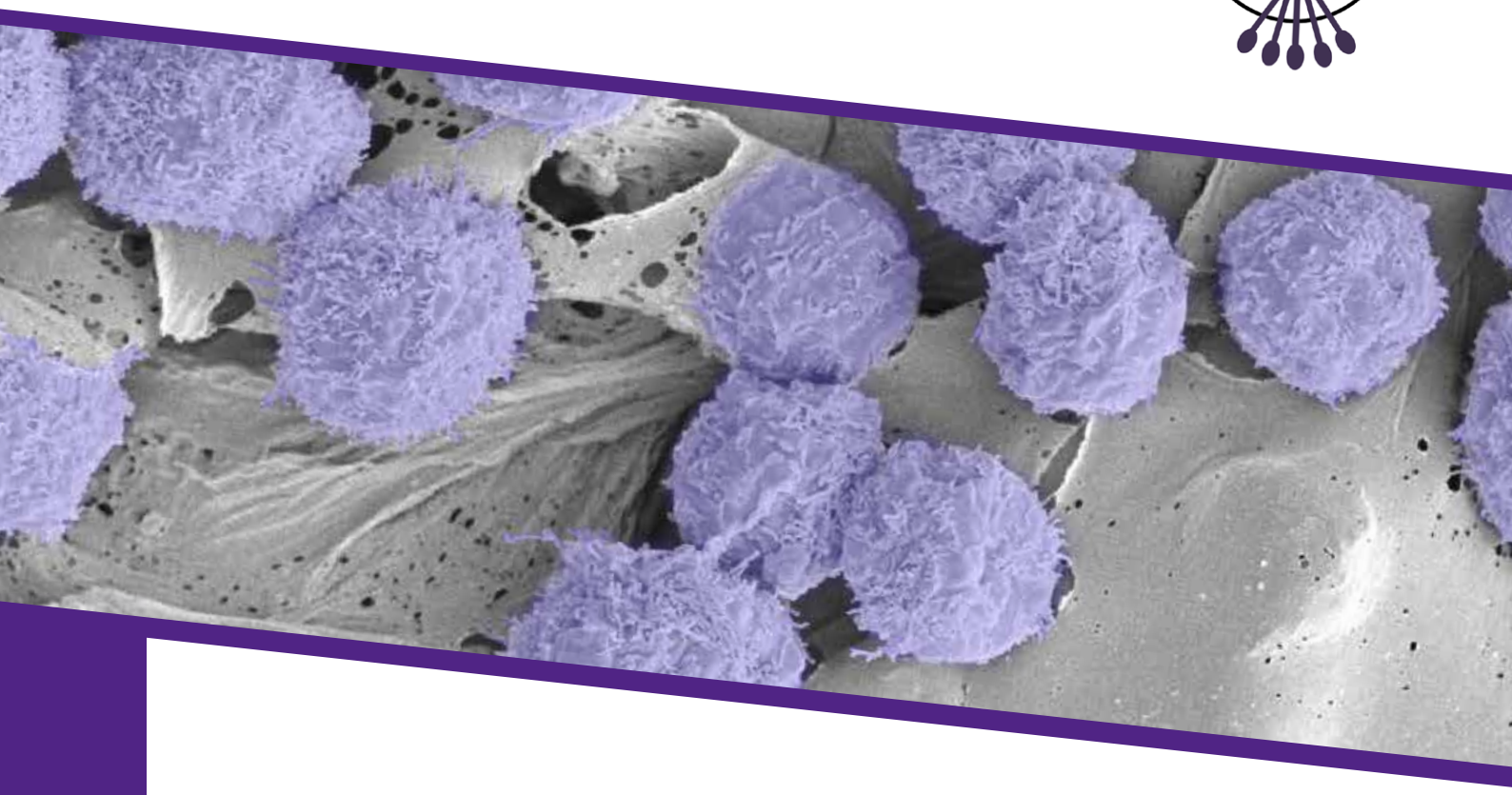

2021 28th INTERNATIONAL COMPLEMENT VIRTUAL WORKSHOP

December 06-10, 2021

ICS INTERNATIONAL COMPLEMENT SOCIETY
Complement... we are the experts!™

WELCOME NOTES

Dear Colleagues,

On behalf of the International Complement Society, we would like to welcome you to the ICW 2021 Virtual Workshop. Having to cancel the ICW 2020 in Berlin due to the impact of the SARS-CoV-2 was a difficult decision for Council and to transition to a fully virtual experience was necessary allowing us to replicate the program for ICW 2021.

We are certain that the virtual experience will serve the purpose of presenting the latest research and provide opportunities for scientific exchange with each other. The poster sessions will be available to visit anytime during the meeting and will be presented live on an interactive platform during the formal poster sessions.

On behalf of the Council and Local Organizing Committee, we thank you for your support and for standing by ICS through the changes, disruptions, and difficulties of the past year. We hope to see each of you in person in New Castle, UK in Sept 2023 for the ICW 2023.

Peter Garred, MD, PhD, President of ICS

Peter Zipfel, PhD, ICW organizer

Christine Skerka, PhD, ICW co-organizer

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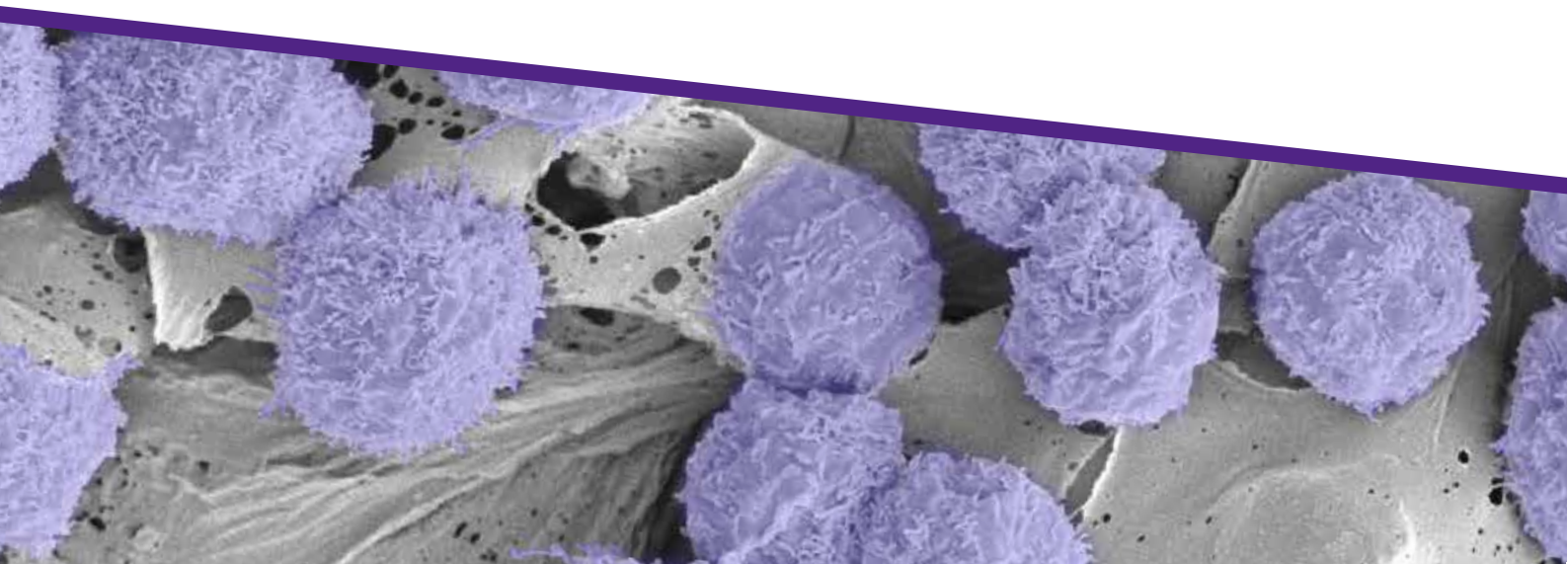

MAIN VIRTUAL PLATFORM

ICW program (December 07 - 10) will take place on Pheedloop platform. Only pre-registered delegates will have the access to platform for ICW program, as well as the contents saved in the platform. The recorded videos saved in ICW virtual platform for play on demand after the conference and until May 31, 2022.

Pheedloop platform for the delegtes: https://pheedloop.com/icw2021/virtual/

POSTER SESSION

Live poster presentations will be held in SpatialChat. All pre-registered delegates are welcome to visit SpatialChat to view all the posters during December 06 - 10.

Poster Session A, Wednesday, December 8, 2021, 18:15 - 20:15 (CET)
Poster Session B, Thursday, December 9, 2021, 17:45 - 19:45 (CET)

SpatialChat platform for the delegates: please find the link in Pheedloop "POSTER HALL" room.

PLATFORM LOG-IN

Log-in information will be sent to all the pre-registered delegates on December 03, 2021.

TEACHING DAY ON DECEMBER 06

Teaching Day will be held in Zoom platform. All pre-registered delegates will receive the access link and information on December 03, 2021.

TEACHING DAY MONDAY DECEMBER 06

CET

14:00 - 14:15 **Introduction to Teaching Day and Modern Aspects of Complement**
Peter Zipfel (Hans Knöll Institute, Germany)

Moderator: Cláudia Vilhena

14:15 - 14:35 **Complement Activation,** Anna Bloom (Lund University, Sweden)

14:35 - 14:55 **Complement Regulation**, Viviana Ferreira (University of Toledo, USA)

14:55 - 15:15 **Complement and Inflammation**, Trent Woodruff (University of Queensland, Australia)

15:15 - 15:30 **Part 1 - Live Q&A**

15:30 - 15:50 **Complement Disease**, Diana Karpman (Lund University, Sweden)

15:50 - 16:10 **Complement Therapy**, Joshua Thurman (University of Colorado , USA)

16:10 - 16:20 **Part 2 - Live Q&A**

16:20 - 17:00 **Break**

Group Exercises I (17:00 - 18:15)

Infections dieases and Inflammation	Gabriele Pradel (Aachen University, Germany) Elena G. de Jorge (Complutense University School of Medicine, Spain)
Modern Complement Techniques	Claire Harris (Newcastle University, UK) Christian Karsten (University of Lübeck, Germany)
Cancer	Ruben Pio (University of Navarra, Spain) Lubka Roumenina (Sorbonne Universités, France)
Neurodegenerative diseases	Simon Clark (University of Manchester, UK) Bärbel Rohrer (Medical University of South Carolina, USA)

Group Exercises II (18:30 - 19:45)

Infections dieases and Inflammation	Gabriele Pradel (Aachen University, Germany) Elena G. de Jorge (Complutense University School of Medicine, Spain)
Modern Complement Techniques	Claire Harris (Newcastle University, UK) Christian Karsten (University of Lübeck, Germany)
Cancer	Ruben Pio (University of Navarra, Spain) Lubka Roumenina (Sorbonne Universités, France)
Neurodegenerative diseases	Simon Clark (University of Manchester, UK) Bärbel Rohrer (Medical University of South Carolina, USA)

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Transforming PNH Treatment

Evaluating oral monotherapy in patients with PNH who have an inadequate response to C5 inhibitor therapy

REDEEM 2
Transforming PNH Treatment

Evaluating oral monotherapy in patients with PNH not currently receiving C5 inhibitor therapy

For more information, visit
www.biocryst.com/PNH

CET

13:50 - 14:15 **WELCOME NOTES**
Peter Zipfel, Peter Garred, Thomas Kamradt, Christine Skerka

14:15 - 15:25 **SESSION I – COMPLEMENT STRUCTURE AND FUNCTION**
Moderators: Nicole Thielens and Peter Garred

(92)
The significance of complex formation of MASP-3 with pattern recognition molecules of the lectin complement pathway in the long-term retention of MASP-3 in the circulation
Machida, Takeshi; Kusakari, Kohei; Ishida, Yumi; Omori, Tomoko; Suzuki, Toshiyuki; Sekimata, Masayuk; Fujita, Teizo; Sekine, Hideharu

