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**UNIVERSITÄT
BERN**

Institut für Parasitologie
der Vetsuisse-Fakultät sowie
der Medizinischen Fakultät
der Universität Bern (IPB)

Nationales Referenzlabor für Toxoplasmose
Nationales Referenzlabor für Trichinellose
Nationales Referenzlabor für Tritrichomonose
Nationales Referenzlabor für Beschälseuche
Nationales Referenzlabor für Neosporose
Nationales Referenzlabor für Besnoitiose



STS 175

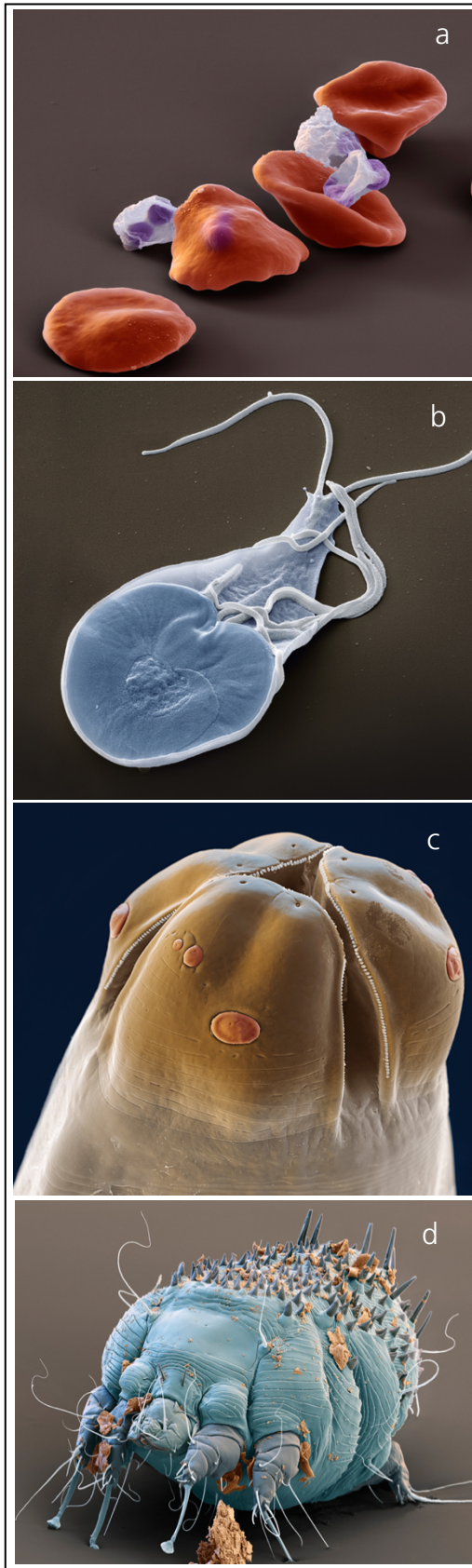
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Direktor: Prof. Dr. B. Gottstein

Jahres- und Tätigkeitsbericht 2018

(Annual scientific reports in English)

26. Berichtsjahr



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[Bildquelle: Bayer Health Care Deutschland, Animal Health, Leverkusen, 2015]

INSTITUTSBEZEICHNUNG

Institut für Parasitologie
der Vetsuisse und der Medizinischen Fakultät der Universität Bern
Departement für Infektionskrankheiten und Pathobiologie
Länggass-Strasse 122
3001 Bern

TEL +41 031 631 24 76 (Sekretariat)
+41 031 631 24 18 (Direktor)

Internet URL [http:// www.ipa.vetsuisse.unibe.ch](http://www.ipa.vetsuisse.unibe.ch)

ARBEITSGRUPPEN DES INSTITUTES

(Anstellungen per 31. Dezember 2018)

Prof. Dr. Bruno Gottstein	[bruno.gottstein@vetsuisse.unibe.ch]
Prof. Dr. Norbert Müller	[norbert.mueller@vetsuisse.unibe.ch]
Ursula Kurath	[ursula.kurath@vetsuisse.unibe.ch]
Bernadette Merkle	[bernadette.merkle@vetsuisse.unibe.ch]
Xuan Lan Vu	[xuanlan.vu@vetsuisse.unibe.ch]
PD Dr. med. vet. Walter Basso	[walter.basso@vetsuisse.unibe.ch]
Liliane Krähenbühl	[liliane.kraehenbuehl@vetsuisse.unibe.ch]
Larissa Hofmann	[larissa.hofmann@vetsuisse.unibe.ch]
Christine Salvisberg	[christine.salvisberg@vetsuisse.unibe.ch]
Caroline Müller	[caroline.mueller@vetsuisse.unibe.ch]
Prof. Dr. Andrew Hemphill	[andrew.hemphill@vetsuisse.unibe.ch]
Dr. Adriana Aguado	[adriana.aguado@vetsuisse.unibe.ch]
Dr. Rita de Amorim	[rita.deamorim@vetsuisse.unibe.ch]
Pablo Winzer	[pablo.winzer@vetsuisse.unibe.ch]
Nicoleta Anghel	[nicoleta.anghel@vetsuisse.unibe.ch]
Vreni Balmer	[vreni.balmer@vetsuisse.unibe.ch]
Prof. Dr. Britta Lundström- Stadelmann	[britta.lundstroem@vetsuisse.unibe.ch]
Dominic Ritler	[dominic.ritler@vetsuisse.unibe.ch]
Reto Rufener	[reto.rufener@vetsuisse.unibe.ch]
Prof. Dr. Norbert Müller	[norbert.mueller@vetsuisse.unibe.ch]
Prof. Dr. Bruno Gottstein	[bruno.gottstein@vetsuisse.unibe.ch]
PD Dr. Joachim Müller	[joachim.mueller@vetsuisse.unibe.ch]
PD Dr. med. vet. Walter Basso	[walter.basso@vetsuisse.unibe.ch]
Dr. Junhua Wang	[junhua.wang@vetsuisse.unibe.ch]
Dr. Ghalia Boubaker	[ghalia.boubaker@vetsuisse.unibe.ch]
Anika Meyer	[anika.meyer@vetsuisse.unibe.ch]
Dr. med. vet. Brigitte Hentrich	[brigitte.hentrich@vetsuisse.unibe.ch]
Alexandra Gerber (Sekretariat)	[alexandra.gerber@vetsuisse.unibe.ch]
A. Läderach (ITPA)	
N. Vukovic (AD)	

Institutsleitung

**Diagnostik
Humanparasitologie**

**Diagnostik
Veterinärparasitologie**

Forschung

Forschung

Forschung div.

Administration

Hausdienst

SCIENTIFIC RESEARCH REPORTS 2018

List of research grants / projects active in 2018

Swiss National Science Foundation SNSF Schweizerischer Nationalfonds SNF

- 1) SEARCH FOR NOVEL IMMUNO- AND CHEMOTHERAPEUTICAL APPROACHES TO TREAT ALVEOLAR ECHINOCOCCOSIS
Gottstein B, Hemphill A
Swiss National Science Foundation No. 31003A_1601081
Project period: 1.4.2015 – 31.3.2018
Project budget: CHF 756'000.—
- 2) THE CROSSTALK BETWEEN CHEMOTHERAPY AND IMMUNITY IN MURINE AND OVINE NEOSPOROSIS DISEASE
Hemphill A
Swiss National Science Foundation No. 310030_165782
PROJECT PERIOD: 1.4. 2016 – 31.3. 2019
PROJECT BUDGET: 678'000 CHF
- 3) FUNCTIONAL ANALYSIS OF NITROREDUCTASES FROM THE INTESTINAL PROTOZOAN PARASITE *GIARDIA LAMBLIA*
MÜLLER N
SWISS NATIONAL SCIENCE FOUNDATION No. 31003A-168330/1
PROJECT PERIOD: 1.3.2016-26.2.2019
PROJECT BUDGET: CHF 291'000.-
- 4) RUTHENIUM COMPLEXES FOR THE TREATMENT OF PROTOZOAN DISEASES OF MEDICAL AND VETERINARY IMPORTANCE
Furrer J, Gasser G, Hemphill A
Swiss National Science Foundation (Sinergia) No. CRSII5_173718
PROJECT PERIOD: 1.9. 2017 – 31.8. 2021
PROJECT BUDGET: 1'547'903 CHF
- 5) TARGETING THE METABOLISM OF *ECHINOCOCCUS MULTILOCULARIS* FOR THE DEVELOPMENT OF NOVEL DRUG TREATMENTS AND IMMUNOTHERAPEUTIC TOOLS
Lundström-Stadelmann B
SWISS NATIONAL SCIENCE FOUNDATION No. 31003A_179439
PROJECT PERIOD: 1.4.2018 - 31.3.2020
PROJECT BUDGET: 350'000 CHF

Research support by other Foundations and other funding agencies (e.g. Industry) Zusprachen Forschungsbeiträge durch andere Stiftungen sowie andere Quellen (z.B. Industrie)

- 6) UniBE ID Grant
G. Beldi & B. Gottstein
"Understanding and modulating hepatic immune responses for the treatment of alveolar echinococcosis"
Project Budget: 148'119 CHF
- 7) United States Department of Agriculture (USDA) / National Institutes of Health (NIH) grant No. 1 R01 HD080670_01
A.Hemphill (subcontractor)
"Dual use therapeutics for cryptosporidiosis, toxoplasmosis and neosporosis"
Project Budget: 115'000 CHF
Project Period: 1.6. 2014 – 31.5. 2018

- 8) Gottfried and Julia Bangerter-Rhyner-Stiftung
 B. Lundström-Stadelmann
 "Starving a deadly pathogen: The metabolism of the fox tapeworm *Echinococcus multilocularis*"
 Project Budget: 100'000 CHF
 Project Period: November 2016 - January 2020
- 9) COST CM1307 through SBF
 A. Hemphill, B. Lundström-Stadelmann
 "Anti-malarials for the chemotherapeutical treatment of Alveolar Echinococcosis"
 Project Budget: 179'841 CHF
 Project Period: 1.12.2015 - 31.3.2018
- 10) Elanco Animal Health
 A. Hemphill, J. Müller
 "Research Collaboration and laboratory Services"
 Project Budget: 421'200 CHF
 Project Period: October 2016 - December 2018
- 11) Novartis Research Foundation
 A. Hemphill
 "Toxoplasmosis: more dangerous than expected: studies on drug susceptibilities of novel parasite isolates."
 Project Budget: 60'000 CHF
 Project period: 1.11. 2018-31.10.2019
- 12) Bundesamt für Lebensmittelsicherheit und Veterinärwesen (BLV)
 C. Frey, B. Hentrich
 "Alveoläre Echinococcosis beim Schlachtschwein: Prävalenzschätzung und Erkennung von Risikofaktoren"
 Project budget: CHF 116'000.-
 Project Period: März 2017 - Juni 2019
- 13) Swiss Government Excellence Research Scholarship (BF)
 J. Dabrowska (supervision Müller N, Frey C)
 "Optimization and comparison of molecular methods for detecting *Tritrichomonas foetus* and genetic characterisation of *T. foetus* from cattle and cats"
 Project budget: CHF 24'000.-
 Project period: 1.9.2017 - 30.8.2018
- 14) Bordier Affinity Products, Crissier
 B. Gottstein
 "Development of new diagnostic tools"
 Project budget: CHF 60'000.-
 Project period: 1.1.2018-31.12.2018
- 15) Fondation Sana
 A. Hemphill
 "Anti-Malaria Wirkstoffe zur chemotherapeutischen Behandlung der alv. Echinokokose"
 Project budget: CHF 30'000.-
 Project Period: 1.12.2015 - 31.11.2018
- 16) Verein zur Förderung der Forschung im Gesundheitssektor von Lamas und Alpakas
 W. Basso, P. Zanolari
 "Epidemiologie der Toxoplasmose und Neosporose bei Neuweltkameliden in der Schweiz und Optimierung von diagnostischen Methoden"
 Project budget: CHF: 17'600.-
 Project period: 1.1.2018 - 31.12.2019

ECHINOCOCCOSIS - IMMUNOLOGY

Prof. Dr. B. Gottstein, Prof. Dr. B. Lundström-Stadelmann, Prof. Dr. A. Hemphill, Prof. Dr. N. Müller, Dr. J. Wang, PD Dr. J. Müller, R. Rufener, D. Rittler, L. Dick, A. Meyer

Cooperative investigations with: Prof. D. Vuitton, Dr. L. Millon, Dr. F. Grenouillet, Dr. J. Knapp, Besançon; Prof. P. Deplazes, Zürich; Prof. G. Beldi, Bern; Dr. C. Göpfert, Bern; Dr. B. Grüner, Ulm; Dr. K. Mätz-Rensing, Göttingen; Dr. F. Wyss, Basel; Dr. C. Wenker, Basel.

