

CURRICULUM VITAE

Name Norbert Müller
Title Prof. Dr. rer. nat (PhD)
Address Institute of Parasitology, University of Berne,
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Date of birth October 2, 1956
Place of birth Constance, Germany
Nationality German

Main research areas (since 2010)

- Experimental chemotherapy in the field of giardiasis including investigations on the mode of action of, and resistance formation against, anti-giardial drugs
- Molecular-epidemiological studies and genetic characterization of free living amoebae (including *Acanthamoeba* and *Naegleria*) and other protozoan parasites (e.g *Leishmania*; *Tritrichomonas*)
- Investigation of the pathogenic mechanisms/potential of *Naegleria* and *Acanthamoeba*
- Development of serological and molecular tools for the diagnosis of different parasite infections

Professional training/career

2003 - present Associated Professor at the Institute of Parasitology, University of Berne, Switzerland; Head of the Human Medical Parasitology Unit, Supervisor of various applied and basic research projects such as investigations on the immunobiology of the protozoan parasite *Giardia lamblia*, experimental chemotherapeutical studies related to giardiasis, genetic characterization of free living amoebae, investigations on the pathogenic potential from free-living amoebae, development of molecular and serological tools for diagnosis of different parasites

1993-2003 “Assistent” and “Oberassistent” (since 1995) at the Institute of Parasitology, University of Berne, Switzerland. Research on immunobiology of the protozoan parasite *Giardia lamblia*, development of molecular and serological tools for diagnosis of different parasites

1993 Habilitation at the Phil. nat. Faculty, University of Berne: Alveolar echinococcosis and African trypanosomiasis: molecular biological approaches in immunodiagnosis and vaccine development

1992 Research fellow at the Dept. of Animal Health and Biomedical Sciences (Prof. Dr. J. Mansfield), University of Wisconsin, Madison, USA

1986-1992 Postdoc at the Institute of General Microbiology, University of Berne: Research on immunological and molecular mechanisms involved in host-parasite interaction (African trypanosomiasis, echinococcosis); Development of serological and molecular tools for diagnosis of parasitic infections

1981-1986 PhD in molecular microbiology, University of Constance, Germany (Supervisor: Prof. Dr. W. Boos): Sugar transport in *Salmonella typhimurium*

1976-1981 Diploma in biology, University of Constance, Germany (Supervisor: Prof. Dr. W. Boos): Focus on molecular biology and microbiology

Most important oral presentations (since 2010):

- Müller N, Nillius D, Leitsch D, Hemphill A, Müller J.: Identification and functional analysis of potential drug target proteins in *Giardia lamblia*. The 8th International Congress of Parasitology, Melbourne, Australia, August 15-20, 2010 (invited).
- Müller N, Nillius D., Hemphill A., Müller J.: Functional analyses of nitro drug activation and resistance formation in *Giardia lamblia*. 5th International *Giardia* and *Cryptosporidium* Conference, Wellington, New Zealand, January 31 – February 3, 2012 (invited)
- Müller N: Drug resistance formation in the intestinal protozoan parasite *Giardia lamblia*. Phil Nat. Faculty, University Basle: May 7, 2012 (invited)
- Müller N.: Chemotherapy of giardiasis: function of nitroreductases in the metabolism of nitro drugs metronidazole and nitazoxanide. Drug Design and Drug Development Seminar, Würzburg, Germany, April 11-13, 2013.
- Müller N.: Chemotherapy of giardiasis: antagonistic function of nitroreductases in (in)activation of nitro drugs metronidazole and nitazoxanide. Annual SSTMP meeting, Basle, October 31, 2013
- Müller, N.: Drug resistance formation in the intestinal protozoan parasite *Giardia lamblia*, University of Havana, Havana, Cuba, February 12, 2016

Further academic activities

- Publications: ca. 145 articles in peer-reviewed scientific journals (e.g. *Trends in Parasitology*, *Journal of Antimicrobial Agents*, *Journal of Clinical Microbiology*, *Infection and Immunity*, *International Journal for Parasitology*)
- Editorial board member of 2 scientific journal (*Parasitology International*, *Molecular and Cellular Probes*)
- Reviewer for >30 scientific journals (e.g. *Nature*, *Science*, *Molecular Biology of the Cell*; *Molecular Microbiology*; *Journal of Antimicrobial Agents*)
- Reviewer for several national and international grant applications (e.g. *Schweizerischer Nationalfonds*, *Deutsche Forschungsgemeinschaft*, *Österreichischer Fonds zur Förderung der wissenschaftlichen Forschung*, *Schweizerisches Staatssekretariat für Bildung und Forschung*)
- Memberships: Swiss Society of Tropical Medicine and Parasitology (SGTP) member of the executive committee), Swiss Society of Biochemistry (SGB), German Society for Parasitology (DGP).

