Nationalbank" we were able to clone several more allergens, for example a thioredoxin. In a new project supported by the Hochschuljubiläumsstiftung der Stadt Wien, we are in the process of studying the prevalence of IgE to *E. kuehniella* antigens in patients' sera from 3 centers from 3 countries. In a collaboration with Prof. Dr. U. Wiedermann-Schmidt and Mag. Elisabeth Hoflehner, we compared recombinant arginine kinase and thioredoxin from *P. interpunctella*, and found that both allergens induced classical Type I allergy in mice. The arginine kinase had a higher potency as measured by the serum IgE levels, strength of T_{H2} cytokine response, and β -hexosaminidase release from RBL cells upon allergen-specific challenge.

Genetic variation of *Bordetella pertussis* isolates

In a collaboration with Dr. Pamela Rendi-Wagner and Dr. Helen Melzer we examined if the high vaccination pressure on *B. pertussis* may lead to a higher rate of sequence variations in clinical isolates from Austrian patients. Dr. Melzer laid a solid foundation of our sample collection but left us to start a new position in summer 2006. We then obtained a grant from the "Jubiläumsstiftung der Österreichischen Nationalbank" to Prof. Dr. Wiedermann to continue the work. In February 2007, Dr. Birgit Wagner started and obtained many more samples. The 80 samples in total were analysed for polymorphisms in the pertussis toxin and pertactin genes using classical PCR and sequence analysis. The same sequence types as in other European countries were found, but the relative frequency of the alleles showed differences.

3. Publications 2007

A. Peer-reviewed papers:

Leitsch, D., D. Kolarich, I. B. H. Wilson, F. Altmann, and M. Duchêne. 2007. Nitroimidazole action in *Entamoeba histolytica*: a central role for thioredoxin reductase. PLoS Biology 5: e211.

Impact: 14.101; correspondence MD

Köhler, M., D. Leitsch, U. Fürnkranz, M. Duchêne, H. Aspöck, and J. Walochnik. 2008. *Acanthamoeba* strains lose their abilities to encyst synchronously upon prolonged axenic culture. Parasitol. Res., in press, published electronically.

Impact: 1.140; correspondence JW

Tasanor, O., B. Brem, D. Leitsch, M. Binder, M. Duchêne, H. Greger, and W. Wernsdorfer. 2007. Development of a pharmacodynamic screening model with *Entamoeba histolytica*.

Wien. Klin. Wochenschr. 119: 88-95 (2007).

Impact: 0.804; correspondence OT

B. Review article:

Clark, C. G., U. C. Alsmark, M. Tazreiter, Y. Saito-Nakano, V. Ali, S. Marion, C. Weber, C. Mukherjee, I. Bruchhaus, E. Tannich, M. Leippe, T. Sicheritz-Ponten, P.

G. Foster, J. Samuelson, C. J. Noël, R. P. Hirt, T. M. Embley, C. A. Gilchrist, B. J. Mann, U. Singh, J. P. Ackers, S. Bhattacharya, A. Bhattacharya, A. Lohia, N. Guillén, M. Duchêne, T. Nozaki, and N. Hall. 2007. Structure and content of the *Entamoeba histolytica* genome.

Adv. Parasitol. 65: 51-190.

Impact: 4.826; correspondence CGC

Impact factors 2007

Sum (in press and published): 20.871

Sum (corresponding author MD): 14.101

Sum (correspondence outside the division): 6.770

4. Cooperations

A. Within the MUW

Elisabeth Hoflehner, Andreas Repa, Ursula Wiedermann-Schmidt (our Department): mouse model of Indianmeal moth allergy immunosuppressive factors in *E. histolytica*,

Eveline Hatzenbichler, Agnes Grünfelder, Martin Schreiber (Department of Obstetrics and Gynecology): *E. histolytica* microarrays

Ursula Wiedermann, Pamela Rendi-Wagner, Herwig Kollaritsch (our Department): genetic variation of clinical *Bordetella pertussis* isolates

Julia Walochnik, Claudia Blaha, Ursula Fürnkranz (Department of Medical Parasitology, Clinical Institute of Hygiene and Medical Microbiology): *Acanthamoeba* and *T. vaginalis* chemotherapy

B. Outside the MUW

Iain Wilson, Katharina Paschinger, Daniel Kolarich, Friedrich Altmann (Department of Chemistry, University for Natural Resources and Applied Life Sciences, Vienna): identification of *E. histolytica* proteins by classical protein sequence analysis and mass spectrometry, glycobiochemistry of the PPG antigen

Jos Brouwers (Dept. of Biochemistry & Cell Biology, Faculty of Veterinary Medicine, Utrecht), Hansjörg Eibl (Max-Planck-Institute of Biophysical Chemistry, Göttingen): *E. histolytica* lipids, chemotherapy

C. Within and outside of the MUW

Julia Walochnik, Martina Köhler (Department of Medical Parasitology, Clinical Institute of Hygiene and Medical Microbiology), Günter Allmaier, Martina Marchetti, Andrea Deutsch (Institute of Chemical Technologies and Analytics, Vienna University

of Technology): *Acanthamoeba* cyst formation - proteomics, identification of induced proteins by mass spectrometry

Walther Wernsdorfer and Oumaporn Tasanor (our Department), Julia Walochnik and Florian Astelbauer (Department of Medical Parasitology, MUW), Brigitte Brem, Christian Szaffich, and Harald Greger (Department of Chemical Ecology and Ecosystem Research, University of Vienna): testing of plant-derived anti-parasitic agents

Ursula Wiedermann-Schmidt, Pamela Rendi-Wagner (our Department), Iain Wilson (Department of Chemistry, University for Natural Resources and Applied Life Sciences, Vienna), Andreas Spittler (Department of Surgical Research, MUW), Kambis Sadeghi (Department of Pediatrics, MUW), Nancy Guillén (Unit of Cellular Biology of Parasitism, Pasteur Institute, Paris), Sam Stanley (Division of Infectious Diseases, Washington University School of Medicine, St. Louis): the EH5 proteophosphoglycan antigen on the surface of *E. histolytica*, localisation, cross-reactivity with immune cells, recombinant antibody EH5

5. Third party funds

Grants in progress

Austrian Science Fund P19044

"Encystment and Excystment in *Acanthamoeba castellanii*: RNA and protein expression in the differentiating cell"

In collaboration with Doz. Dr. Julia Walochnik (Department of Medical Parasitology, Clinical Institute of Hygiene and Medical Microbiology, Project Head) and Prof. Dr. Günter Allmaier (Institute of Chemical Technologies and Analytics, Vienna University of Technology).