Alveolar echinococcosis (AE) is one of the clinically most severe zoonotic helminthic diseases in humans, characterized by chronic progressive hepatic damage caused by the continuous proliferation of the larval stage (metacestode) of *Echinococcus multilocularis*. The proliferative potential of the parasite metacestode tissue is dependent on the nature/function of the periparasitic immune-mediated processes of the host. Immune tolerance and/or down-regulation of immunity are marked characteristics increasingly observed at the chronic (late) stage of infection in both humans and in experimentally infected mice. AE is fatal if not treated appropriately, but the current chemotherapy based on benzimidazoles is far from optimal, and novel options for control are needed. A respective list of own reviews on this overall topic as follows:

- [Meinel TR, Gottstein B, Geib V, Keel MJ, Biral R, Mohaupt M, Brügger J. Vertebral alveolar echinococcosis - a case report, systematic analysis, and review of the literature. *Lancet Infect Dis.* 18(3):e87-e98, 2018]

To elucidate immunological mechanisms that orchestrate the interplay between the parasite and its intermediate host (mice and humans) in view of either parasite survival or host-based parasite elimination, the following projects were carried out.

The PD1/PDL1 pathway: The growth potential of the tumour-like *E. multilocularis* metacestode (causing alveolar echinococcosis, AE) is directly dependent upon the nature/function of the periparasitic adaptive host immune-mediated processes. PD-1/PD-L1 pathway (Programmed Cell Death 1), which inhibits lymphocytic proliferation in tumour development, is over-expressed at the chronic stage of AE. We tested the impact of a PD-1/PD-L1 pathway blockade on the outcome of both acute AE (peroral egg infection) and chronic AE (intraperitoneal (i.p.) metacestode inoculation). To assess the parasite proliferation potential, we measured liver lesion number for the peroral (acute) and parasite mass weight for the i.p. (chronic) infection. In both models, the parasite load was significantly decreased in response to anti-PD-L1 antibody treatment. Peroral infection was associated with fewer lesions in the liver and decreased Treg/Th2 and NKT cell responses. After i.p.-infection, decreased parasite load was associated with increased Th1/Th17 response parameters and decreased Treg responses. Our findings highly suggested that a PD1/PDL1 pathway blockade triggers the host immune responses in favour of an immune-mediated control of *E. multilocularis* proliferation.

- [Wang J, Jebbawi F, Bellanger AP, Beldi G, Millon L, Gottstein B: Immunotherapy of alveolar echinococcosis via PD-1/PD-L1 immune checkpoint blockade in mice. *Parasite Immunol.* 2018 Dec;40(12):e12596]

Tregs in primary murine infection: Using the spleen of mice that were perorally infected with *E. multilocularis* eggs, we assessed the hepatic immune-related gene expression profiles of 15 selected cytokine and chemokine genes upon by qRT-PCR, temporally covering the time span from day 21 to day 120 post infection. Comparative analyses of expression levels showed that a mixed Th1/Th2 immune response marked the early stage of infection in immune competent animals, as characterized by the concomitant presence of IFN- γ and IL-4 and their related chemokines. Subsequently, at late stage of AE, the profile extended to a combined tolerogenic mode including Foxp3, IL-10 and TGF- β as key components. Upon induction of Treg-deficiency (in a model of *E. multilocularis*-infected DEREK mice) by diphtheria toxin (DT)-administration, the parasite lesion sizes were significantly smaller in the affected livers when compared to immunocompetent control animals (infected DEREK mice without DT-treatment). Foxp3+ Tregs appear as one of the key players in immune regulatory processes favoring metacestode survival by affecting antigen presentation and suppressing Th1-type immune responses. For these reasons we suggest that affecting Foxp3+ Tregs could offer an attractive target in the development of an immunotherapy against AE.

- [Wang J, Cardoso R, Marreros N, Müller N, Lundström-Stadelmann B, Siffert M, Vuitton DA, Boué F, Lin R, Wen H, Gottstein B. Foxp3+ Tregs as a potential target for immunotherapy against primary infection with *Echinococcus multilocularis* eggs. *Infect Immun.* 2018 Jul 23. pii: IA1.00542-18. doi: 10.1128/IA1.00542-18]

Experimental vaccination: In collaboration with Fabia Wyss and Chritian Wenker (Zoo Basel), a preliminary vaccine trial was created to address, in a first step, safety parameters of two different vaccines: recEm14-3-3 and recEm95. The design included 4 groups of macaque monkeys, one control group receiving adjuvans only, one receiving recEm14-3-3, one recEm95, and another receiving recEm-14-3-3 plus recEm95 combined. So far, all animals developed a marked humoral immunity against the respective antigen(s). In parallel, a similar study was initiated at the German Primate research center (DPZ) in Göttingen (Dr. K. Mätz-Rensing), but with rhesus monkeys. Here again, humoral immunity developed well in all individuals. A future challenge experiment will have to prove the protective properties of vaccination.

• [Lampe K, Gottstein B, Becker T, Stahl-Hennig C, Kaup FJ, Mätz-Rensing K: Immunization of rhesus macaques with *Echinococcus multilocularis* recombinant 14-3-3 antigen leads to specific antibody response. *Parasitol Res.* 2017 Jan;116(1):435-43]

ECHINOCOCCOSIS - METABOLOMICS AND DRUG TREATMENT

Prof. Dr. B. Lundström-Stadelmann, Prof. Dr. A. Hemphill, Prof. Dr. B. Gottstein, Reto Rufener, Dominic Ritler, Luca Dick, Nelson Marreros, Sabrina Stöckli, Raphael Zurbriggen
Cooperative investigations with: Dr. Jia Li, Imperial College London; Dr. S. Schürch, Universität Bern; Dr. M. Heller, Universität Bern; Prof. Dr. K. Brehm and Dr. M. Spiliotis, Universität Würzburg; Prof. Dr. M. Mevissen, Vetsuisse Bern; Prof. Dr. M.V. Nora de Souza, Fundacao Oswaldo Cruz, Brasil; Prof. Dr. M. Schlitzer and G. Rennar, Universität Marburg; Prof. Dr. S. Dogget, Portland, USA; Dr. T.N.C. Wells, MMV Geneva; Prof. Dr. P. Deplazes, Vetsuisse Zürich; Dr. D. Joekel, Vetsuisse Zürich; Dr. B. Grüner, Universität Ulm; Prof. Dr. D. Czock, Universität Heidelberg; Prof. Dr. T. Junghanss and Dr. M. Stojkovic, Universität Heidelberg; Dr. S. Dion, Université de Rennes; Dr. A. Casulli, Istituto Superiore di Sanita, Rome.

(i) Repurposing of drugs for the treatment of alveolar echinococcosis

The metacestode stage of the fox tapeworm *Echinococcus multilocularis* causes the lethal disease alveolar echinococcosis. Current chemotherapeutic treatment options are based on benzimidazoles (albendazole and mebendazole), which are insufficient and hence alternative drugs are needed. We have established an *in vitro* drug screening pipeline, which allows us to perform whole-organism screenings for anti-echinococcal drugs, as well as the further investigation of active compounds. In one study, we screened the 400 compounds of the Medicines for Malaria Venture (MMV, collaboration TNC Wells) Pathogen Box against *E. multilocularis* metacestodes. We identified ten new compounds with activity against the parasite. The anti-theilerial drug buparvaquone and the endochin-like quinolone ELQ-400 were the most promising compounds against *in vitro* cultured *E. multilocularis* metacestodes. Both drugs were less toxic against mammalian cells than against the parasite. Interestingly, buparvaquone was much less active under anaerobic conditions and seemed to affect mitochondria. To investigate the effect of buparvaquone on mitochondrial respiration, we established a system based on isolated *E. multilocularis* cells using the Seahorse XFp Analyzer and we demonstrated inhibition of the cytochrome bc₁ complex by buparvaquone. Mice with secondary alveolar echinococcosis were treated with buparvaquone, but the drug failed to reduce the parasite burden *in vivo*. Future studies will reveal whether improved formulations of buparvaquone could increase its effectiveness. In addition, novel derivatives of ELQs are tested (collaboration Prof. Dr. S. Dogget) to further investigate the bc₁ complex of *E. multilocularis* cells.

• [Rufener R, Dick L, D'Ascoli L, Ritler D, Hizem A, Wells TNC, Hemphill A, Lundström-Stadelmann B. Repurposing of an old drug: In vitro and in vivo efficacies of Buparvaquone against *Echinococcus multilocularis*. *Int J Parasitol.* 2018 Dec. doi: 10.1016/j.ijppdr.2018.10.011]

In another study we followed our previous investigations on the anti-malarial drug mefloquine, where mefloquine was shown to be active against *E. multilocularis* metacestodes *in vitro*, and in mice infected by intraperitoneal inoculation of metacestodes when administered at 100 mg/kg by oral gavage twice a week for 12 weeks. In the present study, the same dosage regime was applied in mice infected via oral uptake of eggs representing the natural route of infection. We observed a significantly reduced parasite load in mefloquine-treated animals. Assessment of mefloquine plasma concentrations by HPLC (collaboration Prof. Dr. M. Mevissen) and modeling (collaboration Prof. Dr. D. Czock) showed levels were close to concentrations achieved in humans during long-term weekly dosage of 250 mg (dose applied for malaria prophylaxis). *In vitro* structure-activity relationship analysis of mefloquine and

ten derivatives revealed that none of the derivatives exhibited stronger activities than mefloquine (collaboration Prof. Dr. M.V. Nora de Souza). Structure-activity analysis was in line with the anti-malarial activity of mefloquine and further derivatives will be tested in order to further refine this analysis in the future.