Funded projects (principle investigator N. Müller; since 2010)

- Research grant, for "Molecular and biochemical characterization of the cellular functions involved in drug resistance formation in *Giardia lamblia*", from Swiss National Science Foundation (2007-2010) CHF 227'000.-
- Research grant, for "Untersuchung des Lebensraums von freilebenden pathogenen Amöben [FLA] (*Naegleria fowleri* und andere), from Federal Office for Civil Protection (Spiez Laboratory) (2008-2010, together with B. Gottstein, Institute of Parasitology) CHF 190'000.-
- Research grant: "Analysis of pathogenicity mechanisms associated with *Naegleria fowleri* infections", from Federal Office for Civil Protection (Spiez Laboratory) (2011-2014) (together with B. Gottstein, Institute of Parasitology); CHF 223'000.-
- Research grant: "Functional analysis of nitroreductases from the intestinal protozoan parasite *Giardia lamblia*", from Swiss National Science Foundation (since 2012) CHF 223'000.-

- Research Grant: "Das Enzym PDE:Die Achillessehne des Duchfallparasiten *Giardia lamblia*?", from Dürrmüller-Bol Foundation (2014) (together with S. Kunz); CHF 18'000.
- Research grant: "Functional analysis of nitroreductases from the intestinal protozoan parasite *Giardia lamblia*", from Swiss National Science Foundation (approved in September 2015); CHF 291'000.-
- Research grant: Functional analysis of nitroreductases from the intestinal protozoan parasite *Giardia lamblia*. from Swiss National Science Foundation (since 2016) (principle investigator: N. Müller, Institute of Parasitology, Berne); CHF 291'000.-

Scientific co-operations (since 2010)

- Prof. Julia Walochnik; Prof. Michael Duchêne; Dr. David Leitsch, Dept. of Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Vienna, Austria
- Prof. Dr. Adrian Hehl, Institute of Parasitology; University of Zürich, Zürich, Switzerland
- Dr. Alessandro Giuffrè, CNR Institute of Molecular Biology and Patholog, Dept. Biochemical Sciences, Sapienza University of Rome, Rome, Italy
- Prof. Dr. Stephen. L. Leib, Dr. Matthias Wittwer, Labor Spiez, Spiez, Switzerland
- The Pathogen Functional Genomics Research Center; J. Craig Venter Institute, Rockville, Ma., U.S.A.
- PD Dr. Ingrid Felger, Institute of Tropical Medicine and Veterinary Public Health, Basle, Switzerland
- Dr. C. Bovet, Institute for Clinical Chemistry, University of Berne, Switzerland
- PD Dr. J. Furrer, Department of Chemistry, University of Berne, Switzerland

List of Publications (since 2010)

1. Peer-reviewed original articles

Gottstein, B., Wittwer, M., Schild, M., Merli, M., Leib, S.L., Müller, N., Müller, J., Jaggi, R. (2010) Hepatic gene expression profile in mice perorally infected with *Echinococcus multilocularis* eggs. PLoS One 5, e9779 (doi: 10.1371/journal.pone.0009779).

List, C., Qi, W., Maag, E., Gottstein, B., Müller, N., Felger, I. (2010) Serodiagnosis of *Echinococcus* spp. infection: explorative selection of diagnostic antigens by peptide microarray. PLoS Neglected Tropical Diseases 4, e771 (doi: 10.1371/journal.pntd.0000771).

Mejri, N., Müller, N., Hemphill, A., Gottstein, B. (2011) Intraperitoneal *Echinococcus multilocularis* infection in mice modulates peritoneal CD4+ and CD8+ regulatory T cell development. Parasitology International 60, 45-53 (doi: 10.1016/j.parint.2010.10.002).

Gianinazzi, C., Schild, M., Zumkehr, B., Wüthrich, F., Nüesch, I., Ryter, R., Schürch, N., Gottstein, B., Müller, N. (2010) Screening of Swiss hot spring resorts for potentially pathogenic free-living amoebae. Experimental Parasitology 126, 45-53 (doi: 10.1016/j.exppara.2009.12.008).

