ICW2016
KANAZAWA

XXVI[th] INTERNATIONAL
COMPLEMENT
WORKSHOP

September 4-8, 2016 Kanazawa, Japan

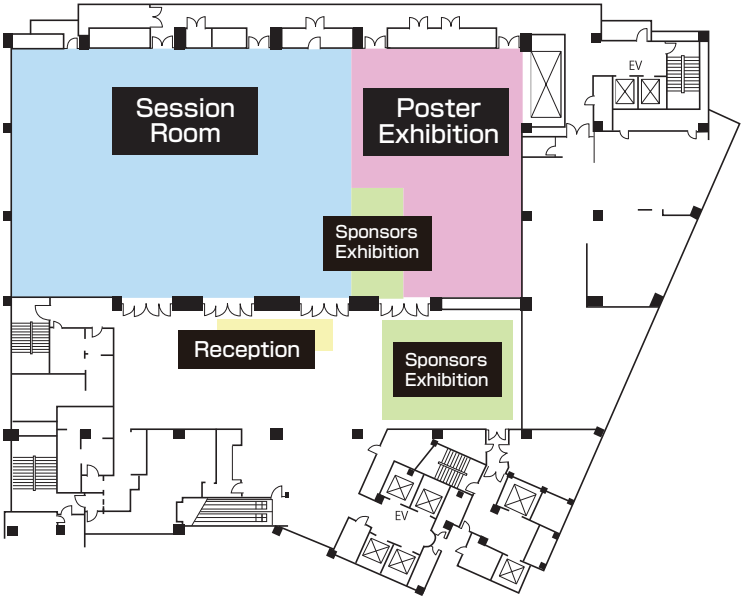
www.icwkanazawa2016.com

JACR

ICS

Hotel Nikko Kanazawa
Floor Map

4F



Dear Colleagues,

It is a great pleasure and an honor to invite you to the 26th International Complement Workshop (XXVI ICW) that will be held in the city of Kanazawa, Japan in September 2016.

The First Japanese Complement Symposium was held in Hakone in 1964. Since then, the Symposia have been held every year and the Japanese Association for Complement Research (JACR) has published reports entitled Proceedings of the Complement Symposium. In 1993, Japan successfully hosted the XV ICW in Kyoto which is one of the most beautiful and ancient cities in the country.

Kanazawa is also one of the most scenic and traditional cities in Japan and was registered as a City of Crafts in UNESCO's Creative Cities Network in June 2009. Kanazawa maintains many historical sites, such as its Samurai Town, Higashi Chaya District (home to its Geisha and tea houses), and the Kenrokuen Garden.

In line with tradition, we aim to organize a high quality scientific meeting that will serve as a platform for enthusiastic discussions that will lead complement scientists to new and insightful research.

We are pleased and impressed by the numerous abstracts that have been submitted to the meeting and which form the basis for the comprehensive scientific program comprising 58 oral and 156 poster presentations.

We hope that, in addition to an exchange of excellent scientific ideas and concepts, you will find time to visit the Kanazawa city and Shirakawa-go, well known for the old Japanese culture and scenery.

We are delighted to welcome you to Kanazawa and we wish you a pleasant and fruitful stay.

Teizo Fujita
From the Local Organizing Committee

International Complement Society Board

Andrea Joan Tenner (Chair of the Program Committee)
ICS President, University of California, Irvine, USA

Michael Holers
ICS President-Elect, University of Colorado, Aurora, USA

Zvi Fishelson
ICS Past President, Tel Aviv University, Tel Aviv, Israel

Claudia Kemper
ICS Secretary, King's College London, London, UK

Wenchao Song
ICS Treasurer, University of Pennsylvania, Philadelphia, USA

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University of Copenhagen, Copenhagen, Denmark

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University of Heidelberg, Heidelberg, Germany

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Santiago Rodriguez de Córdoba
Centro de Investigaciones Biológicas, Madrid, Spain

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Butantan Institute, San Paulo, Brazil

Trent M. Woodruff
University of Queensland, St Lucia, Australia

Peter F. Zipfel
Hans-Knöll-Institute, Jena, Germany

XXVIth ICW Local Organizing Committee

Teizo Fujita (Chair of the Committee)
Fukushima Prefectural General Hygiene Institute, Japan

Nobutaka Wakamiya
Asahikawa Medical University, Japan

Taroh Kinoshita
Osaka University, Japan

Takahiko Horiuchi
Kyushu University Beppu Hospital, Japan

Norimitsu Inoue (Secretary)
Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan

Congress General Information

Congress Venue
Tsuru Hall-4th Floor, Hotel Nikko Kanazawa, Kanazawa, Ishikawa, Japan

Registration Desk Schedule
The Entrance Hall, Kanazawa Chamber of Commerce & Industry Hall
Sunday, September 4, 2016 from **07:45 to 16:00**
Welcome party, Gojukken Nagaya in Kanazawa Castle Park
Sunday, September 4, 2016 from **16:30 to 18:30**
The Entrance Hall-4th Floor, Hotel Nikko Kanazawa
Monday, September 5, 2016 from **07:30 to 18:00**
Tuesday, September 6, 2016 from **08:00 to 18:00**
Wednesday, September 7, 2016 from **08:00 to 12:30**
Thursday, September 8, 2016 from **08:00 to 12:00**

Sponsors Exhibition
The Entrance Hall-4th Floor, Hotel Nikko Kanazawa
There is an accompanying industrial exhibition. The exhibitors are looking forward to welcoming you and to presenting their comprehensive range of innovative products.

Exhibition Schedule
Monday, September 5, 2016 from 08:00 to 19:00
Tuesday, September 6, 2016 from 08:00 to 19:00
Wednesday, September 7, 2016 from 08:00 to 13:00
Thursday, September 8, 2016 from 09:00 to 13:00

Lunches
Lunch will be served for all registered participants for Teaching day. Lunches for registered participants will be served during the Lunchtime seminar indicated in this program on Monday and Tuesday, September 5 (12:30-13:30) and September 6 (12:20-13:20) at the same Tsuru Hall-4th Floor, Hotel Nikko Kanazawa.
On September 7 lunch box will be served for Tours and on September 8 lunch will be served at the same Tsuru Hall-4th and in the other room for JACR meeting.
Badges are required for admission.

Welcome party and Gala Dinner
The **Welcome party** will be held on September 4 from 17:30–19:00 at the Gojukken Nagaya in Kanazawa Castle Park.
The **Gala Dinner** will be held on September 8 from 19:00–21:00 at Hotel Nikko Kanazawa. **Badges are required for participation.**

Tour
Buses for excursion will depart from the hotel front lobby on Wednesday, September 7. **Badges are required for participation.** The buses will leave at **13:15 or 14:00** sharp, with no exception.
Shirakawa-go tour (World Heritage) with lunch box, departure at 13:15 or **Kenrokuen Garden tour**, after taking lunch in the Hotel, **departure at 14:00**

Social Program for Accompanying Persons
On Monday, September 5, City tour will start at 9:30 from Hotel Nikko Kanazawa. On Tuesday, September 6, tour will start at 11:00 from Hotel Nikko Kanazawa.

Certificate of Attendance
Certificate of attendance will be able to receive on the registration desk.

Name Badges
For security, delegates, accompanying persons and exhibitors must wear their name badge at all times in order to access the congress venue and social activities.

Language
The official language of the congress is English.

Awards
Young Investigator Award (YIA) for Research in Complement of the ICS and the Complement Training Award (CTA) sponsored by the Lambris Family were chosen by the members of the ICS Board out of a panel of nominated candidates. Travel awards to oral and poster presenters are given to students and postdoctoral fellows (who applied for awards) based on their research achievements as judged by the members of the ICS Board. Poster Awards and Poster Presenting Awards were also given to the students/postdoc above based on their research achievements.

Disclosure at lecture/ poster presentation
All authors should disclose in their presentations, as a separate second slide in an oral presentation, or a statement in a poster presentation in the bottom left corner, the relevant conflict of interest (COI). In case of no relevant COI, the second slide and poster presentation should state: 'No relevant conflicts of interest to disclose.'

Oral Presentation
The allocated time for oral presentation is 10 minutes followed by 5 minute discussion. Speakers are asked to bring their USB flash drive to the conference reception desk at least 60 minutes prior to the session; presentations in PowerPoint format (PC or Mac) are preferred. Presentation equipment, including a computer, is available in the conference room and we ask all speakers to use the conference computer. Speakers will not be able to use their own personal computer. Please contact the registration desk in advance if you have questions or need assistance.

Poster Presentation
Tsuru Hall-4th Floor, Hotel Nikko Kanazawa

Session I
Posters for Session I should be mounted between **07:30–12:00** on Monday, September 5, 2016 and removed at the end of the session (**17:00**).

Session II
Posters for Session II should be mounted between **07:30–12:00** on Tuesday, September 6, 2016 and removed at the end of the session (**18:00**).

Election/Ballot
Election for members of the ICS Board (President Elect, Secretary, Treasurer, Councilors) will be conducted during the ICW. Ballots are included in the registration package. Please fill it in and insert it into the ballot box placed on the conference registration desk by Tuesday 13:00, September 6, 2016.

No Photographs and Recording Devices
Participants are not allowed to photograph and/or record using cameras, mobile telephones and other recording devices during oral and poster presentations.

Executive Secretariat
The Japanese Association for Complement Research
Research Institute, Osaka Medical Center for Cancer and Cardiovascular Diseases,
1-3-2 Nakamichi, Higashinari, Osaka, 537-8511
TEL: +81 (country code)-6-6972-1181 (Extension number is 4101.)
FAX: +81-6-6973-5691
Email: secretariat@icwkanazawa2016.com

Program overview

	Sunday September 4	Monday September 5	Tuesday September 6	Wednesday September 7	Thursday September 8
08:00					
	08:15–08:30 Welcome and Introduction	08:15–08:30 Opening Remarks			
	08:30–10:10 Teaching Day Lectures I–IV	08:30–9:30 Session I Intra-cellular complement	08:30–09:30 Session IV Complement and Diseases I	08:30–09:30 Session VIII Complement and Diseases II	08:30–09:30 Session X Complement and Diseases III
09:00		09:30–10:30 Plenary lecture I	09:30–10:30 Plenary lecture II	09:30–10:30 Plenary lecture III	09:30–10:30 Plenary lecture IV
10:00	10:10–10:40 Coffee break				
	10:40–12:55 Teaching Day Lectures V–IX	10:30–11:00 Coffee break	10:30–11:00 Coffee break	10:30–11:00 Coffee break	10:30–11:00 Coffee break
11:00		11:00–12:30 Session II Structure and function	11:00–12:20 Session V Lectin pathway and MASP	11:00–12:30 Session IX Host Pathogen interaction	11:00–12:15 Session XI Adaptive Immunity
12:00			12:20–13:20 Lunchtime seminar II		12:15–13:15 Lunch
		12:30–13:30 Lunchtime seminar I			
13:00	12:55–13:45 Lunch			13:15 Departure to Shirakawa-go	
		13:45–15:00 Session III Collectins	13:30–14:45 Session VI Complement and the Nervous System Receptors	14:00 Departure to Kenrokuen Garden	13:45–15:00 Session XII Complement-mediated inhibitors: Therapeutic intervention
14:00	14:00–15:15 Teaching Day Exercise session I				
			14:45–16:45 Coffee break & Poster Session II		
15:00	15:15–15:45 Coffee break	15:00–17:00 Coffee break & Poster Session I			15:00–15:30 Coffee break
	15:45–17:00 Teaching Day Exercise session II				15:30–17:00 Closing
16:00			16:45–18:00 Session VII Receptors		
17:00	17:15 Departure to Welcome Party 17:30–19:00 Welcome Party	17:00–19:00 Standardization Committee of ICW (EQA meeting)			
18:00				from 18:00 ICS Meeting	
19:00					19:00–21:00 Gala Dinner