- [Rufener R, Ritler D, Zielinski J, Dick L, da Silva ET, da Silva Araujo A, Joekel DE, Czock D, Goepfert C, Marques Moraes A, de Souza MVN, Müller J, Mevissen M, Hemphill A, Lundström-Stadelmann B. 2018. Activity of mefloquine and mefloquine derivatives against *Echinococcus multilocularis*. International Journal of Parasitology Drugs and Drug Resistance. doi.org/10.1016/j.ijpddr.2018.06.004]

(ii) Identification of novel drug targets by metabolomics

Apart from the above-described approach of whole-organism screening to identify new drugs, we study the basic metabolism of the parasite, in order to increase basic knowledge, and possibly find new targetable pathways. We do this based on the *in vitro* culture model by assessment of metabolomic and proteomic changes induced by the parasite in culture medium. Metabolites were assessed by nuclear magnetic resonance (NMR, collaboration Dr. J. Li) and liquid chromatography mass spectrometry (LC-MS, collaboration Dr. M. Heller). One interesting aspect we have identified in 2018, is the very high consumption of the amino acid threonine by *E. multilocularis*. We showed that threonine addition to *in vitro* cultures increased the growth of the parasite and that threonine is not simply used in high amounts for protein synthesis. We will further investigate, why the parasite is consuming so much threonine. Another highly interesting aspect is an old pathway we "rediscovered", the malate dismutation. It is an oxygen-independent mitochondrial pathway for energy generation, and mammals do not employ this pathway. As an end product of the pathway, huge amounts of succinate are released into the culture media, and this we could detect *in vitro*. We will further identify the molecular activities and details of the pathway with help of our *in vitro* culture of *E. multilocularis*, and try to identify respective inhibitors.

APICOMPLEXAN PARASITES: NEOSPOROSIS, TOXOPLASMOSIS, BESNOITIOSIS

Prof. Dr. A. Hemphill, PD Dr. Joachim Müller, PD DR. Walter Basso Dr. Adriana Aguado, Prof. Dr. Norbert Müller, Dr. Afonso Basto, Dr. Rita de Amorim Cardoso, Vreni Balmer, Pablo Winzer, Nicoleta Anghel, Anina Bär

Collaborative investigations with: PD Dr. Julien Furrer, Department of Chemistry, Bern; Prof. Gilles Gasser, Paris, France; Prof. Adrian Hehl, University of Zürich; Prof. Alexandre Leitao, Lisbon, Portugal; Dr. Helder Cortes, Evora, Portugal; Prof. Luis Ortega-Mora & Prof. Gema Alvarez, Madrid, Spain; Dr. Gereon Schares, Riems, Germany; Prof. Walter Däubener, Düsseldorf, Germany; Prof. Wes VanVoorhis, Prof. Kajode K Ojo, Seattle; USA; Prof. Richard Haynes, Potchefstroom, South Africa; Bern; Prof. Damer Blake, London, GB; Prof. Peter Buetikofer, IBMM, Bern; Prof. Volker Heussler, IZB, Bern; Prof. Stone Dogget, Portland, USA; Dr. Timothy Wells & Dr. Benoit Laleu, MMV, Geneva; Prof. Isabel Roditi, Dr. Arunasalam Naguleswaran, IZB, Bern; Dr. Manfred Heller, DKF Bern, Dr. Parham Sendi, IFIK, Bern; Prof. Anna Oevermann, Bern; Dr. Kerry Woods & Dr. Philipp Olias, ITPA, Bern

The group is working on cyst-forming apicomplexan parasites that infect farm animals and thus have a considerable economic impact, including *Neospora caninum*, *Toxoplasma gondii*, and *Besnoitia besnoiti*. The identification of targets that could be used for vaccination and/or treatment is of major interest.

In terms of vaccination, we have earlier identified and characterized a series of *N. caninum* vaccine candidates located either on the surface, or within micronemes, rhoptries and dense granules. In non-pregnant mouse models, we assessed respective bacterially expressed recombinant antigens or DNA vaccines for protection against infection and disease, and several promising vaccine candidates were identified. However, most of these initially promising vaccine candidates did not confer protection in the pregnant mouse model. We found that pregnancy-associated immunomodulation can reprogram a polarized protective immune response generated prior to pregnancy, and this highlights the necessity of inducing the adequate Th1/Th2 balance to confer protection during pregnancy. We therefore decided to exploit the crosstalk between innate and adaptive immunity and used an adjuvant that would target Toll-like receptor 2 (TLR2) and would initiate more balanced Th1/Th2 immune responses. In a recent study employing a pregnant mouse model we showed that engagement of TLR2 via Oprl-protein leads to improved immune responses, and vaccination with a cocktail of Oprl-ROP2, Oprl-

ROP40 and Oprl-PDI (O-Ags) conferred significant protection against clinical disease (40% survival) as well as vertical transmission in pups.

- [Aguado-Martínez A, Basto AP, Tanaka S, Ryser LT, Nunes TP, Ortega-Mora LM, Arranz-Solís D, Leitão A, Hemphill A. Immunization with a cocktail of antigens fused with Oprl reduces *Neospora caninum* vertical transmission and postnatal mortality in mice. *Vaccine*. Epub 2018 Nov 27. PubMed PMID: 30497830]

The group was also involved in the characterization of a multi-epitope peptide with selective MHC-binding capabilities encapsulated in PLGA nanoparticles, using predicted T and B cell epitopes of SAG1, AMA1, ROP2, and GRA4 proteins. The expressed protein was encapsulated in PLGA nanoparticles or emulsified in alum. Vaccinated mice challenged with the *T. gondii* RH strain, both with and without PLGA, had greater Th1 immune responses, increased survival rates, antibody titers, and IFN- γ and IL-2 levels than controls, while the alum-adsorbed vaccine stimulated a Th2-type humoral immune response.

- [Roozbehani M, Falak R, Mohammadi M, Hemphill A, Razmjou E, Meamar AR, Masoori L, Khoshmirsafa M, Moradi M, Gharavi MJ. Characterization of a multi-epitope peptide with selective MHC-binding capabilities encapsulated in PLGA nanoparticles as a novel vaccine candidate against *Toxoplasma gondii* infection. *Vaccine*. 2018 Oct 1;36(41):6124-6132]

Drug repurposing was applied in order to identify novel drugs for the treatment of infections with *N. caninum*, *T. gondii* and *B. besnoiti*. We demonstrated excellent in vitro activities of novel artemisinin and decoquinate derivatives against *N. caninum* and *T. gondii* (Beteck et al., 2018), and buparvaquone, diclazuril and decoquinate against *B. besnoiti* (García Lunar et al., 2018). In vitro and in vivo studies in pregnant mice demonstrated the usefulness of a series of endochin-like quinolones (ELQs) against *N. caninum* (Anghel et al., 2018). We also screened both *T. gondii* and *N. caninum* against novel ruthenium complexes previously generated for use in cancer, and demonstrated that ruthenium complexes target the mitochondrion in both cancer cells and *N. caninum* tachyzoites, but were not sufficiently active in vitro to inhibit dissemination in mice experimentally infected with *N. caninum*.

Bumped kinase inhibitors (BKIs) represent a very promising class of compounds, and we have previously described the efficacy of several BKIs against *N. caninum* and *T. gondii* in vitro and in vivo in pregnant mice. One of these compounds, BKI-1553, was taken one step further, and was investigated in a pregnant neosporosis sheep model at the Universidad Complutense in Madrid, and the safety and efficacy of BKI-1553 was confirmed, putting BKIs on the map as future agents for the treatment of neosporosis in small ruminants.

- [Sánchez-Sánchez R, Ferre I, Re M, Vázquez P, Ferrer LM, Blanco-Murcia J, Regidor-Cerrillo J, Pizarro Díaz M, González-Huecas M, Tabanera E, García-Lunar P, Benavides J, Castaño P, Hemphill A, Hulverson MA, Whitman GR, Rivas KL, Choi R, Ojo KK, Barrett LK, Van Voorhis WC, Ortega-Mora LM. 2018. Safety and efficacy of the bumped kinase inhibitor BKI-1553 in pregnant sheep experimentally infected with *Neospora caninum* tachyzoites. *Int J Parasitol – Drug Drug Res*]
- [Beteck R, Seldon R, Coertzen D, van der Watt ME, Reader J, Mackenzie JS, Lamprecht DA, Abraham M, Eribez K, Müller J, Rui F, Zhu G, de Granos RV, Williams ID, Smit FJ, Seyn JC, Winzeler EA, Hemphill A, Birkholtz LM, Warner D, N'Da DD, Haynes RK. 2018. Accessible and distinct decoquinate derivatives highly active against *M. tuberculosis* and apicomplexan parasites. *Nature Comm Chem*, 1:62 | DOI: 10.1038/s42004-018-0062-7]
- [Anghel N, Balmer V, Müller J, Winzer P, Aguado-Martínez A, Roozbehani M, Pou S, Nilsen A, Riscoe M, Dogget JS, Hemphill A. 2018. Endochin-Like Quinolones Exhibit Promising Efficacy Against *Neospora caninum* in vitro and in Experimentally Infected Pregnant Mice. *Front Vet Sci* 5: 285. doi: 10.3389/fvets.2018.00285]

GIARDIASIS

Prof. Dr. N. Müller, PD Dr. J. Müller, Dr. D. Leitsch (3/2014-3/2016 at the IPB, senior Postdoc and Schrödinger'scholarship holder financed by the 'Austrian SWF), Prof. Dr. A. Hemphill
Cooperative investigation with: Prof. Dr. A. Hehl, S. Rout, Institute of Parasitology; Zürich and Dept. of Chemistry and Biochemistry, University Berne; Dr. David Leitsch (since 4/2016), Prof. J. Walochnik; Prof. Michael Duchêne; Dept. of Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Vienna, Austria, Dr. M. Vermathen and Prof. Dr. P. Vermathen, Departement for Chemistry and Biochemistry, University of Berne, .PD Dr. J. Furrer, Department of Chemistry, University of Berne, PD Dr. M. Heller, Proteomics & Mass Spectrometry Core Facility, University of Berne, Prof. Dr. R. Leurs, Medicinal Chemistry, Amsterdam Institute of Molecules, Medicines & Systems, VU University Amsterdam, The Netherlands

Functional analysis of nitroreductases and molecular and cellular mechanisms involved in nitro drug

resistance formation in the intestinal parasite *Giardia lamblia*.

The intestinal protozoan parasite *Giardia lamblia* is a causative agent of diarrhea in humans and various animal species. Currently, treatment of giardiasis mostly relies on the use of nitro drugs such as metronidazole (MET) or nitazoxanide (NTZ), respectively. Unfortunately however, many clinical cases of giardiasis exhibiting resistance particularly against MET have been reported. Our previous research focused on a pre-characterized nitro drug-sensitive versus -resistant in vitro cultivation model of *G. lamblia* demonstrated that nitro drug resistance formation is associated with significant alterations in the expression of two nitroreductases (NR1 and NR2). In subsequent studies, NR1 turned out to be directly involved in activation of nitro drugs whereas NR2 seemed to possess an antagonistic function in that it inactivated these drugs. These findings were achieved by overexpression of the two enzymes in *Escherichia coli* and by subsequent testing of the enzymatic activities in the recombinant bacterial system. In addition, functional assays with purified recombinant NR1 and NR2 revealed that both nitroreductases form a complex and have their strongest activities on the quinone menadione (vitamin K3) and FAD, but also reduction of nitro compounds including the nitro drugs MET and NTZ was observed.

