Targeted Protein Degradation Forum in Japan
At Shonan iPark

DAY-1
10:30~18:30 (Session + Exhibition)
18:30~20:00 (Dinner party)

DAY-2
10:00~15:00 (Session + Exhibition)
15:00~18:00 (Partnering + Exhibition)

Targeted Protein Degradation Forum in Japan
Mail: summit@ibtool.jp
Contact

Taxi
0466-22-2191 (Enoshima Taxi) / 0467-46-5115 (Ofuna Chuo Koutsu)

Bus
Shonan iPark ⇒ Ofuna Station (approx. 18min)
Shonan iPark ⇒ Fujisawa Station North Exit (approx. 18min)

Wi-Fi
SSID: TakedaGuestNet
PW: Takedaism21

Floor map

Transport

Refreshment area
Exhibition
Partnering area
Auditorium
No Entry
No Entry
No Entry
### PROGRAM

#### DAY-1 [8/22]

**9:30**
Registration

**10:30-10:45**
Opening remarks
[Chair person : Gwenn M. Hansen]

**10:45-11:30**
**Key note : Induced protein degradation by chimeric small molecules; recent progress and outlook**
Mikihiko Naito, Chief, Division of Molecular Target and Gene Therapy Products, National Institute of Health Sciences
[Chair person : Gwenn M. Hansen]
Presentation: RaPPIDS: Efficient discovery platform of the targeted protein degradation drugs
Yusuke Tominari, CEO/CSO, Co-Founder FIMECS, Inc.

**11:30-12:00**
iPark company session: Hit compound identification for any target by high-throughput binding screening
Takashi Motoya, Director CTO SEEDSUPPLY INC.

**12:00-12:15**
Luncheon seminar: Protein Degradation as an emerging approach for targeting kinome
Yusuke Kawase, Deputy General Manager, Drug Discovery Support Business Carna Biosciences, Inc.

**12:30-13:00**
Presentation: Molecular mechanisms of cereblon-based drugs
Takumi Hio, Associate Professor, Department of Nanoparticle Translational Research Tokyo Medical University
[Chair person : Michael Plewe]

**13:30-14:00**
Presentation: Autophagy-based targeted degradation
Hirokazu Arimoto, Professor, Graduate School of Life Sciences, Tohoku University

**14:00-14:30**
Presentation: USP8-STAM1 deubiquitinating enzyme complex is a novel drug target for Cushing’s disease
Toshiaki Fukushima, Assistant Professor, Cell Biology Center, Institute of Innovative Research, Tokyo Institute of Technology

**14:30-15:00**
Networking break

**15:00-15:30**
Keynote: Leveraging the dTAG platform to degrade cancer dependencies
Behnam Nabet, Research Fellow Dana-Farber Cancer Institute

**16:00-16:30**
Key note: The Auxin-Inducible-Degron System as a Tool for Target Validation
Masato Kanemaki, Professor, National Institute of Genetics

**16:30-17:00**
Networking break

**17:00-17:15**
iPark company session: Introduction of Axcelead
Takahiro Tanaka, Sales lead, Axcelead Drug Discovery Partners, Inc.

**17:15-18:30**
iPark / Axcelead Drug Discovery Partners, Inc.

**18:30-20:00**
Dinner party

#### DAY-2 [8/23]

**9:00**
Registration

**10:00-10:45**
**Key note : A platform approach for developing E3 ligase inhibitors or effectors for cancer therapy**
Gwenn M. Hansen, Senior Vice President, Research, Nurix Therapeutics

**10:45-11:15**
Presentation: Sulfonamide Small Molecules Target DCAF15-CUL4 Ubiquitin Ligase to Promote Selective Degradation of Splicing Factor CAPER-alpha
Taisuke Uehara, Principal Scientist Eisai Co., Ltd.

**11:15-11:45**
Presentation: Inhibiting DUBs for Targeted Protein Degradation
Benedikt Kessler, Professor of Biochemistry and Life Science, Mass Spectrometry, University of Oxford, UK

**12:00-12:15**
Luncheon seminar: Pharmacology Platform Supporting PROTAC Drug Research
Sun Lingbing, Director WuXi AppTec / HD Biosciences

**12:30-13:00**
Presentation: Inhibiting DUBs for Targeted Protein Degradation
Benedikt Kessler, Professor of Biochemistry and Life Science, Mass Spectrometry, University of Oxford, UK

**13:30-14:00**
Panel discussion

**14:00-14:45**
Closing remarks

**14:45-15:00**
Networking break

**15:00-15:30**
**Key note : Ubiquitin mediated small molecule induced target elimination (uSMITE) for cancer**
Michael Plewe, Vice President - Medicinal Chemistry, Cullgen Inc.