XXVI International Complement Workshop
Teaching Day

Kanazawa Chamber of Commerce & Industry Hall

Morning: Key Lectures on Complement

08:15 – 08:30 **Welcome and Introduction**
Andrea J. Tenner/Michael Holers

08:30 – 08:55 **I Overview of complement system and classical pathway**
Tom E Mollnes – Oslo University Hospital, Norway

08:55 – 09:20 **II Alternative pathway and its regulation**
Peter F. Zipfel – Hans-Knöll-Institut, Germany

09:20 – 09:45 **III Lectin pathway**
Peter Garred – University of Copenhagen, Denmark

09:45 – 10:10 **IV Membrane Attack Complex (MAC)**
Zvi Fishelson – Tel Aviv University, Israel

10:10 – 10:40 Coffee break

10:40 – 11:05 **V Complement and inflammation**
Trent M. Woodruff – The University of Queensland, Australia

11:05 – 11:30 **VI Measuring Complement in the Lab and in the Clinic**
Michael Kirschfink – University of Heidelberg, Germany

11:30 – 11:55 **VII Complement in the nervous system**
Andrea J. Tenner – University of California, USA

11:55 – 12:20 **VIII Linking complement and adaptive immunity**
Claudia Kemper – King's College London, UK

12:20 – 12:45 **IX Challenges and progress in complement therapeutics**
Claire Harris – Newcastle University, UK

12:45 – 12:55 Q & A

12:55 – 13:45 Lunch

Afternoon: Exercise sessions

14:00 – 15:15 **Exercise session I (Select one)**

Theme 1: Complement: focus on immune complex diseases
Bo Nilsson, Leendert Trouw and Masashi Mizuno

Theme 2: Animal and cell models suitable for complement studies
Wenchao Song, Matthew C. Pickering and Hideharu Sekine

Theme 3: Complement deficiencies and diseases
Santiago Rodriguez de Córdoba, Michael Kirshfink and Takahiko Horiuchi

Theme 4: Therapeutic intervention in the complement system
Michael Holers, Tom Eirik Mollnes and Trent M. Woodruff

15:15 – 15:45 Coffee break

15:45 – 17:00 **Exercise session II (Select different one)**
Change the theme

17:15 **Departure to Welcome Party**
About 15-minutes walk to the Gojukken-Nagaya in Kanazawa castle

Welcome Party

Gojukken Nagaya in Kanazawa Castle Park

17:30 **Opening**
19:00 **Closing**

XXVI International Complement Workshop
Scientific Program

Tsuru Hall-4th Floor, Hotel Nikko Kanazawa

8:15 – 8:30 **Opening Remarks**
Teizo Fujita, Fukushima Prefectural General Hygiene Institute, Japan
Andrea Joan Tenner, University of California, USA

Session I

8:30 – 9:30 **Intra-cellular complement**
Chair; Peter F. Zipfel & Claudia Kemper

8:30 – 8:45 **Abstract 108**
The intracellular C5 system is critical to DAMP sensing and cellular responses in human monocytes
Nathalie Niyonzima, Simon Freeley, Giuseppina Arbore, Gaelle Le Friec, Knut Tore, Lappegård, Tom Eirik Mollnes, Claudia Kemper, Terje Espevik

8:45 – 9:00 **Abstract 41**
Presence of an intracellular C3-C3aR system in the human lung epithelium
Hrishikesh S. Kulkarni, Michelle L. Elvington, M. Kathryn Liszewski, Steven L. Brody, John P. Atkinson

9:00 – 9:15 **Abstract 156**
Intracellular C3a regulates cell proliferation in prostate epithelial cells
Hidekazu Yamamoto, Ash Chandra, Len Seymour, Prokar Dasgupta, Claudia Kemper

9:15 – 9:30 **Abstract 145**
A C3(H_2O) recycling and degradation pathway of the intracellular complement system
Michelle L. Elvington, M. Kathryn Liszewski, Hrishikesh S. Kulkarni, John P. Atkinson

Plenary lecture I

9:30 – 10:30 Chair; Andrea J. Tenner
Intracellular innate immune receptors: roles in infection, inflammation and cancer
Jenny PY Ting, UNC School of Medicine, USA

10:30 – 11:00 **Coffee break**

Session II

11:00 – 12:30 **Structure and function**
Chair; Paul Morgan & Piet Gros

11:00 – 11:15 **Abstract 90**
Regulation of the mouse adipose factor D biosynthesis by the endocrine hypothalamic-pituitary-adrenal axis
Xiaobo Wu, Irina Hutson, Dennis Hourcade, Charles Harris, John P. Atkinson

11:15 – 11:30 **Abstract 137**
Structural insights into cofactor activity
Xiaoguang Xue, Jin Wu, Federico Forneris, Daniel Ricklin, Patrizia Di Crescenzio, Christoph Schmidt, Joke Granneman, John D Lambris, Piet Gros

11:30 – 11:45 **Abstract 140**
Imaging complement activation step-by-step on liposomes by phase-plate cryo-electron tomography
Thomas H. Sharp, Abraham J. Koster, Piet Gros

11:45 – 12:00 **Abstract 138**
Complex beauty complements membrane attack.
B. Paul Morgan, Marina Serna, Doryen Bubeck

12:00 – 12:15 **Abstract 111**
Membrane stability of the C5b-9 complexes: a nanoscopical analysis of the interactions of C5b-9 with mortalin and caveolin-1
Niv Mazkereth, Francesco Rocca, Jennifer-Rose Schubert, Claudia Geisler, Yaron Hillman, Alexander Egner, Zvi Fishelson

12:15 – 12:30 **Abstract 78**
A cryptic non-GPI anchored form of CD59 facilitates insulin secretion from pancreatic beta cells
Ben C King, Ewelina Golec, Enming Zhang, David O'Connell, Eitan Netanyah, Rebecca Rosberg, Jose Halperin, Erik Renström, Anna M Blom

Lunchtime seminar I

12:30 – 13:30 Chair; Carl-Wilhelm Vogel
Molecular pathogenesis of paroxysmal nocturnal hemoglobinuria
Taroh Kinoshita, Osaka University, Japan

Session III

13:45 – 15:00 **Collectins**
Chair; Peter Garred & Viviana Ferreira

13:45 – 14:00 **Abstract 187**
Structural characterization of novel collectins, CL-K1, CL-L1, and CL-LK in blood
Yasuyuki Matsuda, Katsuki Ohtani, Nitai Roy, Insu Hwang, Kenichiro Mori, Nobutaka Wakamiya

14:00 – 14:15 **Abstract 106**
Collectin 11 expression by hypoxia-stressed iPSC-derived RPE cells is linked to complement activation
Giorgia Fanelli, Peter Gardner, Anai Gonzalez-Cordero, Peng Qi, Conrad Farrar, Arifa Naeem, Fernando Milan, Robin Ali, Steven Sacks

14:15 – 14:30 **Abstract 72**
Collectin-11 has a critical role in the regulation of phagocytosis of photoreceptor outer segment fragments and cytokine production by retinal pigment epithelial cells
Xia Dong, Weiju Wu, Liang Ma, Chengfei Liu, Conrad A Farrar, Steven H Sacks, Emeline F Nandrot, Yizhi Liu, Wuding Zhou

14:30 – 14:45 **Abstract 61**
Collectin-11 deficiency reduces renal inflammation and ameliorates tubulointerstitial fibrosis following renal ischemia reperfusion injury
Weiju Wu, Chengfei Liu, Conrad A Farrar, Liang Ma, Ke Li, Steve H Sacks, Wuding Zhou

14:45 – 15:00 **Abstract 144**
Collectin-11-mediated renal ischaemia reperfusion: potential of L-fucose as a therapeutic target for intervention
Conrad A. Farrar, Wuding Zhou, Steven H. Sacks

15:00 – 17:00 **Coffee break and Poster Session I**

17:00 – 19:00 **Standardization Committee of ICW (EQA meeting)**
Chair: Michael Kirschfink & Zoltán Prohászka

Tsuru Hall-4th Floor, Hotel Nikko Kanazawa

Session IV

8:30 – 9:30 **Complement and diseases I**
Chair; Michael Holers & Kristina Ekdahl

8:30 – 8:45 **Abstract 181**
C5a drives glucosylceramide accumulation and tissue inflammation in Gaucher disease
Manoj K. Pandey, Thomas A Burrow, Christina Gross, David Witte, Wujuan Zhang, Kenneth D. Setchell, Nancy D Leslie, Gregory A. Grabowski, Jörg Köhl

8:45 – 9:00 **Abstract 130**
Subretinal and sub-RPE deposition in mice with combined factor H mutation and properdin deficiency
Imran Mohammed, Delu Song, Takashi Miwa, Allison Lesher Wlliams, Damodar Gullipali, Sayaka Sato, Joshua L Dunaief, Wen-Chao Song

9:00 – 9:15 **Abstract 6**
The lectin but not classical pathway of activation is important for complement to regulate the development of experimental autoimmune uveitis
Lingjun Zhang, Brent A. Bell, Yan Li, Xiaomin Zhang, John J. Fung, Rachel R. Caspi, Feng Lin

9:15 – 9:30 **Abstract 81**
Essential role of mannose-binding lectin-associated serine proteases-1/3 (MASP-1/3) in the development of lupus-like gromerulonephritis in MRL/lpr mice
Natsumi Sakamoto, Takeshi Machida, Minoru Takahashi, Teizo Fujita, Hideharu Sekine

Plenary lecture II

9:30 – 10:30 Chair; Taroh Kinoshita
Flippase and Scramblase that regulate phospholipid distribution at plasma membrane
Shigekazu Nagata, Osaka University, Japan

10:30 – 11:00 **Coffee break**

Session V

11:00 – 12:20 **Lectin pathway and MASP**
Chair; Wilhelm Schwaeble & Nicole Thielens

11:00 – 11:20 **Abstract 170 – YIA winner**
The lectin complement pathway inhibitor MAP-1 is an upstream regulator of the coagulation cascade
Mikkel-Ole Skjoedt, Vasile Pavlov, Huda Kozarcanin, Anton Willer, Lea Munthe-Fog, Karin Møller Hansen, Kristina Nilsson-Ekdahl, Bo Nilsson, Gregory L. Stahl, Peter Garred