(18)
Complexes between C1q and MASPs are present in the circulation and may mediate complement activation
Rosbjerg, Anne; Bayarri-Olmos, Rafael; Skjoedt, Mikkel-Ole; Garred, Peter

(24)
Structure-Function Studies of Complement Receptor 3 Specific Nanobodies
Lorentzen, Josefine Jensen; Rasmus K. Andersen; Gregers Rom; Vorup-Jensen, Thomas

(176)
Biochemical and X-ray diffraction analysis of the interaction between iC3b and the CR3 αI domain
Fernández, Francisco José Santos-López; Jorge Martínez-Barricarte; Rubén Querol-García, Javier; Martín-Merinero, Héctor; Navas-Yuste, Sergio; Savko, Martin; Shepard, William E.; Rodríguez de Córdoba, Santiago; Vega, M. Cristina

(181)
Visualizing DNA mediated complement activation using cryo-electron tomography
Abendstein, Leoni

15:25 - 15:45 **SESSION I – LIVE Q&A**

15:45 - 16:15 Break

16:15 - 16:45 **KEYNOTE LECTURE I**
Complement: A key regulator of neural circuit degeneration
Introduction: Cláudia Vilhena

Professor Dorothy Schafer
Associate Professor, Department of Neurobiology, University of Massachusetts Chan Medical School, Worcester, USA

CET

16:45 - 17:55 **SESSION II – COMPLEMENT ACTIVATION**

Moderators: Christoph Schmidt and Elena Goicoechea de Jorge

(48)
Complement Gene Expression and Biodistribution of Complement Proteins in the Synovium from Early Rheumatoid Arthritis Patients
Banda Nirmal; Deane, Kevin; Seifert, Jennifer; Strickland, Colin; Bemis, Elizabeth; Jordan, Kimberly; Goldman, Katriona; RA/SLE Network, Accelerating Medicines Partnership (AMP); Morgan, B. Paul; Lewis, Myles J.; Pitzalis, Costantino; Moreland, Larry W.R; Holers, Michael

(222)
Complement downregulation promotes an inflammatory signature that renders colorectal cancer susceptible to immunotherapy
Guglietta, Silvia; Weber, Lukas; Fosso, Bruno; Marzano, Marinella; Hardiman, Gary; Robinson, Mark; Krieg, Carsten

(140)
Inhibition of neuro-inflammation induced gliomagenesis by CSMD1
Tuysuz, Emre Can; Gialeli, Chrysostomi; Blom, Anna M.

(6)
IgA-Complement immune complexes: A novel mechanism for the delivery of complement proteins to the glomerulus in IgA nephropathy
Hamed, Mohamed

(128)
Novel gain-of-function mutations R249C and S250C in complement C2 protein in patients suffering from rare kidney diseases
Kowalska, Daria; Urban, Aleksandra; Kuźniewska, Alicja; Skrobińska, Anna; de Córdoba, Santiago Rodriguez; Arjona, Emilia; Okrój, Marcin

17:55 - 18:15 **SESSION II – LIVE Q&A**

18:15 - 18:45 Break

18:45 - 19:15 **HANS MÜLLER EBERHARDT LECTURE**
Complement in human disease
Introduction: Michael Holers

Professor Mohammed R. Daha
Emeritus Professor, Leiden University Medical Center, Leiden, The Netherlands

CET

19:15 - 20:25 **SESSION III – COMPLEMENT GENETICS; CROSSTALK; AUTOREACTIVITY AND INFLAMMATION**

Moderators: Marina Noris and Kevin Marchbank

(82)
Upregulation of check-point ligand PD-L1 in patients with PNH explained by proximal complement activation
Hafner, Susanne; Anliker, Markus; Drees, Daniela; Loacker, Lorin; Griesmacher, Andrea; Hoermann, Gregor; Fux, Vilmox; Schennach, Harald; Hörtnagl, Paul; Dopler, Arthur; Schmidt, Stefan; Bellmann-Weiler, Rosa; Weiss, Günter, Marx-Hofmann, Astrid; Körper, Sixten; Höchsmann, Britta; Schrezenmeier, Hubert; Schmidt, Christoph Q.

Activation of MASP-3 by PCSK6 links the complement and the proprotein convertase systems in the blood
Dobó, József; Oroszlán, Gábor; Dani, Ráhel; Végh, Barbara M.; Varga, Dóra; Ács, Andrea V. ; Pál, Gábor; Závodszky, Péter; Farkas, Henriette; Gál, Péter

(109)
The lectin pathway is associated with platelet activation during clot formation in a microfluidic bleeding model
Golomingi, Murielle; Dobó, József; Gál, Péter; Pál, Gábor Lam, Wilbur; Schroeder, Verena

(227)
Regulatory architecture of the RCA gene cluster captures an intragenic TAD boundary at the CR1 segmental duplication and long-range enhancer
Cheng, Jessica; Clayton, Joshua; Acemel, Rafael; Zheng, Ye; Taylor, Rhonda; Keleş, Sündüz; Franke, Martin; Harley, John; Quail, Elizabeth; Gómez-Skarmeta, José Luis; Ulgiati, Daniela

(218)
Bulk and single-cell RNA-seq analysis of complement and coagulation cascades in severe inflammation; The whole blood model versus patient data
Emblem, Åse; Slåtsve, Arne Martin; Knutsen, Erik; Mjelle, Robin; Lau, Corinna; Landsem, Anne; Nilsson, Per; Brekke, Ole-Lars; Mollnes, Tom Eirik; Karlsen, Bård

20:25 - 20:45 **SESSION III – LIVE Q&A**

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CET

14:00 - 15:10 **SESSION IV – COMPLEMENT RECEPTORS AND INTRACELLULAR COMPLEMENT**
Moderators: Bärbel Rohrer and Santiago Rodriguez de Cordoba

(146)
Investigation of complement C3 activation and expression in human skeleton muscle myotubes under pro-inflammatory cytokine stress
Licht, Christoph; Jat, Harpreet; Gilbert, Penney

(27)
Intracellular cytosolic C3 protects pancreatic β-cells from IL-1β-driven cytotoxicity
Kulak, Klaudia; Mckay, Marina; Blom, Anna; King, Ben

(22)
The Systemic Absence of C5a Receptor 2 Contributes to an Impaired Establishment of Lung Metastases and a Better Disease Outcome in Mice
Hennig, Caroline; Karsten, Christian M.

(200)
The C5a / C5a receptor 1 axis in platelets controls tissue revascularization through preferential release of CXCL4
Nording, Henry; Baron, Lasse; Emschermann, Frederic; Haberthür, David; Borst, Oliver; Chavakis, Emmanouil; von Hundelshausen, Philipp; Karsten, Christian; Köhl, Jörg; Langer, Harald

(79)
Canonical and non-canonical functions of C1s in cancer
Revel, Margot; Daugan, Marie; Gaboriaud, Christine; Sautes-Fridman, Catherine; Fridman, Wolf Herman; Roumenina, Lubka

15:10 - 15:30 **SESSION I – LIVE Q&A**

15:30 - 15:45 Break

15:45 - 16:15 **SPECIAL LECTURE**
How Complement Wires and Unwires Brain Circuits in Development & Disease
Introduction: Markus Huber-Lang

Beth Stevens, Ph.D
F.M. Kirby Neurobiology Center, Children's Hospital Boston, USA

CET

16:15 - 17:25 **SESSION V – COMPLEMENT REGULATION AND DISEASE**

Moderators: Veronique Fremeaux Bacchi and Leendert Trouw

(76)
Atypical hemolytic uremic syndrome-associated FHR1 isoform FHR1*B accelerates complement activation and inflammation
Kang, Yuqi Xu, Boyang; Du, Yujing; Guo, Weiyi; Zhu, Li; Zhang, Hong

(193)
Implications for properdin, a complement regulatory protein, in disease
Moore, Sara R.; Nigrovic, Peter A.; Sparks, Jeffrey A.; Lee, Janet; Bain, William; Khuder, Sadik; Ferreira, Viviana P.

(175)
MASP3 deficiency in mice reduces but does not abrogate alternative pathway complement activity due to pro-factor D activity
Gullipalli, Damodara; Miwa, Takashi; Golla, Madhu; Sato, Sayaka; Angampalli, Sree; Song, Wenchao

(221)
Modeling the complement system for therapeutics development
Alfonso-González, Lucía; Fernández, Francisco José; Vega, M. Cristina; Abvance Biotech, Centro de Investigaciones Biológicas Margarita Salas (CIB-CSIC)

(25)
Properdin is essential for alternative pathway C5 convertase activity and C5b-9 formation
Michels, Marloes; Maas, Rianne; van der Velden, Thea; van de Kar, Nicole; Volokhina, Elena van den Heuvel, Bert

17:25 - 17:45 **SESSION V – LIVE Q&A**

17:45 - 18:15	Break

CET

18:15 - 20:15 **VIRTUAL POSTER SESSION**
Run in SpatialChat platform

20:15 - 20:45 **PIONEERING WOMEN IN COMPLEMENT**
Moderators:
Andrea Tenner
University of California, Irvine
&
Claudia Kemper
NIH, National Heart, Lung and Blood Institute, Bethesda, MD, USA

20:45 - 21:54 **SESSION VI – COMPLEMENT INFECTIOUS DISEASES**
Moderator: Robert Rieben and Anna Blom

(70)
Activation of human complement and release of complement-dependent cytokines by synthetic oligodeoxynucleotides cpg motifs
De Boer, Eline; Sokolova, Marina; Quang, Huy; McAdam, Karin; Woodruff, Trent; Götz, Maximilian; Garred, Peter; Nilsson; Mollnes, Tom Eirik; Pischke, Søren

(124)
C4b binding protein protects Group A streptococci from killing by phagocytosis and is internalised in human macrophages together with bacteria
Bettoni, Serena; Dziedzic, Mateusz; Blom, Anna M

(67)
Super-resolution microscopy to decipher the subcellular localization of complement regulatory proteins at the surface of Streptococcus pneumoniae
Vilhena, Cláudia; Du, Shanshan; Cseresnyes, Zoltán; Zimmermann, Lioba; Battista, Miriana; Jost, Aurélie; Eggeling, Christian; Kohler, Thomas; Skerka, Christine; Hammerschmidt, Sven; Figge, Marc Thilo; Zipfel, Peter

(65)
The alternative pathway of complement and long pentraxin ptx3 form a functional axis in the immune response to aspergillus fumigatus
Parente, Raffaellae; Possetti, Valentina; Stravalaci, Matteo; Sironi, Marina; Valentino, Sonia; Day, Anthony; Bottazzi, Barbara -; Cunha, Cristina -; Carvalho, Agostinho ; Mantovani, Alberto; Inforzato, Antonio

(154)
FHR1 increases the risk of severe malaria anemia in a cohort study
González Delgado, Andrés; Reiss, Timo; Zipfel, Peter; Fendel, Rolf; Pradel, Gabriele; Skerka, Christine

21:54 - 22:15 **SESSION VI – LIVE Q&A**

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11:00 - 11:30 **KEYNOTE LECTURE II (LIVE PRESENTATION)**
Cell-based Medicine
Introduction: Olaf Strauss

Prof. Nikolaus Rajewsky
Berlin Institute for Medical Systems Biology, Berlin, Germany

14:00 - 15:10 **SESSION VII – COMPLEMENT AND COVID-19**
Moderators: Reinhard Würzner and Nicole van der Kar

(46)
Associations between complement activation and the von Willebrand factor – ADAMTS13 axis in hospitalized COVID-19 patients
Sinkovits, György ; Mező, Blanka ; Réti, Marienn ; Prohászka, Zoltán