As outlined above, the biological function of NR1 and NR2 could be the reduction of quinones and other heterocyclic compounds in essential steps of intermediate metabolism of the parasite. In the present project we raised two main questions: (i) what is the evolutionary benefit of the presence of NR1 and NR2 as well as two other enzymes with potential nitroreductase activity, namely NRfam (in the following referred as to NR3) and thioredoxin reductase (TrxR) in the parasite, and (ii) in as much are these enzymes involved in giardial nitro drug resistance formation?

In particular, we (re-)investigated NR1, NR2, NR3 and TrxR, regarding their enzymatic characteristics, their potential biological function and their participation in nitro drug resistance formation in *G. lamblia*. While NR2 and NR3 were shown to be underrepresented or even absent in *G. lamblia* trophozoites, NR1 and TrxR were clearly detectable and exhibited oxidoreductase and/or nitroreductase activity.

Various metabolic parameters investigated support the hypothesis that resistance formation to nitro drugs is due to a reduction of nitro drug activation rather than to a nitroreductase-mediated elimination of toxic nitro radicals. Possibly, this also means that detoxification of nitro compounds by FAD-dependent nitroreductases and oxidoreductase activities per se is not the only mechanism for protection of trophozoites from nitrosative stress potentially occurring inside the intestinal habitat of the parasite. Here, we evidenced that the reduction of FAD levels and thus reduction of FAD-dependent nitroreductase and also oxidoreductase activities constitutes another important resistance mechanism that avoids the formation of toxic nitro intermediates and/or radicals.

Finally, we found that resistance to nitro drugs in *G. lamblia* did not correlate with a specific pattern of differentially expressed proteins and therefore it seems not to be the result of a directed process. In terms of resistance formation, our results rather suggest the appearance of several distinct anti-nitrosative stress strategies depending on both the *G. lamblia* strain and the particular nitro drug investigated. Here, particularly a down-regulation of the energy production and of intermediate metabolism leading to reduced parasite growth most likely associated with lower uptake/activation of nitro drugs has been mentioned as an alternative mechanism to resist nitrosative stress conditions. Furthermore, resistance formation within *G. lamblia* is supposed to involve clonal selection and expansion of resistant variant-types within a pre-existing and epigenetically pre-determined mix of trophozoites as consequence of nitro drug pressure.

From the evolutionary point of view, we generated strong evidence that nitroreductases provide at least two advantages in that *G. lamblia* gains (i) a higher potential to recycle NAD(P) as electron acceptors for the (fermentative) energy and intermediary metabolism, and (ii) the possibility to inactivate toxic xenobiotics produced by microorganisms living in concurrence inside the intestinal habitat.

- [Müller J., Braga S., Heller M., Müller N. 2019. Resistance formation to nitro drugs in *Giardia lamblia*: No common markers identified by comparative proteomics. International Journal for Parasitology: Drug and Drug Resistance 9, 112-119.]
- [Müller, J., Hemphill, A. & Müller, N. Physiological aspects of nitro drug resistance in *Giardia lamblia*. International Journal for Parasitology: Drug and Drug Resistance 8, 271-277, 2018.]
- [Vermathen M., Müller, J., Furrer J., Müller N, Vermathen P. (1)H HR-MAS NMR spectroscopy to study the metabolome of the protozoan parasite *Giardia lamblia*. Talanta 188, 429-441, 2018.]
- [Müller J. and Müller, N. (2019) Nitroreductases of bacterial origin in *Giardia lamblia*: Potential role in detoxification of xenobiotics. Submitted]

OTHER PROJECTS 2018

(Projects & cooperations funded / supported by extramural grants)

OPTIMISATION AND COMPARISON OF MOLECULAR METHODS FOR DETECTING *TRITRICHOMONAS FOETUS* AND GENETIC CHARACTERISATION OF *T. FOETUS* ISOLATES FROM CATTLE AND CATS

Prof. Dr. N. Müller, PD Dr. C. Frey, Supervision of Joanna Dabrowska ("Swiss Government Excellence Research Scholarship holder at the IPB and doctoral student at the Department of Parasitology, National Veterinary Research in Pulawy, Poland).

Tritrichomonas foetus is a sexually transmitted protozoan parasite that has been identified as an important cause of infertility and abortion in cattle. Several years ago, also *T. foetus* infections in cats supposedly transmitted via the fecal-oral route and associated with lymphocytic inflammation, neutrophilic colitis, and chronic large bowel diarrhoea were identified as an issue of considerable relevance in veterinary medicine. Here, testing of samples via in vitro-cultivation followed by confirmatory PCR specific for *T. foetus* is currently considered the most successful concept for a reliable diagnosis of bovine and feline tritrichomonosis.

In the field of parasitology, loop-mediated isothermal amplification (LAMP) of DNA was successfully applied for molecular diagnosis as an alternative for PCR. LAMP is a simple, rapid, and cost-effective method that basically can be executed without sophisticated equipment by performing a multiple primer-based DNA amplification reaction under isothermal conditions in a transparent tube and a subsequent inspection of a visible colour change by an appropriate dye gradually interchelating into the amplifying double stranded DNA. Referring to various potential methodical advantages, our present study addressed the question if LAMP can serve as a practical alternative to PCR as far as diagnosis of tritrichomonosis is concerned. For this purpose, a LAMP assay specific for *T. foetus* was developed and was subsequently compared to conventional and real-time PCR tests currently applied in our lab for detection of the parasite in bovine and feline samples. Respective investigations revealed that *T. foetus*-LAMP had the same diagnostic sensitivity and specificity as the corresponding real-time PCR and thus can be considered a valuable and practicable assay for diagnosis of bovine and feline tritrichomonosis even under field conditions where no sophisticated lab equipment is available.

IMMUNODIAGNOSIS OF HUMAN ANISAKIDOSIS

Prof. Dr. N. Müller, Prof. Dr. B. Gottstein, Dr. G. Boubaker in cooperation with Maciej Kochanowski, Department of Parasitology, National Veterinary Research in Pulawy, Poland (3-months short-term scientific mission at IPB) and Dr. M. Á. Gómez-Morales, Dept. of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy.

Serodiagnosis of human anisakidosis is presently hampered by the current lack of standardised serological assays that allow sensitive and specific detection of Anisakidae-specific antibodies in human patients. In the present study, we comparatively evaluated the diagnostic value (by IgG-ELISA) of excretory-secretory antigens (ESAg) of *Anisakis simplex*, *Pseudoterranova decipiens* and *Contracaecum osculatum*, representing the most frequently found genera responsible for human infection. In addition, we tested also a mix of the three ES preparations (Mix-ESAg) as well as two recombinant allergens of *A. simplex*, rAni s 1 and rAni s 7. ES antigen from *C. osculatum* yielded the best diagnostic performance in IgG-ELISA-based serodiagnosis of the Spanish anisakidosis patients investigated in this study (relative serodiagnostic sensitivity 100%; specificity 89%) as compared to *A. simplex* ES-antigen (93% versus 57%) and *P. decipiens* (67% versus 93%) or a mix of the three ES antigens (100% versus 44%), respectively. Cross-reactions of *C. osculatum* ES antigen with serum-antibodies from patients suffering from other helminth infections were rare and were exclusively found with few sera from toxocarosis, ascariasis, and filariasis patients. The two recombinant allergens rAni s 1 and rAni s 7 did not prove sufficiently sensitive and specific in order to justify a further evaluation of these antigens regarding their suitability in IgG-ELISA-based serodiagnosis of human anisakidosis. In conclusion, the *C. osculatum*-ESAg-ELISA remains as key candidate to be further assessed for the serodiagnosis of symptomatic anisakidosis in different endemic regions.

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TECHNICAL SERVICES IN RESEARCH

ELECTRON MICROSCOPY

Preparative methods for basic electron microscopical techniques and immunogold-labeling are available. TEM access is ensured at the Institute of Anatomy at the Medical Faculty, University of Bern, SEM is carried out at the Electron Microscope Laboratory of the Department of Chemistry, University of Bern.

PUBLIKATIONEN 2018

Peer-reviewed scientific articles (2018)

- Aguado-Martínez A, Basto AP, Tanaka S, Ryser LT, Nunes TP, Ortega-Mora LM, Arranz-Solís D, Leitão A, Hemphill A. Immunization with a cocktail of antigens fused with Opr1 reduces *Neospora caninum* vertical transmission and postnatal mortality in mice. *Vaccine*. 2018. doi: 10.1016/j.vaccine.2018.11.060. Epub 2018 Nov 27.
- Anghel N, Balmer V, Müller J, Winzer P, Aguado-Martinez A, Roozbehani M, Pou S, Nilsen A, Riscoe M, Doggett JS, Hemphill A. Endochin-Like Quinolones Exhibit Promising Efficacy Against *Neospora Caninum* in vitro and in Experimentally Infected Pregnant Mice. *Front Vet Sci*. 2018 Nov 19;5:285.
- Barkati S, Gottstein B, Müller N, Sheitoyan-Pesant C, Metrakos P, Chen T, Garceau R, Libman MD, Ndao M, Yansouni CP: First Human Case of Metacestode Infection Caused by *Versteria* sp. in a Kidney Transplant Recipient. *Clin Infect Dis*. 2019 Feb 1;68(4):680-683.
- Basso W, Grandt LM, Magnenat AL, Gottstein B, Campos M. *Strongyloides stercoralis* infection in imported and local dogs in Switzerland: from clinics to molecular genetics. *Parasitol Res*. 2018 Dec 14. doi: 10.1007/s00436-018-6173-3.
- Beteck R, Seldon R, Coertzen D, van der Watt ME, Reader J, Mackenzie JS, Lamprecht DA, Abraham M, Eribez K, Müller J, Rui F, Zhu G, de Granos RV, Williams ID, Smit FJ, Seyn JC, Winzeler EA, Hemphill A, Birkholtz LM, Warner D, N'Da DD, Haynes RK. 2018. Accessible and distinct decoquinone derivatives highly active against *M. tuberculosis* and apicomplexan parasites. *Nature Comm Chem*, 1:62 | DOI: 10.1038/s42004-018-0062-7.
- Cardoso R, Wang J, Müller J, Rupp S, Leitão A, Hemphill A. Modulation of cis- and trans- Golgi and the Rab9A-GTPase during infection by *Besnoitia besnoiti*, *Toxoplasma gondii* and *Neospora caninum*. *Exp Parasitol*. 2018 Apr;187:75-85.
- Dawoody Nejad L, Serricchio M, Jelk J, Hemphill A, Bütikofer P. TbLpn, a key enzyme in lipid droplet formation and phospholipid metabolism, is essential for mitochondrial integrity and growth of *Trypanosoma brucei*. *Mol Microbiol*. 2018 Apr 21. doi: 10.1111/mmi.13976. [Epub ahead of print].
- Frey CF, Eicher R, Raue K, Strube C, Bodmer M, Hentrich B, Gottstein B, Marreros N: Apparent prevalence of and risk factors for infection with *Ostertagia ostertagi*, *Fasciola hepatica* and *Dictyocaulus viviparus* in Swiss dairy herds. *Vet Parasitol*. 250:52-59. doi: 10.1016/j.vetpar.2017.12.004 (2018).
- García-Lunar P, Schares G, Sanz-Fernández A, Jiménez-Meléndez A, García-Soto I, Regidor-Cerrillo J, Pastor-Fernández I, Hemphill A, Fernández-Álvarez M, Ortega-Mora LM, Álvarez-García G. Development and characterization of monoclonal antibodies against *Besnoitia besnoiti* tachyzoites. *Parasitology*. 2018 doi: 10.1017/S0031182018001336. Epub 2018 Aug 16.