Stadelmann, B., Spiliotis, M., Müller, J., Scholl, S., Müller, N., Gottstein, B., Hemphill, A. (2010) *Echinococcus multilocularis* phosphoglucose isomerase (EmPGI): a glycolytic enzyme involved in metacestode growth and parasite-host cell interactions. International Journal for Parasitology 40, 1563-1574 (doi: 10.1016/j.ijpara.2010.05.009).

Berger-Schoch, A.E., Herrmann, D.C., Schares, G., Müller, N., Bernet, D., Gottstein, B., Frey, C.F. (2010) Prevalence and genotypes of *Toxoplasma gondii* in feline faeces (oocysts) and meat from sheep, cattle and pigs in Switzerland. *Veterinary Parasitology* 177, 290-297 (doi: 10.1016/j.vetpar.2010.11.046)

Cortes, H.C., Müller, N., Boykin, D., Stephens, C.E., Hemphill, A. (2011) In vitro effects of arylimidamides against *Besnoitia besnoiti* infection in Vero cells. *Parasitology* 138, 583-592 (doi: 10.1017/S0031182011000114).

Nillius, D., Müller, J., Müller, N. (2011). Nitroreductase (GlnR1) increases susceptibility of *Giardia lamblia* and *Escherichia coli* to nitro drugs. *Journal of Antimicrobial Chemotherapy* 66, 1029-1035 (doi: 10.1093/jac/dkr029).

Schweiger, A., Grimm, F., Tanner, I., Müllhaupt, B., Bertogg, K., Müller, N., Deplazes, P. (2011) Serological diagnosis of echinococcosis: the diagnostic potential of native antigens. *Infection* 40, 139-152 (doi: 10.1007/s15010-011-0205-6).

Barlow, A.M., Gottstein, B., Müller, N. (2011) *Echinococcus multilocularis* in an imported captive European beaver (*Castor fiber*) in Great Britain. *Veterinary Record* 169, 339 (doi: 10.1136/vr.d4673).

Burri, D.C., Gottstein, B., Zumkehr, B., Hemphill, A., Schürch, N., Wittwer, M., Müller, N. (2012) Development of a high- versus low-pathogenicity model of the free-living amoeba *Naegleria fowleri*. *Microbiology* 158, 2652-2660 (doi: 10.1099/mic.0.059790-0).

Slapeta, J., Müller, N., Stack, C.M., Walker, G., Lew-Tabor, A., Tachezy, J., Frey, C.F. (2012) Comparative analysis of *Trichostrongylus axei* (Riedmuller, 1928) cat genotype, *T. axei* (Riedmuller, 1928) cattle genotype and *Trichostrongylus axei* (Davaine, 1875) at 10 DNA loci. *International Journal for Parasitology* 42, 1143-1149 (doi: 10.1016/j.ijpara.2012.10.004).

Berzina, I., Müller, N., Krudewig, C., Silaghi, C., Matisse, I., Welle, M. (2013) Histopathological changes in the skin associated with persistent canine granulocytic anaplasmosis. *Journal of Veterinary Internal Medicine* 27, 722-722 (<http://dx.doi.org/10.1016/j.ttbdis.2013.12.010>).

Müller, J., Schildknecht, P., Müller, N. (2013) Metabolism of nitro drugs metronidazole and nitazoxanide in *Giardia lamblia*: characterization of a novel nitroreductase (GlnR2). *Journal of Antimicrobial Chemotherapy* 68, 1781-1789 (doi: 10.1093/jac/dkt106).

Zangger, H., Ronet, C., Desponds, C., Kuhlmann, F.M., Robinson, J., Hartley, M.A., Prevel, F., Castiglioni, P., Pratlong, F., Bastien, P., Müller, N., Parmentier, L., Saravia, N.G., Beverley, S.M., Fasel, N. (2013) Detection of *Leishmania* RNA virus in *Leishmania* parasites. *PLoS Neglected Tropical Diseases* 7, e2006 (doi: 10.1371/journal.pntd.0002006).

Berzina, I., Krudewig, C., Silaghi, C., Matisse, I., Ranka, R., Müller, N., Welle M. (2014) *Anaplasma phagocytophilum* DNA amplified from lesional skin of seropositive dogs. *Ticks and Tick-borne Diseases* 5, 329-335 (doi: 10.1016/j.ttbdis.2013.12.010).

Zysset-Burri, D.C., Müller, N., Beuret, C., Heller, M., Schürch, N., Gottstein, B., Wittwer, M. (2014) Genome-wide identification of pathogenicity factors of the free-living amoeba *Naegleria fowleri*. BMC Genomics 15, 496 (doi: 10.1186/1471-2164-15-496).