(130)
Classical complement pathway responses in vitro differ between SARS-CoV-2 antigens and according to disease severity
Lamerton, Rachel; Marcial Juarez, Edith; Faustini, Sian; Perez-Toledo, Marisol; Goodall, Margaret; Jossi, Sian; Shields, Adrian; Henderson, Ian; Rayes, Julie; Watson, Steve; Crispin, Max; Richter, Alex; Cunningham, Adam

(83)
Development of Immunoassays for Specific Classical and Lectin Pathway Activation Markers and Investigation of Complement Activation in COVID-19
Hurler, Lisa; Toonen, Erik J M; Kajdácsi, Erika; van Bree, Bregje; Sinkovits, György; Cervenak, László; Prohászka, Zoltán

(34)
Local NETosis and Systemic Inflammation and Complement Activation predicts Clinical Outcome of Severe SARS-CoV-2 Infections
Huber, Silke; Massri, Mariam; Grasse, Marco; Fleischer, Verena; Knabl, Ludwig; Knabl Sr., Ludwig; Heiner, Tatjana; Rambach, Günter; Neurauter, Magdalena; Speth, Cornelia; Würzner, Reinhard

(134)
C1 esterase inhibitor and the kinin-kallikrein system in COVID-19
Caccia, Sonia; Berra, Silvia; Parolin, Debora; Suffritti, Chiara; Folcia, Andrea; Zanichelli, Andrea; Cogliati, Chiara; Riva, Agostino; Gidaro, Antonio

15:10 - 15:30 **SESSION VII – LIVE Q&A**

15:30 - 15:45 Break

15:45 - 16:15 **KEYNOTE LECTURE III**
The Genetic History of Plague: What we learn from past pandemics
Introduction: Christine Skerka

Prof. Johannes Krause
Department of Archaeogenetics, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany

CET

16:15 - 17:15 **VIRTUAL SATELLITE SYMPOSIUM - sponsored by Vifor Pharma:**
Pathophysiology of ANCA associated vasculitis and clinical results of the C5-Receptor Antagonist AVACOPAN
Introduction: Peter F. Zipfel

Pathophysiology of ANCA associated vasculitis and the link to the Complement System
Prof. Dr. Ralph Kettritz
Charité and Max-Delbrueck-Center for Molecular Medicine in the Helmholtz Association (MDC), Berlin, Germany

C5-Antagonist AVACOPAN: Results from clinical studies (CLEAR/Ph2 and ADVOCATE/Ph3)
Prof. Dr. Bernhard Hellmich
Medius Klinik Kirchheim, Kirchheim unter Teck, Germany

LIVE Q&A

VIFOR PHARMA

17:15 - 17:45 Break

17:45 - 19:45 **VIRTUAL POSTER SESSION**
Run in SpatialChat platform

19:45 - 20:25 **LAMBRIS COMPLEMENT TRAINING AWARD**
Introduction: Paul Morgan
Presentation by Wioleta Zelek

20:25 - 20:55 **KEYNOTE LECTURE II (REPLAY - NO LIVE Q&A)**
Cell-based Medicine
Introduction: Olaf Strauss

Prof. Nikolaus Rajewsky
Berlin Institute for Medical Systems Biology, Berlin, Germany

20:55 - 21:25 **SOCIAL EVENT - COMPLEMENT BY ART**

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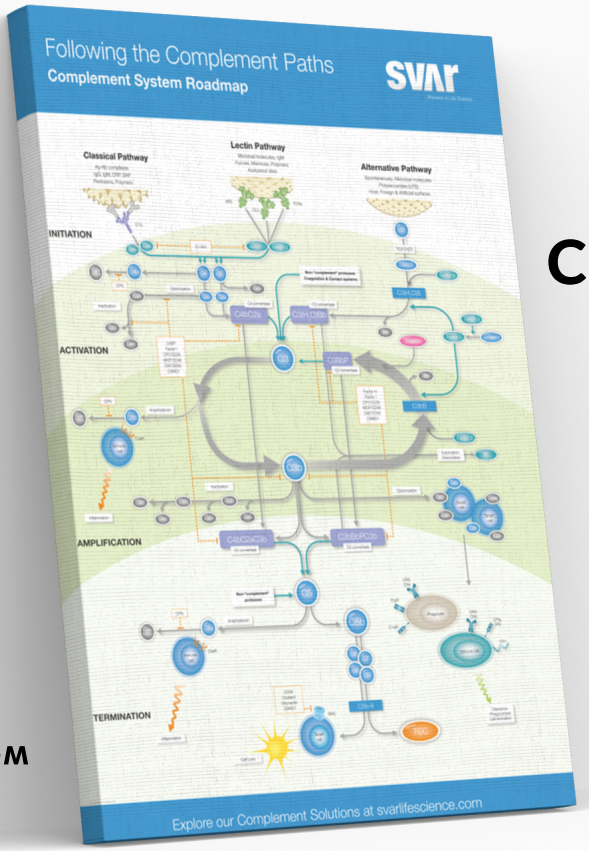

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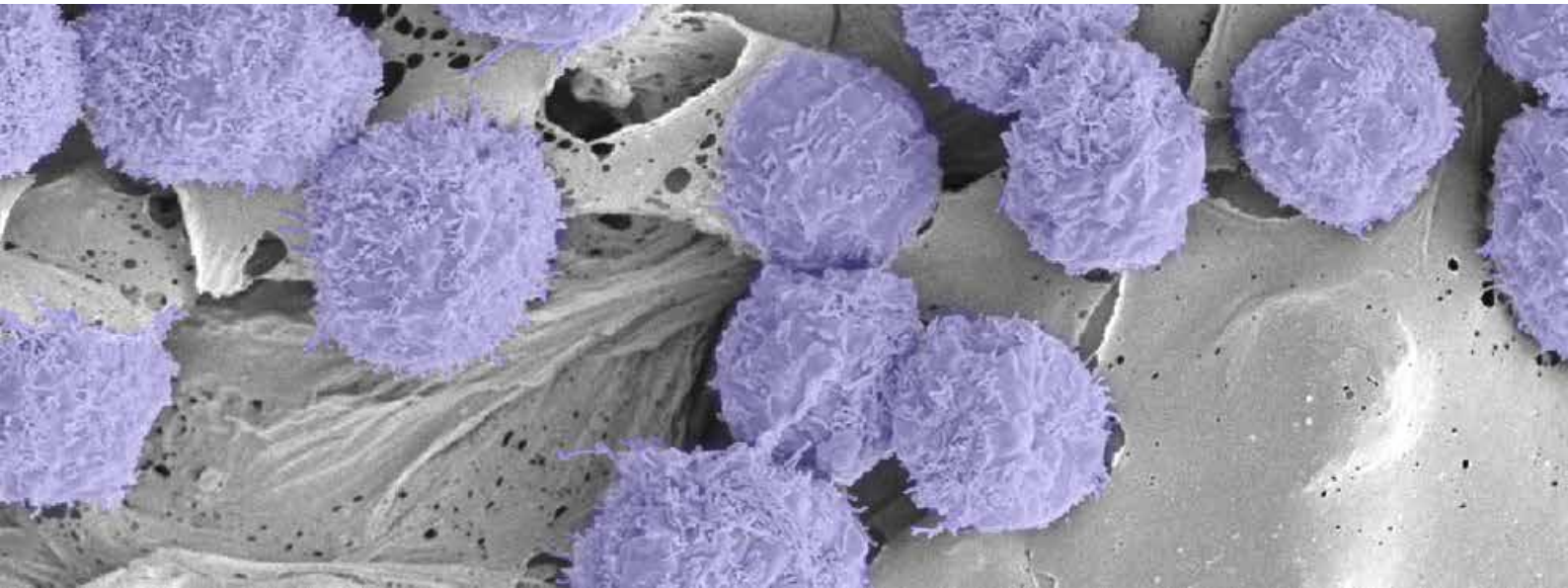


CET

14:00 - 14:42 **SESSION VIII – COMPLEMENT DIAGNOSTICS; STANDARDIZATION AND ANIMAL MODELS**

Moderators: Zoltan Prohaska and Lubka Roumenina

(30)
Immunosuppressive effect of C5a receptor antagonist via macrophage regulation on intestinal transplant in a rat model
Toyama, Chiyoshi; Maeda, Akira; Kogata, Shuhei; Yoneyama, Tomohisa; Ueno, Takehisa; Tazuke, Yuko; Okuyama, Hiroomi; Miyagawa, Shuji

(219)
Normothermic machine perfusion reconstitutes porcine kidney tissue metabolism but stimulates inflammation which is partly complement dependent
De Boer, Eline; Sokolova, Marina; Jager, Neeltina; Weiss, Marc; Schjalm, Camilla; Liavåg, Olav; Thorgersen, Ebbe; Nilsson, Per; Jespersen, Bente; Leuvenink, Henri; Mollnes, Tom Eirik; Pischke, Søren

(161)
Development of an ELISA for characterization of mannose-binding lectin-associated serine protease 2 (MASP-2) in human serum and plasma
Götz, Maximilian; Skjoedt, Mikkel-Ole; Garred, Peter; Bayarri Olmos, Rafael; Rosbjerg, Anne

14:43 - 15:00 **SESSION VII – LIVE Q&A**

15:00 - 15:45 **EARLY CAREER AWARD FOR RESEARCH IN COMPLEMENT**

Introduction: John Atkinson
Presentation by: Hrishikesh Kulkarni

Introduction: Trent Woodruff
Presentation by: John Lee

15:45 - 16:00 **ECCO PhD JOURNAL ARTICLE AWARD**

Introduction: Nicole Schaefer

16:00 - 16:15 Break

CET

16:15 - 17:25 **SESSION IX – COMPLEMENT THERAPEUTICS ON THE WAY TO THE CLINIC**

Moderators: Daniel Ricklin and Claire Harris

(136)
Insight into mode-of-action and structural determinants of the compstatin family of clinical complement inhibitors
Lamers, Christina; Smiesko, Martin; Xue, Xiaoguang; van Son, H; Wagner, Bea; Sfyroera, G; Berger, Nadja; Gros, Piet; Lambris, John D.; Ricklin, Daniel

(100)
Gain-of-function variants of complement C2 support cytocidal activity of anticancer monoclonal antibodies
Urban, Aleksandra; Majeranowski, Alan; Stasiłojć, Grzegorz; Koszałka, Patrycja; Felberg, Anna; Taszner, Michał; Zaucha, Jan M; Okrój, Marcin

(151)
Optimization of Factor H-Binding Peptides for the Protection of Biosurface
Umnyakova, Ekaterina; Bechtler, Clément; Pouw, Richard; Lambris, John; Ricklin, Daniel

(10)
Development of Pharmacodynamic Assays to Assess Ex Vivo MASP-2 Inhibition and Their Use to Characterize the Pharmacodynamics of Narsoplimab (OMS721) in Humans and Monkeys
Freeman, Jeremy; Cummings, Jason; Dudler, Thomas

(168)
Syndrome induced by Shiga-like toxin producing E.coli (STEC-HUS) activation of the complement alternative pathway favors thrombus formation on microvascular endothelial cells
Santarsiero, Donata; Galbusera, Miriam ; Gastoldi, Sara; Schubart, Anna ; Vivarelli, Marina; Bresin, Elena ; Benigni, Ariela ; Noris, Marina; Remuzzi, Giuseppe
#168

17:25 - 17:45 **SESSION IX – LIVE Q&A**

17:45 - 18:10 Break

18:10 - 18:15 **ORAL / POSTER PRESENTATION AWARDS**

CET

18:15 - 19:25 **SESSION X – TRANSLATIONAL COMPLEMENT**

Moderators: Andrea Tenner and Wenchao Song

(170)
Complement C5aR2 contributes to the proliferation of neural progenitor cells during murine neurogenesis
Read, Austin; Lee, John; Woodruff, Trent

(29)
Investigating the role of the complement system in the radioresistance of rectal cancer
O'Brien, Rebecca; Buckley, Croí; Cannon, Aoife; Meltzer, Sebastian; Røe Redalen, Kathrine; Lysaght, Joanne; Lynam-Lennon, Niamh