- Jiménez-Meléndez A, Rico-San Román L, Hemphill A, Balmer V, Ortega-Mora LM, Álvarez-García G. Repurposing of commercially available anti-coccidials identifies diclazuril and decoquinatate as potential therapeutic candidates against *Besnoitia besnoiti* infection. *Vet Parasitol.* 2018 Sep 15;261:77-85.
- Joekel DE, Lundström-Stadelmann B, Müllhaupt B, Hemphill A, Deplazes P. Evaluation of kinase-inhibitors nilotinib and everolimus against alveolar echinococcosis in vitro and in a mouse model. *Experimental Parasitology.* 2018. Apr 3. pii: S0014-4894(17)30572-6. doi: 10.1016/j.exppara.2018.04.002.
- Kegler K, Nufer U, Alic A, Posthaus H, Olias P, Basso W. Fatal infection with emerging apicomplexan parasite *Hepatozoon silvestris* in a domestic cat. *Parasites & Vectors.* 2018 Jul 20; 11(1):428.
- Lippuner C., Ramakrishnan C., Basso W., Schmid MW., Okoniewski M., Smith NC., Hässig M., Deplazes P., Hehl AB. RNA-Seq analysis during the life cycle of *Cryptosporidium parvum* reveals significant differential gene expression between proliferating stages in the intestine and infectious sporozoites. *International Journal for Parasitology.* 2018 48: 413-422.
- Liu J, Peirasmaki D, Ma'ayeh S, Lundström-Stadelmann B, Hellman L and SG Svärd. Secreted *Giardia intestinalis* cysteine proteases disrupt intestinal epithelial cell junctional complexes and degrade chemokines. *Virulence.* 2018; 9(1): 879–894. doi: 10.1080/21505594.2018.1451284.
- Maksimov P, Basso W, Zerweck J, Schutkowski M, Reimer U, Maksimov A, Conraths FJ, Schares G.. Analysis of *Toxoplasma gondii* clonal type-specific antibody reactions in experimentally infected turkeys and chickens. *International Journal for Parasitology.* 2018 48: 845-856.
- Meinel TR, Gottstein B, Geib V, Keel MJ, Biral R, Mohaupt M, Brügger J. Vertebral alveolar echinococcosis - a case report, systematic analysis, and review of the literature. *Lancet Infect Dis.* 18(3):e87-e98. doi: 10.1016/S1473-3099(17)30335-3 (2018).
- Müller J, Manser V, Hemphill A. In vitro treatment of *Besnoitia besnoiti* with the naphto-quinone buparvaquone results in marked inhibition of tachyzoite proliferation, mitochondrial alterations and rapid adaptation of tachyzoites to increased drug concentrations. *Parasitology.* 2018 doi: 10.1017/S0031182018000975. Epub 2018 Jun 20.
- Müller, J, Hemphill A, Müller N. Physiological aspects of nitro drug resistance in *Giardia lamblia*. *International Journal for Parasitology: Drugs and Drug Resistance* 8, 271-277, doi: 10.1016/j.ijpddr.2018.04.008 (2018).
- Roosbehani M, Falak R, Mohammadi M, Hemphill A, Razmjou E, Meamar AR, Masoori L, Khoshmirsafa M, Moradi M, Gharavi MJ. Characterization of a multi-epitope peptide with selective MHC-binding capabilities encapsulated in PLGA nanoparticles as a novel vaccine candidate against *Toxoplasma gondii* infection. *Vaccine.* 2018 Oct 1;36(41):6124-6132.
- Rufener R, Dick L, D'Ascoli L, Ritler D, Hizem A, Wells TNC, Hemphill A, Lundström-Stadelmann B. Repurposing of an old drug: In vitro and in vivo efficacies of Buparvaquone against *Echinococcus multilocularis*. *Int J Parasitol.* 2018 Dec. doi: 10.1016/j.ijpddr.2018.10.011.
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- Schares G, Jutras C, Bärwald A, Basso W, Maksimov A, Schares S, Tuschy M, Conraths FJ, Brodeur V. *Besnoitia tarandi* in Canadian woodland caribou - Isolation, characterization and suitability for serological tests. *International Journal for Parasitology: Parasites and Wildlife* 2018 8:1-9.

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- Wang J, Cardoso R, Marreros N, Müller N, Lundström-Stadelmann B, Siffert M, Vuitton DA, Boué F, Lin R, Wen H, Gottstein B. Foxp3+ Tregs as a potential target for immunotherapy against primary infection with *Echinococcus multilocularis* eggs. *Infect Immun*. 2018 Jul 23. pii: IAI.00542-18. doi: 10.1128/IAI.00542-18. [Epub ahead of print] (2018).
- Wang J, Goepfert C, Mueller N, Piersigilli A, Lin R, Wen H, Vuitton DA, Vuitton L, Mueller C, Gottstein B. Larval *Echinococcus multilocularis* infection reduces dextran sulphate sodium-induced colitis in mice by attenuating T helper type 1/type 17-mediated immune reactions. *Immunology*. 154(1):76-88 (2018).
- Wang J, Jebbawi F, Bellanger AP, Beldi G, Millon L, Gottstein B: Immunotherapy of alveolar echinococcosis via PD-1/PD-L1 immune checkpoint blockade in mice. *Parasite Immunol*. 2018 Dec;40(12):e12596.

Peer-reviewed Reviews, book-chapters and other (peer-reviewed) publications (2018), including books (2018)

- Basso W. (2018). Chapter "Besnoitiosis" in Coetzer J.A.V. and Tustin R.C. (Eds.) *Infectious Diseases of Livestock*. Part I. www.anipedia.org/publications/besnoitiosis/116.
- Olias P, Dettwiler I, Hemphill A, Deplazes P, Steiner A, Meylan M. [The significance of cryptosporidiosis for the health of calves in Switzerland]. *Schweiz Arch Tierheilkd*. 2018 Jun;160(6):363-374.

VORTRÄGE & POSTER (P) 2018

2018

- Anghel Nicoleta, Winzer P, Hemphill A. Comparative study between pregnant mouse interference test and zebrafish embryo development test: a possible replacement in anti-parasitic chemotherapy trials? *Fishclub Bern seminar series*. 29.03.2018.
- Barkati S, Gottstein B, Mueller N, Sheitoyan-Pesant C, Chen T, Metrakos P, Ndao M, Libman M, Yansouni CP: First human case of metacestode larval infection caused by *Versteria* sp. in a renal transplant recipient. *ECCMID*, Madrid, Spain, 21 - 24 April 2018 (P).
- Basso W, Grandt LM, Campos M: *Strongyloides stercoralis* infection in imported and local dogs in Switzerland. *Jahrestagung der DVG-Fachgruppe „Parasitologie und parasitäre Krankheiten“*, Gießen, Germany, 2.-4.7.2018.
- Basso W, Wunderwald C, Gottstein B: Evaluation of the PrioCHECK *Trichinella* AAD kit to detect *T. britovi*, *T. spiralis* and *T. pseudospiralis* in muscle tissues of domestic pigs by the automated digestion method *Trichomatic-TM35*. 13th Workshop of National Reference Laboratories for Parasites, Rome, Italy, 24-25.5.2018.
- Basso W: Cyst-forming coccidian parasites in veterinary medicine: clinical, diagnostic and epidemiological aspects. *Training Course for Diplomates and Residents of the European Veterinary Parasitology College (EVPC) "Very Important Parasites in Zurich – from fundamental to applied research"*, Zurich, Switzerland, 14.September 2018.
- Basso W: Protozoen beim Schwein: Ein Update. 6. Schweizerische Tierärztetagung 2018, Basel, 25.-27.April 2018.

- Basso W: Strongyloidose beim Hund –eine neu auftretende Krankheit? Henry Schein Animal Health/ Provect AG Open-House Days, Lyssach, 9.-10.November 2018.
- Basso W: Toxoplasmose bei Klein und Grosstieren Henry Schein Animal Health/ Provect AG Open-House Days, Lyssach, 9.-10.November 2018.
- Basso W., Gottstein B: Parasitologie in Theorie und Praxis für TPAs (tiermedizinische PraxisassistentInnen). Henry Schein Animal Health/ Provect AG, Lyssach, 13.September 2018.
- Csokai J, Basso W, Heusinger A, Bobadova M, Müller E. Filial infection in the thoracic cavity of a common bat (*Hypsugo savii*) Jahrestagung der DVG-Fachgruppe „Parasitologie und parasitäre Krankheiten“, Gießen, Germany, 2.-4.7.2018.
- Gottstein B: Experimental and applied immunology in alveolar echinococcosis. Immunology seminar, University of Rennes, 21 November 2018.
- Gottstein B: Research review on parasitoses. Key noote lecture, SSTMP doctoral/PhD meeting, Sigriswil, November 1-2, 2018.
- Hemphill A, Augado-Martinez A, Winzer P. Bumped kinase inhibitor 1294 induces the formation of multinucleated complexes and alters protein expression in *Neospora caninum*. Deutsche Gesellschaft für Parasitologie Annual Meeting, Berlin 21.03.2018 (P).
- Hemphill A. Drug and drug targets for the treatment of *Toxoplasma gondii* infections. CIISA congress, Faculty of Veterinary Medicine, Lisbon. 16.11.2018.
- Hemphill A. Drugs and drug targets in pregnant models for toxoplasmosis and neosporosis. European coccidiosis discussion group, Royal Veterinary College London. 17.05.2018.
- Hemphill A. Studies on novel preventive and therapeutic tools to tackle diseases caused by apicomplexans parasites. Seminarios investigación platera, Universidad Complutense de Madrid, Spain, Madrid, 24.04.2018.
- Hemphill A. Vaccination against neosporosis - studies in the mouse model. Invited seminar. Royal Veterinary College London, 16.05.2018.
- Lundström-Stadelmann B, Frey C. Presentation for interview for Professorship in Parasitology at Vetsuisse Bern: Helminth control: from the field to the molecule and back, Vetsuisse Bern, CH, May 31, 2018.
- Lundström-Stadelmann B. "Career experience report", VetMENT kick-off meeting, Bern, 20.4.2018
- Lundström-Stadelmann B. To live or let die: novel treatments against parasitic diseases. Habilitation lecture, Vetsuisse Faculties Bern and Zürich, Bern, Switzerland, Mar. 15, 2018.
- Lundström-Stadelmann B: Seminar an der Universität Rennes, Frankreich, im Rahmen des Programms " Master Microbiologie fondamentale et appliquée", 21 November 2018.
- Müller J, Hemphill A, Braga S, Heller M, Müller N. Physiology and proteomics of nitro drug resistance in *Giardia lamblia*. Joint Annual Meeting 2018 SSI | SSHH | SSTMP | SSTTM, Interlaken, 13.9.2018.
- Müller J, Hemphill A, Müller N. Phenotypic characterization of a nitro drug resistant *Giardia lamblia* strain, Host-Pathogen Interactions and Drug Resistance Symposium, Bern, Switzerland, 4.5.2018.
- Müller J, Hemphill A, Müller N. Phenotypic characterization of a nitro drug resistant *Giardia lamblia* strain. 28th Annual Meeting DGP, Berlin, Germany, 21.3.2018 (P).
- Müller N. Recent advances in chemo- and immunotherapy in canine giardiasis, Seminar at Elanco Animal Health Inc. Basel, Switzerland, 1.11.2018.

