

XXXVth Winter School
on
Proteinases and Their Inhibitors

Tiers am Rosengarten
February 28 – March 4, 2018



35th Winter School on Proteinases and Their Inhibitors
in Tiers (Italy)
February 28 – March 4, 2018

Organizing Committee

Klaudia Brix (Bremen)

Thomas Reinheckel (Freiburg)

Christian Sommerhoff (Munich)

Boris Turk (Ljubljana)

Hans Brandstetter (Salzburg)

Editors

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University of Salzburg

Supported by



GENERAL INSTRUCTIONS

Accommodation

All Winterschool participants are accommodated in one of the three hotels Rose, Paradies or Laurin, all of which are in five minutes walking distance. If you are unsure, please ask at the registration of Hotel Paradies. They have a list of all participants and are happy to help you.

While accommodation and meals including mineral water are covered, any extras are not:

- Please pay all drinks (except mineral water) directly after the meal.
- Please do not forget to pay your good night-drinks before you leave for sleeping.
- Please do not forget to pay all your extras (personal orders, ...) at your hotel before departure.

If you want to rent ski equipment, please ask at the Hotel Paradies.

Scientific sessions

All lectures will take place at the *Haus der Dorfgemeinde* (City Hall).

Social events

- Thursday evening, Paradies: *Meet and Make Friends in Proteolysis Research*
- Friday evening, City Hall: *Night session with the InhibiTiers Allstar Band*
- Saturday afternoon *Several hiking tours, excursions*
- Saturday evening, Castle Prösels *Gala Dinner & Farewell*

Disclaimer

To enable and foster the unrestrained presentation and discussion of new results and ongoing research, every Winter School attendee must respect that all contents presented and discussed at the Winter School are private communications, not allowed for public use. Consequently, recording of lectures or photographing/copying of slides or presentations is prohibited.

PRELIMINARY PROGRAM

Regular talks are 8 min lecture plus **4 min discussion**.

WEDNESDAY, FEBRUARY 28

18:00 Dinner

20:00 – 21:45 Wednesday evening session: Immunity

20:00 – 20:05 Opening

20:05 – 20:15 **Chairs:** Dieter JENNE & Yoshifumi ITOH: *Background, open questions, approaches*

20:15 – 20:27 Seda SEREN (Centre d'Etude des Pathologies Respiratoires) *Consequences of cathepsin C inactivation on membrane expression of proteinase 3, the target antigen in autoimmune vasculitis*

20:27 – 20:39 Salome REHM (Helmholtz Center Munich) *Preemptive inhibition of cathepsin C in candidates for transplantation improves early graft functions*

20:39 – 20:51 Alejandro PUCHOL-TARAZONA (University of Natural Resources and Life Sciences, Vienna) *Degradation of anti-HIV antibodies 2F5 and PG9 by proteases of *Nicotiana benthamiana**

20:51 – 21:03 Yoan MACHADO (University of Salzburg) *Fold-stability is a key factor for allergenicity and immunogenicity of the major birch pollen allergen Bet v 1*

21:03 – 21:08 **FLASH TALK:** Wai Tuck SOH (University of Salzburg) *Relevance of Bet v 2 Conformation to Its Proteolytic Resistance to Cathepsin S*

21:08 – 21:20 Inga TUNEEW (University of Southern Denmark) *FVa-stabilizing monoclonal antibodies that interfere with aPC-mediated degradation of FVa*

21:20 – 23:00 Chris OVERALL (University of British Columbia) *A Twist of the TAILS: An Allosteric Inhibitor Rescues Mutant MALT1 in an Immunodeficient Patient*

22:00 **REFRESHING SENSES & MEMORIES IN THE PARADIES BAR**

THURSDAY, MARCH 1

09:00 – 10:30 Thursday morning session I: Cancer

09:00 – 09:10 **Chairs:** Christoph PETERS & Thomas REINHECKEL: *Background, open questions, approaches*

09:10 – 09:25 Nermina TOPCAGIC (University of Vienna) *Role of lysosomal cathepsins in cyclohexadepsipeptide induced cell growth inhibition of cancer cells*

09:25 – 09:37 Maria Alejandra PARIGIANI (Albert-Ludwigs-Universität Freiburg) *Cell specific functions of the lysosomal protease Cathepsin L in breast cancer*

09:37 – 09:49 Stefanie WEISS (Helmholtz-Zentrum München) *Tumor-derived granulocyte chemotactic protein 2 cooperates with neutrophil elastase and proteinase 3 to drive lung adenocarcinoma*

