



UNIVERSITÀ
DEGLI STUDI
FIRENZE

DICUS
DIPARTIMENTO DI CHIMICA
"UGO SCHIFF"

ECCELLENZA 2018-22



UNIVERSITÀ
DEGLI STUDI
FIRENZE

PhD
Chemical Sciences

Prof Dr DIANA IMHOF

*Department of Pharmaceutical Biochemistry and Bioanalytics, Pharmaceutical
Institute, University of Bonn, An der Immenburg 4, 53121 Bonn, Germany*
22-23 and 26-27 February 2024

Chemistry and biology of regulatory heme: demystification of a multifaceted molecule

LECTURE TOPICS

Thursday 22.02.2024 - Lesson 1 Introduction into heme (as a prosthetic group) and hemoprotein chemistry, biochemical background (physiology), heme-related diseases (pathophysiology).

3 pm–6 pm aula 18, G3 (Blocco aule), via Gilberto Bernardini 6, Sesto Fiorentino.

Join online: <https://meet.google.com/sys-pyws-dyw>

Friday 23.02.2024 - Lesson 2 Heme research with focus on heme as an effector molecule (not as a prosthetic group), analysis methods based on peptides and proteins, elucidation of hemebinding/regulatory motifs in proteins, introduction into spectroscopic analysis of heme binding

3 pm–6 pm aula 11, G3 (Blocco aule), via Gilberto Bernardini 6, Sesto Fiorentino.

Join online: <https://meet.google.com/gyt-hncu-opv>

Prof.ssa Anna Maria Papini
Coordinatore del Dottorato

Prof.ssa Anna Maria Papini
Organizzatore



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LECTURE TOPICS

Monday 26.02.2024 - Lesson 3 Methods for heme binding studies and structural analysis of heme-peptide/protein complexes (UV/Vis, rRaman, cwEPR, 2D NMR), prediction of heme-binding motifs.

2 pm – 6 pm aula Speroni, P2 (Dipartimento di Chimica), via della Lastruccia 13, Sesto Fiorentino.

Join online: <https://meet.google.com/dae-ogmk-wuq>

Tuesday 27.02.2024 - Lesson 4 Applications and clinical relevance (from bacteria to humans).

9 am – 11 am aula Speroni, P2 (Dipartimento di Chimica), via della Lastruccia 13, Sesto Fiorentino.

Join online: <https://meet.google.com/jus-grkt-smk>

Note: Interaction with students is encouraged and desired through the processing of worksheets and question papers

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Course program and objectives

Labile heme, released from hemoglobin of ruptured red blood cells, has been considered an „alarmin“ for around 30 years because of its cytotoxic, proinflammatory and procoagulant properties. The molecular and structural basis of the heme-protein interactions and their consequences, however, were unknown for a long time. Labile heme is a regulator of protein function and thus an effector molecule in biochemical processes, yet also disease development (e.g., thrombosis, inflammation). Heme associates with proteins as an axial ligand, based on a coordinate bond between the central iron ion and an amino acid side chain containing heteroatoms and significant contributions of adjacent amino acids. The use of combinatorial peptide library screening, molecular and structural analysis by different spectroscopic methods enabled the establishment of a classification scheme for Cys-, His- and Tyr-based heme-binding motifs (HBMs). The course will teach the interdisciplinary approach to elucidating the molecular basis of heme-protein interactions, including verification of protein function, and the importance of this knowledge for the development of biomedical applications in diagnosis and therapy.

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Suggested reading

1. Heme Biology: The Secret Life of Heme in Regulating Diverse Biological Processes (Book) Edited By: Zhang Li, World Scientific, <https://doi.org/10.1142/7484> | July 2011, Pages: 228
2. Heme and erythropoiesis: more than a structural role. (Review) Chiabrando D, Mercurio S, Tolosano E. *Haematologica*. 2014 Jun;99(64.):973-83. doi: 10.3324/haematol.2013.091991.
3. Regulatory Fe(II/III) heme: the reconstruction of a molecule's biography. (Review) Kühl T, Imhof D. *Chembiochem*. 2014 Sep 22;15(14):2024-35. doi: 10.1002/cbic.201402218.
4. Red alert: labile heme is an alarmin. (Review) Soares MP, Bozza MT. *Curr Opin Immunol*. 2016 Feb;38:94-100. doi: 10.1016/j.coi.2015.11.006.
5. Other references (including e.g., Ref 1) will be announced and/or provided during the course.