**15:30-16:00**
**Key note : Targeted IRAK-M degradation as a novel approach in cancer immunotherapy overcoming innate-driven immunosuppression**
Kanae Gamo, Vice President, Biology, Co-Founder FIMECS, Inc.

**16:00-16:30**
**Panel discussion**
Yusuke Tominari / Mikihiko Naito / Gwenn M. Hansen / Michael Plewe / Kanae Gamo

**16:30-17:00**
Networking break

**17:00-17:15**
iPark company session: Introduction of Axcelead
Takahiro Tanaka, Sales lead, Axcelead Drug Discovery Partners, Inc.

**17:15-18:30**
iPark / Axcelead Drug Discovery Partners, Inc.

**18:30-20:00**
Dinner party

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**GOLD Sponsors**
- Carna Biosciences

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**Chair person : Gwenn M. Hansen**
**Chair person : Mikihiko Naito**
**Chair person : Yusuke Tominari**
**Chair person : Michael Plewe**
**Chair person : Kanae Gamo**
Induced protein degradation by chimeric small molecules: recent progress and outlook

- An overview of the protein degradation induced by small molecules.
- What we can do and we can not do with degrader molecules.
- Advantage of the protein degradation over enzyme inhibition.
- Future prospects of the protein degradation.

Dr. Naito was granted PhD degree from the University of Tokyo in 1987, then started his carrier at the Cancer Institute, Japanese Foundation in Cancer Research, as a postdoctoral fellow. In 1989, Dr. Naito was engaged in the Institute of Applied Microbiology, the University of Tokyo, as an assistant professor, and in 2009 he became a chief of the division of Biochemistry and Molecular Biology at the National Institute of Health Sciences in Japan. Since 2014, he has been a chief of Molecular Target and Gene Therapy Products at the institute. Dr. Naito has had a long-standing interest in understanding the mechanisms how cancer cells undergo cell death or survive after anticancer treatment, and has made significant contributions in the areas of (1) anticancer drug resistance, (2) cancer cell death and (3) molecular function of anti-apoptotic proteins. Dr. Naito performed in-depth studies on inhibitor of apoptosis protein (IAP) ligands, and established a protein degradation system with SNIPERs.

RaPPIDS: Efficient discovery platform of the targeted protein degradation drugs

- Efficient degrader discovery platform; RaPPIDS
- Feature of proprietary E3 ligase binders
- Strategy of FIMECS research

Yusuke Tominari is a CEO and CSO, and manages the entire projects and strategy of FIMECS, Inc. He co-founded FIMECS with his colleagues in 2018 as a spin-out biotech from Takeda Pharmaceutical Company Limited. He started his career of a medicinal chemist at Takeda in 2006 after getting a PhD at the University of Tokyo in Japan. His expertise is medicinal chemistry in immunology, oncology and immuno-oncology areas, Natural product synthesis and Chemical biology (Bifunctional molecules, Photo-affinity labeling probes and Cleavable linkers). Through his 13 years of the pharmaceutical experience, he contributed 2 out-licensing and 1 IND filing. He is currently challenging “Drugging Undruggable Targets” by the targeted protein degradation technology with a proprietary RaPPIDS platform in FIMECS.

Autophagy-based targeted degradation

- Identification of cereblon using thalidomide-immobilized FG beads
- Molecular mechanisms of therapeutic effects of thalidomide and its derivatives
- Molecular mechanisms of thalidomide teratogenicity

Takumi Ito received BS in 2004, MSE in 2006, and PhD in Engineering in 2010 from Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology. From 2004-2008, he was a JSPS research fellow. From 2008-2012, he was a researcher at the Integrated Research Institute of Tokyo Institute of Technology. From 2012-2013, he was an assistant professor of Graduate School of Bioscience and Biotechnology at Tokyo Institute of Technology. From 2013-2016, he was an assistant professor at Department of Nanoparticle Translational Research of Tokyo Medical University. Now he is an associate professor at the same affiliation.
Recent advances with the dTAG system including:

- Case studies highlighting functional evaluation and drug target validation of cancer dependencies using the dTAG system
- Development of the dTAG platform to enable immediate and selective degradation of drug target proteins
- Recent advances with the dTAG system including model system development and in vivo evaluation

USP8-STM1 deubiquitinating enzyme complex is a novel drug target for Cushing’s disease

- Dysregulation of deubiquitinating enzymes is implicated in many human diseases.
- Cushing’s disease is an endocrine disorder in which pituitary tumors secrete adrenocorticotropic hormone (ACTH), leading to the onset of hypercortisolism symptoms.
- Missense mutations of ubiquitin-specific protease 8 (USP8) are very frequently occurring in the pituitary tumors.
- We show the pathogenic mechanisms of Cushing’s disease induced by USP8 mutations, and propose USP8-STM1 complex as a novel drug target.