Gottstein, B., Schneeberger, M., Boubaker, G., Merkle, M., Huber, C., Spiliotis, M., Müller, N., Garate, T., Doherr, M. G. (2014) Comparative assessment of ELISAs using recombinant Saposin-like protein 2 and recombinant cathepsin L-1 from *Fasciola hepatica* for the serodiagnosis of human fasciolosis PLOS Neglected Tropical Diseases 8, e2860 (doi: 10.1371/journal.pntd.0002860)

Gottstein, B., Müller, N., Frey, C.F. (2014) *Tritrichomonas foetus*: prevalence study in naturally mating bulls in Switzerland. Veterinary Parasitology 200, 289-294 (doi: 10.1016/j.vetpar.2013.12.029).

Müller, J., Vaithilingam, J., Rosner, L.R., Müller, N. (2014) *Escherichia coli* are susceptible to thiazolides if the TolC efflux system is inhibited. Journal of Developing Drugs 3, 2 (doi:10.4172/2329-6631.1000124).

Bernasconi, C., Bodmer, M., Doherr, M.G., Janett, F., Thomann, A., Spycher, C., Iten, C., Hentrich, B., Gottstein, B., Müller, N., Frey, C.F. (2014) *Tritrichomonas foetus*: prevalence study in naturally mating bulls in Switzerland. Veterinary Parasitology 200, 289-294 (doi: 10.1016/j.vetpar.2013.12.029).

Müller, J., Rout, S., Leitsch, D., Vaithilingam, J., Hehl, A., Müller, N. (2015) Comparative characterisation of two nitroreductases from *Giardia lamblia* as potential activators of nitro compounds, International Journal for Parasitology: Drug and Drug Resistance 5, 37–43 (<http://dx.doi.org/10.1016/j.ijpddr.2015.03.001>).

Chaignat, V, Boujon, P, Frey, C.F, Hentrich, B, Müller, N, Gottstein, B. (2015) The brown hare (*Lepus europaeus*) as a novel intermediate host for *Echinococcus multilocularis* in Europe. Parasitology Research 114, 3167-3169 (doi: 10.1007/s00436-015-4555-3).

Wang, J., Vuitton, D.A., Müller, N., Hemphill, A., Spiliotis, M., Blagosklonov, O., Grandgirard, D., Leib, S.L., Shalev, I., Levy, G., Lu, X., Lin, R., Wen, H., Gottstein, B. (2015) Deletion of fibrinogen-like protein 2 (FGL-2), a novel CD4⁺ CD25⁺ Treg effector molecule, leads to improved control of

Echinococcus multilocularis infection in mice. PLoS Neglected Tropical Diseases 9, e0003755 (doi: 10.1371/journal.pntd.0003755)

Lopes, A.P., Vila-Viçosa, M.J., Coutinho, T., Cardoso, L., Gottstein, B., Müller, N., Cortes, H.C. (2015) *Trichinella britovi* in a red fox (*Vulpes vulpes*) from Portugal. Veterinary Parasitology, in press (doi: 10.1016/j.vetpar.2015.03.025)

Müller, N., Hentrich, B., Frey, C.F., Welle, M. (2015) Quantitative PCR for the diagnosis of cutaneous leishmaniasis from formalin-fixed and paraffin-embedded skin sections. Molecular and Cellular Probes, 29, 507-510 (doi:10.1016/j.mcp.2015.09.008)

Jerez Puebla, LE, Núñez, F.A, Martínez Silva, I., Rojas Rivero, L, Martínez González, M., Méndez Sutil, Y., Ayllón Valdés, L., Atencio Millán, I., Müller, N. (2015) Molecular characterization and risk factors of *Giardia duodenalis* among school children from La Habana, Cuba. *Journal of Parasitology Research* 378643 (doi: 10.1155/2015/378643)

Müller, N., Hentrich, B., Frey, C.F., Welle, M. (2015) Quantitative PCR for the diagnosis of cutaneous leishmaniasis from formalin-fixed and paraffin-embedded skin sections. *Molecular and Cellular Probes*, 29, 507-510.

2. Review articles

Hemphill, A., Stadelmann, B., Scholl, S., Müller, J., Spiliotis, M., Müller, N., Gottstein, B., Siles-Lucas, M.. (2010) *Echinococcus* metacestodes as laboratory models for the screening of drugs against cestodes and trematodes. *Parasitology* 137, 569-87 (doi: 10.1017/S003118200999117X).

Frey, C. F., Müller, N. (2012) *Tritrichomonas* - Systematics of an enigmatic genus. *Molecular and Cellular Probes* 26, 132-136 (PMID: 22662341).

