ISNAC 2022

The 49th International Symposium on Nucleic Acids Chemistry
The 6th Annual Meeting of Japan Society of Nucleic Acids Chemistry

第49回 国際核酸化学シンポジウム
日本核酸化学会第6回年会

Program & Abstracts

Period November 2(Wed)–4(Fri), 2022

Venue Tokyo University of Science
Katsushika Campus,
Library Big Hall

Organizer Hidetaka Torigoe
Tokyo University of Science

ISNAC2022 Program at a Glance

November 2 (Wed)

9:55～10:00 **Opening Remarks**

10:00～11:00
Oral Presentations
10:00 1O-01 Takashi Osawa
10:15 1O-02 Akash Chandela
10:30 1O-03 Ahmed M. Abdelhady
10:45 1O-04 Dipanwita Banerjee

11:00～11:15 **Break**

11:15～12:05
Invited Lecture 1
IL-01
Katherine Seley-Radtke

12:05～13:25
Lunch Break

13:25～15:25
Poster Presentations
1P-01～1P-67

15:25～16:25
Oral Presentations
15:25 1O-05 Kane McQuaid
15:40 1O-06 Shiyu Wang
15:55 1O-07 Shigeyoshi Matsumura
16:10 1O-08 Jun Wang

16:25～16:40 **Break**

16:40～17:30
Invited Lecture 2
IL-02
Bengang Xing

17:30～18:30
Oral Presentations
17:30 1O-09 Takeshi Tabuchi
17:45 1O-10 Natsuhisa Oka
18:00 1O-11 Yasuaki Kimura
18:15 1O-12 Takehiko Wada

November 3 (Thu)

10:00～11:00
Oral Presentations
10:00 2O-01 Bimolendu Das
10:15 2O-02 Yudai Yamaoki
10:30 2O-03 Tatsuya Nishihara
10:45 2O-04 Shigeori Takenaka

11:00～11:15 **Break**

11:15～12:05
Invited Lecture 3
IL-03
Anh Tuan Phan

12:05～13:25
Lunch Break

13:25～15:25
Poster Presentations
2P-01～2P-67

15:25～15:40 **Break**

15:40～16:10
Special Lecture 1 SL-01
Hiroshi Sugiyama

16:10～16:40
Special Lecture 2 SL-02
Ichiro Hirao

16:40～16:50 **Break**

16:50～18:00
JSNAC General Meeting

November 4 (Fri)

10:00～10:50
Invited Lecture 4
IL-04
Xingguo Liang

10:50～11:05 **Break**

11:05～12:05
Oral Presentations
11:05 3O-01 Michiko Kimoto
11:20 3O-02 Kazunori Ikebukuro
11:35 3O-03 Arivazhagan Rajendran
11:50 3O-04 Ryosuke Ueki

12:05～ **Closing Remarks**

ISNAC 2022

The 49th International Symposium on Nucleic Acids Chemistry 2022
The 6th Annual Meeting of Japan Society of Nucleic Acids Chemistry

Program & Abstracts

Period

November 2(Wed)–**4**(Fri)**, 2022**

Venue

Tokyo University of Science
Katsushika Campus,
Library Big Hall

6-3-1 Niijuku, Katsushika-ku, Tokyo 125-8585, JAPAN

Symposium Organizer

Prof. **Hidetaka Torigoe**

Tokyo University of Science

Sponsored by

Japan Society of Nucleic Acids Chemistry

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Greeting

On behalf of the organizing and executive committees of the 49th International Symposium on Nucleic Acids Chemistry (ISNAC2022), I would like to invite all of you to attend ISNAC2022 to be held from November 2 (Wed) to November 4 (Fri), 2022 at Katsushika Campus in Tokyo University of Science. Because ISNAC2020 was canceled and ISNAC2021 was held online due to the COVID-19 pandemic, ISNAC2022 is the first onsite ISNAC after the COVID-19 pandemic is going down. However, the COVID-19 pandemic has not been completely finished. To avoid the expansion of the COVID-19 pandemic, our organizing committee has decided that the exchange meeting will not be held where many scientists usually gather to eat and drink in the second day evening of the symposium.

ISNAC started in 1973 as an annual domestic meeting of nucleic acid chemists in Japan, and developed into an international symposium in 2005 for nucleic acid scientists from all over the world. ISNAC may be one of the largest symposiums with the active discussions of nucleic acid chemistry in the world. Nucleic acid chemistry is based on various fields, such as organic chemistry, physical chemistry, biochemistry, and medicinal chemistry. Recently, nucleic acid chemistry is quite important and expanding to bridge various related fields, such as medicine, pharmacy, and engineering, to develop novel nucleic acid medicines and materials. COVID-19 vaccines are one of the nucleic acid medicines. Under these situations, the discussion subjects of ISNAC have been basically based on “chemistry” and they are now expanding the scope to include diverse aspects of molecular biology, gene regulation, epigenetics, bioengineering, biotechnology, biomaterials, therapeutic and diagnostic applications, etc.