11:20 – 11:35 **Abstract 31**
MASP-1 enhances clot formation in a microvascular flow model
Lorenz Jenny, József Dobó, Péter Gál, Wilbur Lam, Verena Schroeder

11:35 – 11:50 **Abstract 84**
Utility of MASP-2 inhibition in murine models of cerebral ischemia
Franca Orsini, Elvina Chrysanthou, Thomas Dudler, Jason Cummings, Minoru Takahashi, Teizo Fujita, Gregory Demopulos, Maria-Grazia De Simoni, Wilhelm Schwaeble

11:50 – 12:05 **Abstract 2**
Targeted inhibition by RNA interference-mediated gene silencing of mannan-binding lectin-associated serine protease (MASP)-1/3 expression attenuates collagen antibody-induced arthritis (CAIA)
Nirmal K. Banda, Sumitra Acharya, Robert I. Scheinman, Gaurav Mehta, Minoru Takahashi, Simon Mortensen, Steffen Thiel, Hideharu Sekine, Teizo Fujita, V Michael Holers

12:05 – 12:20 **Abstract 166**
MASP-3 is the major activator, and the exclusive "resting blood" activator of pro-FD
Gábor Oroszlán, Dávid Szakács, Elod Kortvely, András Szilágyi, Péter Závodszky, Gábor Pál, Péter Gál, József Dobó

Lunchtime seminar II

12:20 – 13:20 Chair; Michael Kirschfink
Angioedema due to C1 inhibitor deficiency: from research on complement to treatments tailored to patients
Marco Cicardi, University of Milan, Italy

Session VI

13:30 – 14:45 **Complement and the nervous system receptors**
Chair; Trent M. Woodruff & Jörg Köhl

13:30 – 13:45 **Abstract 42**
Microglia specific ablation of C1q gene definitively demonstrates microglia as the dominant source of C1q in both normal mouse brain and in models of Alzheimer's disease
Maria I. Fonseca, Shu-Hui Chu, Michael Hernandez, Melody Fang, Lila Modarresi, Andrea J.Tenner

13:45 – 14:00 **Abstract 125**
Role of microglial C5aR1 in the arctic alzheimer's disease mouse model
Michael X. Hernandez, Maria I. Fonseca, Shu-Hui Chu, Andrea J. Tenner

14:00 – 14:15 **Abstract 131**
Complement C5a activates microglial NLRP3 inflammasomes and drives neurodegeneration in Parkinson's disease through C5aR1
Richard Gordon, Eduardo A Albornoz, Vinod Kumar, Kiane Zhou, Ashoka Garin-Michaud, Susanna Mantavani, Anumantha G Kanthasamy, Trent M. Woodruff

14:15 – 14:30 **Abstract 171**
A pathogenic role for the C5a receptor, C5aR2, in mouse models of Huntington's and Parkinson's disease
Rui Li, John D. Lee, Samantha Levin, Richard Gordon, Trent M. Woodruf

14:30 – 14:45 **Abstract 82**
The lectin complement pathway in human contusions
Daiana De Blasio, Stefano Fumagalli, Luca Longhi, Franca Orsini, Fabrizio Ortolano, Elisa R Zanier, Silvia Ferrari, Giulio Goti, Peter Garred, Edoardo Picetti, Marco Locatelli, Anna Bernardi, Marco Gobbi, Nino Stocchetti, Maria-Grazia De Simoni

14:45 – 16:45 **Coffee break and Poster Session II**

Session VII

16:45 – 18:00 **Receptors**
Chair; Rick Wetsel & Maria Botto

16:45 – 17:00 **Abstract 141**
C3a and C5a control central and peripheral circadian rhythms
Anna Czabanska, Julia Kilian, Christiane Koch, Anthony Tsang, Yves Laumonnier, Jörg Köhl, Henrik Oster

17:00 – 17:15 **Abstract 109**
Defining C3aR expression in myeloid and lymphoid cells using a novel Td-Tomato-C3aR reporter knockin mouse
Yves Laumonnier, Christian M Karsten, Anna Czabanska, Inken Schmudde, Daria Briukhovetska, Anna Wiese, Jing Sun, Katharina Quell, Konstantina Antoniou, Tillman Vollbrandt, Jörg Köhl

17:15 – 17:30 **Abstract 153**
The C5a/C5aR1 axis is critical for the activation of a novel vacuolated eosinophil population in experimental allergic asthm
Anna Valeska Wiese, Fanny Ender, Jing Sun, Tillman Vollbrandt, Peter König, Jörg Köhl, Yves Laumonnier

17:30 – 17:45 **Abstract 129**
Role of granulocyte C5a receptor expression in complement-mediated diseases as assessed by conditional gene targeting
Sayaka Sato, Yuan Wang, Damodar Gulipalli, Lin Zhou, Brenal Singh, Takashi Miwa, Wen-Chao Song

17:45 – 18:00 **Abstract 43**
Investigating the role of Complement Component C5a Receptor 2 (C5aR2/C5L2) in Spinal Cord Injury
P. J. C. Biggins, F. H. Brennan, S. M. Taylor, T. M. Woodruff, M. J. Ruitenberg

Tsuru Hall-4th Floor, Hotel Nikko Kanazawa

Session VIII

8:30 – 9:30 **Complement and diseases II**
Chair; Santiago Rodriguez de Cordoba & Matthew C. Pickering

8:30 – 8:45 **Abstract 13**
A novel C3 gain of function mouse model of atypical haemolytic uraemic syndrome
Kate Smith-Jackson, Harriet Denton, Katie Cook, Mathew C. Pickering, Terrence H. Cook, Kevin J. Marchbank

8:45 – 9:00 **Abstract 128**
Genetic and antibody targeting of properdin ameliorates atypical hemolytic uremic syndrome in a mouse model
Yoshiyasu Ueda, Takashi Miwa, Damodar Gullipalli, Lin Zhou, Sayaka Sato, Matthew Palmer, Wen-Chao Song

9:00 – 9:15 **Abstract 152**
Towards a complete functional characterization of the disease-associated genetic variants found in the *CFH* gene
Héctor Martín Merinero, Sheila Pinto García, Jesús García-Fernández, Emilia Arjona, Agustín Tortajada and Santiago Rodríguez de Córdoba

9:15 – 9:30 **Abstract 195**
Collectin-12 and long pentraxin PTX3 crosstalk synergizes resistance against *N. meningitides* via the alternative pathway of complement
Ying Jie Ma, Andrea Doni, Bernt Christian Hellerud, Tom Eirik Mollnes, Alberto Mantovani, Peter Garred

Plenary lecture III

9:30 – 10:30 Chair; Nobutaka Wakamiya
Functions of macrophage/monocyte subsets revealed by gene targeting
Shizuo Akira, Osaka University, Japan

10:30 – 11:00 **Coffee break**

Session IX

11:00 – 12:30 **Host pathogen interaction**
Chair; Anna Blom & Sanjay Ram

11:00 – 11:15 **Abstract 95**
The complement anaphylatoxins provide host protection against *Listeria monocytogenes* infection by inhibiting a distinct innate cytosolic surveillance pathway that regulates IFN-ß gene expression
Stacey L Mueller-Ortiz, Daniel G Calame, Nancy Shenoi, Yi-Dong Li, Rick A Wetsel

11:15 – 11:30 **Abstract 87**
C5a controls Toxoplasma gondii infection in the brain
Daria Briukhovetska, Fabian Mey, Birte Ohm, Kasper Hoebe, Julio Aliberti, Jörg Köhl, Christian M. Karsten

11:30 – 11:45 **Abstract 56**
Hijacking host complement regulators: mechanisms of *Plasmodium falciparum* complement evasion
Alexander T. Kennedy, Christoph Q. Schmidt, Jennifer K. Thompson, Greta E. Weiss, Tana Taechalerpaisarn, Paul R. Gilson, Paul N. Barlow, Brendan S. Crabb, Alan F. Cowman, Wai-Hong Tham

11:45 – 12:00 **Abstract 32**
Complement evasion by *staphylococcus aureus* Bbp and SdrE that act on the C3 convertase
Mingsong Kang, Sheila Thomas, Vannakambadi K. Ganesh, Ya-Ping Ko, Magnus Hook

12:00 – 12:15 **Abstract 66**
Human ficolin-1 interacts with Ebola virus glycoprotein: a novel case of lectin-dependent enhancement of viral infection
Anne-Laure Favier, Evelyne Gout, Olivier Reynard, Olivier Ferraris, Jean-Philippe Kleman, Viktor Volchkov, Christophe Peyrefitte, Nicole M Thielens

12:15 – 12:30 **Abstract 190**
In vitro* and *in vivo* roles in Collectin Kidney 1 (CL-K1) with innate immunity against *Streptococcus pneumoniae
Insu Hwang, Kenichiro Mori, Katsuki Ohtani, Yasuyuki Matsuda, Nitai Roy, YounUck Kim, Nobutaka Wakamiya

Excursion **Shirakawa-go tour (World Heritage), departure at 13:15**
Kenrokuen Garden tour, departure at 14:00

18:00 **ICS Meeting: Matsu Hall-5th Floor, Hotel Nikko Kanazawa**

Tsuru Hall-4th Floor, Hotel Nikko Kanazawa

Session X

8:30 – 9:30 **Complement and diseases III**
Chair; Bo Nilsson & Reinhard Wurzner

8:30 – 8:45 **Abstract 3**
Antibodies that efficiently form hexamers upon antigen binding can induce complement-dependent cytotoxicity under complement-limiting conditions
Ronald P. Taylor, Margaret A. Lindorfer, Erika M. Cook, Frank J. Beurskens, Hilma van der Horst, Simone Oostindie, Janine Schuurman, Clive Zent, Richard Burack, Paul W.H.I. Parren

8:45 – 9:00 **Abstract 177**
Anaphylatoxin-signaling through C5a and C3a receptor alters signaling in Retinal Pigment Epithelial (RPE) cells
Bärbel Rohrer, Catharina Busch, Kannan Kunchithapautham, Balasubramanian Annamalai, Christine Skerka, Peter Zipfel, Carl Atkinson, Olaf Strauß

9:00 – 9:15 **Abstract 126**
FH-IgG fusion proteins as novel therapeutics against group A streptococcal infections
Lisa Kohl, Michal Magda, Jutamas Shaughnessy, Sanjay Ram, Anna M Blom, David Ermert

9:15 – 9:30 **Abstract 162**
Molecular modelling showed optimal fit between TSR5 in trimeric properdin and C345C in the C3b moiety for stabilization of the alternative convertase, whereas binding to molecular patterns in myeloperoxidase, endothelial cells and *Neisseria meningitides* was indirectly mediated by initial C3 activation
Morten Harboe, Christina Johnson, Stig Nymo, Karin Ekholt, Camilla Schjalm, Julie K. Lindstad, Anne Pharo, Bernt C. Hellerud, Kristina N. Ekdahl, Tom E. Mollnes, Per H. Nilsson

Plenary lecture IV

9:30 – 10:30 Chair; Zvi Fishelson

The ubiquitin proteolytic system: From basic mechanisms thru pathogenesis of diseases and on to drug targeting