(144)
Acquisition of complement-dependent cytotoxicity by type II anti-CD20 therapeutic antibody Obinutuzumab
Kuźniewska, Alicja; Majeranowski, Alan; Kowalska, Daria; Urban, Aleksandra; Henry, Sara; Okroj, Marcin

(135)
Liver targeted gene therapy is far superior to protein infusions of HDM-FH in long term dosing studies
Kamala, Ola; Smith Jackson, Kate; Hallam, Thomas; Gibson, Beth; Pappworth, Isabel; Cox, Tom; Alexander, Ian; Logan, Grant; Pickering, Mathew; Marchbank, Kevin

(85)
Complement Activation Contributes to Hydrocephalus Development following Germinal Matrix Hemorrhage
Mallah, Khalil; Alshareef, Mohammed; Vasas, Tyler; Alawieh, Ali; Borucki, Davis; Couch, Christine; Cutrone, Jonathan; Shope, Chelsea -; Eskandari, Ramin; Tomlinson, Stephen

19:25 - 19:45 **SESSION X – LIVE Q&A**

19:45 - 19:50 Break

19:50 - 20:50 **CLOSING SESSION**

Closing Remarks - Christine Skerka
ICS Election Results - Claudia Kemper
Farewell by the ICS President - Peter Garred
European Complement Network 2022 – Bern, Switzerland, Robert Rieben
ICW 2023 – Newcastle, UK, Claire Harris & Kevin Marchbank
Farewell by the LOC - Peter Zipfel

LIST OF POSTERS

Poster #	Presenter	Abstract Title
A01	Yue Li	Variability of opsonization of iron oxide nanoparticles with complement C3 in different species and strains: a quest for a predictive animal model
A02	Verena Harpf	Complement evasion of Candida albicans is glucose-dependent: The role of the factor H binding molecule Hgt1
A03	Pedro Miguel Coelho Medeiros	Vitamin C, hydrocortisone, and the combination thereof significantly inhibited two of nine inflammatory markers induced by E. coli but not by S. aureus – when incubated in human whole blood
A04	Kristina Yucius	The Importance of Ascertaining Hc null Allele Status in Mouse Models of Complement-Mediated Diseases.
A05	Shunxin Jin	Complement factor D and C3 are associated with arterial stiffness, independent of age, sex, heart rate and blood pressure but not of cardiometabolic factors: The Maastricht Study
A06	Mercedes Noriega	In-situ analysis of complement convertases in glomerulonephritis using deep learning based on explainable artificial intelligence
A07	Olaf Penack	Narsoplimab (OMS721), a MASP-2 Inhibitor, for the Treatment of Adult Hematopoietic Stem Cell Transplant-Associated Thrombotic Microangiopathy (HSCT-TMA)
A08	Thomas Dudler	Characterization of Narsoplimab, a Selective Inhibitor of Lectin Pathway-Mediated Complement Activation and Thrombosis
A09	Peter Kraiczy	CipA of Acinetobacter baumannii inhibits complement activation by interacting with different complement components
A10	Marina Malinchik	Mannose-binding protein-associated serine protease (MASP-2) gene rs72550870 variants among the newborns of Russian Arctic populations
A11	Meike Heurich	Complement Regulator Factor H is a Cofactor for Thrombin in both Pro- and Anticoagulant Roles
A12	Hrishikesh Kulkarni	Increased complement activation is a distinctive feature of severe SARS-CoV-2 infection
A13	Mariam Massri	Complement C7 - strong association with clusterin, but no indication for the presence of a modulating alternatively spliced C7-like protein
A14	Chantal DUMESTRE-PERARD	Evaluation of anti-HMGB1 and anti-C1s autoantibodies for the diagnosis and follow-up of systemic lupus erythematosus
A15	Mikel Rezola Artero	C4bp hijacking by Plasmodium falciparum circumsporozoite protein
A16	Zhongli Xu	The anti-C5a antibody vilobelimab efficiently inhibits C5a in severe COVID-19 patients.
A17	Christine Gaboriaud	Engineering recombinant headless C1q to study its interaction with LAIR-1 Ig-like domain.
A18	Ying Tan	The role of renin in the pathogenesis of postpartum hemolytic uremic syndrome
A19	Alessandra Zarantonello	Structural basis for nanobody mediated inhibition of the classical pathway
A20	Wioleta M Zelek	Targeting Membrane Attack Complex for therapy in Kidney Ischaemia Reperfusion Injury.
A21	M. Cristina Vega	Crystal structure and SAXS analysis of the immune evasive factor GAPDH from Leptospira interrogans
A22	Jean-Baptiste REISER	Biophysical characterization of recombinant IgMs and their interactions with C1q
A23	Anne GRUNENWALD	Complement implication in the acute kidney injury associated with rhabdomyolysis
A24	Scott Barnum	Development of a Rapid and Inexpensive Soluble Membrane Attack Complex Lateral Flow Assay for Diagnosis of Bacterial Meningitis
A25	Tilo Freiwald	SARS-CoV-2 drives JAK1/2-dependent local complement hyperactivation
A26	Nikolina Papac-Milicevic	Humoral immune responses targeting malondialdehyde-epitopes in kidney transplantation patients
A27	Praveen Mathews Varghese	Soluble complement regulators as pattern recognition molecules of Influenza A virus
A28	Candace Fox	Human Coronavirus Infected Lung Cells Recruit Complement Inhibitors Vitronectin and Clusterin and Delay Complement-Mediated Lysis
A29	Ganna Stepanova	TGF-β-induced renal complement expression is associated with fibrosis and depends on the genetic background of mice
A30	Sára Kellnerová	Complement components C3b and C5 bind to Shiga toxin 2a and their gene expression in human cell lines is upregulated upon in vitro stimulation with the toxin
A31	Josh Garlich	APL-1030: A Novel Nanofitin Drug Candidate Demonstrating Specific and High Affinity to C3 and C3b for Inhibition of Complement
A32	Giulia Bertacchi	COMPLEMENT-OPSONIZED HIV-1 INCREASES TNTs FORMATION IN DCs
A33	Xaria Li	C5a receptors synergize with Dectin-1 to modulate cytokine responses in primary human macrophages
A34	Mustapha Dahmani	Classical Complement Activation and IgM Contribute to Control of Rickettsia Infection

Poster #	Presenter	Abstract Title
A35	Sandra Parker	Visualising Complement: Validation of C5aR1-specific fluorescent peptide probes
A36	Douwe Dijkstra	Circulating levels of anti-C1q and anti-Factor H autoantibodies and their targets in preeclampsia
A37	Laura Pérez Alós	Reduction of urinary levels of lectin pathway complement components in an IgA vasculitis patient after MASP-2 inhibition with narsoplimab
A38	Nikoleta Daskoulidou	Demonstrating microglial CR1 expression in the human brain
A39	Lucie Colineau	Cytosolic C3 is deposited on invasive Staphylococcus aureus in lung epithelial cells and decreases their survival
A40	Svitlana Babych	C.albicans inhibits phagocytosis by recruiting human extracellular vesicles onto the surface via opsonisation
A41	Charles Booth	Structure-function analysis of immunomodulatory lipoproteins from Borrelia miyamotoi
A42	Masaaki Ishii	Mitochondrial C3a Receptor Activation in Oxidatively Stressed Epithelial Cells
A43	Szilvia Lukácsi	The role of β2-integrins in the migration and receptor recycling of human myeloid cells
A44	Ji Zhang	Development of a Differentiated Human Primary Retinal Pigmented Epithelial Cell Culture System for the Study of Complement-Mediated RPE cell Injury
A45	Hee Jung Kang	Absence of N-glycolylneuraminic acid on porcine cells does not increase the risk of complement alternative pathway activation in human serum
A46	Michal Magda	Clinical isolates of Acinetobacter spp. are highly serum resistant despite efficient recognition by the complement system.
A47	Ewelina Golec	Novel intracellular isoforms of CD59 mediate insulin secretion, and are downregulated in diabetic islets.
A48	A. Itzam Marin	Sex and age-related comparisons in complement factors among patients with intermediate age-related macular degeneration
A49	Bianca Brandus	Development of immunotherapeutic complexes that elicit complement activation towards multidrug-resistant Pseudomonas aeruginosa
A50	Paul Tamburini	Generation and in vitro properties of ALXN1720 a bispecific VHH antibody against complement C5 designed for subcutaneous administration.
A51	Cláudia Vilhena	Role of C5b-9 on Streptococcus pneumoniae-induced Hemolytic Uremic Syndrome (Sp-HUS)
A52	Anna Pittaluga	The complement system, a synaptic organizer controlling glutamate transmission in the CNS of healthy and EAE mice.
A53	Martin Lo	SARS-CoV-2 causes delayed complement activation in an ex vivo whole blood model
A54	Joshua Dubowsky	Dengue Virus Infection Induces Factor H production, Relocation to the Nucleus and binding to cell surface Heparan Sulphate
A55	Cedric Cui	An in-vivo pharmacodynamic method to investigate complement C5a receptor antagonists
A56	Shanshan Du	Streptococcus pneumoniae diverse surface proteins act as guards against complement attack
A57	Katelyn Cranmer	A Factor H-Fc Fusion Protein Boosts Complement-mediated Opsonophagocytosis and Killing of Methicillin-resistant Staphylococcus aureus
A58	Simon Clark	Beyond Factor H: Impact of genetic-variants associated with age-related macular degeneration on circulating FHR protein levels
A59	Marco Mannes	Complement-induced prothrombotic activation of platelets necessitates terminal pathway mediated cytolysis
A60	Yongsen Zhao	Comparative Evaluation of Complement Factor D and C3 Inhibitors on Serum Bactericidal Activity Against Nongroupable Neisseria meningitidis
A61	Corinna Lau	Cell specific contributions in the human whole blood model of inflammation
A62	Beatrice Fageräng	Characterization of a novel anti-C1s clone inhibiting the classical complement pathway
A63	Khalil Mallah	Complement Mediates Cognitive Decline In Chronic Phases Post Traumatic Brain Injury
A64	Héctor Martín Merinero	Functional characterization of 105 Factor H variants associated with atypical HUS: lessons for variant classification
A65	April Joy Baral	Association of CR1 and C3 polymorphisms in C3-mediated extravascular haemolysis in PNH
A66	Xilin Chen	Preclinical Characterization of BCX9930, a Potent Oral Complement Factor D Inhibitor, for the Treatment of Alternative Pathway Mediated Diseases
A67	Mario Alejandro Duque Villegas	The impact of MBL on the outcome of infection with representative mycobacterial strains of the Mycobacterium tuberculosis complex
A68	Sofiya Pisarenka	Assembly and regulation of C3 convertase on the surface of an in vitro model of glycomatrix
A69	Lazara Elena Santiesteban Lores	Analysis of Complement Factor H gene polymorphisms and their influence on leptospirosis susceptibility
A70	Larisa Viazmina	Role of factor H and apolipoprotein E in resolution of neuroinflammation