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Coordinatore del Dottorato

Prof.ssa Anna Maria Papini
Organizzatore



Diana Imhof is Professor for Pharmaceutical Biochemistry and Bioanalytics at the Pharmaceutical Institute Rheinische Friedrich-Wilhelms-University of Bonn

Research interests

Peptide and protein biochemistry, peptide chemistry (in particular solid-phase synthesis) and analysis with focus on multiple disulfide-bonded peptides, peptide folding studies, combinatorial peptide

libraries and screening, bioactive peptides and peptide complexes as tools for structurefunction relationship studies, peptide therapeutics, protein-protein and protein-ligand (e.g. heme) interactions, peptides as tools

ACADEMIC EDUCATION AND DEGREES

1990 – 1994 Chemistry studies at University of Jena

1994 – 1995 Biology studies at Dublin City University, Dublin/Ireland

1996 Diploma in Chemistry, Chem.-Geol. Faculty, University of Jena

SCIENTIFIC EDUCATION AND DEGREES

1996 – 1999 Doctoral studies in Biochemistry, Biol.-Pharm. Faculty, University of Jena

1999 PhD in Biochemistry (summa cum laude), University of Jena

2008 Habilitation, venia legendi in Biochemistry, University of Jena

PROFESSIONAL CAREER

2017 – Head of the Core Facility for Protein Synthesis and Bioanalytics, Univ. of Bonn

2016 – Professor (W3) for Pharmaceut. Biochemistry and Bioanalytics, Univ. of Bonn

2011 – 2016 Professor (W2) for Medicinal Chemistry and Drug Synthesis, Univ. of Bonn

2007 – 2010 Head of Junior Research Group “Peptide Chemistry”, CMB/University of Jena

2005 – 2006 HWP grant for habilitation, CMB/University of Jena

2004 – 2005 Postdoc with Prof. Dr. Dehua Pei, Johnston Laboratory, Department of Chemistry, Ohio State University, Columbus, USA

2003 – 2004 Research assistant, University of Jena

2002 Research assistant, University Hospital Jena

2001 HWP grant for habilitation, University of Jena

2000 – 2001 Head of Service Unit “Peptide Libraries“ of IZKF, University Hospital Leipzig

1999 – 2000 Research assistant, University of Jena

SERVICE TO SCIENTIFIC COMMUNITY AND HONOURS (SELECTION)

9/1994-6/1995 Foreign exchange student, Erasmus program, DCU Dublin, Ireland

6/2000 PhD award of the Faculty of Biology and Pharmacy, University of Jena

7/2001-12/2001 Research grant for habilitation, "Hochschulwissenschaftsprogramm zur Nachwuchs- und Frauenförderung des Freistaates Thüringen"

2005-2006 Research grant for habilitation, "Hochschulwissenschaftsprogramm zur Nachwuchs- und Frauenförderung des Freistaates Thüringen"

2005, 2006 Grants of the Fonds der Chemischen Industrie

2015, 2018, 2022 DAAD travel/congress grants (invited lectures)

9/2011 Organizer of Workshop "Biomolecules in Ionic Liquids: synthesis, structure elucidation, biological activity" within DFG SPP1191, Heimerzheim

1/2012-6/2015 Finance representative, Pharmacy, University of Bonn, deputy since 7/2015

4/2014-9/2015 Member of the senate, University of Bonn

5/2020-6/2023 Member (Vice chair) of the Gender Equality Committee, University of Bonn

2014-15/2020-21 Executive director, Pharmaceutical Institute, deputy 2015-16, 2021-23

since 8/2020 Founder and patron of the network WHATS-UB (Women in higher education and top science – University of Bonn), University of Bonn

BIBLIOMETRIC DATA

> 130 publications, 1 text book, 2 book chapters, >2500 citations, > 30 invited lectures/oral Presentations