It is a great pleasure of our organizing committee to host ISNAC2022 with the invitation of excellent speakers from abroad. We will arrange an exciting scientific program to bring together the scientific community of nucleic acid chemistry and to enjoy fruitful discussions. We sincerely expect that as many scientists as possible including young and senior scientists from both academia and industry will attend ISNAC2022. We are looking forward to meeting all of you in Tokyo.

Chairman of ISNAC 2022
Hidetaka Torigoe
Graduate School of Science, Tokyo University of Science

Information for Participants, Chairs, and Presenters

General Information for Participants

1. Reception

   On-site registration, certificate issuing, cloak and other general inquiries are available during the following hours at the venue.

Date	Open Hours
Nov. 2 (Wed)	8:30 – 19:00
Nov. 3 (Thu)	9:00 – 18:30
Nov. 4 (Fri)	9:00 – 13:00

〈 On-site Registration fee 〉

*Regular: 30,000JPY
*Student: 15,000JPY
*Recommended Students: 14,000JPY

Only payment in Japanese yen in cash is acceptable.

2. Internet

   Wireless Internet service is available at the venue.

3. Exhibition

   Nov. 2 (Wed) 10:00 – 17:00
   Nov. 3 (Thu) 10:00 – 17:00
   Nov. 4 (Fri) 10:00 – 12:30

4. Awards of Young Scientist

   ISNAC2022 offers “ISNAC Outstanding Oral Presentation Award for Young Scientist in 2022” and “ISNAC Outstanding Poster Award in 2022”.

Instruction for Chairs

1. Arrival

   Chairpersons are requested to be seated at the “next chairs’ sheet” located in the right front of the hall no later than 10 minutes before the start of the presentations.

2. Session Progress

   Chairpersons are asked to ensure that all presentations start and finish punctually as scheduled. Staffs will assist with timing. Remaining time will be notified with bell signal as follows;

   - 1 ring: Warning – at 3 minutes left to the end of talk
   - 2 rings: End of talk – time for discussion
   - 3 rings: End of presentation – time for the next speaker

Instruction for Oral Presenters

1. Time Allocation

   Invited Lectures: Presentation 45 min. + Discussion 5 min. (Total: 50min.)

   Oral Presentations: Presentation 12 min. + Discussion 3 min. (Total: 15min.)

2. Presentation Materials

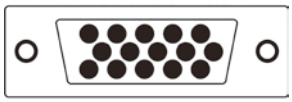
   Only computer-based Powerpoint presentations will be accepted, and no sound output equipment will be available.

3. Laptop Computer

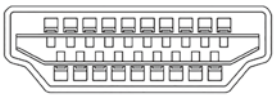
   Please be sure to bring your own laptop computer. We ask you to bring your presentation file in USB for back up as well.

   < Technical Requirements for Your Laptop Computer >

   - Ensure that your computer is equipped with the proper monitor connector (Type A for HDMI or mini D-sub 15 pin for VGA) as shown below. If your computer does not have this connection, please bring an appropriate converter with you.
   - Be sure to bring an AC adaptor. Please note that voltage in Japan is 100 V and the frequency ranges 50 – 60 Hz depending on the area (50 Hz in Tokyo).
     The socket is type A, which has two flat plug holes. If your laptop is not convertible, transformers and/or plug adaptors are necessary.
   - Adjust the settings to prevent activation of the screen saver of power-saving mode.

   mini D-sub 15 pins

   HDMI Type A

4. Preparation

   Please bring your computer to the Oral Presentation Hall stage during coffee or lunch break before your presentation.

5. Timing

   In order to maintain the schedule, you are requested to keep time allocation strictly.

   Remaining time will be notified with bell signal as follows;

   - 1 ring: Warning – at 3 minutes left to the end of talk
   - 2 rings: End of talk – time for discussion
   - 3 rings: End of presentation – time for the next speaker

Instruction for Poster Presenters

1. Set-up and Removal

   Poster No. 1P-X (X=1-67)

   Set-up: Nov. 2 (Wed) 9:00-13:20

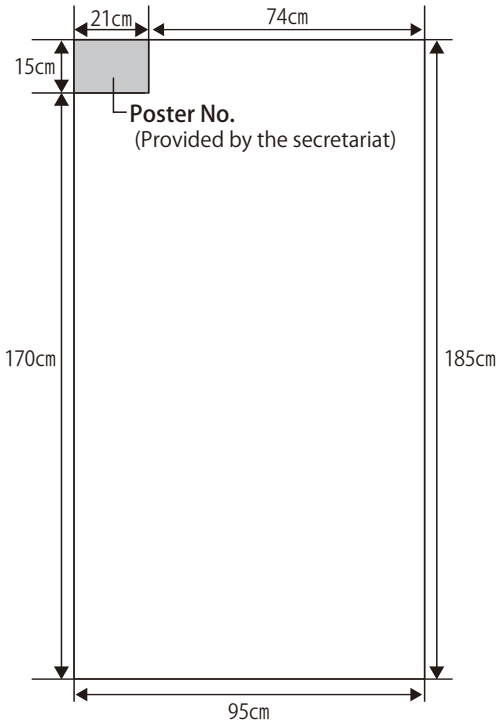
   Removal: Nov. 2 (Wed) 18:30-19:00

   Poster No. 2P-X (X=1-67)

   Set-up: Nov. 3 (Thu) 9:00-13:20

   Removal: Nov. 3 (Thu) 18:00-18:30

   * Any posters remaining on panels after the removal time will be discarded by the secretariat.