Poster #	Presenter	Abstract Title
A71	Christine Couch	Cigarette Smoking and Age Amplifies Complement-Dependent Injury After Stroke
A72	Matthew Davidson	BCX9930, an Oral Factor D Inhibitor for the Potential Treatment of Paroxysmal Nocturnal Hemoglobinuria and other Alternative Pathway (AP) Mediated Diseases, Inhibits the AP in Healthy Subjects
A73	Kristóf G. Kovács	CR2 is an inhibitory coreceptor of BCR on human B cells
A74	Flavio Bruni	Complement and endothelial cell activation in COVID-19 patients compared to controls with suspected SARS-CoV-2 infection – a prospective cohort study
A75	Julia ROQUIGNY	Identification of anti-C3bBb antibodies enhancing the formation of the C3 convertase: a new mechanism of dysregulation of the complement in C3 glomerulopathy
A76	Pascal Rabatscher	Anti-C1q Autoantibodies From Systemic Lupus Erythematosus Patients Induce TNF Secretion in Monocytes via CD40 Signaling
A77	Anne Landsem	The complement-dependent transcriptome dynamics in platelet activation
A78	Kim Vanderliek	Monitoring Complement Biomarkers in C3 Glomerulopathy Patients with Factor H or FHR Gene Mutations before and after Treatment with Eculizumab or Ravulizumab
A79	Daniel Chauss	An autocrine Vitamin D-driven Th1 shutdown program can be exploited for COVID-19
A80	Irene Gómez Delgado	Increased levels of FHR-4A and other Factor H-Related proteins in Spanish patients with severe cutaneous adverse reactions
A81	Mieke C. Louwe	Heart failure patients display alternative complement pathway activation
A82	Esther Boer	The contribution of the alternative pathway to complement activation depends on the strength of classical pathway initiation
A83	Richard Pouw	Platelet activation by commercial C4a preparations is mediated by trace impurities of thrombin
A84	MARINA NORIS	In thrombotic microangiopathy associated with stem cell or bone marrow transplantation (HSCT/BMT-TMA) activation of the lectin pathway induces C5b-9 formation on endothelium and favors thrombosis
A85	Kelly Fahnoe	Design and characterization of C3d targeted fusion proteins for tissue localized inhibition of complement activation
A86	Rafael Bayarri-Olmos	COLEC11 splice variants found in the circulation are functionally distinct in their interaction with the MASPs
A87	Nicole Schartz	C5aR1 deletion delays amyloid-associated inflammatory gene expression and microglial activation in the Arctic model of Alzheimer's disease.
A88	Margot Revel	Intracellular Factor H Drives Tumor Progression Independently of the Complement Cascade
A89	Angela Armento	Loss of intracellular Complement Factor H (CFH) in Retinal Pigment Epithelium (RPE) cells causes retinal degeneration in a novel human RPE-porcine retinal explant co-culture system.
A90	Eylul Tuncer	Cholesterol Crystals, Complement C1q and von Willebrand Factor are Present in Atherosclerotic Human Carotid Arteries
A91	Dorottya Csuka	SARS-CoV-2 infection as a potent trigger of first aHUS symptoms in patients with CD46 mutations
A92	Sarah Walachowski	Novel single cell proteotranscriptomics reveals new insights into C5a receptor functions during pneumococcal pneumonia

Poster #	Presenter	Abstract Title
B01	Myriam Martin	Severe congenital thrombocytopenia characterized by decreased platelet sialylation and moderate complement activation caused by novel compound heterozygous variants in GNE
B02	Margot Revel	C4d as a prognostic biomarker in renal cancer
B03	Sheila Thomas	Elucidating the structure and function of a novel class of complement inhibitors of the Lyme disease agent, Borrelia burgdorferi
B04	Amanda Heiderscheit	The Role of Factor H, Factor H-related 1, and Factor H-related 5 in C3 Glomerulopathy
B05	Steven Podos	Clinical and biomarker characteristics of patients with C3G enrolled in two phase II studies investigating the Factor D inhibitor danicopan
B06	Rachel Washburn	Complement inhibition by immunoregulatory Sertoli cells: Paving the road to allograft and xenograft survival
B07	Tiffany Petrisko	Alterations to gut microbiota in mice lacking C1q or C5aR1 in Alzheimer's mouse model do not account for protective effects in disease progression.
B08	Frerich Masson	Differences in complement activation and killing of Klebsiella pneumoniae isolates
B09	Serena Bettoni	Serum complement activation by C4BP-IgM fusion protein can restore susceptibility to antibiotics in Neisseria gonorrhoeae
B10	Hrishikesh Kulkarni	Increased complement activation in recipients is associated with worse long-term outcomes after lung transplantation.
B11	Rosa Lammerts	Successful second kidney transplantation after plasmapheresis for suspected anti-endothelial cell antibodies
B12	Yingying Zhang	Spatial transcriptomic profiling of the complement system in mouse brain
B13	Carla Plüss	Establishing a screening platform for the biological evaluation and modulation of complement-related integrin receptors
B14	Lydia Gonzalez del Barrio	MAP-2:CD55 chimeric construct effectively modulates complement activation
B15	Mieke van Essen	Initial properdin binding contributes to alternative pathway activation on necrotic cells
B16	Amer Toutonji	The Role of Complement in Propagating Neuroinflammation in Chronic Traumatic Brain Injury – A Transcriptomic Analysis
B17	Aleksandra Blagojevic	Structure-activity assessment of the leech-derived complement inhibitor BD001
B18	Alexandra Gerogianni	Heme interferes with the regulatory properties of complement factor I in human plasma
B19	Xin Gao	The N-linked glycans at the SCR-17 and SCR-18 domains mediate a C-terminal dimerization site in human Factor H - implications for its regulatory function
B20	Ingrid Lopatko Fagerström	Kallikrein-kinin system activation triggers complement deposition on cells
B21	Daniel Seiler	C5aR2 deficiency ameliorates inflammation in antibody transfer-experimental epidermolysis bullosa acquisita and suggests enhancing action on C5aR1 signaling
B22	sigridur aradottir	Genetic variants in complement factor H-related protein 5 and their phenotype in complement-associated renal diseases
B23	Audrey Crowther	A Tale of Two Isoforms: The Role of Complement Regulatory Protein, CD46, Splicing in Lung Adenocarcinoma
B24	Fei Liu	C3d-Targeted Factor H Achieves Potent Tissue-Directed Complement Inhibition and Disease-Modifying Efficacy Without Affecting Systemic Complement
B25	Thais Akemi Amamura	Proteolytic Activity of Secreted Enzymes from Pathogenic Leptospira on Phagocytosis by Murine Macrophages
B26	Andrea Balduit	Role of the Complement Protein C1q in the Regulation of Hyaluronic Acid Cleavage in Malignant Pleural Mesothelioma
B27	Thomas Hallam	A novel method for characterisation of rare genetic variants in CFH and CFI and identification of a dominant negative effect: implications for AMD
B28	Stephen Perkins	The solution structure of the collagen triple helix in mannan-binding lectin is bent: implications for complement activation
B29	Bert Veuskens	Development and validation of novel specific monoclonal antibodies against members of the Factor H protein family
B30	Nick Deerain	Identification of potent small peptides targeting human C3a receptor
B31	Maartje Inklaar	Turning strength into weakness – Exploiting Factor H recruitment by Plasmodium falciparum gametes as a malaria transmission blocking strategy
B32	Karolina Smolag-Klosowska	Factor H promotes survival of CD4+ T-cells via interaction with the activating immune checkpoint protein inducible T-cell costimulator (ICOS)
B33	Rachel Hevey	Development of glycomimetic antagonists to reduce CL-11-mediated ischemia-reperfusion injury

Poster #	Presenter	Abstract Title
B34	Leon Cyranka	Generation of anaphylatoxin receptor-targeted monoclonal antibodies
B35	John Lee	A pathogenic role for complement C5aR1 activation in Huntington's Disease
B36	Elena Guillen	Potential involvement of terminal complement pathway overactivation in the pathogenesis of ANCA-associated vasculitis
B37	Timo Reiß	P. falciparum merozoites bind and utilize plasminogen during the asexual replication phase
B38	Anna Felberg	ASSESSMENT OF THE ROLE OF FACTOR I IN NON-SMALL CELL LUNG CANCER (NSCLC) PROGRESSION
B39	Jørund Asvall	Increased local inflammatory response to MOC31PE immunotoxin after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy
B40	M. Cristina Vega	Functional and structural characterization of mouse monoclonal antibodies against human C5a
B41	Wioleta M Zelek	Mechanism of inhibition of membrane attack complex by disulphide-locked C9.
B42	Arthur Dopler	Factor H-related protein 5 binds sialic acid and deregulates Factor H on host surfaces
B43	Anna Adler	A novel method to store complement C3 with superior ability to maintain the native structure and function of the protein
B44	Janti Haj Ahmad	Generation of monoclonal antibodies targeting murine C5aR2
B45	Marina Malinchik	Bronchial asthma in children and Mannose-binding lectin gene polymorphism: association with disease severity and recurrent wheezing.
B46	Marina Malinchik	Distribution of polymorphisms of genes FCN2, FCN3 and MASP-2 among MBL2-deficient genotypes in populations of the Arctic territories in Russia
B47	Madhu Golla	Evidence of contribution by the classical but not Masp2 and lectin pathway of complement in a murine model of TMA caused by factor H mutation
B48	Aoife Cannon	A novel role for the complement cascade in chemoradiation therapy resistant oesophageal adenocarcinoma
B49	Paolo Macor	Analysis of autoantibodies and complement activation in bronchoalveolar lavage of COVID-19 patients
B50	Vivek Manivel	The role of prostasomes and tissue Kallikreins in coagulation disorder associated with the prostate cancer
B51	Rémi PHILIP	Autoantibodies against complement proteins in patients with antiphospholipid syndrome
B52	Chloe Connelly	Establishing a porcine ex vivo normothermic kidney perfusion model for testing complement therapies
B53	Samyr Kenno	The C5a/C5aR1 axis drives autoimmune inflammation in pemphigoid disease through the control of early Tfh cell activation, IgG autoantibody formation and IgG Fc-glycan composition
B54	Larissa Seifert	The classical pathway triggers pathogenic complement activation in membranous nephropathy
B55	Richard Pouw	A high-throughput, flow cytometry-based screening of FDA-approved drugs that induce complement regulator expression on hypoxic human endothelial cells
B56	Valeria Ramaglia	Complement-associated loss of CA2 inhibitory synapses in the demyelinated hippocampus impairs memory
B57	Barbro Persson	COVID-19 organ damage and outcome are strongly linked to thromboinflammation elicited by the complement and kallikrein/kinin systems
B58	Norimitsu Inoue	Early elevation of complement factor Ba following allo-HSCT provides a predictive biomarker of transplant-associated thrombotic microangiopathy in adults
B59	Jutamas Shaughnessy	Development of complement factor H based immunotherapeutic molecules in tobacco plants against multidrug-resistant Neisseria gonorrhoeae
B60	Rabia Ülkü Korkmaz	C5a signaling axes in myeloid cells favor the development of type 2 Innate Lymphoid cells
B61	Nicole Schartz	C5a overexpression alters gene expression and microglial activation in brain of the Arctic model of Alzheimer's disease.
B62	Sára Kellnerová	Kallikrein-kinin system activation in EHEC-associated hemolytic uremic syndrome
B63	Danlei Zhou	Analyses Human Complement C4B of Genotypes and Phenotypes, Identifications of Sequence Bases for Polymorphisms and Deficiencies, and Segregation of their HLA Haplotypes
B64	Ole-Lars Brekke	Effects of complement C3, C5 and CD14 inhibitors on bacterial survival and thromboinflammation induced by two different live E.coli-strains in human whole blood
B65	Baerbel Rohrer	Peptide-based immunotherapy against oxidized elastin ameliorates pathology in mouse model of smoke-induced ocular injury