09:49 – 10:01 Lena HÖLZEN (Albert-Ludwigs-Universität Freiburg) *Combining PI3K-pathway inhibition with a degradome-wide genetic interference screening in murine breast cancer cells*

10:01 – 10:13 Weiwei GONG (Technical University of Munich) *Clinical relevance of kallikrein-related peptidase 4 (KLK4) mRNA expression levels in tumor tissue of high-grade advanced (FIGO III/IV) serous ovarian cancer patients*

10:13 – 10:18 **FLASH TALK:** Xiaocong GENG (Technical University of Munich) *Tumor tissue protein expression levels of kallikrein-related peptidase (KLK) 10 and 11 are associated with prognosis of advanced high-grade serous ovarian cancer patients*

10:18 – 10:30 Yueyang LIU (Technical University of Munich) *Quantitative assessment of KLK 10 and 11 mRNA expression in triple negative breast cancer: KLK10 is a novel independent prognostic marker for disease-free survival in this major breast cancer subtype*

10:30 – 11:00 COFFEE BREAK

11:00 – 12:00 Thursday morning session II: Life time of achievements of Manfred SCHMITT

11:00 – 11:10 **Chair:** Hans BRANDSTETTER: *A tribute to Manfred SCHMITT (1947 – 2018)*

11:10 – 11:35 Judith CLEMENTS (Queensland University of Technology Brisbane) *A KLK journey: the Munich Brisbane connections*

11:35 – 12:00 Viktor MAGDOLEN (Technical University of Munich) *Personalized Medicine: Identification of Cancer-related Biomarkers to Predict Prognosis and Treatment Success*

12:15 LUNCH (Paradies, Rose)

THURSDAY AFTERNOON SESSIONS

14:30 – 16:21 Thursday afternoon session I: MMP – TIMP (patho-)biology

14:30 – 14:40 Chairs: Rama KHOKHA & Achim KRÜGER: **Background, open questions, approaches**

14:40 – 14:52 Benjamin SCHOEPS (Technical University of Munich) *TIMP-1 induces formation of neutrophil extracellular traps to create a pre-metastatic liver niche*

14:52 – 15:04 Paulina KASPERKIEWICZ (Wroclaw University of Science and Technology) *The role of Neutrophil serine proteases in netosis*

15:04 – 15:16 Jennifer VANDOOOREN (Rega Institute for Medical Research - University of Leuven) *MMP-9 cleaves secretory leukocyte peptidase inhibitor and modulates its anti-proteolytic activity, a new link in the balance between proteases and inhibitors*

15:16 – 15:28 Chris HERMANN (Technical University of Munich) *Correlation of elevated systemic TIMP-1 with clinical markers of cachexia in the development of pancreatic cancer*

15:28 – 15:40 Johanna KARBE (Technical University of Munich) *Purification of Flag-tagged recombinant TIMP-1 variants*

15:40 – 15:52 Barbara GRÜNWALD (University of Toronto) *Delineation of the TIMP–protease–substrate network in pancreatic tumor stroma*

15:52 – 16:04 Simonas SAVICKAS (Technical University of Denmark) *High-throughput targeted degradomics analysis of matrix metalloproteinases in murine skin using pressure cycling technology*

16:04 – 16:16 Valentina GIFFORD (University of Oxford) *Intracellular trafficking of the invasion promoting cell surface proteinase MT1-MMP*

16:16 – 16:21 **FLASH TALK:** Isabel PABLOS (University of British Columbia) *Proteolytic regulation of high mobility group box 1 (HMGB1) activity by matrix metalloproteinase 7 (MMP7) processing*

16:21 – 16:45 COFFEE BREAK

16:45 – 18:07 Thursday afternoon session II: Signaling

16:45 – 16:55 Chairs: Ruth GEISS-Friedlander & Brice KORKMAZ: **Background, ...**

16:55 – 17:07 Aleksander KRAJNC (Jožef Stefan Institute) *Secretomic analysis of the effects of TNF α on macrophages and cancer cells*

17:07 – 17:19 Hung-En HSIA (German Center for Neurodegenerative Diseases (DZNE)) *Proteolytic processing and function of death receptor 6 in the peripheral nervous system*

17:19 – 17:31 Waheed SHABBIR (University of Vienna) *Proteases mediated activation of epithelial sodium channel*

17:31 – 17:43 Marina KLEMENČIČ (University of Umeå, University of Ljubljana) *Metacaspases and calcium: disentangling the role of the p10 domain*

17:43 – 17:55 Oguz BOLGI (University of Medical Center Göttingen) *Role of DPP9 in cell signalling*