Duration 36 months starting September 1, 2006

Total sum: EUR 372.960.--

Sum in the reporting period 2007: EUR 55.825.--

FFG (Österreichische Forschungsförderungsgesellschaft) Bridge B1 Project 814280:

"Wirkprofil pflanzlicher Naturstoffe bei pathogenen Protozoen und Pilzen"

In collaboration with Prof. Dr. Harald Greger and Dr. Brigitte Brem (Comparative and Ecological Phytochemistry, Faculty Center of Botany, University of Vienna, Project Head), Dr. Andreas Obwaller, Orphanidis, Vienna, Doz. Dr. Julia Walochnik (Department of Medical Parasitology, Clinical Institute of Hygiene and Medical Microbiology, Medical University of Vienna), Prof. Dr. Walther Wernsdorfer (Department of Specific Prophylaxis and Tropical Medicine).

Duration 36 months, starting November 1, 2007

Total sum for all partners: EUR 296.900.--, part for MD and WW EUR 47.500.--

Sum in the reporting period 2007: EUR 0.00, no funds used in 2007.

Hochschuljubiläumsstiftung der Stadt Wien

Project H1760/2006 "The allergenic potential of the common household moth *Plodia interpunctella* "

Total sum: EUR 5.000.--.

Sum in the reporting period 2007: EUR 3.863.--

6. PhD theses, lectures

A. PhD theses – dissertations

- Mag. Margit Tazreiter (maiden name Margit Hofer) (starting November 1, 2002, FWF grant P15960): "Characterization of the molecular response of the human protozoan parasite *Entamoeba histolytica* to alkylphosphocholines and metronidazole on the level of mRNA expression"
3rd publication was published this year (Clark *et al.*, 2007). Fourth publication and dissertation in preparation. Son Jakob born September 2007.
- Mag. David Leitsch (Starting September 22, 2003, FWF grant P15960, from Sept. 1, 2006, FWF grant P19044): Characterization of the molecular response of the human protozoan parasite *Entamoeba histolytica* to alkylphosphocholines and metronidazole on the level of protein expression.
2 Publications (Leitsch *et al.*, 2007; Koehsler *et al.*, 2008) were published this year. Final PhD exam was on July 10, 2007. Grade: "summa cum laude".

B. Teaching

- WS2006/2007: 514042 Seminar für funktionelle Pathologie (Pflichtlehrveranstaltung gem. § 5/3 StG.), zu besuchen ab dem 2. theoretisch-klinischen Semester (Parallelkurs 1) 2 SStd. Michael Duchêne, Jürg Graf, Peter Pietschmann, Rudolf Valenta, Ursula Wiedermann-Schmidt, Kira Brämswig 519069 SE Infektions- und Tropenkrankheiten (Wahlfachausbildung § 13 StG. Med.). Seminartitel: "Tuberkulose und Lepra"
- SS 2007: 514081 Kombinations-Wahlfach § 13 lit.a: Ausgewählte Themen aus funktioneller Pathologie 7 SStd. Heide Cross, Michael Duchêne, Renate Fuchs, Martin Willheim. Teilvorlesung MD "Molekularbiologie genetisch verursachter Erkrankungen des Menschen".
2 Wochen Blockseminar
- SS 2007: 501824 Impfwesen und Tropenmedizin 1 SStd. Michael Duchêne, Herwig Kollaritsch, Ursula Wiedermann-Schmidt, Pamela Rendi-Wagner, Harald Nödl Teilvorlesung "*Entamoeba histolytica*, *Trichomonas vaginalis*, *Giardia intestinalis*"

7. Awards

No awards 2007

8. International mobility

Presentation of data in 4 international congresses (see below).

9. Reviewer for journals and grant organizations 2007

A. Journals

Biochemistry and Cell Biology
 FEMS Immunology and Medical Microbiology (2)
 Journal of Proteome Research
 Molecular and Biochemical Parasitology
 Parasite Immunology
 PLoS Neglected Tropical Diseases (2)

B. Grant organizations

Wellcome Trust

10. Presentations at meetings 2007

1. Chemotherapie von *Entamoeba histolytica*: Erkenntnisse aus dem Genom und dem Proteom.

David Leitsch, Margit Hofer, Marina Binder, Nicola Mason, Michael Duchêne
 (M. Duchêne, oral presentation)

Zentrumssymposium des Zentrums für Physiologie und Pathophysiologie
 Wien, 15. - 16. Februar 2007

2. Targets of nitroimidazole action in *E. histolytica* - a central role for thioredoxin reductase.

David Leitsch, Daniel Kolarich, Iain B. Wilson, Friedrich Altmann, Michael Duchêne
 (D. Leitsch, oral presentation)

Amoebiasis Satellite Meeting
 5th European Congress of Tropical Medicine and International Health
 Amsterdam, May 24-25, 2007

3. The interaction of metronidazole with amitochondriate protist parasites.

David Leitsch, Margit Tazreiter, Daniel Kolarich, Marina Binder, Evelyn Hatzenbichler, Agnes Grünfelder, Iain B. Wilson, Ralf Steinborn, Friedrich Altmann, Martin Schreiber, Michael Duchêne
 (Michael Duchêne, invited oral presentation)

Drug Development for Parasite Diseases - COST B22 Annual Congress
 Dundee, Scotland, UK, June 10-13, 2007

4. Metronidazole action in *Entamoeba histolytica* and other microaerophilic parasites.

David Leitsch, Daniel Kolarich, Marina Binder, Iain B. H. Wilson, Friedrich Altmann, Michael Duchêne

(D. Leitsch, poster)
 32nd FEBS Congress. Molecular Machines.
 Vienna, Austria. July 7-12, 2007.

5. Anti-*Acanthamoeba* efficacy and toxicity of miltefosine in an organotypic skin model.

Julia Walochnik, Andreas Obwaller, Florian Gruber, Michael Mildner, Erwin Tschachler, Miranda Suchomel, Michael Duchêne, Herbert Auer
(J. Walochnik, oral presentation)

12th International Meeting on the Biology and Pathogenicity of Free-living Amoebae. Wako City, Japan, 27.-30. August 2007

6. Losses of the encystment potential of *Acanthamoeba* spp. involve epigenetic regulation.

Martina Köhler, David Leitsch, Michael Duchêne, Ursula Fürnkranz, Horst Aspöck, Julia Walochnik
(M. Köhler, oral presentation)

12th International Meeting on the Biology and Pathogenicity of Free-living Amoebae. Wako City, Japan, 27.-30. August 2007

7. Encystment in *Acanthamoeba* spp.: application of two-dimensional gel electrophoresis for the elucidation of stage-specific proteins involved in the developmental process.

David Leitsch, Martina Köhler, Andrea Deutsch, Günter Allmaier, Michael Duchêne, Julia Walochnik

(D. Leitsch, oral presentation)

12th International Meeting on the Biology and Pathogenicity of Free-living Amoebae. Wako City, Japan, 27.-30. August 2007

8. *Entamoeba histolytica* and metronidazole: desperate amoebae and no resistance in sight.