Recent publications of our group:
2. Kawaguchi et al. (2018) Ubiquitin-specific protease 8 deubiquitinates Sec31A and decreases large COPII carriers and collagen IV secretion. BBRC 499, 635-641
5. Behnam Nabet, Ph.D. is a Postdoctoral Research Fellow in the laboratory of Dr. Masayuki Komada in the Tokyo Institute of Technology. From 2015 to the present, I studied the physiological and pathological actions of some deubiquitinating enzymes in the laboratory of Dr. Masayuki Komada in the Tokyo Institute of Technology. Recent publications of our group:

- DNA encoded library discovery as a resource for binders and modulators of E3 ligases
- A platform approach for developing E3 ligase inhibitors or effectors for cancer therapy
- DNA encoded library discovery as a resource for binders and modulators of E3 ligases
- Small molecule inhibitors of the E3 ligase, Cbl-b, are potential novel, immuno-therapies
- Targeted degradation of resistance mutations in oncology

Behnam Nabet, Ph.D. is a Postdoctoral Research Fellow in the laboratory of Dr. Nathanel Gray at the Dana-Farber Cancer Institute. Dr. Nabet received his Ph.D. in Cancer Biology from Northwestern University and B.A. in Biology from the University of Pennsylvania. In his postdoctoral research, Dr. Nabet developed a generalizable technology platform known as the dTAG system to rapidly degrade any target protein of interest. The dTAG system pairs potent small molecule degraders and extensible tagging strategies to achieve selective degradation of divergent proteins. This technology facilitates biological exploration and drug target validation in cells and animal models. Dr. Nabet is currently applying the dTAG platform to investigate pancreatic cancer dependencies and has been sharing the technology with the global scientific community in an open-source manner. Dr. Nabet is supported by an American Cancer Society Postdoctoral Fellowship and is a recipient of the Claudia Adams Barr Program for Innovative Cancer Research award.

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- Targeted degradation of resistance mutations in oncology
**Day 2**

**Presentation**

**10:45~11:15**

**Taisuke Uehara**
Principal Scientist
Eisai Co., Ltd.

**Sulfonamide Small Molecules Target DCAF15-CUL4 Ubiquitin Ligase to Promote Selective Degradation of Splicing Factor CAPER-alpha**

- Proteome wide analysis revealed that anti-cancer sulfonamides induce proteosomal degradation of splicing factor CAPER-alpha.
- Anticancer sulfonamides are novel molecular glue that assemble a protein complex between CAPER-alpha and DCAF15.
- Molecular mechanism of the sulfonamides suggests DCAFs are promising drug targets through the promotion of selective protein degradation.

**11:15~11:45**

**Benedikt Kessler**
Professor of Biochemistry and Life Science Mass Spectrometry
University of Oxford, UK

**Inhibiting DUBs for Targeted Protein Degradation**

- Small molecule development against deubiquitinating enzymes (DUBs)
- Drugging the undruggables through the ubiquitin system
- Discovery of critical DUBs that modulate stability of oncoproteins and tumor suppressor genes
- Proteomics and ubiquitomics

**Key Note**

**13:00~13:30**

**Michael Plewe**
Vice President - Medicinal Chemistry
Cullgen Inc.

**Ubiquitin mediated small molecule induced target elimination (uSMITE) for cancer**

Case studies of targeted protein degraders for oncology targets will be presented; progress in development of orally active degraders will be shared; the importance of considering physico-chemical properties for successful degrader design will be discussed.

**13:30~14:00**

**Kanae Gamo**
Vice President, Biology, Co-Founder
FIMECS, Inc.

**Targeted IRAK-M degradation as a novel approach in cancer immunotherapy overcoming innate-driven immunosuppression**

- Generation of IRAK-M degraders by RaPPIDS
- In vitro mode of action analysis and in vivo studies of IRAK-M degraders
- Targeting IRAK-M as an effective cancer immunotherapy strategy
**LUNCHEON SEMINAR**

**DAY-1 12:30~13:00**

**Yusuke Kawase**  
Deputy General Manager, Drug Discovery Support Business  
Carna Biosciences, Inc.

**Protein Degradation as an emerging approach for targeting kinome**

Conventional approaches in kinase inhibitor drug discovery had been heavily focused on suppressing kinase activity. However, such modality wouldn't work on some intractable kinases which have additional functions such as adaptor protein. Recent discovery of new bifunctional compound groups such as PROTAC and SNIPER could open up new avenues for those kinases by hijacking the ubiquitin degradation system and pulling a targeted kinase into it.