17:55 – 18:07 Janja BOŽIČ (Jožef Stefan Institute) *Glucosamine prevents cell-mediated cytotoxicity of the natural killer cell line NK-92*

18:30 DINNER (PARADIES, ROSE)

20:00 – 23:00 MEETING AND MAKING FRIENDS IN PROTEOLYSIS RESEARCH (PARADIES)

FRIDAY, MARCH 2

09:00 – 10:49 Friday morning session I: Lysosomal proteases & inhibitors

09:00 – 09:10 **Chairs:** Dušan TURK & Lukas MACH: *Background, open questions, approaches*

- 09:10 – 09:22 Monika BIASIZZO (Jožef Stefan Institute, Ljubljana) *The role of cystatin C in inflammatory response and endotoxemia*
- 09:22 – 09:27 *FLASH TALK:* Andreja BRATOVŠ (Jožef Stefan Institute) *Stefin A as a ligand for cathepsins S and L-targeted drug delivery*
- 09:27 – 09:39 Janja ZAVRŠNIK (Jozef Stefan Institute) *Ablation of stefin B and cystatin C results in smaller tumors in a breast cancer model*
- 09:39 – 09:51 Nataša KOPITAR-JERALA (Jozef Stefan Institute) *Anti-inflammatory effect of cysteine cathepsin inhibitor stefin B in macrophages is mediated by autophagy*
- 09:51 – 10:03 Elfriede DALL (University of Salzburg) *Legumain inhibitory cystatin E transforms to multimers with distinct function*
- 10:03 – 10:15 Alejandro GOMEZ-AULI (Albert-Ludwigs-Universität Freiburg) *Cysteine Cathepsin B can regulate the abundance of the antitumoral-like glycoprotein CREG1*
- 10:15 – 10:27 Friederike ZUNKE (University of Kiel) *α -Synuclein aggregation mechanisms and how they might affect maturation of lysosomal cathepsins*
- 10:27 – 10:49 James BURROWS (Queen's University Belfast) *Does USP17 regulate lysosome positioning?*

10:49 – 11:10 COFFEE BREAK

11:10 – 12:25 Friday morning session II: Pathogens

11:10 – 11:20 **Chairs:** Maria Luiza OLIVA & Jan POTEMPA: *Background, open questions, approaches*

- 11:20 – 11:32 Christian PICHLO (University of Cologne) *Structural Insights into the Mechanism and Specificity of Proline-Proline Endopeptidase-1 from Clostridium difficile*
- 11:32 – 11:44 Fabian WOJTALLA (University of Cologne) *Production, biochemical characterization and structure of a PPEP-1 related metalloprotease from Aeromonas hydrophila, Vibrio cholerae and Vibrio vulnificus.*
- 11:44 – 11:56 Ulrich ECKHARD (University of Salzburg) *Bacterial Flagella in the Moonlight of Proteolysis.*
- 11:56 – 12:08 Irena WALIGÓRSKA (Jagiellonian University) *Novel proteases from human pathogen Tannerella forsythia*
- 12:08 – 12:20 Dóra BALOGH (Technical University of Munich) *Stimulation of ClpXP proteolysis by partial inhibitor binding and hetero-oligomerization*
- 12:20 – 12:25 *FLASH TALK:* Isabel HOPPE (University of Salzburg) *Biochemical and enzymatic characterization of bacterial collagenases*

12:30 LUNCH (Paradies, Rose)

FRIDAY AFTERNOON SESSIONS

14:30 – 16:09 Friday afternoon session I: Metalloproteases

14:30 – 14:40 **Chairs:** Uli DEMUTH & Walter STÖCKER: *Background, open questions, approaches*

14:40 – 14:52 Michael KUSKE (Johannes Gutenberg University of Mainz) *Modes of Ovastacin Activation in vitro and in vivo*

14:52 – 15:04 Hagen KÖRSCHGEN (Johannes Gutenberg University of Mainz) *Intracellular activation of ovastacin facilitates premature hardening of the Zona pellucida*

15:04 – 15:16 Milan FOWKES (University of Oxford) *Screening for ADAMTS-4 and ADAMTS-5-selective substrates to detect and monitor proteinase activity in vivo*

15:16 – 15:28 **THUNDER TALK:** Franka SCHARFENBERG (University of Kiel) *Degradome of soluble ADAM10 and ADAM17*

15:28 – 15:36 Martin SAMMEL (University of Kiel) *Ectodomain shedding of interleukin receptors*