David Leitsch, Margit Tazreiter, Daniel Kolarich, Marina Binder, Evelyn Hatzenbichler, Iain B. Wilson, Ralf Steinborn, Friedrich Altmann, Martin Schreiber, Michael Duchêne

(M. Duchêne, invited oral presentation)

COST B22 WG5 Expert Meeting on Drug Resistance and Parasites
Québec City, Québec, Canada, October 22-24, 2007

9. Enzystierung bei *Acanthamoeba* spp.: Anwendung der zweidimensionalen Gelelektrophorese für die Identifizierung von Entwicklungsphase-spezifischen Proteinen.

David Leitsch, Martina Köhler, Andrea Deutsch, Günter Allmaier, Michael Duchêne and Julia Walochnik

(D. Leitsch, Vortrag)

41. Jahrestagung der Österreichischen Gesellschaft für Tropenmedizin und Parasitologie

Wien VUW, 22.-24. November 2007

10. Epigenetic regulation of encystment and protease activity in *Acanthamoeba* spp.
Martina Köhler, David Leitsch, Michael Duchêne, Julia Walochnik
 (M. Köhler, Vortrag)

41. Jahrestagung der Österreichischen Gesellschaft für Tropenmedizin und Parasitologie
 Wien VUW, 22.-24. November 2007

11. N-Chlortaurin (NCT): zytotoxische Effekte auf amastigote Leishmanien und die Bestätigung des vermuteten Wirkmechanismus anhand von *Trichomonas vaginalis*
Ursula Fürnkranz, Markus Nagl, Waldemar Gottardi, Michael Duchêne, Horst Aspöck, Julia Walochnik
 (U. Fürnkranz, Vortrag)

41. Jahrestagung der Österreichischen Gesellschaft für Tropenmedizin und Parasitologie
 Wien VUW, 22.-24. November 2007

12. Metronidazol - neue Erkenntnisse über einen Klassiker

David Leitsch, Margit Tazreiter, Daniel Kolarich, Marina Binder, Evelyn Hatzenbichler, Ralf Steinborn, Martin Schreiber, Iain B. Wilson, Friedrich Altmann und Michael Duchêne
 (M. Duchêne, Vortrag)

41. Jahrestagung der Österreichischen Gesellschaft für Tropenmedizin und Parasitologie
 Wien VUW, 22.-24. November 2007

Meeting contributions 2007: 12

Invited oral presentations (international): 2

Oral presentations (not invited, own group): 5

Oral presentations (not invited, collaborations): 4

Poster: 1

III: “ Epidemiology and Travel Medicine”

Unit Leader: A.o. Univ. Prof. Dr. H. Kollartisch, MD

Co-workers:

Dr. med. Pamela Rendi-Wagner (until Nov.2007)

Dr. Maria Paulke-Korinek

Dr. Renate Kronik

Dr. Ana Grac

Mag. Brigitte Laaber

1. Research projects

Ongoing research projects:

- Epidemiological hospital-based surveillance of vaccine preventable diseases (VPD) in Austria (hospitalized cases in children, since 1997): Hepatitis A, Hepatitis B, Hepatitis C, Measles, Mumps, Rubella, Haemophilus B, Rotavirus, Pertussis
- Epidemiological lab-based surveillance of VPD of all age classes (laboratory based cases, since 1999) Hepatitis A, Hepatitis B, Hepatitis C, Measles, Mumps, Rubella, Haemophilus B, Rotavirus, Pertussis
- Tick-Borne-Encephalitis:
A phase IV, uncontrolled, open-label, single-center study in adults: Evaluation of immunogenicity and safety of the polyglycine-free TBE vaccine in adults, when used as booster at least 3 years after primary or booster TBE immunization :
Long term Follow up
- Epidemiological surveillance of Invasive Pneumococcal Disease (IPD) in children below 5 years of age in Austria (ongoing since 2000)
- JEV-vaccine (Intercell) phase III clinical trial (immunogenicity and reactogenicity): IC 51-301 – long term follow up

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Newly initiated research projects

- An Open Label Phase III study of a Vero Cell-Derived whole Virus H5N1 influenza vaccine to Assess the Immunogenicity and Safety and to Investigate the Need for and Timing of a Booster Vaccination. Started June 2007, ongoing to 2010
- Seroprevalence of vaccine induced antibodies in Austrian schoolchildren (Ministry of Health, Austria); started last quarter of 2007, ongoing until end 2008.

2. Publications

Tauber E, Kollaritsch H, Korinek M, Rendi-Wagner P, Jilma B, Firbas C, Schranz S, Jong E, Klingler A, Dewasthaly S, Klade CS.

Safety and immunogenicity of a Vero-cell-derived, inactivated Japanese encephalitis vaccine: a non-inferiority, phase III, randomised controlled trial. Lancet. 2007, 370(9602):1847-53.

IPF: 25,800

Kollaritsch H, Wenisch C, Hatz C, Laer G, Bauer B, Hollenstein U, Haditsch M, Diridl G, Malinowski W, Jeschko E, Payer-Neundlinger G, Speiser-Remp N, Pichler HE, Rumpold H, Stemberger H, Eder G, Wiedermann G, Wiedermann U. [Medical clearance for missions abroad (EEU): definitions, recommendations for use and performance.] Wien Klin Wochenschr. 2007, 119 Suppl 3:13-25. German.

IPF: 0,804

Rendi-Wagner P, Paulke-Korinek M, Stanek G, Khanakah G, Kollaritsch H. Impact of a pertussis booster vaccination program in adolescents and adults on the epidemiology of pertussis in Austria. *Pediatr Infect Dis J.* 2007, ;26(9):806-10.
IPF: 3,215

Rendi-Wagner P, Korinek M, Mikolasek A, Vécsei A, Kollaritsch H. Epidemiology of travel-associated and autochthonous hepatitis A in Austrian children, 1998 to 2005. *J Travel Med.* 2007, 14(4):248-53.
IPF: 1,333

Rendi-Wagner P, Paulke-Korinek M, Kundi M, Wiedermann U, Laaber B, Kollaritsch H. Antibody persistence following booster vaccination against tick-borne encephalitis: 3-year post-booster follow-up. *Vaccine.* 2007,25(27):5097-101.
IPF: 3,159

Nothdurft HD, Dahlgren AL, Gallagher EA, Kollaritsch H, Overbosch D, Rummukainen ML, Rendi-Wagner P, Steffen R, Van Damme P; ad hoc Travel Medicine Expert Panel for ESENEM. The risk of acquiring hepatitis A and B among travelers in selected Eastern and Southern Europe and non-European Mediterranean countries: review and consensus statement on hepatitis A and B vaccination. *J Travel Med.* 2007, 14(3):181-7.
IPF: 1,333