Aaron Ciechanover, Technion-Israel Institute of Technology, Israel

10:30 – 11:00 **Coffee break**

Session XI

11:00 – 12:15 **Adaptive Immunity**

Chair; John Atkinson & Berhane Ghebrehiwet

11:00 – 11:15 **Abstract 18**

Regulation of TLR9-mediated human B cell functions by C3a and C3adesArg - a novel anti-inflammatory effect of C3a on the humoral immune response

Mariann Kremlitzka, Zsófia Csáti, Christian M. Karsten, Jörg Köhl, Anna Erdei

11:15 – 11:30 **Abstract 202**

In response to C3a/C5a, Human Vascular Endothelial Cells Transmigrate and Mediate the Activation of B-cells and Polarization of T-cells

Pooja Shivshankar, Stacey L. Mueller-Ortiz, Rick A. Wetsel

11:30 – 11:45 **Abstract 88**

C5a regulates homeostasis and egress of peritoneal B1 cells

Katharina Bröker, Christian M. Karsten, Rudolf A. Manz, Jörg Köhl, Julia Figge

11:45 – 12:00 **Abstract 143 – CTA winner**

Tissue extravasation induces 'complement-licensing' required for immune cell effector function

Martin Kolev, Sarah Dimeloe, Paul Lavender, Cristoph Hess, Andrew Cope, Claudia Kemper

12:00 – 12:15 **Abstract 112**

Regulation of complement-dependent cytotoxicity by microRNAs

Yaron Hillman, Noam Shomron, Zvi Fishelson

12:15 – 13:15 **Lunch**

12:15 – 13:15 **JACR meeting (Japanese members only)**
Kujaku Hall-3rd Floor, Hotel Nikko Kanazawa
ECN meeting: Matsu Hall-5th Floor, Hotel Nikko Kanazawa

Session XII

13:45 – 15:00 **Complement-mediated inhibitors: Therapeutic intervention**
Chair; Wenchao Song & Claire Harris

13:45 – 14:00 **Abstract 89**
TNT009, a monoclonal antibody inhibitor of C1s, induces a rapid and complete remission of anemia in primary cold agglutinin disease patients
Sandip Panicker, Graham C. Parry, Michael Fillitz, Thomas Schenk, Christian Sillaber, Johann Bartko, James C Gilbert, Ulrich Jäger, Bernd Jilma

14:00 – 14:15 **Abstract 63**
Design and preclinical characterization of ALXN1210: a next generation anti-C5 monoclonal antibody with improved pharmacokinetics and duration of action
Douglas Sheridan, Zhao-Xue Yu, Yuchun Zhang, Rekha Patel, Melissa Lasaro, Keith Bouchard, Bruce Andrien, Andre Marozsan, Yi Wang, Paul Tamburini

14:15 – 14:30 **Abstract 176**
Anti-human properdin monoclonal antibody dose-dependently inhibits complement-mediated lysis of PNH erythrocytes in Ham's test and prevents extravascular hemolysis in a human properdin transgenic mouse model
Damodar Gullipalli, Fengkui Zhang, Sayaka Sato, Yoshiyasu Ueda, Yuko Kimura, Takashi Miwa, Jianxiang Wang, Wen-Chao Song

14:30 – 14:45 **Abstract 59**
Improved complement regulation on host surfaces by a potentiating antibody against complement factor H as a new therapeutic strategy
Richard B. Pouw, Mieke C. Brouwer, Arie van der Ende, Taco W. Kuijpers, Diana Wouters

14:45 – 15:00 **Abstract 179**
Treatment of a murine model of human lupus with a monoclonal antibody that blocks binding of C3d to its receptors decreases anti-DNA autoantibodies and proteinuria: implications for the CR2:C3d interaction as a therapeutic target in lupus and other autoimmune diseases
V. Michael Holers, Jennifer Laskowski, Joshua M. Thurman, Liudmila Kulik

15:00 – 15:30 **Coffee break**

15:30 – 17:00 **Closing:**

Announce newly elected ICS officers
YIA; Mikkel-Ole Skjødt
CTA; Martin Kolev
Travel Awards
Poster Awards
Poster Presenting Awards
Closing remark; Andrea Tenner
Next ICW
Next EMCHD

19:00 – 21:00 **Gala Dinner**

XXVI International Complement Workshop

Poster Session I

Tsuru Hall-4th Floor, Hotel Nikko Kanazawa

1 **Lectin complement proteins in infectious diseases**
Thirumalaisamy P Velavan, Tong Van Hoang, Olusola Ojurongbe, Kumarasamy Thangaraj, Ngyuen Linh Toan, Le Huu Song, Iara J. Messias-Reason, Christian G Meyer

4 **Human DAF suppresses macrophage-mediated xenogeneic cytotoxicity and phagocytosis through the binding of SCR-4 to the inhibitory receptor**
Rieko Sakai, Akira Maeda, Thuy-Vy Choi, Pei-Chi Lo, Rei Matsuura, Tasuku Kodama, Kazuaki Yamanaka, Kengo Nakahata, Tomomi Kawai, Hiroshi Eguchi, Hiroomi Okuyama, Shuji Miyagawa

5 **Painting factor H onto mesenchymal stem cells protects the cells from complement- and neutrophil-mediated damage**
Yan Li, Wen Qiu, Lingjun Zhang, John Fung, Feng Lin

7 **Absence of Complement Protects Against Bone Loss in a Model of Postmenopausal Osteoporosis**
Danielle L. MacKay, Thomas J. Kean, Kristina G. Bernardi, G. Adam Whitney, James E. Dennis, Feng Lin

8 **Differential diagnosis between hereditary and mast cell-mediated angioedema**
Isao Ohsawa, Daisuke Honda, Atsuko Hisada, Hiroyuki Inoshita, Kisara Tsueshita, Satoshi Mano, Nobuyuki Sato, Satoshi Horikoshi

9 **The alternative complement pathway is associated with oxidative stress in human autoimmunity: preliminary results**
Kheireddine Kerboua, Amina Boumediene, Hamid Zeggaoui, Ahmed Mohammedi Bouzina, Reda Djijik, Kamal Djenouhate

10 **A Simple method to abolish the plasma factor H function in a reversible manner without affecting the alternative complement pathway activity**
Kheireddine Kerboua, Hamid Zeggaoui, Ahmed Mohammedi Bouzina, Amina Boumediene, Reda Djijik, Kamal Djenouhate

11 **No complement exhaustion or factor H increases in B cell non Hodgkin lymphoma patients under rituximab therapy**
Kheir eddine Kerboua, Noureddine Belkasmaoui, Aissa Bachiri, Amina Boumediene, Ahmed Mohammedi Bouzina, Mohammed Hamid Zeggaoui, Kamal Djennouhat

12 **Activity of cleaving enzymes for bradykinin in sera from patients with hereditary angioedema**
Daisuke Honda, Isao Ohsawa, Hiroyuki Inoshita, Nobuyuki Sato, Satoshi Mano, Satoshi Horikoshi, Yasuhiko Tomino

14 **Excretions/secretions from medicinal larvae (*Lucilia sericata*) inhibit complement activation by two mechanisms**
Tetsuro Tamura, Gwendolyn Cazander, Suzan H. M. Rooijakkers, Leendert A. Trouw, Peter H. Nibbering

15 **The roles of ribosomal protein S19 polymer in acute pleurisy model C57BL/6J mice**
Hiroshi Nishiura, Koji Yamanegi, Nahoko Yamada, Yasuko Yagaki, Keiji Nakasho

16 **Ficolins promote fungal clearance and modulate the inflammatory cytokine response in host defense against Aspergillus fumigatus**
Genster Ninette, Cramer Elisabeth Præstekjær, Rosbjerg Anne, Pilely Katrine, Cowland Jack, Garred Peter

17 **Cholesterol crystals activate the lectin complement pathway via ficolin-2 and MBL – implications for the progression of atherosclerosis**
Katrine Pilely, Anne Rosbjerg, Ninette Genster, Peter Gal, Gábor Pál, Bente Halvorsen, Sverre Holm, Pål Aukrust, Siril Skaret Bakke, Bjørnar Sporsheim, Ingunn Nervik, Nathalie Niyonzima, Emil D. Bartels, Gregory L. Stahl, Tom Eirik Mollnes, Terje Espevik, Peter Garred

19 **No association between dysplasminogenemia with p.Ala620Thr mutation and atypical hemolytic uremic syndrome**
Toshiyuki Miyata, Yumiko Uchida, Yoko Yoshida, Hideki Kato, Masanori Matsumoto, Koichi Kokame, Yoshihiro Fujimura, Masaomi Nangaku

20 **Lack of Functional Immunogenicity of Humanized Cobra Venom Factor in Mice: Analysis of the IgG response against CVF and Human C3**
Mathieu Ing, Brian E. Hew, David C. Fritzinger, Ivan Peyron, Srinivas V. Kaveri, Sébastien Lacroix-Desmazes, Carl-Wilhelm Vogel, Julie Rayes

21 **Genetic changes predisposing to complement dysregulation and infection may play role in a case of atypical hemolytic uremic syndrome**
Elena Volokhina, Omaima El Tahir, Martin Kömhoff, Servaas Morre, Marceline van Furth, Birendra Singh, Marcin Okroj, Nicole van de Kar, Kristian Riesbeck, Anna Blom, Lambertus van den Heuvel

22 **C5 Promotes Histone-Induced Lethal Thromboembolism**
Tomohiro Mizuno, Kengo Yoshioka, Masashi Mizuno, Naotake Tsuboi, Shoichi Maruyama, Tadashi Nagamatsu, Masaki Imai

23 **Pharmacokinetics and pharmacodynamics of eculizumab in individualized treatment of atypical hemolytic uremic syndrome**
Elena Volokhina, Kioa Wijnsma, Fred Sweep, Roger Brüggemann, Jack Wetzels, Nicole van de Kar, Lambertus van den Heuvel

24 **Characterization of the stoichiometry of the complex formed by Staphylococcal toxin LukSF and human C5a receptor**
Karita Haapasalo-Tuomainen, Adam Wollman, Carla de Haas, Piet Aerts, Esther van 't Veld, Karin Strijbis, Richard Wubbolts, Kok van Kessel, Mark Leake, Jos van Strijp

25 **Complement promote releasing transglutaminase 2 from cytoplasm**
Kaori Hara, Tomohiro Mizuno, Kazuo Takahashi, Masashi Mizuno, Akihiro Kato, Takanori Onouchi, Yutaka Tsutsumi, Hideki Tatsukawa, Tadashi Nagamatsu, Kiyotaka Hitomi, Yukio Yuzawa

26 **C5a play an important role in high fat diet-induced neutrophil activation**
Mizuko Osaka, Masaki Honda, Yukihiro Inomata, Kensuke Egashira, Masayuki Yoshida

27 **Functional activity of complement factor H is impaired in patients with ANCA-positive vasculitis**
Su-Fang Chen, Feng-Mei Wang, Zhi-Ying Li, Feng Yu, Min Chen, Ming-Hui Zhao

28 **Association of *C4B* copy number variation and serum complement activation *in vitro* in patients with Pediatric-Onset Inflammatory Bowel Disease**
Eija Nissilä, Riitta Paakkanen, Marja-Liisa Lokki, Sakari Jokiranta, Willem de Vos, Kaija-Leena Kolho, Seppo Meri