Poster #	Presenter	Abstract Title
B66	Erik Toonen	Complement Activation in the Disease Course of Coronavirus Disease 2019 and Its Effects on Clinical Outcomes
B67	Bilal Ben Brahim	The Role of Complement in Ischemia/Reperfusion Injury of Amputated Limbs from Ex Vivo and In Vivo Reperfusion
B68	Kelly Fahnoe	Design and characterization of ADX-097: A C3d targeted antibody – fH1-5 fusion protein for the treatment of complement alternative pathway driven disease
B69	MARINA NORIS	Cell surface-targeted complement inhibitors prevent C3 deposits on cultured endothelial cells exposed to serum from patients with atypical uremic syndrome (aHUS)
B70	Pascal Rabatscher	Epitope-Specific Anti-C1q Autoantibodies in Systemic Lupus Erythematosus
B71	Ryan Garrigues	Insights into the endogenous regulation of the classical pathway of complement based on microbial complement evasion mechanisms
B72	LAURA LUCIENTES	The influence of the complement alternative pathway in anti-neutrophil cytoplasmic antibody-associated vasculitis.
B73	Andrea E. Schneider	Factor H family proteins modulate monocyte and neutrophil granulocyte functions
B74	Alexandra Matola	AUTOANTIBODIES AGAINST FACTOR B AND FACTOR H IN A PATIENT WITH MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS
B75	Alexandra Papp	Complement factor H-related proteins FHR1 and FHR5 interact with extracellular matrix ligands, reduce factor H regulatory activity and enhance complement activation
B76	Xiaobo Wu	A Comparison of Kallikrein and FD in activating complement alternative pathway
B77	Sourav Roy	Molecular basis of interaction of Borrelial inhibitors with C1r: A molecular dynamics and functional study
B78	Beth Gibson	Mice with hyperfunctional complement develop non-alcoholic steatohepatitis
B79	michael carroll	Overexpression of human C4A promotes excessive synapse loss and alteration in behavior
B80	Trine Gadeberg	Structural insight in initiation and amplification of the alternative pathway
B81	Pooja Sakthivel	C1q as a Positive Autocrine Regulator of Microglial Inflammation
B82	Silvia Guglietta	High dimensional analysis by mass cytometry reveals the immune landscape in traumatic brain injury following targeted complement inhibition
B83	Hang Zhong	Role of pentraxin 3 and interaction with complement in immune defence against opportunistic infections
B84	Nathaniel Parsons	Regulatable complement inhibition of the alternative pathway mitigates age-related macular degeneration pathology
B85	Barbara Marquez Tirado	Identification of novel binding partners for the Factor H protein family
B86	Maria Maqsood	A novel role for neutrophils and NETs in the pathogenesis of C3 glomerulopathy
B87	Barbara Rolfe	Immunoregulatory Role for Complement Receptors in Murine Breast Cancer
B88	Shunxin Jin	Diet-induced Weight Loss Lowers Plasma Complement C3 via Reduction of Visceral Adipose Tissue: a Randomized Controlled Trial in Abdominally Obese Men
B89	Paul Tamburini	Formation of multivalent complexes in the presence of more than one conventional antibody to complement factor C5
B90	Björn Laffer	Strong complement activation in Fabry Disease patients at the level of C3
B91	Mihály Józsi	A panel of monoclonal antibodies against complement proteins for potential research, diagnostic and therapeutic applications

LATE BREAKING ABSTRACTS

A panel of monoclonal antibodies against complement proteins for potential research, diagnostic and therapeutic applications

Józsi, Mihály[1,2]; Uzonyi, Barbara[2]; Papp, Alexandra[2]; Matola, Alexandra[2]; Nagy, Mátka[2]; Kovács, Boglárka[2]; Rabb, Márton[1]; Szabó, Zsóka[2]; Cserhalmi, Marcell[2]; Csincsi, Ádám I.[2]; Lázár, József[3]; Takács, László[3]

1. MTA-ELTE Complement Research Group, Eötvös Loránd Research Network (ELKH), Department of Immunology, Eötvös Loránd University, Budapest, Hungary
2. Department of Immunology, Eötvös Loránd University, Budapest, Hungary
3. Biosystems Immunolab Zrt., Debrecen, Hungary

Monoclonal antibodies (mAbs) represent a powerful tool for research, diagnostics and as therapeutics. Given the multifaceted role that complement plays in health and disease, there is increasing need for complement specific reagents to reliably detect components and diagnose diseases, as well as to manipulate this complex protein network. Novel anti-complement mAbs with well-characterized specificity, epitopes and functional effects could thus be valuable tools.

To this end, we tested mAbs from Biosystems' QuantiplasmaTM library produced against natural protein epitopes by a protected technology1,2. A total of 156 mAbs reacting with either C1q, C3, C4, C5, C6, C7, C8, C9, C4b-binding protein (C4BP) or factor H (FH) were further analyzed in ELISA, complement activation and hemolysis assays.

From these mAbs, we identified altogether 42, among them 5 C3, 4 C4, 3 C5, 7 C6, 4 C7 and 8 C9 specific mAbs that could inhibit hemolysis of rabbit and/or hemolysin-sensitized sheep erythrocytes to various extent. In a solid-phase assay, the 5 anti-C3 mAbs inhibited the activity of the C3bBbP convertase. In addition, one anti-C4 mAb rather enhanced hemolysis. From the antibodies that recognized the classical/lectin pathway regulator C4BP, one mAb enhanced and three mAbs inhibited complement activation. Among the 69 mAbs that recognized FH, 22 cross-reacted with factor H-related protein 1 (FHR1), of which 7 also recognized both FHR2 and FHR5. 19 anti-FH mAbs bound to the N-terminal complement regulatory domains and 17 to C-terminal domains 19-20; 5 and 12 mAbs, respectively, induced alternative pathway-mediated hemolysis of sheep erythrocytes. However, 8 anti-FH mAbs inhibited complement activation.

In summary, we generated and characterized a panel of novel mAbs that could be useful as research and diagnostic tools, to develop specific ELISAs, and as potential therapeutics to inhibit complement activation at various levels of the cascade.

Reference 1:
Guergova-Kuras M, Kurucz I, Hempel W, Tardieu N, Kádas J, Malderez-Bloes C, Jullien A, Kieffer Y, Hincapie M, Guttman A, Csánky E, Dezso B, Karger BL, Takács L. Mol Cell Proteomics. 2011 Dec;10(12):M111.010298. doi: 10.1074/mcp.M111.010298. PMID: 21947365

Reference 2:
Laszlo Takacs, Andras Guttman, William S. Hancock, Barry L. Karger, Manuel Duval,Patrick Berna: Monoclonal antibody based biomarker discovery and development platform US 20070172887 A1

Cholesterol Crystals, Complement C1q and von Willebrand Factor are Present in Atherosclerotic Human Carotid Arteries

Tuncer, Eylul

Atherosclerosis is an inflammatory disease characterized by the formation of cholesterol crystals (CC) within atherosclerotic plaques. CC can trigger complement activation and hemostasis with growing evidence on the cross-talk between both systems, including the interaction between complement C1q and von Willebrand factor (vWF). We have previously shown that the interaction of C1q and vWF also occurs on CC surfaces in vitro forming CC-C1q-vWF complexes, and leading to downstream anti-inflammatory effects on human macrophages. However, the role of C1q and vWF in human atherosclerosis is not well established. Therefore, we examined the presence and localization of C1q and vWF in human carotid artery tissues of individuals with or without atherosclerotic manifestations by immunohistochemistry on paraffin-embedded sections and by immunofluorescence on frozen sections. We observed by immunohistochemistry that C1q and vWF localize around CC clefts of atherosclerotic carotid artery tissue. C1q and as well as vWF signal intensities were stronger in tissues from individuals with atherosclerotic compared to individuals with normal arteries. The signal intensity between C1q and vWF correlated strongly and in specimens with atherosclerotic manifestations but only weakly in specimens without atherosclerotic manifestations. Last, the overlap of vWF staining patterns into C1q staining patterns (colocalization) was significantly higher in tissues of atherosclerotic patients compared to non-atherosclerotic donors. In conclusion, our ex vivo study demonstrates that C1q and vWF are concomitantly

present in human atherosclerotic plaques. This observation suggests that C1q-vWF and also CC-C1q-vWF complex formation can occur in vivo and thus might play a role in the pathogenesis of atherosclerosis.

Loss of intracellular Complement Factor H (CFH) in Retinal Pigment Epithelium (RPE) cells causes retinal degeneration in a novel human RPE-porcine retinal explant co-culture system

Armento, Angela; Murali, Aparna; Marzi, Julia; Arango-Gonzalez, Blanca; Kilger, Ellen; Clark, Simon; Schenke-Layland, Katja; Ueffing, Marius

Background: The Y402H polymorphism in the Complement Factor H gene (CFH/FH) represents one of the major genetic risk loci for Age related macular degeneration (AMD), a progressive and degenerative disease of the macula, leading cause of blindness in the elderly population. In our previous work, we show that FH holds additional functions beside regulating complement system in the extracellular space. We showed that intracellular FH is important for RPE cells homeostasis and FH loss impairs metabolic capacity and oxidative balance of RPE cells. In this study we investigated the impact of RPE cells damaged by FH loss on the neuroretina.

Methods: We established a co-culture model comprising hTERT-RPE1 cells and porcine retinal explants, obtained from the visual streak of the porcine retina and rich in cone photoreceptors (PR). We silenced CFH in hTERT-RPE1 cells (siCFH) prior to co-culture initiation. Additionally, cultures were supplemented with exogenous complement sources (FH and C3). Cultures were maintained for 3 days, then fixed and sectioned for imaging and Raman microspectroscopy analyses.

Results: RPE cells deprived of FH causes retinal degeneration in the co-cultured retinal explants compared to retinae cultured with RPE controls. In detail, we observed a reduction in retinal thickness, outer nuclear layer (ONL) thickness and number of PR cells in the ONL. Raman analyses revealed that CFH-silenced RPE cells leads to reduced mitochondrial activity and increased levels of oxidized lipids in the ONL. Moreover, no beneficial or detrimental effects were observed in response of additional complement sources and the damage was not directly mediated by the activation of either microglia or Müller glia cells.

Conclusions: Our data support the hypothesis that RPE-derived FH plays a wider role in retinal homeostasis out with its known complement-regulatory function. As a result of CFH silencing, RPE cells are unable to properly metabolically support the neuroretina and protect it from oxidative stress, ultimately leading to photoreceptor loss, primarily rods. These findings may help elucidate the function of FH in the retina and our co-culture system may provide a suitable model to test medical interventions.

MAP-2:CD55 chimeric construct effectively modulates complement activation

Gonzalez del Barrio, Lydia[1]; Pérez Alós, Laura[1]; Garred, Peter[1]; Bayarri Olmos, Rafael[1]

1. Copenhagen University Hospital

Background: The complement system is a complex tightly regulated protein cascade involved not only in the defence against pathogens but also in the pathogenesis of several diseases. Thus, development of complement modulators has risen as potential treatment for complement-driven inflammatory pathologies. Mannose-binding lectin (MBL)/ficolin/collectin-associated protein-2 (sMAP or MAP-2) has been reported as an inhibitor of the lectin pathway (LP) by competing with its homologous MASP-2. On the other hand, CD55 is a membrane-bound complement regulator that acts on the C3/C5 convertase level, thus modulating the activation of the three pathways of the complement system. In this study, we produced a recombinant chimeric inhibitor to modulate complement activation at two different levels of the complement cascade.

Methods: The recombinant inhibitor was designed using the full-length sequence of MAP-2 followed by the CCP domains 1 to 4 of CD55 (CD551-4). MAP-2:CD551-4, and also MAP-2 and CD551-4 alone, were produced in ExpiCHO cells and purified by affinity chromatography using a C-terminal FLAG-tag. The structural properties of the recombinant proteins were assessed by size exclusion chromatography (SEC). Binding and complement deposition assays were performed on ELISA-based assays.

Results: Proteins were successfully expressed and purified. Size exclusion chromatography (SEC) results suggest that MAP-2:CD551-4 forms dimers in the presence of calcium, and that dimers are resistant to 24 hours incubation with EDTA and EGTA. MAP-2:CD551-4 bound to the LP pattern recognition molecules MBL,

ficolin-3, and collectin-11 in a calcium-dependent manner. Using the WIELISA total complement screen, we demonstrate an efficient inhibition of the LP (IC50 0.14 nM) as well as the classical and the alternative pathways (IC50 8.908 nM and 14.05 nM, respectively).

Conclusion: Here we showed that MAP-2:CD551-4, a protein-based chimeric inhibitor, is effective in vitro at modulating all three pathways of the complement system, probably due to the unique combination of a targeting (MAP-2) and a potent regulatory moiety (CD55).