Kollaritsch H, Wiedermann U.
[Examples for vaccines against diarrheal diseases--rotavirus and traveller's diarrhea]
Wien Med Wochenschr. 2007, 157(5-6):102-6.
IPF: 0,000

Rendi-Wagner P, Korinek M, Winkler B, Kundi M, Kollaritsch H, Wiedermann U. Persistence of seroprotection 10 years after primary hepatitis A vaccination in an unselected study population. *Vaccine* 2007, 25(5):927-31.
IPF: 3,159

3. Cooperations

A. Cooperations within the MUW:

Prof. Wiedermann-Schmidt: Evaluation of humoral and cellular longterm-immunity after hepatitis A vaccination

Prof. Kundi; Institute of Environmental Medicine; Statistical analysis of epidemiological data

Prof. Holzmann, Institute of Virology,; Serology post FSME, hepatitis B, A vaccination

Prof. G. Stanek, Institute for Hygiene; Surveillance of pertussis epidemiology

Prof. Burgmann; Univ. Clinic of Internal Medicine: Serotyping and antimicrobial resistance testing of *Strep. Pneum.* Isolates

B. Cooperations outside MUW:

Prof. Zenz: Kinderklinik Graz
 Prof. Mutz: Kinderklinik Leoben
 Prof. Waldner, Institute for Hygiene, Medical University Innsbruck
 Prof. Mittermayer, Institute for Hygiene, Krankenhaus Elisabethinen, Linz
 Prof. Harald Stoiber, Medical University Graz
 Austrian Federal Ministry of Health and Women
 GlaxoSmithKline
 SanofiPasteur MSD

C. International cooperations:

Clinical studies together with:
 Novartis Vaccines (TBE vaccination: Long-term protection)
 Wyeth Pharma (epidemiology of invasive pneumococcal diseases)
 Intercell (Japan Encephalitis vaccine phase III)
 Baxter (H5N1 Vero-cell vaccine)

4. Third party funding

The clinical studies were directly sponsored by the respective companies.

Identification and source of support	Title and head of project and cooperation partners	Duration of research project	Total sum of grant (€)	Aliquot for 2007 (€)
§ 27 Baxter AG H5N1 influenza	Vero-cell influenza vaccine	2007-2010	500.000.-	120.000
§ 26 BMWF	SEROPRÄV	2007-2008	49.440.-	24.720.-
Sum			549.440.-	144.720.-

5. Lectures

Impfpraktikum (Pflichtpraktikum for medical students), 2,5 h
 Wahlfach Tropenmedizin, 3std
 Repetitorium Tropenmedizin 2std
 Grundlagen der Reisemedizin 1std
 MCW Block 22 Präventivmedizin 1std
 SSM3: Methodenseminar: Impfungen und Tropenmedizin (4 Std)

6. Reviewer activity:**Prof. Kollartisch:**

Vaccine
 Journal of Travel Medicine
 Wr. Klin. Wochenschrift

Pamela Rendi-Wagner:

Vaccine

Journal of Travel Medicine

European Journal of Pediatrics

7. Appointments

Prof. Kollaritsch:

- Member and vice-chair of the „Impfausschuss des Obersten Sanitätsrates der Republik Österreich“
- Member of the „Arzneimittelbeirat“ (Ausschuss für Arzneimittelsicherheit) der Republik Österreich
- President of the Austrian Society for Travel and Touristic Medicine.
- Member of the “Board for International Development” of the Austrian Academy of Sciences
- Member of the Scientific Board of the Ministry of Defense, Republic of Austria
- Scientific Chair for CISTM10, Vancouver, Canada 2007
- President of the Austrian Committee for Vaccinations
- Co-Editor (special duties) of The Journal of Travel Medicine

P. Rendi-Wagner:

- Member of the Scientific Committee of the International Society of Travel Medicine (ISTM)

8. Presentations at meetings 2007**Pamela Rendi-Wagner:****Invited oral presentations:**

- | | |
|----------|---|
| 26.1.07 | 9th Annual Meeting of the International Scientific Working Group of Tick-borne Encephalitis (ISW-TBE), Wien: Invited oral: “TBE Cases & Vaccination Status in 2006: Czech Republic, Slovenia, Austria” |
| 27.2.07 | „Giftiger Dienstag“, Fortbildungsveranstaltung der Österreichischen Gesellschaft für Infektiologie und der Ärztekammer für Wien: Invited oral: „Epidemiologie invasiver Pneumokokkenkrankungen bei Kindern“ |
| 10.3.07 | 12. Linzer Reisemedizinische Tagung: Invited oral: „Impf-Up-Date“ |
| 24.3.07 | 16. Österreichischer Impftag, Salzburg: Invited oral: „FSME Impfung – Schutzdauer“ |
| 17.4.07 | Fortbildungsveranstaltung der Österreichischen Gesellschaft für Tropenmedizin und Parasitologie (ÖGTP), Wien: Invited oral: „Epidemiologie invasiver Pneumokokkenkrankungen“ |
| 24.5.07 | 10th Conference of the International Society of Travelmedicine: Vancouver, B.C., Canada. May 2007. Invited oral: “ABC’s of Travel Immunizations“ |
| 16.10.07 | Pressegespräch - Cervarix Launching, Wien: Invited oral: “Adjuvans System 04” |

Maria Paulke-Korinek

Poster at IX International Jena Symposium on Tick-borne Diseases; (Jena, 15-17 March 2007): Seroprotection four years following booster vaccination against tick-borne encephalitis. Rendi-Wagner P, Paulke-Korinek M, Kundi M, Wiedermann U, Laaber B, Kollaritsch H.