29 **Impact of IgG oligomerization state on the potency of complement-dependent cytotoxicity**
Frank J. Beurskens, Rob N. de Jong, Guanbo Wang, Marleen Voorhorst, Ewald T.J. van den Bremer, Aran F. Labrijn, Janine Schuurman, Albert J. R. Heck, Paul W.H.I. Parren

30 **Endothelin-1 as an endothelial cell biomarker in atypical hemolytic uremic syndrome**
Bálint Mikes, György Sinkovits, Ágnes Szilágyi, Dorottya Csuka, Zoltán Prohászka

33 **Two cases of atypical hemolytic uremic syndrome due to anti-factor H autoantibodies successfully treated by plasma exchange, corticosteroids and mizoribine**
Toshihiro Sawai, Yusuke Okuda, Toshiki Masuda, Tomoyuki Sakai, Toshinaga Maeda, Agustín Tortajada, Santiago Rodríguez de Córdoba

34 **Peptide Therapy in Sepsis and Inflammation: A novel strategy to suppress inflammation**
Hidechika Okada, Alan Okada

35 **Suppression of C5a decreases ischemia/reperfusion injury and increases proliferation of epithelial cells in the rat small intestine**
Eszter Tuboly, Mitsuru Futakuchi, Gabriella Varga, Dániel Érces, András Mészáros, Gábor Kisvári, Mihály Boros, Hidechika Okada, Noriko Okada

36 **An acetylated anti-C5a complementary peptide (AcPepA) reduced cytokines and free radicals and prolonged survival time in a neonatal piglet sepsis model**
Mohamed Hamed Hussein, Tatenobu Goto, Ineko Kato, Noriko Okada, Ghada Abdel-Hamid Daoud, Hidechika Okada

37 **Anti-C1q autoantibodies from systemic lupus erythematosus patients induce C1q production by macrophages**
Sophia Thanei, Marten Trendelenburg

38 **Malondialdehyde epitopes act as hubs for complement activation on dying cells**
Nikolina Papac-Milicevic, Frida C. Mohlin, David Weismann, Mirlinda Ademi, Clara J Busch, Manuele Rebsamen, Barbara Bartolini Gritti, Maria Gorna, Mate Kiss, Lejla Alic, Anna M. Blom, Christoph J. Binder

39 **Development of autologous C5 vaccines to block complement activity in vivo**
Lingjun Zhang, Wen Qiu, Stephen Crook, Yan Li, John Fung, M.G. Finn, Feng Lin

40 **Therapeutic potential of staphylococcal superantigen-like protein 7 for acute complement activation-mediated diseases**
Yan Li, Fiona Clow, John J. Fung, John D. Fraser, Feng Lin

44 **Identification of *CFHR5* variations and analyzing their effect on plasma CFHR5 level in patients with atypical hemolytic uremic syndrome or with C3-glomerulopathies**
Dorottya Csuka, Nóra Garam, Ágnes Szilágyi, Mihály Józsi, Michael Rudnicki, Gere Sunder-Plassmann, Alice Schmidt, George S Reusz, Zoltán Prohászka

45 **An autoimmune epitope on C-reactive protein targets complement regulation in lupus nephritis**
Qiuyu Li, Haiyun Li, Feng Yu, Yi Wu, Minghui Zhao

46 **Recognition of mumps virus by mannan-binding lectin**
Yoshiki Kodama, Hiroaki Hiramatsu, Masashi Honda, Yasuo Suzuki, Yasuhiko Ito, Toshisuke Kawasaki, Kazuhide Uemura

47 **The very first kinetic follow-up of a single edematous attack of a C1-INH-HAE patient: classical pathway components in focus**
Nóra Veszeli, Kinga Viktória Kőhalmi, Erika Kajdácsi, Márta Kókai, Dominik Gulyás, László Cervenak, Henriette Farkas, Lilian Varga

48 **Autoantibodies to C1 inhibitor in SLE are associated with higher SLEDAI 2K score and with autoantibodies to cardiolipin**
Tina Linnér, Birgitta Gullstrand, Elizabeth Huynh, Anders Bengtsson, Lillemor Skattum

49 **LDL apheresis activates the complement system and the cytokine network, whereas PCSK9 inhibition induces no inflammatory response**
Anders Hovland, Judith Krey Ludviksen, Tom Eirik Mollnes, Knut Tore Lappegård

50 **C5aR1 participates in the pathogenesis of ascending urinary tract infection through enhancement of adhesion and colonisation of uropathogenic E coli**
Yun Song, Kun-Yi Wu, Zhao-Yang Duan, Steve H Sacks, Wuding Zhou, Ke Li

51 **Japanese internet-based patient registration system for hereditary angioedema: results of clinical characteristics**
Takahiko Horiuchi, Shin-Ichi Harashima, Chikako Kiyohara, Kaoru Nomura, Chinami Hashimura

52 **Japanese internet-based patient registration system for hereditary angioedema: results of genetic analysis**
Takahiko Horiuchi, Hisaaki Miyahara, Chikako Kiyohara, Osamu Kohara, Chinami Hashimura

53 **PRELP Enhances Host Innate Immunity against Respiratory Tract Pathogen *Moraxella catarrhalis***
Guanghui Liu, David Ermert, Martin E. Johansson, Kristian Riesbeck, Anna M. Blom

54 **Production of C3 and its secretion into the mucus by intestinal epithelial cells correlates with disease activity in experimental chronic colitis**
Kerstin Skibbe, Karen Ebbert, Sophie Preisker, Annika Sünderhauf, Petra Langenstrassen, Christian Sina, Stefanie Derer

55 **A highly specific ELISA based assay for screening of complement capacity using EDTA plasma related to different pathways of the complement system**
Jytte Bryde Clausen, Jesper Andresen, Katrine Pilely, Peter Garred

57 **The complement inhibitor CSMD1 acts a tumour suppressor for breast cancer**
Chrysostomi Gialeli, Astrid Escudero-Esparza, Michael Bartoschek, Matthias Mörgelin, Petter Storm, Marcin Okroj, Sioned Owen, Karin Jirström, Akira Orimo, Wen G. Jiang, Kristian Pietras, Anna M. Blom

58 **Cartilage Oligomeric Matrix Protein affects prostate cancer development by altering main cellular functions**
Konstantinos Papadakos, Emelie Englund, Giacomo Canesin, Emma Persson, Neelanjan Vishnu, Bart Reitsma, Aseem Anand, Laila Jacobsson, Leszek Helczynski, Hindrik Mulder, Anders Bjartell, Anna M. Blom

60 **Activation of complement by pigment epithelium derived protein in synovial fluid of rheumatoid arthritis patients**
Leonie M. Vogt, Simone Talens, Carsten Scavenius, Jan J. Enghild, Tore Saxne, Anna M. Blom

62 **Assessment of Complement-Mediated Bacterial Killing and the Effect of a Small Molecule Factor D Inhibitor *in Vitro***
Yongsen Zhao, Manuel Galvan, Steven D. Podos, Jane A. Thanassi, Guangwei Yang, Dharaben Patel, Joanne Fabrycki, Amanda Luu, Wengang Yang, Jason Wiles, Avinash Phadke, Joel Barrish, Mingjun Huang

64 **Paroxysmal nocturnal hemoglobinuria caused by PIGT mutations; Atypical PNH**
Yoshiko Murakami, Norimitsu Inoue, Michi Kawamotoi, Nobuo Kohara, Taroh Kinoshita

65 **Recombinant human C1q variants with differential ligand binding capacities**
Isabelle Bally, Christophe P Moreau, Barbara Bottazi, Christine Gaboriaud, Nicole M. Thielens

67 **Molecular dissection of the interaction of C1q with CD91**
Isabelle Bally, Evelyne Gout, Catherine Wicker-Planquart, Anne Chouquet, Philippe Frachet, Nicole M. Thielens, Jean-Philippe Kleman, Véronique Rossi

68 **Parasite calreticulins: structure, C1q binding and dual carbohydrate/ peptide interaction properties**
Christophe P. Moreau, Isabelle Bally, Marina Iannello, Emmanuelle Laffly, Anne Chouquet, Arturo Ferreira, Nicole M. Thielens, Christine Gaboriaud

69 **Three cases of C3 glomerulonephritis associated with group A streptococcus infection**
Sohshi Matsumura, Koichi Kamei, Yuji Kano, Takahisa Yoshikawa, Hiroko Nagata, Ken Saida, Mai Sato, Masao Ogura, Yu Kamigaki, Aya Inaba, Hiroyuki Machida,Takashi Oda, Kenji Ishikura, Shuichi Ito

70 **Bactericidal assay with autologous serum demonstrates increased bactericidal activity after Hib vaccination in C2 deficiency**
Göran Jönsson, Christina Hansson, Cecilia Sahl, Lillemor Skattum

71 **The complement regulator C4b-binding protein inhibits islet amyloid polypeptide-induced inflammasome activation**
Klaudia Kulak, Gunilla Westermark, Nikolina Papac-Milicevic, Erik Renström, Anna M. Blom, Ben C. King

73 **Infantile thrombotic microangiopathy following *Bordetella pertussis* infection: difficulty in differentiating aHUS from secondary TMA**
Ken Saida, Sohshi Matsumura, Takahisa Yoshikawa, Yuji Kano, Hiroko Nagata, Mai Sato, Masao Ogura, Koichi Kamei, Yoko Yoshida, Hideki Kato, Masaomi Nangaku, Shuichi Ito, Kenji Ishikura

74 **Effects of C1-INH on complement deposition and endothelial cell activation in a rat hind limb ischemia/reperfusion injury model**
Shengye Zhang, Jane Shaw-Boden, Yara Banz, Anjan K. Bongoni, Adriano Taddeo, Rolf Spirig, Marc W. Nolte, Peter J. Cowan, Robert Rieben

75 **The *Candida albicans* evasion molecule Hgt1p – *in vitro and in vivo* evidence that it functions as virulence factor**
Samyr Kenno, Dorothea Orth-Höller, Reinhard Würzner

76 **Promoting adaptive immunity: a new aspect to Immune Adherence?**
Steven P. Broadley, Ann Plaumann, Raffaele Coletti, Christin Lehmann, Steffen Massberg, Dirk H. Busch, Menno van Lookeren Campagne, Admar Verschoor

77 **The protective role of C1-INH on ischemia reperfusion injury in a porcine limb amputation and reperfusion model**
Mai M. Abdelhafez, Jane Shaw, Damian Sutter, Jonas Schnider, Hansjörg Jenni, Esther Voegelin, Mihai A. Constantinescu, Robert Rieben

79 **Unraveling the role of Sushi-domain containing protein 4 (SUSD4) in pancreatic islets by means of a SUSD4 knockout mouse model**
Wouter Van Overbeke, Karolina Danestig, Ulrika Krus, Ben C. King, Erik Renström, Anna M. Blom

80 ***In silico* identification of CCP sequence motifs allow identification of novel complement regulators**
Hina Ojha, Gaurang Mahajan, Shekhar Mande, Arvind Sahu