SELECTION OF THE 10 MOST PROJECT-RELEVANT PUBLICATIONS

[1] Kühl, T., Wißbrock, A., Goradia, N., Sahoo, N., Galler, K., Neugebauer, U., Popp, J., Heinemann, S.H., Ohlenschläger, O., Imhof, D. (2013) Analysis of Fe(III) heme binding to cysteine-containing heme regulatory motifs in proteins, *ACS Chem. Biol.*, 8(8), 1785-1793. Doi: 10.1021/cb400317x

[2] Wißbrock, A., Kühl, T., Silbermann, K., Becker, A. J., Ohlenschläger, O., Imhof, D. (2017) Synthesis and evaluation of Abeta-derived and Abeta-independent enhancers of the peroxidase-like activity of heme. *J. Med. Chem.*, 60(1), 373-385. Doi: 10.1021/acs.jmedchem.6b01432

[3] Kumar, A., Wißbrock, A., Goradia, N., Bellstedt, P., Ramachandran, R., Imhof, D., Ohlenschläger, O. (2018) Heme interaction of the intrinsically disordered N-terminal peptide segment of human cystathionine- β -synthase. *Sci. Rep.*, 8, 2474. Doi: 10.1038/s41598-018-20841-z

[4] Wißbrock, A., Goradia, N.B., Kumar, A., Paul George, A.A., Kühl, T., Bellstedt, P., Ramachandran, R., Hoffmann, P., Galler, K., Popp, J., Neugebauer, U., Hampel, K., Zimmermann, B., Adam, S., Wiendl, M., Krönke, G., Hamza, I., Heinemann, S.H., Frey, S., Hueber, A.J., Ohlenschläger, O., Imhof, D. (2019) Structural insights into heme binding to IL-36 α proinflammatory cytokine. *Sci. Rep.*, 9, 16893. Doi: 10.1038/s41598-019-53231-0

- [5] Humayun, F., Domingo-Fernandez, D., Paul George, A.A., Hopp, M.-T., Syllwasschy, B.F., Detzel, M.S., Hoyt, T.C., Hofmann-Apitius, M., Imhof, D. (2020) A computational approach for mapping heme biology in the context of hemolytic disorders. *Front. Bioeng. Biotechnol.*, 8, 74. Doi: 10.3389/fbioe.2020.00074
- [6] Paul George, A.A., Lacerda, M., Syllwasschy, B.F., Hopp, M.-T., Wißbrock, A., Imhof, D. (2020) HeMoQuest: A webserver for qualitative prediction of transient heme binding to protein motifs. *BMC Bioinformatics*, 21, 124. Doi: 10.1186/s12859-020-3420-2
- [7] Hopp, M.-T., Alhanafi, N., Paul George, A.A., Hamedani, N. S., Biswas, A., Oldenburg, J., Pötzsch, B., Imhof, D. (2021) Molecular insights and functional consequences of the interaction of heme with activated protein C. *Antioxid. Redox Signal.*, 34(1), 32-48. Doi: 10.1089/ars.2019.7992
- [8] Hopp, M.-T., Domingo-Fernández, D., Gadiya, Y., Detzel, M.S., Graf, R., Schmalohr, B.F., Kodamullil, A.T., Imhof, D., Hofmann-Apitius, M. (2021) Linking COVID-19 and heme-driven pathophysiologies: A combined computational-experimental approach. *Biomolecules*, 11, 644. Doi: 10.3390/biom11050644
- [9] Hopp, M.-T., Rathod, D., Imhof, D. (2022) Host and viral proteins involved in SARS-CoV-2 infection differentially bind heme. *Protein Sci.*, e4451. Doi: 10.1002/pro.4451
- [10] Mubeen, S., Domingo-Fernández, D., Días del Ser, S., Solanki, D. M., Kodamullil, A. T., Hoffmann-Apitius, M., Hopp, M.-T., Imhof, D. (2022) Exploring the complex network of heme-triggered effects on the blood coagulation system. *J. Clin. Med.*, 11(19), 5975. Doi: 10.3390/jcm11195975