Presentation: „Update Impfungen 2007“ (20.9.07) at Fortbildungsseminar: „Ethik in der Medizin“ für Mitglieder der österreichischen Ethikkommissionen (St. Pölten)

Prof. Dr. Herwig Kollaritsch (invited oral presentations only)

- 18.1.07 Fortbildung Novartis Wien: Tollwut Zecken & Co
- 15.2.07 Naturhistorisches Museum Wien, Pharmazeuten: Neue Impfungen
- 1.3.07 Saalfelden, Öst.Apothekertage. Reisemedizin update
- 9.3.07 ESIDOG: Impfseminar f. Gynäkologen Oberösterreich
- 10.3.07 Linzer Reisemedizinische Tagung: Entsendungseignungsuntersuchung
- 17.3.07 Öst.Kongress für Infektionskrankheiten: Reiseimpfungen
- 23.3.07 Öst.Bundesheerimpftag. Japan Encephalitis
- 24.3.07 Öst.Impftag. Infektionssurveillance
- 9.5.07 Mini-Med-Studium Donauuniversität: Impfungen
- 1.6.07 ESIDOG: Impfseminar für Gynäkologen Salzburg
- 7.5.07 Ärzteakademie Grado: Lunchsymposium Reisemedizin
- 8.5.07 Ärzteakademie Grado: Impfupdate öst.Impfplan
- 26.9.07 Fortbildungsakademie Innsbruck: Impfupdate
- 27.9.07 Impfsymposium Gmunden: Pneumokokkensusveillance
- 2.10.07 Ärztekammer Wien: Giftiger Dienstag. Der öst.Impfplan
- 11.10.07 Gesellschaft der Ärzte, Novartis: Influenza
- 7.11.07 AGES Zukunftskonferenz, Messe Wien: Klimaveränderungen und Tropenkrankheiten

9. Educational Activities outside MUW

Prof. Kollaritsch:

Scientific Co-chair of the 10th international Conference on Travel Medicine, Vancouver, Canada

Impfpratgeber, 11th ed. 312 pages, Müllerverlag Wien

Traveler's diarrhea textbook (Ericsson, Steffen, DuPont, eds), 2nd ed., Chapter on „Probiotics in Traveler's diarrhea“

IV. Tropical Medicine and Field Research

Unit Leader: Univ. Doz. Harald Noedl, MD, MCTM, PhD

Staff Austria:

- Kamala Thriemer, MD
- Peter Starzengruber, MD
- Oumaporn Tasanor, Msc, PhD Student
- Matthias Vossen, MD Student
- Benedikt Ley, MD Student
- Paul Swoboda, MD Student
- Mariella Jung, MD Student

Staff Bangladesh:

7 technicians, nurses, and field workers

- Mun Thawn Bawm, Lab Technician
- Nayebur Rahman, Lab Technician
- Ching Sang Thwe, Health Worker
- Moug Thing Hla, Health Worker
- Thawn Sang Bawm, Health Worker
- Al Mamun, Health Worker
- Lal Dawt Sang Bawm, Health Worker

1. Projects 2007:

- Prevalence of malaria and non-malaria febrile illnesses among febrile patients in Bandarban. ICDDR,B: #2006-033. Prevalence survey among 752 fever patients (primary objective) and 2,077 healthy subjects (secondary objective) in Bandarban Province, Southeastern Bangladesh. Project ongoing. Collaboration with the International Centre for Diarrhoeal Disease Research (ICDDR,B), Bangladesh.
- Malaria Baseline Prevalence Survey in Bangladesh. GFATM- funded nationwide, cross-sectional prevalence survey for malaria throughout Bangladesh. Enrollment completed. Collaboration with the International Centre for Diarrhoeal Disease Research (ICDDR,B), Bangladesh.
- Glucose-6-phosphate-dehydrogenase deficiency in Bandarban District, Bangladesh and its impact on the epidemiology of malaria.
- Seroprevalence of typhoid, leptospirosis, and dengue in southeastern Bangladesh.

- Diagnosis of influenza A and B among febrile patients in southeastern Bangladesh
- Randomized, controlled, Phase II/III GCP clinical trial with azithromycin - artesunate combination therapy for the treatment of uncomplicated falciparum malaria in Bangladesh. Study site: Bandarban Sadar Hospital, Bangladesh. "Azithromycin Combination Therapy for the Treatment of Uncomplicated Falciparum Malaria in Bangladesh: an Open Label Randomized Controlled Trial", Protocol Identifier: ICDDR,B #2006-024; MUW #218/2006, enrollment completed. Collaboration with the International Centre for Diarrhoeal Disease Research (ICDDR,B), Bangladesh.
- Randomized, controlled GCP trial with artesunate monotherapy with the aim of identifying artemisinin resistance along the Cambodian-Thai border. Study site: Tassan Health Center, Batambong Province, Cambodia. "Artemisinin Resistance in Cambodia", Protocol Identifier: WRAIR Protocol #1296, enrollment completed. Collaboration with USAMC-AFRIMS, Bangkok and the The National Center for Parasitology, Entomology and Malaria Control, Cambodia.
- *In vitro* antimalarial activity of propafenone and analogs; 2D and 3D quantitative structure activity relationship (QSAR) studies; identification of candidate drug targets after separation of plasmodial proteins on 2D gels (Collaboration with the Institute of Medicinal Chemistry, Medical University of Vienna, P. Chiba).
- Development of novel ELISA-based assays for measuring *P. vivax* biomass as an indicator of parasite growth and inhibition and its application in drug sensitivity testing (Collaboration with USAMC-AFRIMS and ICDDR,B).
- *In vitro* antimalarial activity of novel antibiotic compounds and interaction with conventional antimalarials.
- Building research and diagnostic capacities at the Bandarban Sadar Hospital in Southeastern Bangladesh
- Antimalarial drug resistance surveillance in Thailand, Cambodia, and Bangladesh (Collaboration with USAMC-AFRIM, Thai Ministry of Public Health, Thamassat University, The National Center for Parasitology, Entomology and Malaria Control, Cambodia, and the ICDDR,B, Bangladesh)

2. Grants 2007

Identification and source of support	Title and head of project	Duration of research project	Total sum of grant (€)
Austrian Science Fund; FWF P18350-B02	New assays for <i>P. vivax</i> drug and vaccine development; H. Noedl	1/2006 – 12/2007	156.302.00
Austrian Academy of Sciences P154-II	Building Research and Diagnostic Capacities at Bandarban Sadar Hospital in Southeastern Bangladesh; H. Noedl	12/2006 – 5/2008	25.000.00

3. Publications:

- Noedl H., S. Krudsood, W. Leowattana, N. Tangpukdee, W. Thanachartwet, S. Looareesuwan, RS. Miller, M. Fukuda, K. Jongsakul, Y. Kritsanai, S. Sriwichai, C. Ohrt, C. Knirsch. 2007. In vitro antimalarial activity of azithromycin, artesunate, and quinine in combination and correlation with clinical outcome. *Antimicrob. Agents Chemother.* 51(2):651-6
Impact 4.153
- Haque R., K. Thriemer, Z. Wang, K. Sato, Y. Wagatsuma, MA. Salam, S. Akther, J. Akter, M. Fukuda, RS. Miller, H. Noedl. 2007. Therapeutic efficacy of artemether-lumefantrine for the treatment of uncomplicated *Plasmodium falciparum* malaria in Bangladesh. *Am. J. Trop. Med. Hyg.* 76(1):39-41.
Impact 2.546
- Vossen M.G., R. Haque, P. Starzengruber, W. Ali Khan, K. Thriemer, AS.Marma, S. Akther, M. Fukuda, H. Noedl. 2007. In vitro interaction studies of azithromycin and dihydroartemisinin in *Plasmodium falciparum* isolates from Bangladesh. *Wien. Klin. Wochenschr.* 119 Suppl 3:71-5.
Impact 0.804
- Thriemer K., WA. Khan, P. Starzengruber, R. Haque, MG. Vossen, ASP. Marma, S. Akther, M. Fukuda, H. Noedl. 2007. In vitro interaction of dihydroartemisinin and lumefantrine in clinical field isolates from Bangladesh. *Wien. Klin. Wochenschr.* 119 Suppl 3:67-70.
Impact 0.804
- Tasanor O., M. Ernst, K. Thriemer, GF. Ecker, H. Noedl, P. Chiba. 2007. Characterization of a novel class of antimalarials and its applicability to plasmodial target identification. *Wien. Klin. Wochenschr.* 119 Suppl 3:83-87.
Impact 0.804