Novel single cell proteotranscriptomics reveals new insights into C5a receptor functions during pneumococcal pneumonia

Walachowski, Sarah[1]; Jayaraman, Archana[1]; Dudek, Markus[2]; Campbell, Joshua D.[3]; Mizgerd, Joseph P.[1]; Bosmann, Markus[1,2]

1. Pulmonary Center, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, 02118, USA
2. Center for Thrombosis and Hemostasis, University Medical Center Mainz, Germany
3. Computational Biomedicine, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, 02118, USA

Background
Bacterial pneumonia is a life-threatening infection with a high risk of acute respiratory distress syndrome (ARDS) and subsequent death. The complement system is pivotal for the clearance of encapsulated bacteria such as Streptococcus pneumoniae (Spn), a major pathogen of pneumonia. Complement activation liberates C5a which activates its two homologous receptors, C5aR1 and C5aR2. While many experimental studies have suggested that C5a aggravates the severity of ARDS, it is not entirely clear whether C5a has beneficial or detrimental effects on the outcome of Spn infection. Moreover, the extent of functional overlap and role distribution between C5aR1 and C5aR2 remains enigmatic.

Materials and Methods
We generated homozygous C5aR1/2-/- double-knockout mice using CRISPR/Cas9 guided gene editing for phenotyping and functional studies using BALF cells after Spn TIGR4 infection. To further profile alveolar cell populations at the single cell level, we performed TOTAL-seq on FACSorted live CD45+ BALF cells. This novel and innovative single cell proteotranscriptomics workflow utilizes ~200 oligonucleotide-conjugated antibodies (ADT) to enable simultaneous detection of surface protein markers and RNA (Figure 1a).

Results
The C5a-induced influx of neutrophils to the airways was abrogated in C5aR1/2-/- mice. Surprisingly, the dual genetic absence of C5a receptors was associated with a stronger inflammatory response in alveolar spaces after Spn TIGR4 infection, as suggested by higher numbers of neutrophils, increased amount of inflammatory cytokines and chemokines such as IL-6, TNFα, CXCL1, CXCL10 and exacerbated lung vascular permeability. Single cell data analysis revealed 26 distinct cell clusters including 8 subclusters of alveolar macrophages and 8 subclusters of neutrophils after Spn infection (Figure 1b). C5aR1/2-/- mice showed higher neutrophils but lower macrophage counts than C57BL/6J wildtype (WT) mice. WT alveolar cells exhibited heterogeneous levels of C5aR1 ADT and C5aR2 RNA expression among macrophage and neutrophil clusters (Figure 1c). We also observed a small subset within the alveolar macrophage cluster in the WT mice that was barely detectable in the C5aR1/2-/- mice. Further studies are needed to fully decipher its nature and functions.

Conclusion
TOTAL-seq is a powerful method for characterization of immune cell phenotypes in C5aR1/2-/- mice after bacterial pneumonia and will help to elucidate potential synergisms and redundancies of C5aR1 and C5aR2.

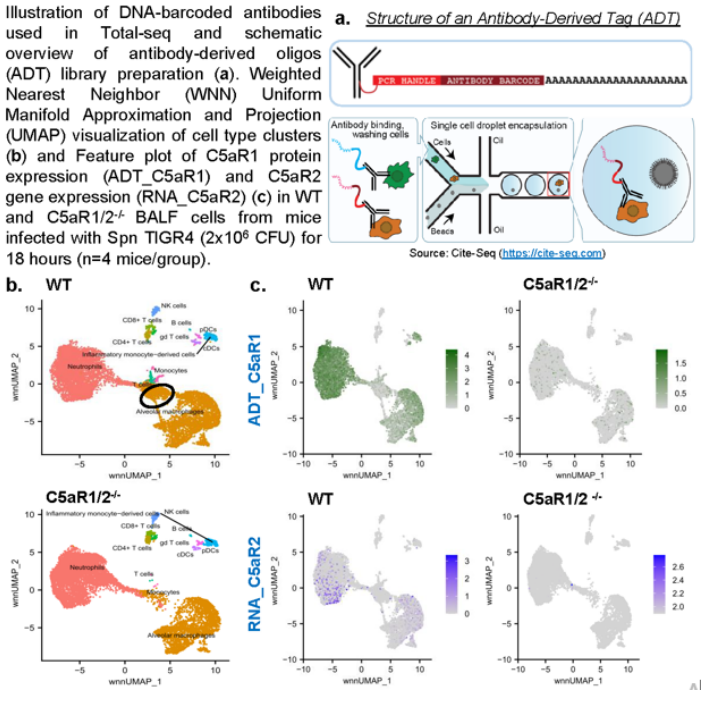


Illustration of DNA-barcoded antibodies used in Total-seq and schematic overview of antibody-derived oligos (ADT) library preparation (**a**). Weighted Nearest Neighbor (WNN) Uniform Manifold Approximation and Projection (UMAP) visualization of cell type clusters (**b**) and Feature plot of C5aR1 protein expression (ADT_C5aR1) and C5aR2 gene expression (RNA_C5aR2) (**c**) in WT and C5aR1/2$^{-/-}$ BALF cells from mice infected with Spn TIGR4 (2x10^6 CFU) for 18 hours (n=4 mice/group).

Potential involvement of terminal complement pathway overactivation in the pathogenesis of ANCA-associated vasculitis

Guillén-Olmos, Elena[1]; Palomo, Marta[2,3]; Alba, Marco A.[4]; Hernández-Rodríguez, José[4]; Cid, Maria C.[4]; Espígol-Frigolé, Georgina[4]; Prieto-González, Sergio; Xipell, Marc[1]; Quintana, Luis F.[1]; Diaz-Ricart, Maribel; Blasco, Miquel

1. Department of Nephrology and Renal Transplant, Hospital Clinic of Barcelona (Spain). Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)
2. Josep Carreras Leukaemia Research Institute, 3. Hemopathology, Hospital Clínic of Barcelona (Spain). Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)
4. Vasculitis Research Unit. Department of Autoimmune Diseases, Hospital Clínic of Barcelona (Spain). Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)

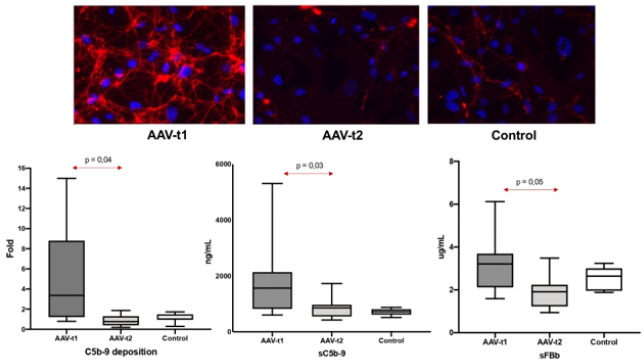
Background: Clinical, in vitro, and animal model-derived evidence has demonstrated a critical involvement of the alternative complement pathway in the pathogenesis of ANCA-associated vasculitis (AAV). However, the role of the terminal complement pathway (TCP) is less well studied (1). The current study aimed to explore new experimental approaches to assess the potential role of TCP in this condition.

Methods: A prospective, observational, multicenter study analyzing first episodes and relapses of patients with AAV, with a minimum follow-up of 6 months, was performed. Blood samples were collected at diagnosis (AAV-t1) and at remission (AAV-t2). Control population consisted of age and sex-matched individuals. Complement activation was assessed by analyzing the complement membrane attack complex (C5b-9) deposition on cultured endothelial cells (HMEC-1), by indirect immunofluorescence, after exposing them to activated plasma (patient's citrated plasma mixed with healthy subjects' sera pool, 1:1). C5b-9 deposits induced by patient's activated plasma were calculated as percentage of labeled area with respect to the total area analyzed. Results from patient and control samples were expressed as fold increase (mean±SEM) vs. those obtained with the pool of activated plasma from healthy subjects. TCP soluble factors in plasma, such as sFBb and sC5b-9, were also measured (mean±SEM).

Results: The present results are those obtained with samples from 13 AAV-MPO patients who achieved complete remission (38% men, age 63±14 years) and 10 controls (45% men, age 66±6 years). At AAV-t1, there was a significant increase ($p<0.05$) of C5b-9 deposition on endothelial cells in response to patients' plasma (fold increase of 5.3±1.3) compared to controls (fold increase of 1.2±0.2). Samples obtained at AAV-t2 induced less C5b-9 deposition than at AAV-t1 (fold increase of 0.9±0.2; $p<0.05$), with values similar to controls. Regarding TCP soluble factors, levels were significantly increased in AAV-t1 (1882±418 for sC5b-9, and 3.2±0.4 for sFBb; $p<0.05$) vs. AAV-t2 (852±104 for sC5b-9, and 1.9±0.2 for sFBb; $p<0.05$). Levels at AAV-t2 were similar to controls (708±42 for sC5b-9, and 2.4±0.2 for sFBb).

Conclusion: Our results suggest that TCP may be dysregulated in AAV. Further characterization of this dysregulation may lead to new diagnostic or disease activity biomarkers, as well as new therapeutic options for the management of patients with AAV.

Reference 1:
Moiseev S, Lee JM, Zykova A, Bulanov N, Novikov P, Gitel E, Bulanova M, Safonova E, Shin JI, Kronbichler A, Jayne DRW. The alternative complement pathway in ANCA-associated vasculitis: further evidence and a meta-analysis. Clin Exp Immunol. 2020;202(3):394-402.



Strong complement activation in Fabry Disease patients at the level of C3

Laffer, Björn[1]; Hoffmann, Inken[1]; Muschol, Nicole[2]; Köhn, Anja Friederike[2]; vom Dahl, Stephan[3]; Miglinas, Marius[4]; Degulys, Andrius[4]; Suvajdzic, Nada[5]; Fekete, György[6]; Kovac, Arpat[6]; Canaan-Kühl, Sima[7]; Tylki-Szymańska, Anna[8]; Dostálová, Gabriela[9]; Germain, Dominique[10]; Lenders, Malte[11]; Heidenreich, Karin[12]; Brand, Eva[11]; Köhl, Jörg[1]

1. Institute for Systemic Inflammation Research, University of Lübeck, Lübeck, Germany
2. International Center for Lysosomal Disorders (ICLD), University Medical Center Hamburg-Eppendorf, Hamburg, Germany
3. University Hospital Düsseldorf, Clinic for Gastroenterology, Hepatology and Infectiology, Düsseldorf, Germany

4. Vilnius University, Hospital Santaros Clinics, Vilnius, Lithuania
5. Clinical Centre of Serbia, Department of Haematology, Belgrade, Serbia
6. Semmelweis University, 2nd Department of Pediatrics, Budapest, Hungary
7. Charité – Medical University Berlin, Division of Nephrology and Internal Intensive Care Medicine, Berlin, Germany
8. Children's Memorial Health Institute, Department of Pediatrics, Nutrition and Metabolic Diseases, Warsaw, Poland
9. Charles University Prague, Prague, Czech Republic
10. University of Versailles, Versailles, France
11. Department of Internal Medicine D, and Interdisciplinary Fabry Center (IFAZ), University Hospital Münster, Germany
12. Eleva GmbH, Freiburg, Germany

Background
Lysosomal storage disorders (LSD) are characterized by accumulation of specific substrates in lysosomes resulting from mutations encoding lysosomal enzymes or the receptors for their delivery to this organelle. Recently, we found strong complement activation in Gaucher disease, driving the inflammation in this LSD (Pandey et al. Nature 2017). Here, we determined complement activation in Fabry disease (FD), an X-linked LSD caused by mutations in the α-galactosidase A gene. Such mutations lead to the cellular accumulation of globotriaosylceramide (Gb3) associated with several clinical manifestations including cardiac disease, renal failure and cerebrovascular disease.