83 **Insights into the role of FHR5 in C3 glomerulopathy**
Marieta M Ruseva, Talat H Malik, Matthew C Pickering

85 **The role of Complement Receptor 1 (CD35) in chronic Chagas Disease**
Thaisa Lucas Sandri, Hoang van Tong, Christina Schieber, Fabiana Antunes Andrade, Kárita Cláudia Freitas Lidani, Iara J. T. de Messias-Reason, Thirumalaisamy P. Velavan

86 **Comparison of Complement Functional Assays: Differential Sensitivities of Hemolysis and Wieslab Assays to Levels of Complement Proteins C5, Factor B, and Factor D**
Jane A. Thanassi, Dharaben Patel, Guangwei Yang, Manuel Galvan, Yongsen Zhao, Joanne Fabrycki, Amanda Luu, Wengang Yang, Avinash Phadke, Jason Wiles, Joel Barrish, Mingjun Huang, Steven D. Podos

91 **C4d as New Biomarker in Systemic Lupus Erythematosus**
Myriam Martin, Karolina I Smoląg, Albin Björk, Birgitta Gullstrand, Marcin Okroj, Jonatan Leffler, Andreas Jönsen, Jan-Åke Nilsson, Anders A. Bengtsson, Anna M. Blom

92 **Complement Biomarkers in the Management of Peritoneal Dialysis**
Wioleta Zelek, Claire L. Harris, Nicholas Topley, Ian Weeks, Mark Lambie, Simon J Davies, B. Paul Morgan

93 **Complement System Biomarkers in Demyelinating Disease**
Wioleta Zelek, Dina Fathalla, Rowan P. Orme, Angharad Morgan, Samuel Touchard, Caroline O'Hagan, Sam Loveless, Neil Robertson, B. Paul Morgan

94 **RGC-32 promotes Th17 cell differentiation and enhances experimental autoimmune encephalomyelitis**
Violeta Rus, Vinh Nguyen, Alexandru Tatomir, Dallas Boodhoo, Armugam P. Mekala, Cornelia Cudrici, Tudor C. Badea, Horea Rus

96 **Complement component expression in primary human glomerular endothelial cells subjected to a diabetic-like insult**
Kamilla Pajęcka, Troels Krarup Hansen, Julie Marie Williams

185 ***Candida albicans* modulates the immune response of human blood monocytes**
Emeraldo A.H. Jo, Luke D. Halder, Susanne Ackermann, Ilse M Jacobsen, Peter F. Zipfel, Christine Skerka

Late Breaking Abstracts

210 **Additive effect of methotrexate (MTX) and anti-TNF agents on the inhibition of TNF-producing cells: clarification of the mechanism(s) focused on" reverse" signal and complement-dependent cytotoxicity (CDC)**
Qiaolei Wang, Hiroki Mitoma, Yasunao Ueda, Takahiko Horiuchi

211 **An analysis of thrombotic microangiopathy associated with antibody to complement factor H antibody in Japanese**
Yasufumi Ohtsuka, Masafumi Oka, Kumiko Jinnouchi, Hidehiko Ohgushi, Tadashi Sato, Muneaki Matsuo

212 **Characterisation of mutations in recombinant full-length factor H affords fresh molecular insights into complement-disease link**
Heather Kerr, Edwin K Wong, Elisa Makou, Yi Yang, Kevin J Marchbank, David Kavanagh, Anna Richards, Andrew P Herbert, Paul N Barlow

213 **Visualising complement activation and regulation on a tunable chemically defined biomimetic surface**
Elisavet Makou, Heather J Johnson, Richard G Bailey, Andrew P Herbert, Alison N Hulme, Georg Haehner, Paul N Barlow

214 **Role of factor H and effects of C-terminal mutations on control of human platelet/granulocyte aggregate formation**
Adam Z. Blatt, Gurpanna Saggu, Claudio Cortes, Andrew P. Herbert, David Kavanagh, Daniel Ricklin, John D. Lambris, Jesus G. Valenzuela, Viviana P. Ferreira

215 **Recommendations on biomarker analysis for alternative pathway-mediated renal diseases**
Yuzhou Zhang, Kristofer S May, Dingwu Shao, Adam Keenan, Carla M Nester, Richard JH Smith

216 **Characterization and development of ANX005, a novel function blocking anti-C1q antibody for treatment of autoimmune and neurodegenerative disease**
Sethu Sankaranarayanan, Haiyan Qiu, Mario Saltarelli, Susan Kramer, Ted Yednock

217 **Mortalin mimetic peptides sensitize cancer cells to complement-dependent cytotoxicity**
Ritta Jubran, Moran Saar-Ray, Natalie Donin, Lea Ziporen, Zvi Fishelson

218 **Cell surface activation of the antibody dependent complement system by the E protein of dengue virus**
Nuntaya Punyadee, Jintana Jaiyen, Pijitra Petcharat, Somchai Thiemmeca, Chunya Puttikhunt, Panisadee Avirutnan

Poster Session II

Tsuru Hall-4th Floor, Hotel Nikko Kanazawa

97 **Variants in Complement Factor H Affect Complement Activation in Henoch-Schonlein Purpura Nephritis**
Weiyi Guo, Li Zhu, Yalin Zhai, Hong Zhang

98 **Activation of complement and coagulation in xenotransplantation: Effect of growth hormone receptor knockout on porcine aortic endothelial cells**
Riccardo Sfriso, Nikolai Klymiuk, Annegret Wuensch, Joerg D. Seebach, Eckhard Wolf, Robert Rieben

99 **A vessel-like microfluidic system to study complement and coagulation in the context of xenotransplantation**
Riccardo Sfriso, Shengye Zhang, Colette Andrea Bichsel, Oliver Thierry Guenat, Robert Rieben

100 **Characterization of the patients with atypical hemolytic uremic syndrome by combination of hemolytic assay and gene analysis in Japan**
Yoko Yoshida, Hideki Kato, Madoka Fujisawa, Yuka Sugawara, Yumiko Uchida, Masanori Matsumoto, Yoshihiro Fujimura, Toshiyuki Miyata, Masaomi Nangaku

101 **In vitro evaluation of a CRIg-Factor H hybrid complement inhibitor**
Marcell Cserhalmi, Mario Hebecker, Tamás Mészáros, János Szebeni, Mihály Józsi

102 **Functional characterization of a disease-associated N-terminal factor H mutation**
Marcell Cserhalmi, Barbara Uzonyi, Dorottya Csuka, Edgar Meusburger, Karl Lhotta, Zoltán Prohászka, Mihály Józsi

103 **Factor H-related protein 3 (FHR-3) inhibits factor H binding to pentraxins and malondialdehyde epitopes, and activates the alternative pathway via C3b binding**
Ádám I Csincsi, Richard B Pouw, Agustín Tortajada, Santiago Rodríguez de Córdoba, Diana Wouters, Mihály Józsi

104 **Mechanisms responsible for differential bactericidal activities of human and rabbit complement for *Neisseria meningitidis***
Scott Jones, Holly Humphries, Andrew Gorringe, Dominique Walters, B. Paul Morgan, Stephen Taylor, Claire L. Harris

105 **Auto-regulation of Th1 responses through carboxypeptidase M-generated C5a-desArg**
Simon Freeley, Gaelle Le Friec, Martin Kolev, Nathalie Niyonzima, Terje Espevik, Tom Eirik Mollnes, Knut Lappegard, Trent M. Woodruff, Pete Monk, Claudia Kemper

110 **Complement C5 is essential for *E. coli*-induced coagulation activation, independent of inhibition of cytokines inducing tissue factor**
Anne Landsem, Hilde Fure, Judith Krey Ludviksen, Dorte Christiansen, Monica Dammen Mathisen, Grethe Bergseth, Knut Tore Lappegård, Tom Eirik Mollnes, Ole-Lars Brekke

113 **Domain swapping reveals functional modularity present in the decay-accelerating factor (CD55)**
Hemendra Singh Panwar, Hina Ojha, Payel Ghosh, Sunil Raut, Arvind Sahu

114 **Activation of Complement in Crescentic IgA Nephropathy**
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Additive effect of methotrexate (MTX) and anti-TNF agents on the inhibition of TNF-producing cells: clarification of the mechanism(s) focused on" reverse" signal and complement-dependent cytotoxicity (CDC)

Qiaolei Wang[1], Hiroki Mitoma[2], Yasunao Ueda[2], Takahiko Horiuchi[1]

[1]*Kyushu University Beppu Hospital, Beppu, Japan*

[2]*Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan*

Methotrexate (MTX) and anti-TNF agents are both important drugs for the treatment of chronic inflammatory disorders, such as rheumatoid arthritis (RA). The combination therapy of MTX and anti-TNF agents exerts more potent effect on the control of disease activity and joint destruction of RA compared with the effect obtained by single administration of MTX or anti-TNF agents. The mechanism(s) of this synergistic effect caused by the concomitant administration of MTX and anti-TNF agents have not been clearly understood. It is considered that MTX contributes at least in part to strengthen the effect of anti-TNF agents by inhibiting the generation of anti-drug neutralizing antibody. In order to identify unknown mechanisms for the synergism of MTX and anti-TNF agents, we shed light on the direct effects of these drugs on TNF-producing cells.
A human Jurkat T cell line stably expressing transmembrane TNF (Harashima et al. J Immunol 2001) was stimulated with 0.1uM of MTX alone for 36h, 0.01uM of anti-TNF agents lone (infliximab, etanercept, or certolizumab pegol) for 12h or 0.1uM of MTX plus 0.01uM of anti-TNF agents which was subjected to FACS analysis to detect cell death. Heat-inactivated bovine serum was used for the "reverse" signal assay, while human serum without heat-inactivation was for CDC assay. "Reverse" signal is a newly proposed action mechanism of anti-TNF agents, which is totally different from CDC or antibody-dependent cell-mediated cytotoxicity (ADCC) (Horiuchi et al. Rheumatology 2010). "Reverse" signal is a death signal transmitted through the intracellular domain of transmembrane TNF upon binding of anti-TNF agents. The percentages of early apoptotic cells induced by "reverse" signal were 15.7% for MTX alone, 45.6% for infliximab alone, 4.7% for etanercept alone, 8.5% for certolizumab pegol alone, 59.9% for MTX+infliximab, 17.8% for MTX+etanercept, and 17.7% for MTX+certolizumab pegol, respectively. There were additive effects between MTX and all of the anti-TNF agents. Especially, the combination of MTX and infliximab achieved the most clear additive effect. In contrast, the additive synergistic or additive effect of MTX was not prominent for the CDC activities of these anti-TNF agents. It is thus concluded that "reverse" signal of anti-TNF agents through transmembrane TNF was augmented by concomitant MTX, which culminated in the increased apoptosis of TNF-producing cells. Our in vitro data might explain at least in part the superiority of the combination of MTX+anti-TNF agents to MTX alone or anti-TNF agent alone in the treatment of RA.