- Coldren RL., K. Jongsakul, S. Vayakornvichit, H. Noedl, MM. Fukuda. 2007. Apparent Relapse of Imported Plasmodium ovale Malaria in a Pregnant Woman. Am. J. Trop. Med. Hyg. 77(5):992-4.
Impact 2.546
- Chretien JP., M. Fukuda, H. Noedl. 2007. Improving surveillance for antimalarial drug resistance. JAMA. 23;297(20):2278-81.
Impact 23.175

Impact total 2007: 34.83 Impact corresponding author: 9.11

4. Cooperations

Within home institution:

- Institut für Medizinische Chemie, Center for Physiology and Pathophysiology, Medical University of Vienna (P. Chiba)

International:

- Walter Reed Institute (WRAIR), Washington, DC / USAMC-Armed Forces Research Institute of Medical Sciences (AFRIMS), Bangkok, Thailand (M. Fukuda)
- International Centre for Diarrheal Disease Research, Bangladesh (ICDDR,B), Dhaka, Bangladesch (R. Haque, WA Khan)
- Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand (S. Looareesuwan)
- Thai Ministry of Public Health, Nonthaburi, Thailand (J. Sirichaisinthop)
- World Health Organization, Geneva, Switzerland (P. Ringwald)
- University of Tsukuba, Graduate School of Comprehensive Human Sciences, Tsukuba, Japan (Y. Wagatsuma)
- Bandarban Sadar Hospital, Bangladesh (AS. Prue Marma)
- Thamassat University, Bangkok, Thailand (K. Na-Bangchang)

5. Reviewer activity

- JAMA, The Journal of the American Medical Association
- Trends in Parasitology (formerly Parasitology Today)
- Antimicrobial Agents and Chemotherapy
- American Journal of Tropical Medicine and Hygiene

6. Presentations

- Harald Noedl, Lon Chan Thap, Youry Se, Sabaithip Sriwichai, Sok Peou, Kurt Schaecher, Paktiya Teja-Isavadharm, Krisada Jongsakul, Bryan Smith, Wiriya Rutvisuttinunt, Delia Bethell, Sittidech Surasri, Duong Socheat, Mark M. Fukuda. Artemisinin Resistance in Cambodia. Annual Meeting of the American Society of Tropical Medicine and Hygiene, Philadelphia Nov 2007 (oral)
- Kamala Thriemer, Rashidul Haque, Aung Swi Prue Marma, Wasif Ali Kahn, Peter Starzengruber, Selim Akter, Matthias Vossen, Mark Fukuda, Harald Noedl. Azithromycin combination therapy for the treatment of uncomplicated falciparum malaria. in Bangladesh: an open label randomized controlled trial. Annual Meeting of the American Society of Tropical Medicine and Hygiene, Philadelphia Nov 2007 (oral)
- Harald Noedl. Artemisinins and amino alcohols: in vitro and clinical data from Thailand and the region. WHO Expert Meeting on Drug Resistance, Phnom Penh Jan 2007 (invited)
- Harald Noedl, Lon Chan Thap, Youry Se, Duong Suheat, Sok Peou, Bryan Smith, Kurt Schaecher, Krisada Jongsakul, Sabaithip Srivichai, Sittidech Surasri, Ses Sarim, Mark Fukuda. Artemisinin Resistance in Cambodia? WHO Informal consultation on Malaria Multi Drug Resistance in the Mekong Region, Phnom Penh Jan 2007 (invited)

- Harald Noedl. In vivo / in vitro drug resistance monitoring in Bangladesh, Thailand, and Cambodia. Kisumu, Kenya, 2007 (invited)
- Harald Noedl, Lon Chan Thap, Youry Se, Duong Suheat, Sok Peou, Kurt Schaecher, Sabaitip Srivichai, Paktiya Teja-Isavadharm, Bryan Smith, Krisada Jongsakul, Sittidech Surasri, Mark M. Fukuda. Artemisinin Resistance in Cambodia? 5th European Congress on Tropical Medicine and International Health, Amsterdam, May 2007 (oral)
- Oumaporn Tasanor, Marlies Ernst, Peter Starzengruber, Adolf Ellinger, Gerhard F. Ecker, Harald Noedl and Peter Chiba. Quantitative structure activity relationship studies on a novel class of antimalarial compounds derived from the class 1c antiarrhythmic drug propafenone. 5th European Congress on Tropical Medicine and International Health, Amsterdam, May 2007 (poster)
- Harald Noedl. Malaria in Bangladesh. Microscopy Training Workshop, ICDDR,B, Dhaka, Bangladesh Sept 2007 (invited)
- Benedikt Ley, Wasif Ali Khan, Peter Starzengruber, Kamala Thriemer, Rashidul Haque, Harald Noedl. Typhoid fever and leptospirosis. Significant causes of fever in Bangladesh? 41. Jahrestagung der ÖGTP, Vienna, Austria, Nov 2007 (oral)
- Harald Noedl. Artemisinin Resistance of Plasmodium falciparum in Southeast Asia. 41. Jahrestagung der ÖGTP, Vienna, Austria, Nov 2007 (oral)
- Mariella Jung, Benedikt Ley, Wasif Ali Khan, Peter Starzengruber, Kamala Thriemer, Rashidul Haque, Harald Noedl. G6PD deficiency and its impact on malaria in southeastern Bangladesh. 41. Jahrestagung der ÖGTP, Vienna, Austria, Nov 2007 (oral)
- Matthias G. Vossen, Sandra Pferschy, Peter Chiba, Harald Noedl. The SYBR Green I assay. A potential candidate for malaria field drug sensitivity testing? The SYBR Green I assay. A potential candidate for malaria field drug sensitivity testing? 41. Jahrestagung der ÖGTP, Vienna, Austria, Nov 2007 (poster)