- Ritler D, Li J, Lundström-Stadelmann, B. In vitro metabolomic studies on the *Echinococcus multilocularis* metacestode. Joint Annual Meeting 2018 SSI | SSHH | SSTMP | SSTTM. Interlaken, CH, Sept. 13-14, 2018. (P, poster flash).
- Ritler D, Rufener R, Li J, Lundström-Stadelmann, B. Starving a deadly parasite: in vitro metabolomic studies on the *Echinococcus multilocularis* metacestode. 28th annual meeting of the German Society of Parasitology, Berlin, DEU, Mar. 21-24, 2018.
- Rufener R, Dick L, Ritler D, Hemphill A, Lundström-Stadelmann B. *Echinococcus multilocularis*: from drug screening to the energy metabolism. 28th annual meeting of the German Society of Parasitology, Berlin, DEU, Mar. 21-24, 2018.
- Sydler X, Grimm F, Rosato G, Polster S, Klausmann S, Hadorn D, Basso W: *Blastocystis* infection in Swiss pigs of different age categories. 25th International Pig Veterinary Society (IPVS) Congress, Chongqing, China, 11.06. to 14.06.2018 (P).
- Winzer P, Anghel N, Hemphill A. Comparative study between pregnant mouse interference test and zebrafish embryo development test. Host-pathogen interactions symposium, Vetsuisse Bern. 4.5.2018.
- Winzer P, de Amorim Cardoso R, Hemphill A. Bumped kinase inhibitor 1294 induced formation of multinucleated complexes in *Neospora caninum*. Graduate School of Life Science Symposium, University of Bern. 1.2.2018. (P).

AUS-, FORT- UND WEITERBILDUNG

AUSBILDUNG – Veterinärparasitologie (HS: Herbstsemester; FS: Frühjahrsemester)

VETSUISSE - CURRICULUM

- Gottstein B, Lundström-Stadelmann B: Oekologie mit Beispielen aus der Parasitologie. [8 Stunden, 1. Studienjahr] (FS).
- Gottstein B, zusammen mit Basso W, Hentrich B, Sager H, Lundström-Stadelmann B: Integralunterricht (Vorlesung und Kurs/Praktikum) "Veterinärmedizinische Parasitologie" im NOZ ("Nicht-organzentrierter Unterricht") sowie in verschiedenen Organblöcken gemäss neuem Vetsuisse Studienplan (HS und FS).
- Gottstein B, zusammen mit Basso W, Hentrich B und Sager H: "Klinische Parasitologie" (Kern- und Mantelunterrichts) gemäss neuem Vetsuisse Studienplan [4. Vetsuisse Studienjahr]. (HS und FS).
- Basso W: „Parasitologische Fälle“. Blockstudium gemäss neuem Vetsuisse Studienplan [4. Vetsuisse Studienjahr] (HS und FS).

AUSBILDUNG - Medizinische Parasitologie (Human- und Veterinärparasitologie)

Ganze Veranstaltung (3 ECTS)

- Müller N, Hemphill A, Lundström-Stadelmann B, Basso W, Gottstein B: Medizinische Parasitologie und tropische Parasitosen, 3 Stunden/Woche. Für Biologen (Block M9P) und Mediziner (HS).
- Gottstein B, Müller N, Hentrich B, Basso W: Diagnostische Methoden im Bereich Parasitologie; einwöchiger Blockkurs (HS).

Teilpensum

- Müller N: Vorlesung im Rahmen der "Zell- und Molekularbiologie", Block M5, 2 h
- Lundström-Stadelmann B: Vorl. im Rahmen der "Zell- und Molekularbiologie", Block M5, 2h

FORT- UND WEITERBILDUNG Veterinär- und Humanparasitologie

Für die institutsinterne Fort- und Weiterbildung wurden regelmässig Seminare / Journal-Clubs sowie wöchentliche diagnostische Kolloquien abgehalten.

Das Institut hat 2018 folgende Weiterbildungsveranstaltungen organisiert und durchgeführt:

- PhD candidate meeting, B. Lundström-Stadelmann, K. Woods, T. Voss, P. Mäser, Swiss Society of Tropical Medicine and Parasitology (SSTMP), Sigriswil, CH, Nov. 2018
- Host-Pathogen Interactions Symposium, K. Woods, B. Lundström-Stadelmann, Vetsuisse Faculty, University of Bern, CH, May 2018

Habilitationen, Dissertationen und Diplom/Master-Arbeiten, Abschlüsse im 2018

- Nina Hari (Maturandin), Titel: „Der Fuchsbandwurm – Die Auswirkung von Medikamenten auf das Stadium im Zwischenwirt“, Gymnasium Neufeld Bern, Supervisor B. Lundström-Stadelmann
- Raphael Zurbriggen (BSc), Titel: "Development of new drugs against *Echinococcus multilocularis* metacestodes", Supervisor B. Lundström-Stadelmann
- Luca Dick (MSc), Titel: "New treatments against alveolar echinococcosis", Supervisor B. Lundström-Stadelmann
- Lundström-Stadelmann B. (Habilitation), Titel: "Strategies for the identification of novel treatment options against parasitic diseases"
- Sabrina Stöckli (BSc), Titel: "Looking for alternatives – new drugs against the parasite *Echinococcus multilocularis*", Supervisor B. Lundström-Stadelmann

SEMINARE / GÄSTE / GASTFORSCHERINNEN 2018

Gäste und Besucher, Seminaristen:

- Dr. Renate Edelhofer, Institut für Parasitologie, Veterinärmedizinische Universität Wien: Seminar: Diagnostische Methode in der Parasitologie und Inspektor Columbo ermittelt; Blutparasiten (Präparatensammlung mikroskopische Diagnose) (14-16 Februar 2018).
- M.Sc. Nadja Morf, Forensische Genetik Institut für Rechtsmedizin Universität Zürich. Seminar: Elephant meets roe deer: Wildlife forensics in Zurich (4.12.2018).
- Dr. Simona Stäger NRS-Institut Armand-Frappier, Laval, Canada (18.12.2018)
- Dr. Charlotte Admaczick, Deutsche Gesellschaft für Tropenpädiatrie und Internationale Kindergesundheit. Seminar: Schistosomiasis revisited: How a neglected tropical disease is challenging doctors and epidemiologists alike in Europe (8.6.2018).

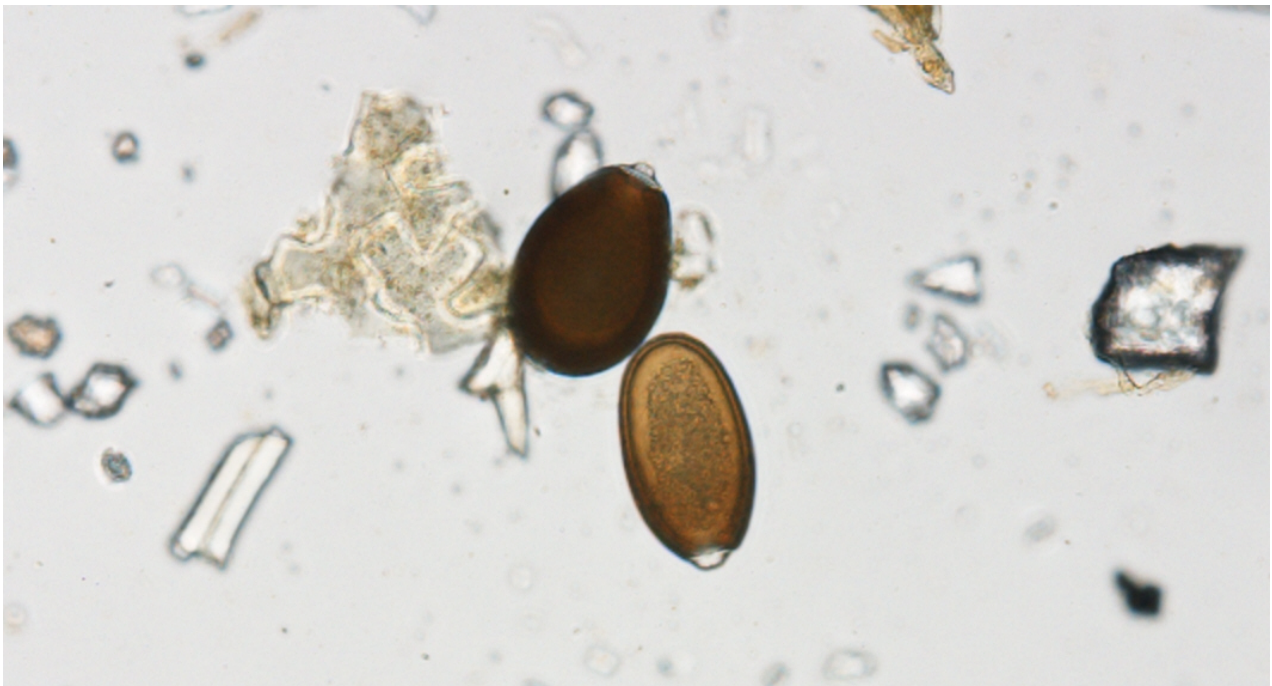
Gastwissenschaftlerinnen:

Dr. Lucía María Campero (Post-Doc aus dem Labor für Immunparasitologie der Veterinärmedizinische Fakultät La Plata, Argentinien) (15.10. bis 12.12.2018) Projekte:

Nachweis von AK gegen *Toxoplasma gondii* in Speichel von Schweinen; Diagnose von *Neospora caninum* Infektionen bei Kleinwiederkäuern.

Dr. Marine Carlus, Institut Galli Valerio, Lausanne, (22.11. bis 4.12.2018): *Trichinella*-Nachweis, Koprologische, Serologische und PCR-Diagnose.

J. Dąbrowska, Department of Parasitology and Invasive Diseases, National Veterinary Research Institute, Partyzantów Avenue 57, Puławy, Poland (1.9. 2017-30.8.2018). *Tritrichomonas*-Projekt.