An analysis of thrombotic microangiopathy associated with antibody to complement factor H antibody in Japanese

Yasufumi Ohtsuka[1], Masafumi Oka[1], Kumiko Jinnouchi[1], Hidehiko Ohgushi[1], Tadashi Sato[1], Muneaki Matsuo[1]

[1]Department of Pediatrics, Faculty of Medicine, Saga University

Autoantibody to complement factor H (anti-CFH antibody) causes 10%–15% of atypical hemolytic uremic syndrome (aHUS) cases. Homozygous deletion of *CFHR1* is the primary genetic background. Because the frequency of *CFHR1* deletion is very low in the Japanese population, it was predicted that aHUS caused by anti-CFH antibody would be rare. We analyzed anti-CFH antibodies and genes encoding 13 complement factors (CFH, CFHR1-5, C3, CFI, CFB, MCP, THBD, DGKE, and PLG) in Japanese subjects with thrombotic microangiopathy (TMA).

We examined 61 serum samples from 47 subjects (mean age = 38.56 ± 27.5 y; 40.4% males). Subjects diagnosed with aHUS once TTP or STEC-HUS were ruled out. ELISA analysis showed that seven of the 47 subjects possessed the anti-CFH antibody. 2 of the 7 subjects were newly diagnosed in this study. All showed childhood onset. Levels of anti-CFH antibody were remarkably high in the acute phase and decreased in remission (10,779 ± 5,603 vs. 476 ± 906). In addition, anti-CFH antibody levels decreased remarkably several years after onset. The frequency of aHUS caused by anti-CFH antibody was found to be 4.7% (2/42) in TMA except TTP or STEC-HUS. Genetic analysis revealed that 5 subjects had a homozygous deletion of *CFHR1* and 1 subject had a homozygous deletion of *CFHR1* combined with a *C3* mutation. One subject showed no mutations in the 13 genes analyzed.

We detected seven cases of aHUS caused by anti-CFH antibody among Japanese subjects. The pathologic and clinical conditions were similar to those reported in previous reports. We conclude that aHUS caused by anti-CFH antibody is a critical disease that occurs in the Japanese population at frequency almost similar to that reported in previous studies.

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Characterisation of mutations in recombinant full-length factor H affords fresh molecular insights into complement-disease link

Heather Kerr[1], Edwin K Wong[2], Elisa Makou[3], Yi Yang4, Kevin J Marchbank[4], David Kavanagh[2], Anna Richards[1], Andrew P Herbert[3], Paul N Barlow[3,5]

[1]*Queen's Medical Research Institute, University of Edinburgh, Edinburgh, UK*
[2]*Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne, UK*
[3]*School of Chemistry, University of Edinburgh, Edinburgh, UK*
[4]*Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, UK*
[5]*School of Biological Sciences, University of Edinburgh, Edinburgh, UK*

Inherited variants of the human complement regulator factor H (FH) increase risks of age-related macular degeneration, atypical haemolytic uraemic syndrome (aHUS) and C3 glomerulopathy. Patient-derived purified mutant proteins may be difficult to obtain. Therefore many previous mutagenesis studies used recombinant FH fragments containing just a few of the 20 complement-control protein (CCP) modules that make up full-length FH. It is, however, now widely accepted that FH function necessitates simultaneous deployment of multiple recognition sites across all 20 CCP modules. Here, we used *Pichia pastoris* to overcome the challenges of producing full-length FH mutants recombinantly. We assayed their activities on host-like sheep erythrocytes (SE), in the non-host contexts of surface plasmon-resonance (SPR) chips and rabbit erythrocytes surfaces, and in complex with PspCN, a *Streptococcus pneumoniae* protein domain that binds FH very tightly and enhances its regulatory functions. In benchmarking work we showed that recombinant allotypic variants, I62,Y402,D936-FH (IYD-FH) and V62, Y402, E936-FH (VYE-FH), behaved like their respective plasma-purified equivalents; recombinant IYD-FH (I62 protects against age-related macular degeneration) marginally outperforming recombinant VYE-FH. Results with the recombinant aHUS-linked mutant R53H-FH, which is mutated in the N-terminal module, mirrored those obtained previously for the four-module FH fragment, R53H FH 1-4. The aHUS-linked mutation D1119G, in CCP 19, had negligible impact on SPR-based assays but, on sheep erythrocytes, reduced C3bBb-decay accelerating activity by an order of magnitude, and almost abolished factor I-cofactor activity. The aHUS-linked CCP 20 mutation S1191L/V1197A, yielding a C-terminal CCP module-pair identical to that of FH-related 1, had wild-type functionality on SPR. While its decay accelerating activity on sheep erythrocytes is slightly diminished, its cofactor activity on sheep erythrocytes is very severely reduced and its ability to protect sheep erythrocytes from haemolysis severely degraded. PspCN did not improve decay-accelerating activity for R53H-FH and S1191L/V1197A-FH on sheep erythrocytes. Conversely, PspCN boosted IYD-FH and VYE-FH and partially rescued R53H-FH and S1191L/V1197A-FH in sheep-erythrocyte-based cofactor activities and in its protection against haemolysis. PspCN could, therefore, in selected cases, therapeutically boost cofactor activity levels of a defective FH variant.

Visualising complement activation and regulation on a tunable chemically defined biomimetic surface

Elisavet Makou[1], Heather J Johnson[1], Richard G Bailey[2], Andrew P Herbert[1], Alison N Hulme[1], Georg Haehner[2], Paul N Barlow[1,3]

[1]School of Chemistry, University of Edinburgh, Edinburgh, UK

[2]School of Chemistry, University of St Andrews, St Andrews, UK

[3]School of Biological Sciences, University of Edinburgh, Edinburgh, UK

The abundant soluble complement regulator, factor H (FH), selectively protects self-surfaces from complement-mediated damage by recognizing molecular patterns comprising glycosaminoglycans and sialic acids on healthy host cells and tissue. Conversely, FH does not normally prevent C3b amplification and complement activation on non-host surfaces. Numerous previous studies have examined FH in the contexts of foreign surfaces, such as those of non-human erythrocytes or surface-plasmon resonance (SPR) chips in which, by design, FH performs poorly. We hypothesized that FH exists in different conformations depending upon its surface context, which dictate its regulatory efficacy. To test whether FH can switch its conformation from “OFF” to “ON” in response to its surroundings, and to explore the effect this has on its biological activity, we created biomimetic surfaces that provide chemically defined environments. By employing organic chemical synthesis, alkanethiol monomers were manufactured and used to create tailored self-assembled monolayers on flat gold surfaces. The placement of various terminal groups on the monolayers, such as OH, COOH, maleimide, and alkyne, allows the simultaneous conjugation of C3b and specific carbohydrate molecules at defined densities, depending on the type of monomer used. The aim is to create environments resembling the surfaces of extracellular matrix or glycocalyx. By using SPR we are able to quantify the attachment or non-covalent binding of molecules in real time, and by combining SPR with atomic-force microscopy we can count and visualize the locations of proteins on the surface. For the first time, we have been able to measure the affinity of FH for C3b on host-like surfaces and to study the acceleration of decay of C3 convertase by FH in this context. In more elaborate experiments we have simulated activation of the alternative pathway by seeding with C3b, and then flowing C3, factor B and factor D over the surface. By repeating this process in the presence and absence of wild-type and disease-linked FH variants we can analyse the resultant distributions of newly-generated C3b molecules. The microfluidics available within the SPR instrument are allowing us to compare the effects of various carbohydrate chemistries on the regulatory properties of FH. Thus our novel platform is providing unique insights into the link between surface chemistry, the primary structures of FH variants, and the regulation of complement activation.

Role of factor H and effects of C-terminal mutations on control of human platelet/granulocyte aggregate formation

Adam Z. Blatt[1], Gurpanna Saggu[1], Claudio Cortes[2], Andrew P. Herbert[3], David Kavanagh[4], Daniel Ricklin[5], John D. Lambris[5], Jesus G. Valenzuela[6], and Viviana P. Ferreira[1]

[1]Department of Medical Microbiology and Immunology, University of Toledo College of Medicine and Life Sciences, Toledo, Ohio

[2]Department of Biomedical Sciences, Oakland University William Beaumont School of Medicine, Rochester, Michigan

[3]The School of Chemistry, University of Edinburgh, Scotland, UK

[4]Institute of Genetic Medicine, International Centre for Life, Newcastle upon Tyne, UK

[5]Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

[6]Vector Molecular Biology Section, LMVR, National Institute of Allergy and Infectious Diseases, NIH, Rockville, Maryland

Atypical hemolytic uremic syndrome (aHUS) is characterized by renal damage and thrombosis, as a result of dysregulated complement alternative pathway (AP) activity on cell surfaces. Platelets activated during thrombosis can bind to granulocytes to form stable platelet/granulocyte aggregates (PGA), which can enhance thromboinflammation in the vasculature. Mutations in the C-terminal domains, 19 and 20, of the AP negative regulator factor H are a common cause of aHUS. We have recently shown that domains 19-20 are also critical for control of PGA formation in human whole blood stimulated with thrombin receptor-activating peptide (TRAP), yet there are no known associations between aHUS and PGA formation. Here, we determined that (a) domains 19-20, were the most critical regions of factor H for controlling the AP on human platelets and neutrophils, and in TRAP-stimulated human whole blood, (b) factor H limits PGA formation primarily by preventing AP-mediated C5a generation, (c) aHUS-related mutations in domains 19-20 have differential effects on control of TRAP-mediated PGA formation and AP activity, as measured by C3b deposition and C5a generation, and (d) the effects of mutations in 19-20 have similar differential effects on AP activity on isolated platelets and neutrophils. Our results indicate a key role for factor H C-terminal domains in controlling AP activity on cells involved in PGA formation, and suggest that mutations associated with aHUS result in varying degrees of impairment of complement regulation on cell surfaces. These data have important implications for understanding pathophysiologic mechanisms of PGA formation and potential treatment options for aHUS.

Recommendations on biomarker analysis for alternative pathway-mediated renal diseases

Yuzhou Zhang[1], Kristofer S May[1], Dingwu Shao[1], Adam Keenan[1], Carla M Nester[1,2], Richard JH Smith[1,2]

[1]Molecular Otolaryngology and Renal Research Laboratories, Carver College of Medicine, University of Iowa, Iowa City, IA 52242, USA

[2]Department of Internal Medicine, Division of Nephrology, Carver College of Medicine, University of Iowa, Iowa City, IA 52242, USA

Overactivity of the alternative pathway (AP) of complement underlies two prototypical ultra-rare renal diseases, atypical hemolytic uremic syndrome (aHUS) and C3 glomerulopathy (C3G). In these two diseases, quantitating circulating levels of complement proteins and their activation products and measuring complement activity are predictive of disease type, provide insight into disease activity, and offer prognostic significance for disease outcome. These tests are usually performed by a few specialized laboratories on samples received from around the world.

Proper sample preparation is critical. Normally, complement activation products are present in only trace amounts *in vivo* although they can be rapidly generated *in vitro*, making correct sample collection and storage critical to avoid errors. Guidelines for sample collection and handling (standard operating procedures, SOPs) are typically provided by the testing laboratory. Herein, we assess sample variability on 350 samples collected from three different centers (cohorts 1-3) across the United States using the same SOP. All samples were shipped to a reference laboratory (MORL) on dry ice and received in good condition. As a reference, 200 samples (cohort 4) were collected locally. All samples were analyzed using complement assays applicable for the evaluation of complement activity in aHUS and C3G, and included C3, C4, C5, FB, FH, FI, properdin, C3c, Ba, Bb, sC5b-9, CH50, AP functional assay (APFA) and hemolytic assays.