- Oumaporn Tasanor, Stephan Kopp, Matthias Vossen, Peter Chiba, Harald Noedl. The growth inhibitory potential of propafenone in combination with chloroquine and dihydroartemisinin against *Plasmodium falciparum* in vitro. 41. Jahrestagung der ÖGTP, Vienna, Austria, Nov 2007 (poster)
- Paul Swoboda, Oumaporn Tasanor, Rashidul Haque, Wasif Ali Khan, Kamala Thriemer, Peter Starzengruber, Peter Chiba, Harald Noedl. In vitro activity of propafenone against clinical field isolates of *Plasmodium falciparum*. 41. Jahrestagung der ÖGTP, Vienna, Austria, Nov 2007 (poster)
- Peter Starzengruber, Kamala Thriemer, Rashidul Haque, Aung Swi Prue Marma, Wasif Ali Khan, Matthias Vossen, Selim Akter, Mark Fukuda, Harald Noedl. Azithromycin combination therapy for the treatment of uncomplicated falciparum malaria. An open label randomized controlled trial in Bangladesh. 41. Jahrestagung der ÖGTP, Vienna, Austria, Nov 2007 (oral)

6. Theses and Training

- Oumaporn Tasanor, PhD student: thesis, characterization of the antimalarial activity of propafenone and its analogues
- Matthias Vossen, MD student: thesis, azithromycin combinations in vitro
- Mariella Jung, MD student: thesis, G6PD deficiency in Bangladesh
- Paul Swoboda, MD student: thesis, activity of propafenone and its analogues in clinical field isolates
- Benedikt Ley, PhD student, typhoid fever and leptospirosis. Significant causes of fever in Bangladesh.
- Kamala Thriemer, MD: medical training in Specific Prophylaxis and Tropical Medicine
- Peter Starzengruber, MD: medical training in Specific Prophylaxis and Tropical Medicine

7. Lectures/Workshops

- In vitro workshop Phnom Penh 2007: HRP2-Based Drug Sensitivity Testing. Phnom Penh, Mar 2007
- „Spezifische Prophylaxe und Tropenmedizin“ (MCW, SS 2007).

V. Malaria and Diagnostics

Leader: Prof. Walther H. Wernsdorfer, M.D. (Visiting Professor)

Co-workers

Florence Peace Amito, B.Sc., Master Student
 Ampai Darakapong, Technical Officer
 Maj. Dr. Klaus Hochleutner, M.D., Scientific Co-worker
 Dr. Ariane Knauer, M.D., Scientific Co-worker
 Lt.Col. Dr. Robert Kollermann, M.D., Scientific Co-worker
 Dr. Florentina Kosely, M.D., Scientific Co-worker
 Benedikt Ley, B.Sc., Diploma Student
 Dr. Gernot Müller, M.D., Scientific Co-worker
 Armin Sadjed, cand.med., Doctoral Student
 Christin Sisowath, M.Sc., Doctoral Student
 Oumaporn Tasanor, M.Sc., Doctoral student

1. Scientific Activities 2007

Work in 2007 was focused on the investigation of specific pharmacodynamic activities of antiparasitic compounds in *Plasmodium falciparum* and *Plasmodium vivax*, the elucidation of drug sensitivity of *Plasmodium falciparum* in study sites in SE-Asia and Uganda, and the final analysis of the response of *Crithidia fasciculata* and *Entamoeba histolytica* to plant extracts and pure, structurally identified plant-derived substances.

A. *Plasmodium falciparum*

In May-July 2007 a working group assessed the in vitro response of *P. falciparum* to antimalarial drugs in the area of Mae Sot, Thailand, in the framework of the monitoring programme of the Ministry of Public Health of Thailand. This is a collaborative project. The sensitivity studies, including chloroquine, artemisinin, mefloquine, quinine, atovaquone, pyronaridine, lumefantrine, and monodesbutylbenflumetol, were supplemented by molecular-biological investigations in cooperation with the Karolinska Institute, Stockholm. In addition, the following studies were carried out:

1. Specific pharmacodynamic interaction between quinine and retinol in *P. falciparum*. Earlier investigations with atovaquone, artemisinin and other blood schizontocidal compounds produced evidence of significant enhancement of their specific activity by the addition of retinol concentrations in the physiological concentration range. Such observations were lacking for members of the 4-quinolinemethanol group. Therefore the specific activity of quinine alone was compared with that of quinine supplemented with retinol at concentrations corresponding to the 50th, 65th and 80th percentile of the physiological range in the serum of healthy adults. Despite the presence of substantial quinine resistance, the addition of retinol reduced the mean EC₉₉ values to less than half, i.e. to a level within the therapeutic range. This was even more evident with the geometric cut-off concentrations of schizont maturation (GMCOC), dropping from 13668 nM for quinine alone to 1990 nM for QNN-RET low, 1462 nM for QNN-RET medium, and 1344 nM for QNN-RET high.
2. Investigations of the specific pharmacodynamic interaction between lumefantrine and monodebutyl-benflumetol (DBB) were expanded from the 999:1 to the 995:5 combination. These studies confirmed the earlier findings with the 999:1 combination and indicated significantly higher synergism with the 995:5 combination of lumefantrine and DBB. The GMCOC values for lumefantrine alone, DBB alone, LUM:DBB 999:1, and LUM:DBB 995:5 were 555.55 nM, 245.95 nM, 243.74 nM and 149.94 nM, respectively. Berenbaum analysis confirmed high-grade synergism between lumefantrine and DBB at a ratio of 995:5, with mean Σ FIC values consistently <0.5.
3. In view of earlier observations on synergism between lumefantrine and artemether it was of interest to investigate the interaction between monodesbutyl-benflumetol (DBB) and artemisinin. The EC₉₉ levels observed with DBB alone, artemisinin alone and DBB:artemisinin 1:1 were 312.52 nM, 371.18 nM and 57.99 nM, and the GMCOC levels 279.05 nM, 494.05 nM and 49.25 nM, respectively. Berenbaum analysis indicated moderate synergism at the EC₅₀ level, and strong synergism at the EC₉₀ and EC₉₉.
4. Retrospective analysis of results obtained with a DBB:proguanil 3:1 m/m combination in *P. falciparum* yielded evidence of moderate, albeit significant ($p < 0.01$) synergism between the two compounds in analogy to that observed between atovaquone and proguanil. This indicates an interesting potential of DBB.

B. Plasmodium vivax

The analysis of the sensitivity data of *P. vivax* for 2006 indicated a further significant rise of the therapeutically relevant ECs for chloroquine, but still adequate clinical-parasitological response to treatment with chloroquine and primaquine in the study area. Considering the particular pharmacokinetic profile of amodiaquine, little benefit could be expected from replacing chloroquine by amodiaquine. Therefore, studies in 2007 concentrated on re-checking the susceptibility status regarding chloroquine and amodiaquine and the in vitro evaluation of potential replacement drugs other than the 4-aminoquinolines, e.g. lumefantrine, mefloquine, DBB, artemisinin and atovaquone. The material is still under evaluation.