In our talk, we present
• New discoveries about targeting kinases in this modality
• How Carna’s tagged kinases will assist your target protein degradation research by contributing to acquire accurate data.

**DAY-2 12:00~12:30**

**Sun Lingbing**  
Director  
WuXi AppTec / HD Biosciences

**Pharmacology Platform Supporting PROTAC Drug Research**

- Introduce in vitro pharmacology platform at WuXi AppTec in supporting early-stage PROTAC R&D with strategy of critical steps on PROTAC functions including binary/ternary complex formation, target ubiquitination and target degradation
- Share our knowledge and expertise to provide solution and recommendation on assay selection at different development stages
- Showcase and share our experience in the desirable PROTAC working pattern through case studies.

**iPark COMPANY SESSION**

**DAY-1 12:00~12:15**

**Takashi Motoyaji**  
Director CTO  
SEEDSUPPLY INC.

**Hit compound identification for any target by high-throughput binding screening**

Affinity based screening for any drug target (soluble protein, membrane protein, RNA chain)

**DAY-1 17:00~17:15**

**Takahiro Tanaka**  
Sales lead  
Axcelead Drug Discovery Partners, Inc.

**Introduction of Axcelead**

- Axcelead is a spin-out company from Takeda Pharmaceutical inheriting its unique and proprietary drug discovery platform, “People”, “Infrastructure” and “Historical Data”
- We offer integrated services tailored to your needs, from early stage exploration studies to optimization of candidate compounds and even a bridge process to clinical development.
- Company overview will be introduced in advance to specific capability offer of our DMPK team
**Biotinylated Kinases**

Carna's biotinylated kinases are best materials for your study of compound affinity and other kinase-molecule interactions!

**No Additional Labeling Required!**

**ACTIVE & STABLE**
- Native, catalytically active kinase domains well preserved
- Each batch activity measured using a relevant specific substrate

**Site specific, Single biotin labeling**

**HIGH QUALITY**
- All produced in-house
- Produced via Baculovirus expression system

**ASSURING**
- DNA sequence confirmed prior to expression
- Amino acid sequence confirmed by Peptide Mass Fingerprinting (PMF)

**RELIABLE**
- Ensured batch-to-batch consistency
- Constructs carefully selected from literature

You may find how easy-to-use Carna's biotinylated kinases are in various assays including homogenous proximity-based binding assays such as Tri-FRET, AlfaScreen™/AlfaLISA™, HTRF® to interrogate inhibitor binding affinity, determine on-off rates, and measure binding kinetics. Please experience effortless immobilization of target proteins onto sensor surface without impairing their structure and activity by utilizing Carna’s biotinylated kinases.

Carna Biosciences, Inc.
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TEL: 078-302-7091 | FAX: 078-302-7086
info@carnabio.com / www.carnabio.com
Combining Strengths. Sharing Success.

TCG Lifesciences has been catalyzing drug discovery and early development efforts of its global client base over the past 16 years. Our alliances span from functional chemistry, biology to integrated drug discovery as well as API development, globally across North America, Europe and Asia.

Key Achievements
- Five development candidates delivered, including three in the clinic.
- Discovered and optimized several lead molecules.
- Developed a novel biomarker for liver disease.
- Supplied key intermediates of a marketed cosmeceutical.
- Live cell chem synthesist/sAR and rapid scale up for pharma/biotech clients have led to hundreds of patents and numerous stage transitions.
- Wide range of technology platforms in solid phase peptide synthesis, library synthesis, GLP analytical, molecular pharmacology, ADMET/PK, pre-clinical models deliver unique value.
- Extensive experience in providing high end discovery, development and analytical services to other allied industries like crop science, animal health, cosmeceutical and nutraceutical.
- Enhanced portfolio of services for supporting an "end to end" solution for discovery, development, and commercialization.

TCG Lifesciences Pvt. Ltd. is a Discovery and Pre-clinical Research Company that provides an integrated platform to global pharmaceutical and biotech companies to expedite discovery of new small molecule drug candidates.

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