Hemphill, A, Stadelmann, B., Rufener, R., Spiliotis, M., Boubaker, G., Müller, J., Müller, N., Gorgas, D., Gottstein, B. (2014) Treatment of echinococcosis: albendazole and mebendazole-what else? *Parasite* 21, 70 (doi: 10.1051/parasite/2014073)

Gottstein, B., Wang, J., Blagosklonov, O., Grenouillet, F., Millon, L., Vuitton, D.A., Müller, N. (2014) *Echinococcus* metacestode: in search of viability markers. *Parasite*. 9, e0003755 (doi: 10.1051/parasite/2014063).

Gottstein, B., Wang, J., Boubaker, G., Marinova, I., Spiliotis, M., Müller, N., Hemphill, A.. (2015) Susceptibility versus resistance in alveolar echinococcosis (larval infection with *Echinococcus multilocularis*). *Veterinary Parasitology*, in press (doi: 10.1016/j.vetpar.2015.07.029)

3. Book chapters

Müller, J., Hemphill, A., Müller, N. (2011) Treatment of giardiasis and drug resistance. In: *Giardia - a model organism*. Springer Verlag Wien, Austria

Top ten publications (only peer-reviewed, original articles listed)

Bienz, M., Siles-Lucas, M., Wittwer, P., Müller, N. (2001). *vsp* gene expression by *Giardia lamblia* clone GS/M-83-H7 during antigenic variation in vivo and in vitro. *Infection and Immunity* 69, 5278-5285 (PMID: 11500396).

von Allmen, N., Bienz, M., Hemphill, A., Müller, N. (2004) Experimental infections of neonatal mice with cysts of *Giardia lamblia* clone GS/M-83-H7 are associated with an antigenic reset of the parasite. *Infection and Immunity* 72, 4763-4771 (PMID: 1150039).

Müller, J., Sterk, M., Hemphill, A., Müller, N. (2007) Characterization of *Giardia lamblia* WB C6 clones resistant to nitazoxanide and to metronidazole. *Journal of Antimicrobial Chemotherapy*, 60, 280-287 (doi: 10.1093/jac/dkm205).

Müller, J., Ley, S., Felger, I., Hemphill, A., Müller, N. (2008) Identification of differentially expressed genes in a *Giardia lamblia* WB C6 clone resistant to nitazoxanide. *Journal of Antimicrobial Chemotherapy* 62, 72-82 (doi: 10.1093/jac/dkn142.).

Gianinazzi, C., Schild, M., Zumkehr, B., Wüthrich, F., Nüesch, I., Ryter, R., Schürch, N., Gottstein, B., Müller, N. (2010) Screening of Swiss hot spring resorts for potentially pathogenic free-living amoebae. *Experimental Parasitology* 126, 45-53 (doi: 10.1016/j.exppara.2009.12.008).

Nillius, D., Müller, J., Müller, N. (2011). Nitroreductase (GlnR1) increases susceptibility of *Giardia lamblia* and *Escherichia coli* to nitro drugs. *Journal of Antimicrobial Chemotherapy* 66, 1029-1035 (doi: 10.1093/jac/dkr029).

Burri, D.C., Gottstein, B., Zumkehr, B., Hemphill, A., Schürch, N., Wittwer, M., Müller, N. (2012) Development of a high- versus low-pathogenicity model of the free-living amoeba *Naegleria fowleri*. *Microbiology*, 158, 2652-2660 ((doi: 10.1099/mic.0.059790-0)

Müller, J., Schildknecht, P., Müller, N. (2013) Metabolism of nitro drugs metronidazole and nitazoxanide in *Giardia lamblia*: characterization of a novel nitroreductase (GlnR2). *Journal of Antimicrobial Chemotherapy* 68, 1781-1789 (doi: 10.1093/jac/dkt106).

Zysset-Burri, D.C., Müller, N., Beuret, C., Heller, M., Schürch, N., Gottstein, B., Wittwer, M. (2014) Genome-wide identification of pathogenicity factors of the free-living amoeba *Naegleria fowleri*. *BMC Genomics* 15, 496 (doi: 10.1186/1471-2164-15-496).

Müller, J., Rout, S., Leitsch, D., Vaithilingam, J., Hehl, A., Müller, N. (2015) Comparative characterisation of two nitroreductases from *Giardia lamblia* as potential activators of nitro compounds, *International Journal for Parasitology: Drug and Drug Resistance* 5, 37-43 (<http://dx.doi.org/10.1016/j.ijpddr.2015.03.001>).