C. Malaria baseline survey in Gulu District, Uganda

Throughout September 2007 a malaria baseline survey was conducted in the internally displaced population (IDP) of Gulu District in northwestern Uganda, an area severely affected by raids of the LRA. Nearly 90 % of the district's population lives in refugee camps. The survey was based at St. Mary's Hospital, Gulu and supported by a grant from the Italian Government. The survey included a representative, stratified sample of the refugee population, and a wide range of environmental, medical-physical, haematological parameters in addition to those specific for malaria. The area was classified as hyper-endemic for malaria, with *P. falciparum* as the lead species. The assessment of drug sensitivity of local *P. falciparum* yielded evidence of practically universal, solid resistance to chloroquine and amodiaquine and reduced sensitivity to artemisinin and lumefantrine as compared to the baseline sensitivity observed in Tanzania, obviously the result of the liberal use of the lumefantrine-artemether (coartem) combination for the treatment of febrile conditions in the absence of evidence-based treatment of malaria in the district. Sensitivity of *P. falciparum* to quinine is still within the drug's therapeutic range.

E. *Crithidia fasciculata* and *Entamoeba histolytica*

The results obtained with the recently developed micro-test systems, using control drugs as well as extracts from higher tropical plants and pure, structurally identified plant-derived compounds were re-analysed and consolidated for inclusion in the dissertation of Ms Oumaporn Tasanor.

2. WHO Assignments

1. As a resource-person to the consultative meeting of the Managers of Malaria Control Programmes in the Eastern Mediterranean Region of WHO, Dubai, 11-14 March 2007.
2. Restructuring of Department of Malaria Control into Department for the Control of Vector-Borne Diseases of the United Arab Emirates. Sharjah and Dubai, UAE, 15-19 June 2007.
3. Consultation on the future orientation of the WHO initiative "Roll-back malaria", WHO, Geneva, 14-16 May 2007.
4. Review and outlook of malaria control activities in countries of eastern Africa, Entebbe, Uganda, 11-16 August 2007.
5. Strategic review of malaria control in countries of southern Africa, and consideration of activities aiming at the elimination of malaria. Victoria Falls, Zimbabwe, 6-11 October 2007.

3. Academic activities and lectures

- Medical University of Vienna
Hygiene: SS 2007: 2 lectures (malaria)
Dissertation adviser to candidates of medicine, MUW
Diploma thesis adviser and examiner (biosciences), University of Vienna

- Thammasat University, Bangkok, Faculty of Allied Health Sciences
Lecture series (introduction to tropical communicable diseases), June 2007
Thesis adviser to M.Sc. and Ph.D. students
- Universiti Sains Malaysia, Penang, Centre for Drug Research
Thesis adviser and External Examiner (M.Sc. and Ph.D. students)
- Karolinska Sjukhus and Karolinska Institutet, Stockholm
Research and thesis adviser to Ph.D. students

Meetings, special lectures and workshops

IP = invited participant; IS = invited speaker; SCM = session chairman;

P = presenter

- Center for International Collaborative Research, Nagasaki University (CICORN), meeting of the Advisory Committee, Nagasaki 15-18 January 2007. **IP, IS**
- Cost B22 (EU) conference on “Vitamin and cofactor biosynthesis in protozoan parasites”, Seggau, Styria. **IP, IS**
- Annual Meeting of the Austrian Society of Tropical Medicine and Parasitology, Vienna, 22-24 November 2007. **SCM, P**

4. Reviewer activities

Acta Tropica

American Journal for Tropical Medicine and Hygiene

Antimicrobial Agents and Chemotherapy

BMC Clinical Pharmacology

Eastern Mediterranean Health Journal

Experimental Parasitology

Journal of Infectious Diseases

Transactions of the Royal Society of Tropical Medicine and Hygiene

Tropical Medicine and International Health

5. Publications

Exner B, Wernsdorfer G, Sirichaisinthop J, Rojanawatsirivet C, Kollaritsch H, Wernsdorfer WH (2007) Synergistic interaction between atovaquone and retinol in *Plasmodium falciparum* *in vitro*. *Wien Klin Wochenschr* 119 (Suppl 3): 45-52.

Parizek M, Sirichaisinthop J, Wernsdorfer G, Noedl H, Kollaritsch H, Wernsdorfer WH (2007) Synergistic interaction between monodesbutyl-benflumetol and retinol in *Plasmodium falciparum*. *Wien Klin Wochenschr* 119 (Suppl 3): 53-59.

Starzengruber P, Wernsdorfer G, Parizek M, Rojanawatsirivet C, Kollaritsch H, Wernsdorfer WH (2007) Specific pharmacokinetic interaction between lumefantrine and monodesbutyl-benflumetol in *Plasmodium falciparum*. *Wien Klin Wochenschr* 119 (Suppl 3): 60-66.

Tasanor O, Brem B, Leitsch D, Binder M, Duchêne M, Greger H, Wernsdorfer WH (2007) Development of a pharmacodynamic screening model with *Entamoeba histolytica*. *Wien Klin Wochenschr* 119 (Suppl 3): 88-95.

Wernsdorfer WH, Congpuong K, Sirichaisinthop J, Wernsdorfer G (2007) Drug sensitivity of *Plasmodium falciparum* and *Plasmodium vivax* in the area of Mae Sot, Tak Province, northwestern Thailand. *Trop Med Health* 35: 1-9.

Woitsch B, Wernsdorfer G, Congpuong K, Rojanawatsirivet C, Sirichaisinthop J, Wernsdorfer WH (2007) Susceptibility to chloroquine, mefloquine and artemisinin of *Plasmodium vivax* in northwestern Thailand. *Wien Klin Wochenschr* 119 (Suppl 3): 76-82.

Wongsrichanalai C, Barcus MJ, Muth S, Sutamijardja A, Wernsdorfer WH (2007) A review of malaria diagnostic tools: microscopy and rapid diagnostic tests (RDT). *Am J Trop Med Hyg* 77 (Suppl 6): 119-127.

List of the Members of the SPTM

(P: university positions; G: employed by grants; KV (receipts); w.s. without salary)
 In training for "Facharzt für "Spezifische Prophylaxe und Tropenmedizin" FA

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 Secr. Christina Hössel P3/4
 Secr. Elisabeth Brunner P1/2
 Indrid Demel G/KV

Group leader:

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 Herwig Kollaritsch P (1/2)
 Harald Noedl P
 Walter Wernsdorfer w.s.
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 Eva Jeschko G
 Pamela Rendi-Wagner G
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