Only plasma levels of C3, C4, C5, FB, FH, FI and properdin were comparable across cohorts. While CH50 and APFA were comparable in cohorts 1, 2 and 4, in cohort 3 they were reduced in 5% of controls. Consistent with this finding, hemolytic assay results using rabbit erythrocytes were low. Complement activation products were also observed in cohort 3: 10% had increased Ba and Bb and ~50% had increased C3c and sC5b-9. An elevated C3c/C3 ratio was consistent with *in vitro* activation.

These data highlight an important fact - there is no method to ensure samples are collected correctly even when an SOP is provided. Our results show that multiple complement assays must be performed on every sample to generate a composite picture. By so doing, it is possible to recognize global over-activation of complement with consumption of multiple factors, which is typical of *ex vivo* activity. If results suggest sample mishandling, another aliquot of serum and plasma should be requested.

Characterization and development of ANX005, a novel function blocking anti-C1q antibody for treatment of autoimmune and neurodegenerative disease

Sethu Sankaranarayanan[1], Haiyan Qiu[1], Mario Saltarelli[1], Susan Kramer[1], Ted Yednock[1]

[1]Annexon Biosciences, South San Francisco, USA

The classical complement cascade is implicated in antibody-mediated disease and in complement-mediated synapse loss in neurodegenerative diseases. Autoantibody binding to target tissue leads to recruitment of the C1 complex that is followed by the sequential cleavage of C4, C2, C3, C5, and eventual assembly of the terminal complement complex. Tissue damage is driven by three concurrent steps including production of pro-inflammatory and chemotactic molecules (e.g. C4a, C3a, C5a), tissue deposition of C4b and C3b promoting phagocytosis, and assembly of the lytic complex leading to tissue damage.

C1q is the initiating molecule of the classical complement cascade and plays a key role in synaptic pruning in early brain development. During normal aging, there is a robust increase in C1q levels at synaptic locations throughout the central nervous system. In neurodegenerative diseases such as Alzheimer's, Parkinson's, and glaucoma, C1q-mediated removal of weakened synapses is triggered following a variety of insults, culminating in neuronal cell death. This mechanism of complement-mediated neurodegeneration (CMND) has been demonstrated in multiple neurodegenerative disease models where C1q plays a critical role in synapse elimination.

In order to directly target complement-mediated diseases, we developed a humanized monoclonal antibody (ANX005) that binds with high-affinity (~10 pM) to C1q and blocks classical complement cascade activation. ANX005 inhibits deposition of activated complement components (e.g. C4b, C4d, C3b, and C3d) and blocks hemolysis when co-incubated with serum and red blood cells *in vitro*. Following parenteral administration of the murine parent of ANX005 in preclinical species, significant serum and cerebrospinal fluid antibody levels are detected for up to 1 week after a single dose. At time points when antibody levels were elevated, a robust reduction in free levels of C1q in serum and CSF was seen, along with elimination of C1q-mediated hemolytic activity *ex vivo*. In summary, ANX005 is a potent anti-C1q antibody with drug-like properties that blocks the classical complement cascade and is active in a variety of autoimmune and neurodegenerative disease models.

Mortalin mimetic peptides sensitize cancer cells to complement-dependent cytotoxicity

Ritta Jubran, Moran Saar-Ray, Natalie Donin, Lea Ziporen and Zvi Fishelson
Department of Cell and Developmental Biology, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

Cancer therapy confronts numerous obstacles that restrain its therapeutic potential to kill tumor cells. Resistance to complement is one of the prominent issues for concern, particularly when immunotherapy is applied, as cancer cells have evolved different strategies to withstand complement-dependent cytotoxicity (CDC). The mitochondrial stress-70 protein, mortalin, is one of the challenging cancer protectors. It is a constitutively expressed house-keeper in normal tissues and, in tumors, its expression level is elevated. Mortalin inhibition was shown to sensitize cancer cells to apoptosis and to CDC. We have focused on mortalin as a drug target for cancer therapy. Previously, we targeted mortalin synthesis with specific siRNA and demonstrated that intervention with synthesis of mortalin in cancer cells enhanced their sensitivity to CDC. Recently, we designed mimetic mortalin peptides with sequences corresponding to predicted epitopes on mortalin that are involved in protein-protein interactions. Several mortalin peptides that inhibit direct C9-mortalin binding were identified. To facilitate peptides entry into the cells, the peptides were synthesized with a TAT cell-penetrating sequence. The impact of the peptides on CDC was examined and our data showed that pretreatment of leukemia/lymphoma cells with these mortalin peptides, prior to antibody and complement treatment, led to an increase in C5b-9 deposition and cytotoxicity. Interestingly, certain peptides were also found to be highly toxic to cancer cells in the absence of complement. The peptides induced mitochondrial depolarization and caused necrotic cell death. Further analysis of the mechanism of action of these mortalin peptides is ongoing. In summary, this study has identified mortalin peptides that may potentially promote cancer cell death as single agents and as enhancers of complement-dependent cytotoxicity.

Cell surface activation of the antibody dependent complement system by the E protein of dengue virus

Nuntaya Punyadee[1], Jintana Jaiyen[1,2], Pijitra Petcharat[1,2], Somchai Thiemmeca[1,2], Chunya Puttikhunt[1,3], and Panisadee Avirutnan[1,3]

[1]Division of Dengue Hemorrhagic Fever Research, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

[2]Graduate Program in Department of Immunology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

[3]Medical Biotechnology Research Unit, National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Bangkok, Thailand

Severe vascular leakage and shock are the major causes of death in patients with dengue hemorrhagic fever or dengue shock syndrome (DHF/DSS), a disease caused by dengue virus (DENV). Massive complement activation and vascular leakage are the hallmarks of DHF/DSS, but the underlying mechanism has remained unclear. Our previous studies have shown that immune complexes formed on the surface of infected cells efficiently activate human complement to completion without causing cell lysis. Nonstructural protein NS1, a non-virion associated protein yet present extracellularly as soluble hexamers and on the surface of infected cells, is a major viral antigen responsible for complement activation in DENV infection. Membrane associated NS1 activates complement via the antibody-dependent classical and alternative pathways. Here, we show the capability of another major viral antigen i.e., envelope (E) protein which is a major structural component of DENV virion but also present on the surface of infected cells, to activate the human complement system. Complement activation as shown by C3d deposition on the surface of DENV-infected cells and cells stably expressing premembrane-envelope protein (prM-E) was triggered by E specific monoclonal antibodies. Analogous to the NS1 immune complexes, the complement fixing ability of membrane associated E-anti-E antibody complexes efficiently reaches the terminal pathway resulting in the deposition of C5b-9 membrane attack complexes on cell surfaces but was unable to induce cell lysis. Biological relevance of our in vitro findings was demonstrated in plasma of DENV-infected patients collected during acute infection. Contribution of complement activation by cell-surface associated E compared to NS1 protein in patients plasma will be further assessed. Our results suggest that the complement system can be activated in vivo by infected cells via specific anti-DENV antibodies and may be one of the key events responsible for massive complement activation and vascular leakage occurring in DHF/DSS.

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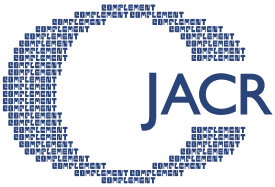
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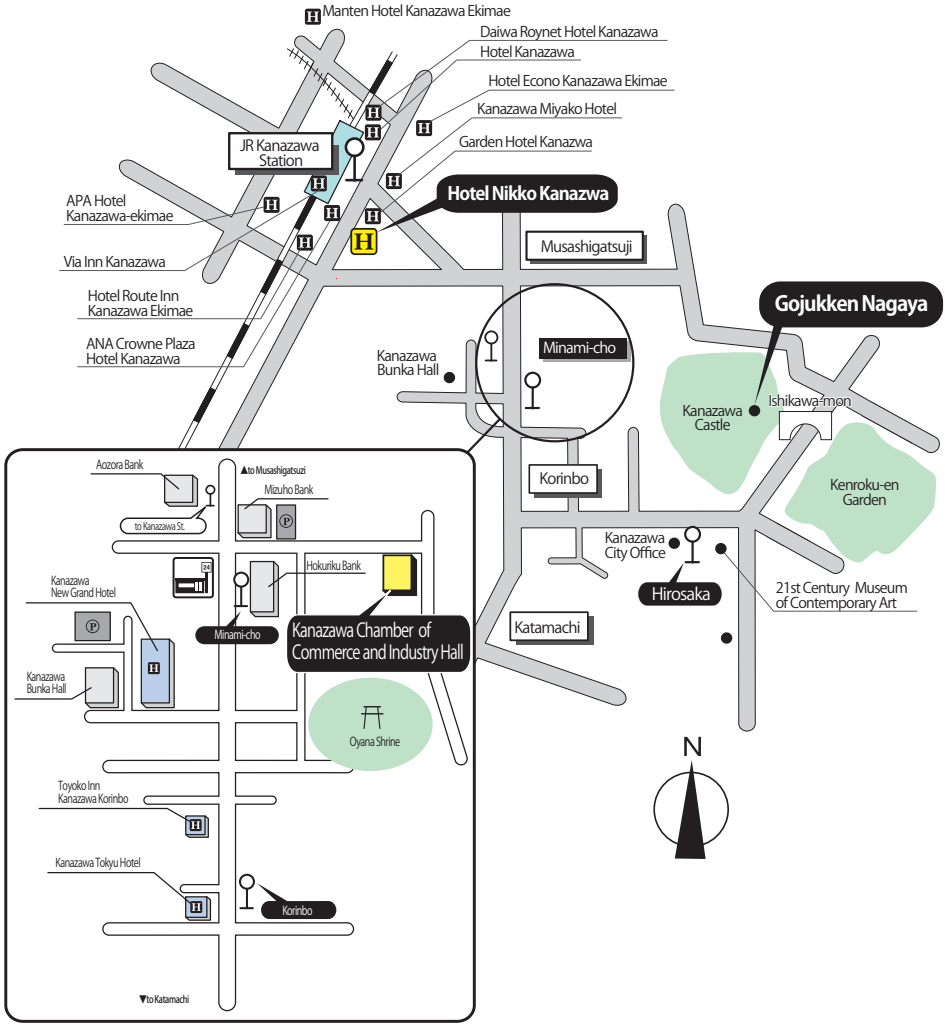
Conference Secretariat
The Japanese Association for Complement Research
Osaka Medical Center for Cancer and Cardiovascular Diseases
1-3-2 Nakamaichi, Higashinari-ku, Osaka, 537-8511, Japan
TEL: +81-6-6972-1181 (extension number: 4101)
FAX: +81-6-6973-5691
E-mail: secretariat@icwkanazawa2016.com

Kanazawa Area Map



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