15:36 – 15:48 Claudia SPAHN (Fraunhofer Institute for Cell Therapy and Immunology, Halle/Saale) *The structure of meprin β in complex with a specific inhibitor*

15:48 – 16:00 Kathrin TAN (Fraunhofer Institute for Cell Therapy and Immunology, Halle/Saale) *Towards selective inhibitors of Meprin α*

16:00 – 16:09 **THUNDER TALK:** Luisa WESSOLOWSKI (University of Kiel) *Proteolytic processing of TREM2 by Meprin β*

16:09 – 16:40 COFFEE BREAK

16:40 – 17:28 Friday afternoon session II: Posttranslational control of meprin function

Chairs: Uli DEMUTH & Walter STÖCKER

16:40 – 16:52 Philipp ARNOLD (University of Kiel) *Proteolytic regulation of cancer associated variants of meprin β*

16:52 – 17:04 Rielana WICHERT (University of Kiel) *Mucus detachment in the small intestine requires shedding of host metalloprotease meprin β , which is abrogated by pathogenic protease RgpB*

17:04 – 17:16 Fred ARMBRUST (University of Kiel) *Phosphorylation of meprin β diminishes its proteolytic activity*

17:16 – 17:28 Florian PETERS (University of Kiel) *A single glycosylation motif determines the unique oligomeric structure of meprins*

18:00 **DINNER (PARADIES, ROSE)**

20:30 – 23:45 **NIGHT SESSION WITH THE INHIBITORS (CITY HALL)**

SATURDAY, MARCH 3

09:00 – 10:15 Saturday morning session I: Inhibitor & substrate recognition

09:00 – 09:10 **Chairs:** Esther SCHÖNAUER & Dorian LAMBA: *Background, open questions, approaches*

09:10 – 09:22 Tomasz JANISZEWSKI (Wrocław University of Science and Technology) *Cathepsin K extended substrate specificity determination*

09:22 – 09:34 Jure LOBODA (Jožef Stefan Institute) *Structural insight in peptidyl substrate binding to cysteine cathepsins*

09:34 – 09:46 Ilka WOIWODE (University of Cologne) *A family of unconventional deubiquitinases with modular chain specificity determinants*

09:46 – 09:51 **FLASH TALK:** Sven DAHMS (University of Salzburg) *Substrate specificity determinants of the proprotein convertase furin beyond the S4 pocket.*

09:51 – 10:03 Johannes KRAML (Leopold-Franzens-University of Innsbruck) *Electrostatic Substrate Recognition in Serine Proteases*

10:03 – 10:15 Ursula KAHLER (Leopold-Franzens-University of Innsbruck) *The E – E* Equilibrium of Thrombin*

10:15 – 10:45 COFFEE BREAK

10:45 – 11:36 Saturday morning session II: Substrate discovery

10:45 – 10:55 Chairs: Ulrich AUF DEM KELLER & Pitter HUESGEN: *Background, open questions, approaches*

10:55 – 11:07 Sonia KOLT (Wrocław University of Science and Technology) *IQF substrates for proteases activity profiling*

11:07 – 11:19 Wioletta RUT (Wrocław University of Science and Technology) *Combinatorial approach to substrate specificity of deubiquitinating enzymes*

11:19 – 11:24 **FLASH TALK:** Elizabeta MADZHAROVA (Technical University of Denmark) *Cutting it in four: an improved TMT-TAILS workflow*

11:24 – 11:36 Dilza Trevisan SILVA (Butantan Institute, Brazil) *Proteomic characterization of the in vivo effects of the hemorrhagic metalloproteinase HF3 from Bothrops jararaca venom on mouse kidney*

12:00 LUNCH

SATURDAY AFTERNOON: HIKING, EXCURSION, ROUND TABLE DISCUSSIONS

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| 12:15 – 17:00 | “Extreme” hiking tour (lunch package will be provided) |
| 13:30 – 17:00 | Relaxed hiking tour |
| 12:15 – 17:00 | Locally organized skiing tours (ski equipment can be rent at the Hotel Paradies; lunch package will be provided) |
| 12:45 – 16:00 | Bus tour to Bozen (Guided Tour of Bozen, Visit Ötzi & more) |
| 16:40 | Bus to Castle Prösels for Guided Tour (17.00 – 18.00) |
| 18:00 | First shuttle bus to Castle Prösels |
| 18:30 | Second shuttle bus to Castle Prösels |

19:00 GALA DINNER AT CASTLE PRÖSELS

SUNDAY, MARCH 4

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| 10:00 | Bus departure |
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ABSTRACTS

Available in the printed program only.