Dienstleistungen

AKKREDITIERUNG DURCH DIE SCHWEIZERISCHE AKKREDITIERUNGSSTELLE (SAS)

Die Erstakkreditierung erfolgte am 15. März 2000 durch die Schweizerische Akkreditierungsstelle, mit der damaligen STS 251. Die Prüfstelle für parasitologische Diagnostik in den Bereichen Veterinär- und Humanmedizin (IPB) wurde im Jahr 2010 zusammen mit den Prüfstellen der Institute für Tierpathologie (inklusive der Nationalen Fischuntersuchungsstelle), Veterinär-Bakteriologie sowie dem NeuroCenter zu den Diagnostischen Labors der Vetsuisse-Fakultät der Universität Bern (DLVB; www.dlvb.unibe.ch) zusammengefasst (STS 175). Die erfolgreiche Reakkreditierung fand 2015 statt. Diese Organisation ist unter einem gemeinsamen QM-Handbuch vereinigt. Nähere Details zum Thema "Akkreditierung" siehe Management-Review 2018.



Interne Audits / Qualitätskontrollen

Der Auditplan, anfangs Jahr durch die Institutsleitung freigegeben, beinhaltet die Durchführung der Audits für Prüfungsabläufe und Geräte während des ganzen Jahres.

In den auditierten Prüfungsabläufen wurden keine relevanten Abweichungen oder Mängel festgestellt. Nachaudits waren somit nicht notwendig.

Grundsätzlich arbeitet das Laborpersonal gewissenhaft und präzise, ausserdem wird die interne Qualitätskontrolle aufgrund von Arbeitsvorschriften, Checklisten und Richtlinien systematisch durchgeführt.

Externe Audits / Qualitätskontrollen

Wir haben uns an allen parasitologischen Qualitätskontrollen des „U.K. National External Quality Assessment“ in London beteiligt. Die Resultate sind sowohl für koprologische als auch serologische Untersuchungen überdurchschnittlich und somit sehr befriedigend ausgefallen.

Die Evaluation der IPB-Leistung im Rahmen der UK NEQAS Parasitology Quality Assessment ist im internationalen Quervergleich (siehe nebenstehende Graphik) festgehalten.

2018:

	Mean score of all participants	Score of IPB
Faecal parasitology	31.96	32.49
Serology	38.00	38.74

Im Veterinärbereich nimmt das IPB jährlich an zwei internationalen Ringversuchen (ISS, Rome; BfR, Berlin) zum Nachweis von *Trichinella*-Larven im Fleisch teil und schnitt dabei immer sehr gut ab. Seit 2011 nimmt das IPB auch an einer internationalen Qualitätskontrolle (ISS, Rome) zur molekularen Diagnostik von *Trichinella*-Larven teil. Seit 2014 nimmt das IPB an den RV der VetQas, England, zum Nachweis von anti-Toxoplasma-AK in Schafseren (3 x jährlich) und anti-*Neospora*-AK in Rinderseren (2x jährlich) teil. Die Ergebnisse fielen sehr gut aus. Zudem nimmt das IPB an den jährlichen RV zur Dourine Serologie organisiert durch das Anses, Frankreich, teil. Auch hier fielen die Resultate immer gut aus.

Das IPB organisiert jährlich eine Qualitätskontrolle zum *Trichinella*-Nachweis im Fleisch und führt diese auch durch. Zudem bietet das IPB regelmässig eine Qualitätskontrolle zum serologischen Nachweis von *Neospora* und *Toxoplasma* an.

Labor für Veterinärparasitologie*

(*BLV-bewilligtes Labor für Tierseuchendiagnostik)
 (Beteiligung per 31.12.2018): Dr. W. Basso (Leitung), Prof. Dr. B. Gottstein, Dr. B. Hentrich, L. Krähenbühl, L. Hofmann, C. Salvisberg. QS-Leitung: Dr. W. Basso
 Ausserdem beteiligt:
 Prof. Dr. N. Müller, B. Merkle, U. Kurath, H.T.T. Nguyen, C. Müller

Das IPB amtet als **Nationales Referenzlabor** für folgende Tierseuchen:

Trichinellose: Statistiken sind dem entsprechenden BLV- Bericht zu entnehmen.,

Beschälseuche (Trypanosoma equiperdum): Der Parasit wurde 2018 in der Schweiz weder serologisch noch direkt nachgewiesen.

Toxoplasmose: Statistiken sind dem entsprechenden BLV- Bericht zu entnehmen.

Tritrichomonose: 2018 wurden beim Rind keine Fälle gemeldet. Der Parasit tritt jedoch gehäuft bei der Katze auf.

Neosporose: Statistiken sind dem entsprechenden BLV- Bericht zu entnehmen.

Besnoitiose: 2018 wurde der Parasit in der Schweiz nicht festgestellt.

Dienstleistungsvolumen "Veterinärparasitologie" 2018:

Untersuchung	Tierart	Anzahl erbrachter Leistungen	
		2018	(2017)
Direktnachweis:	Diverse	4'642	(6'373)
Blut- und serologische Untersuchungen:	Diverse	2'489	(1'069)
Molekulare Diagnostik:	Diverse	653	(1'304)
Parasitennachweis in vitro	Diverse	819	(764)
Gesamttotal:		8603	(9'510)

Labor für medizinische Parasitologie*

(*BAG-anerkanntes Labor für Serologie und Parasitologie, AL 3.3)
 (Beteiligung per 31.12.2018): Prof. Dr. N. Müller (Leitung), Prof. Dr. B. Gottstein, B. Merkle, U. Kurath, H.T.T. Nguyen, X.L. Vu. QS-Leitung: Dr. W. Basso
 Ausserdem beteiligt: L. Krähenbühl, L. Hoffmann, C. Salvisberg

Untersuchungen Leistungen	Anzahl erbrachter	
	2018	(2017)
Blut- und serologische Untersuchungen:	8342	(8546)
Molekularbiologische Diagnostik:	162	(166)
Parasitennachweis in Zellkulturen:	-	(0)
Direktnachweis:	5	(4)
Gesamttotal	8509	(8716)
Internationale Qualitätskontrollen:		
UK NEQAS Parasitology Quality Assessment	8 cycles	
AM CNQ	2 cycles	

FUNKTIONEN UND INTERNATIONALE TÄTIGKEITEN DES KADERS (STAND 31.12.2018)

Prof. Dr. B. Gottstein, Prof. hc, CBA

Gesellschaften, Kommissionen u.ä.:

- Schweizerische Gesellschaft für Tropenmedizin und Parasitologie (SGTP): Mitglied
- Schweizerische Gesellschaft für Mikrobiologie (SGM): Mitglied
- Schweizerische Gesellschaft für Zell- und Molekularbiologie & USGEB: Mitglied (SGZB)
- Schweizerischer Vertreter in der International Commission on Trichinellosis (ICT)
- Deutsche Gesellschaft für Parasitologie: Mitglied (DGP)
- Mitglied der Schweizerischen Vereinigung der Veterinär-Labordiagnostiker (SVVLD)
- Mitglied der Schweizerischen Vereinigung für Tierproduktion (SVT)
- Mitglied der Schweizerischen Gesellschaft für Versuchstierkunde (SGV)
- Mitglied der World Association for the Advancement of Veterinary Parasitology (WAAVP)
- Mitglied der Deutschen Akademie der Naturforscher Leopoldina
- ESCCAP Schweiz, Vizepräsident
- Ehrenmitglied der "Bulgarian Society for Parasitology"

Peer Reviewer von Projektgesuchen:

- International Science Foundation
- Deutsche Akademie der Naturforscher Leopoldina
- Deutsche Forschungsgemeinschaft (DFG)
- INSERM

Universität Bern:

Finanzchef der Vetsuisse Fakultät Bern

Université de Franche-Comté, France:

Professeur Honoraire

Editorial or Advisory Boards bei wissenschaftlichen Zeitschriften:

- Mitglied des Editorial Boards der Zeitschrift Parasitology Research
- Mitglied des Editorial Boards der Zeitschrift "Schweizer Archiv für Tierheilkunde"
- Mitglied des Editorial Boards der Zeitschrift Acta Parasitologica
- Mitglied des Editorial Boards der Zeitschrift Helminthologia

Prof. Dr. A. Hemphill

Gesellschaften:

- Mitglied der Schweizerischen Gesellschaft für Tropenmedizin und Parasitologie (SGTP)
- Mitglied der British Society of Parasitology (BSP)
- Mitglied der Deutschen Gesellschaft für Parasitologie (DGP)
- Mitglied der World Association for the Advancement of Veterinary Parasitology (WAAVP)
- Mitglied der American Society of Parasitology
- Mitglied der American Society of Tropical Medicine and Hygiene (ASTMH)
- Mitglied der American Society for Microbiology (ASM)

Peer Reviewer von Projektgesuchen:

- United States Department of Agriculture (USA)
- Welcome Trust (GB)
- Deutsche Forschungsgemeinschaft (DFG)
- Schweizerischer Nationalfonds (SNF)
- National Health and Medical Research Council, Australia (NHMRC)

Gutachten von Dissertationen und Diplomarbeiten:

- University of Technology Sydney (Australia)
- University of Liverpool (UK)
- Universidad Complutense Madrid (Spain)
- Faculty of Veterinary Sciences, Lisbon, Portugal
- University of Evora, Portugal
- Infection Biology, University of Glasgow, UK

Editorial Board:

- Editor: Parasitology, Parasitology Open
 - Editorial board member: The Open Journal of Parasitology, Scientifica, Experimental Parasitology
 - Guest editor thematic issues: Exp Parasitol 2008; Int J Parasitol 2012;2017, Parasitology 2010, 2013,
- External advisory board: Swissmedic: Veterinary Medicines Advisory Board (VMEC)

Prof. Dr. N. Müller

Gesellschaften:

- Mitglied der Schweizerischen Gesellschaft für Tropenmedizin und Parasitologie (SGTP)
- Mitglied der Diagnostikkommission der SGTP
- Mitglied der Deutschen Gesellschaft für Parasitologie (DGP)

Peer Reviewer von Projektgesuchen:

- Schweiz. Nationalfonds
- Deutsche Forschungsgemeinschaft (DFG)
- Schweiz. Staatssekretariat für Bildung und Forschung (SBF)
- Fonds zur Förderung der wissenschaftlichen Forschung, Österreich

Gutachter/Examinator bei Dissertationen:

- University of Technology Sydney (Australia)
- University of Melbourne (Australia)
- Karlsuniversität, Prague (Czech Republic),
- Institute of Parasitology, University of Zürich

Editorial Board:

Editorial board member für die Zeitschriften Parasitology International, Molecular and Cellular Probes

PD Dr. med. vet. Walter Basso, FVH, Dipl EVPC

Gesellschaften:

- Diplomate of the European Veterinary Parasitology College (Dipl. EVPC).
- Member of the Credentials Committee of the European Veterinary Parasitology College (EVPC).
- Präsidiumsmitglied European Scientific Counsel Companion Animal Parasites (ESCCAP) Schweiz.
- Vertreter der Schweiz in der International Commission on Trichinellosis (ICT)
- Mitglied Swiss Vector Entomology Group (SVEG)

Peer Reviewer von Projektgesuchen:

- Austrian Science Fund (FWF)

Universität Bern:

Mittelbau Vetsuisse-Fakultät, Universität Bern: Institutsvertreter

Gutachter/Examinator bei Dissertationen und Diplomarbeiten:

- Facultad de Ciencias Veterinarias, Universidad Nacional de La Plata, Argentina
- Facultad de Ciencias Agrarias, Universidad Nacional de Mar del Plata, Argentina
- Faculty of Veterinary Medicine, Univ. of Vet. and Pharm. Sciences Brno, Czech Republic
- School of Agricultural, Forest and Food Sciences (HAFL), Bern, Switzerland
- Facultad de Ciencias veterinarias, Universidad Complutense Madrid (Spain)
- UPMC Sorbonne Universités, Ecole Doctorale "Complexité du Vivant" Université Pierre et Marie Curie, Paris, France

Prof. Dr. B. Lundström-Stadelmann, Assistenzprofessorin Host-Pathogen Interactions

Gesellschaften:

- Vorstand der Schweizerischen Gesellschaft für Tropenmedizin und Parasitologie (SGTP), Vizepräsidium
- Vorstand Mittelbauvereinigung Vetsuisse Bern
- Mitglied der Deutschen Gesellschaft für Parasitologie (DGP)
- Mitglied der Schwedischen Gesellschaft für Mikrobiologie (SFM, Svenska Föreningen för Mikrobiologi)
- SGV, Schweizerische Gesellschaft für Versuchstierkunde (Swiss Laboratory Animal Science)

Association)

Editorial Board:

- Gasteditorin Food and Waterborne Parasitology (FAWPAR)

Anderes:

- Mentorin im Vetment Programm

Dr. med. vet. B. Hentrich, Fachtierärztin für Veterinärparasitologie

Gesellschaften:

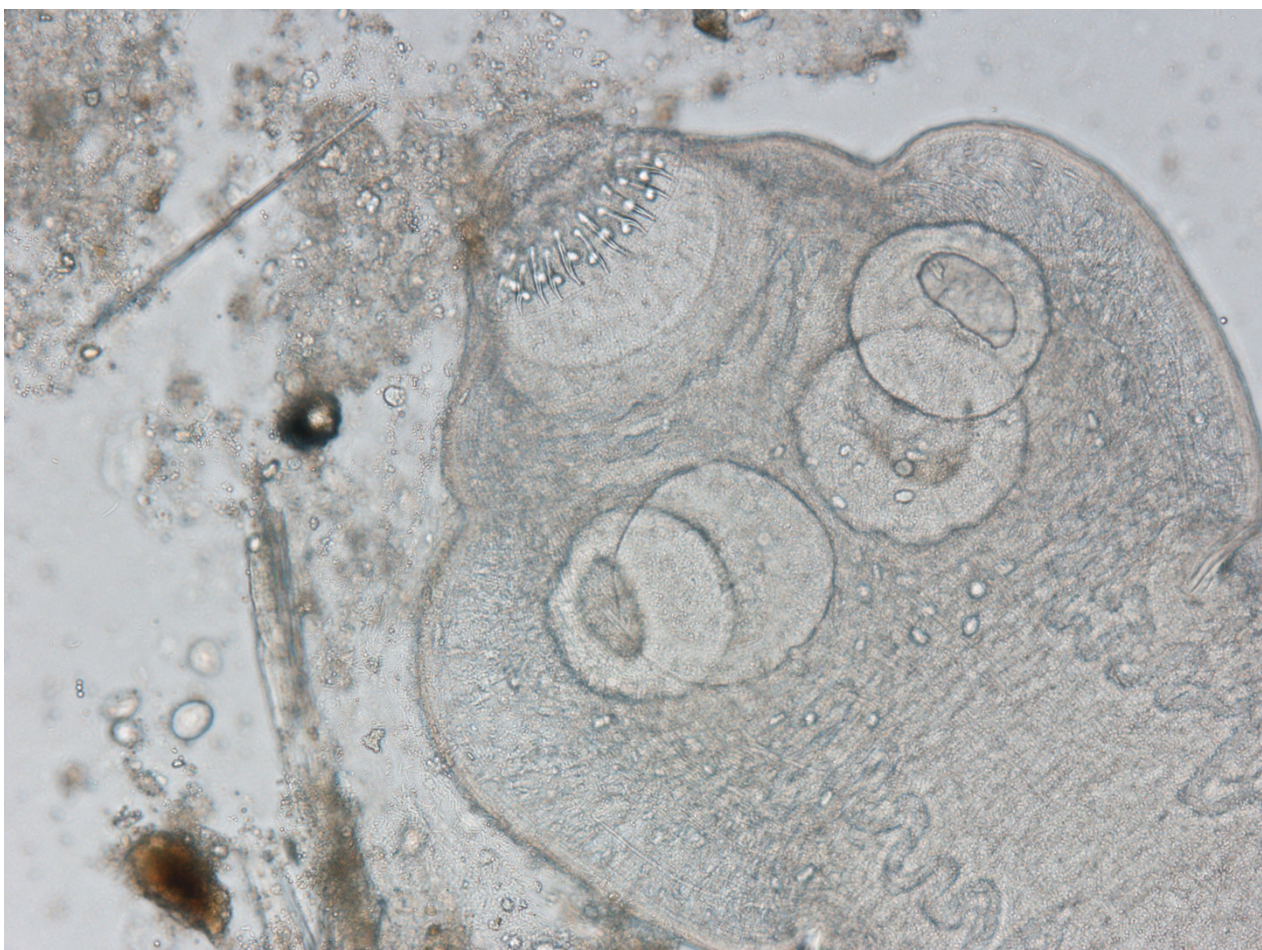
- Mitglied der Schweizerischen Gesellschaft für Tropenmedizin und Parasitologie (SGTP)

- Mitglied der Deutschen Gesellschaft für Parasitologie (DGP)

- Mitglied der Deutschen Veterinärmedizinischen Gesellschaft (DVG)

- Mitglied der Schweizerischen Vereinigung der Veterinär-Labordiagnostiker (SVVLD)

- Mitglied der Gesellschaft Schweizerischer Tierärztinnen und Tierärzte (GST)



PERSONELLES / PERSONAL

Austritte 2018: Dr. Rita de Amorim (Assistentin)

Eintritte 2018: Nicoleta Anghel (Doktorandin)

Personalbestand des Institutes (Stand 01.01.2019):

Prof. Dr. B. Gottstein (Direktor)	(K)
Prof. Dr. A. Hemphill (Dozent 1)	(K)
Prof. Dr. N. Müller (Dozent 1)	(K)
Prof. Dr. B. Lundström-Stadelmann (Assistenzprofessur)	(K)
PD Dr. W. Basso (Oberassistent)	(K)
Dr. B. Hentrich (Assistentin)	(K/D)
PD Dr. J. Müller (wiss. MA)	(D)
Dr. G. Boubaker (Assistentin)	(D)
Dr. J. Wang (Assistentin)	(D)
Dr. R. de Amorin Cardoso (Assistentin)	(D)
Dr. A. Aguado (Assistentin)	(D)
A. Meyer (Doktorandin)	(D)
R. Rufener (Doktorand)	(D)
P. Winzer (Doktorand)	(D)
D. Ritler (Doktorand)	(D)
V. Balmer (Laborantin)	(D)
L. Krähenbühl (MTA)	(K)
B. Merkle (MTA)	(K)
C. Müller (MTA)	(K/D)
L. Hofmann (MTA)	(K)
U. Kurath (MTA)	(D)
C. Salvisberg (MTA)	(D)
XL. Vu (MTA)	(D)
A. Gerber (Sekretariatsleiterin)	(K, DIP)
A. Läderach (techn. Dienst)	(K/ITPA)
N. Vukovic (Reinigung)	(UniBE)

Anstellungsverhältnis: (K) Kantonal, (KDE) Kantonal/Dienstleistungseinnahmen; (DM) Drittmittel.

Bern, den 30. April 2019

Der Direktor, Prof. Dr. B. Gottstein

Auflösung der Fragen auf Seite 2 (Was ist was ?)

- (a) *Babesia canis*
- (b) *Giardia duodenalis*
- (c) Vorderende von *Toxocara canis*
- (d) *Sarcoptes* spp.

Rückblick in die IPB-Zeit von 1992-2018 und Ausblick in die Jahre \geq 2019*Bruno Gottstein*

Liebe Kolleginnen und Kollegen, liebe Freunde der Parasitologie

2018 werde ich als das Jahr in Erinnerung behalten, in dem das Institut für Parasitologie (IPB) nach 26 Jahren Forschung, Lehre und Dienstleistung, beginnend mit seiner Gründung als eigenständiges Institut im Oktober 1992, die Umstellung auf eine neue Institutsleitung vorbereitete, welche auf den 1.8.2019 anfallen wird, dies aufgrund meiner bevorstehenden Pensionierung. Das Institut, aber im besseren Sinne die Institutsmitarbeiterinnen und Institutsmitarbeiter, haben sich in diesen letzten 26 Jahren, im Rahmen von ergebnisoffenen Prozessen, aber auch mit einem planvollen Vorgehen, mit dem aktuell wissenschaftlich Erschliessbaren der Parasitologie auseinandergesetzt. Rückblickend denke ich dabei an einige "Highlights" wie z.B. an die neuen Parasitosen, bei welchen das IPB eine federführende Rolle gespielt hat, sowohl bei der Entwicklung neuer diagnostischer Test als auch bei der Sensibilisierung der öffentlichen Gesundheitsbehörden über die respektive Problematik: Im veterinärparasitologischen Bereich waren dies insbesondere die hier früher unbekannte bovine Neosporose sowie dann später die bovine Besnoitiose. Im humanparasitologischen Bereich erforschten wir erstmalig für die Schweiz die Naegleriose und andere freilebende pathogene Amöben, dies nur um ein paar Beispiele zu nennen. Hauptschwergewicht der Forschung war sicherlich die alveoläre Echinokokkose, was in den jeweiligen Jahresberichten klar zum Ausdruck kommen konnte. Die internationale Bedeutung unserer Echinokokkose-Forschung wurde in einem soeben erschienen interessanten Artikel klar kommuniziert (Zitat)¹: "*The top three productive institutions were the Univ Zurich (German, 229 articles), Univ Bern (Switzerland, 203 articles) and Univ Salford (England, 173 articles)*".

Das IPB konnte sich nur deshalb auf eine so vielfältige und erfolgreiche Weise an der parasitologischen Forschung beteiligen, weil sich alle unserer Mitarbeiterinnen und Mitarbeiter gemeinsam an den Forschungsideen, an deren Verwirklichung und Veröffentlichung beteiligten. Hierfür gilt ihnen allen mein ganz herzlicher Dank, und ich werde mich freuen, wenn die neue Institutsleitung (Frau Prof. Dr. med. vet. Caroline Frey zusammen mit Frau Prof. Dr. phil. nat. Britta Lundström-Stadelmann) ab 1.8.2019 mit Hilfe ihrer Engagements weiterhin wirksame Akzente in der parasitologischen Forschung, aber auch in der Lehre und Dienstleistung setzen werden. Ihnen beiden und der ganzen IPB-Belegschaft wünsche ich viel Erfolg und berufliche Freude,

Ihr



Bruno Gottstein

¹ Ma et al. Knowledge domain and emerging trends on echinococcosis research: A scientometric analysis. *Int. J. Environ. Res. Public Health* 2019, 16, 842; doi:10.3390/ijerph16050842