Material and Methods
We analyzed blood samples from "classic" FD patients (18-55 years). Patient were either treatment-naïve or received enzyme replacement therapy (ERT). Lyso-Gb3 serum concentrations in both groups were >0.5 nmol/l. Samples were collected from 9 European hospitals. Further, blood from healthy controls was collected at the University Medical Center Schleswig-Holstein. The concentrations of C3a and C5a from healthy controls (n=28), treatment-naïve FD patients (n=25) and FD patients treated with ERT (n=13) were determined by ELISA (Hycult Biotech). The study was approved by the Ethics Committee of the University of Lübeck (Ref No: 20-151).

Results
C3a and C5a serum levels in treatment-naïve and ERT-treated FD patients were significantly higher than in healthy controls, whereas they were similar in treatment-naïve and ERT-treated FD patients. Of note, 40% of treatment-naïve and 23% of ERT-treated FD patients had C5a levels in the range of healthy controls. In contrast, C3a serum levels from treatment-naïve and ERT-treated FD patients were consistently higher than those in healthy controls (Figure 1). Regression analysis showed no significant correlation between C3a and C5a serum levels.

Conclusions
Our findings demonstrate strong complement activation in treatment-naïve and ERT-treated FD patients. Surprisingly, C3 cleavage was more pronounced than C5 cleavage suggesting canonical and non-canonical C3 activation. The high C3a and C5a serum levels after ERT treatment suggest sustained complement activation despite enzyme substitution. This ongoing complement activation may explain endothelial dysfunction and the high risk of thrombotic events observed in FD patients. Follow-up studies need to define the mechanisms underlying primary and ongoing C3 cleavage in FD patients.

Reference 1:
M.K. Pandey, T.A. Burrow, R. Rani, L.J. Martin, D. Witte, K.D. Setchell, M.A. McKay, A.F. Magnusen, W. Zhang, B. Liou, J. Köhl, and G.A. Grabowski, Complement drives glucosylceramide accumulation and tissue inflammation in Gaucher disease. Nature 543 (2017) 108-112.

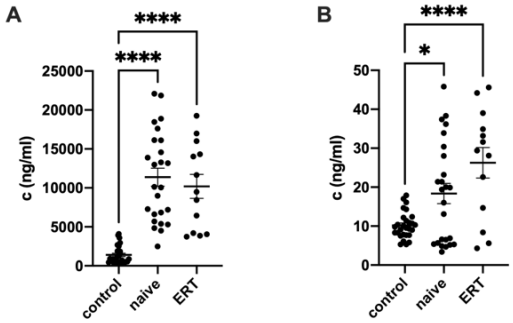


Figure 1: Serum concentrations of C3a and C5a in FD patients. C3a (A) or C5a (B) concentrations in serum samples from healthy controls (n=28) as well as from treatment-naïve (n=25) and ERT-treated (n=13) patients as assessed by ELISA. Data shown are the mean ± SEM. Differences between groups were determined by ANOVA with Tukey posthoc test. ****p<0.0001; *p<0.05.

Successful second kidney transplantation after plasmapheresis for suspected anti-endothelial cell antibodies

Lammerts, Rosa[1]; van den Born, Jaap; Huberts-Kregel, Magdalena; Gomes-neto, Antonio; Daha, Mohammed; Hepkema, Bouke; Sanders, Jan-Stephan; Pol, Robert; Diepstra, Arjan; Berger, Stefan

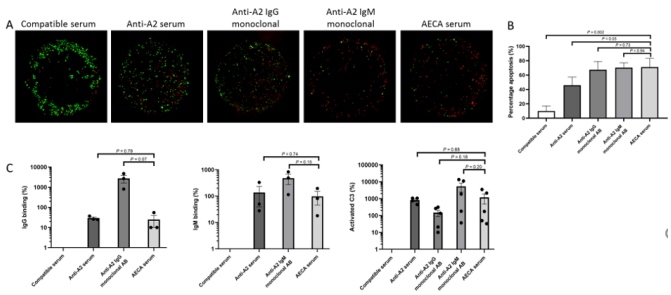
1. Univerisity Medical Center Groningen

Tissue specific non-HLA antigens can play crucial roles in allograft immunity and have been shown to trigger humoral responses leading to rejection of HLA-matched kidney allografts. Interest in the role of endothelial

specific antigens has grown over the past years in which antibodies reacting with endothelial cells (ECs) are associated with rejection. Such antibodies escape the detection in conventional crossmatch tests, as they do not react with lymphocytes. We present a case of a 69 year old male patient, whose kidney allograft was rejected hyperacute, in spite of the absence of pre-transplant HLA-specific antibodies. The patient's serum was reactive with primary renal ECs, demonstrated by antibody binding and complement-dependent-cytotoxicity. Antibodies from this patient did not react with lymphocytes, nor were HLA donor-specific-antibodies (DSAs) found. Two years later the patient successfully received a second kidney transplant after treatment with rituximab and plasmapheresis before and after transplantation. We demonstrated that removal of antibodies against non-HLA ECs specific molecules can be monitored using a renal EC crossmatch test, possibly contributing to a successful transplantation outcome.

Reference 1:
Reindl-Schwaighofer R, Heinzel A, Gualdoni GA, Mesnard L, Claas FHJ, Oberbauer R. Novel insights into non-HLA alloimmunity in kidney transplantation. Transpl Int. 2020;33(1):5-17. doi:10.1111/tri.13546

Reference 2:
Lammerts RGM, Lagendijk LM, Tiller G, et al. Machine perfused donor kidneys as a source of human renal endothelial cells. Am J Physiol Physiol. March 2021:ajprenal.00541.2020. doi:10.1152/ajprenal.00541.2020



Complement dependent endothelial cytotoxicity crossmatch assay using machine perfusion derived primary renal endothelial cells (MP-PRECs).

A) A representative experiment of a complement dependent endothelial cytotoxicity crossmatch assay (CDC) using MP-PRECs (HLA typing A2 B62 B60 Bw6 Bw6 Cw10 DR1 DR4 DR53 DQ7 DQ5 and bloodgroup A, incubated with blood group and HLA compatible serum, blood group and HLA incompatible serum (anti-A2 serum), a monoclonal antibody directed against A2 IgG, a monoclonal antibody directed against A2 IgM, and the patients' serum having AECA. Rabbit complement was used as the complement source. Living cells are depicted in green and apoptotic cells in red.

B) Quantification of n=3 experiments of apoptotic (red) cells. *P* values are depicted in the figure.

C) Flow cytometry showing IgG, IgM and activated C3 binding in percentages after incubation of MP-PRECs with blood group and HLA compatible serum, blood group and HLA incompatible serum (anti-A2 serum), a monoclonal antibody directed against A2 IgG, a monoclonal antibody directed against A2 IgM, and the patients' serum having AECA. 20% human serum was used as the complement source. MP-PRECs that were Propidium Iodide negative were included in the analysis, indicating living cells. *P* values are depicted in the figure. Experiments with a positive result for IgG, IgM and activated C3 binding after incubation with anti-A2 serum were included in the analyzes . Data are normalized to the negative control (Bloodgroup and HLA compatible serum) are presented on a logarithmic scale. Dots represent individual values.

TGF-β-induced renal complement expression is associated with fibrosis and depends on the genetic background of mice

Stepanova, Ganna[1]; Foss, Amelia1; Fazekas, Krisztina[1]; Mozes, Miklos[1]; Kokeny, Gabor[1]

1. Semmelweis University

Aims: Renal fibrosis is a hallmark of chronic kidney disease (CKD) and represents a significant health concern due to the increasing number of patients. However, progression rates vary among patients, presumably due to individual genetic differences. We have previously described the strain-dependent progression of renal fibrosis in TGFβ-transgenic mice, with C57BL/6J (B6) mice showing resistance (1). As renal complement expression has been associated with experimental and human kidney diseases, we hypothesize that intrarenal complement expression in TGFβ-transgenic mice depends on the genetic background.

Methods: Kidneys of B6-TGFβ (B6-Tg) and CBAxB6-TGFβ F1 (CBA-Tg) male transgenic mice and their wild-type (WT) controls (B6 and CBAxB6 F1) were investigated at 14 days (n=6/group) for mRNA and protein expressions. Statistical significance was determined via the Kruskal-Wallis test and set at $p<0.05$.

Results: The survival rate of CBA-Tg transgenic mice was one-tenth of the B6-Tg mice, although plasma TGF-β1 levels were comparably elevated in both transgenic strains. However, only CBA-Tg mice had elevated urinary protein creatinine ratio. In CBA-Tg mice, we observed severe glomerulosclerosis and tubulointerstitial fibrosis, accompanied by a 60-fold increase in complement C3, a 7-fold increase in complement C4, and a 4-fold increase in C3aR mRNA expressions. Immunohistochemistry for C3 protein revealed abundant staining in CBA-Tg kidneys with mostly intra-tubular localization. There was no difference in any of the abovementioned parameters between WT groups.

Conclusion: Genetic background determines the intrarenal complement components expression rates in our murine model of renal fibrosis. The genetically altered renal complement expression might influence the progression of renal fibrosis.

Reference 1:
Kokeny G, Fekeshazy O, Fang L, Rosivall L, Mozes M (2011) "Genetic susceptibility to TGF-beta induced renal fibrosis is associated with altered TIMP-1 expression" Nephrol Dial Transplant Plus, 4 (S2): 421-429 (Sa248)

The complement system, a synaptic organizer controlling glutamate transmission in the CNS of healthy and EAE mice.

Pittaluga, Anna

Background: The term "synaptic organizers" indicates those molecules which regulate the formation, the development, the functions and the removal of synapses in selected regions of the central nervous system (CNS). These molecules include "presynaptic organizers" that control the specialization of the synaptic boutons (in term of functional efficiency and structural refinement) and therefore their participation to synaptic communications. In recent years we provided evidence that complement selectively releases glutamate from nerve terminals of different CNS regions including the cortex, the hippocampus and the spinal cord (Merega et al., 2014; Olivero et al., 2019).

Methods and Results: Complement (dilution 1:10 to 1:10000) elicited per se the release of glutamate from isolated nerve endings (synaptosomes) isolated from the above-mentioned CNS regions in mouse and rats as well as from the release of glutamate from human cortical nerve, leaving unaltered the release of GABA, noradrenaline or acetylcholine. A comparable releasing activity was also observed in astrocytic processes (gliosomes) isolated from mouse cortex. Interestingly, the complement-evoked releasing activity in both cortical synaptosomes and gliosomes involves a carrier-mediated mechanism, being almost totally prevented by the concomitant presence of the excitatory aminoacid transporters (EAAT) blocker DL-tBOA. In both particles, the complement-evoked releasing activity depended on the C1q and the C3 component of the immune-complex. We extended the study of the releasing activity in the cortex of mice suffering from the experimental autoimmune encephalomyelitis (EAE) an animal model of demyelinating disorder. We found a significant increase of the endogenous levels of both C1q and C3 proteins in both cortical synaptosomes and gliosomes of EAE mice at the acute stage of the disease (21 days post immunization), but a reduced efficiency of the complement-evoked releasing activity in the synaptosomes but not in gliosomes.

Conclusion: These results unveiled that th
e presynaptic organizer activity of complement on glutamate transmission is altered in a cell-dependent fashion during the course of the disease. The impact of these vents on the onset of the clinical symptoms that typify MS remains to be established.

Reference 1:
Merega E, Prisco SD, Lanfranco M, Severi P, Pittaluga A. (2014) Complement selectively elicits glutamate release from nerve endings in different regions of mammal central nervous system. J Neurochem. 129: 473-483.

Reference 2:
Olivero G, Vergassola M, Cisani F, Usai C, Pittaluga A. Immuno-Pharmacological Characterization of Presynaptic GluN3A-Containing NMDA Autoreceptors: Relevance to Anti-NMDA Receptor Autoimmune Diseases. Mol Neurobiol. 2019

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