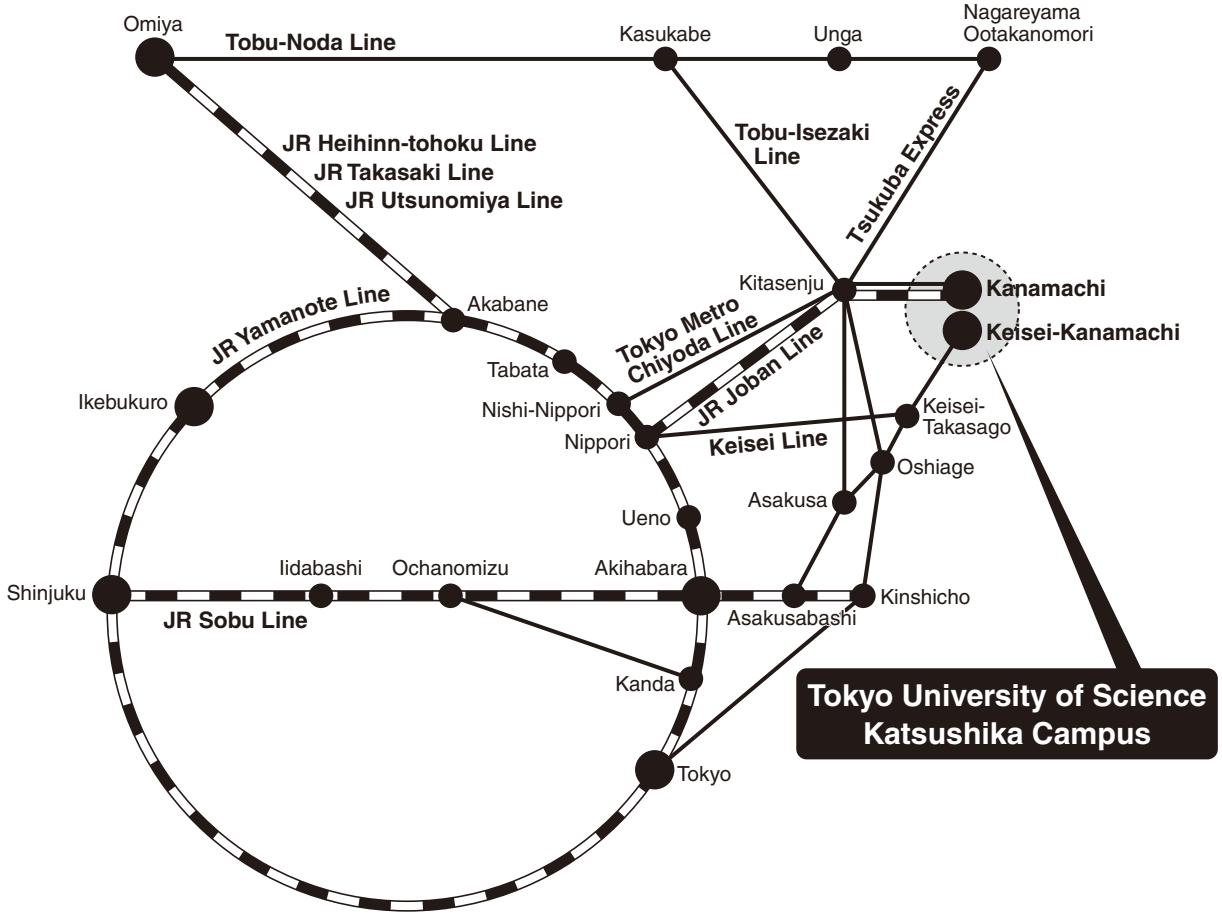


2. Poster Presentations

   1P numbers: Nov. 2 (Wed) 13:25-15:25

   2P numbers: Nov. 3 (Thu) 13:25-15:25

Around the Venue



■ From Narita Airport

Take the Keisei Honsen/main Line to Keisei-Takasago Station.
Transfer to the Keisei Kanamachi Line and take it to Keisei-Kanamachi Station.
Travel time : about 1 hour 29 minutes.

■ From Haneda Airport

Take the Tokyo Monorail to Hamamatsucho Station.
Transfer to the JR Yamanote Line / Keihin-Tohoku Line and take it to Nishi-Nippori Station.
Transfer to the Tokyo Metro Chiyoda Line and take it to Kanamachi Station.
Travel time : about 1 hour 14 minutes.

Take the Keikyu Line to Sengakuji Station. Transfer to the Toei Asakusa Line and take it to Keisei-Takasago Station (via Oshiage Station).

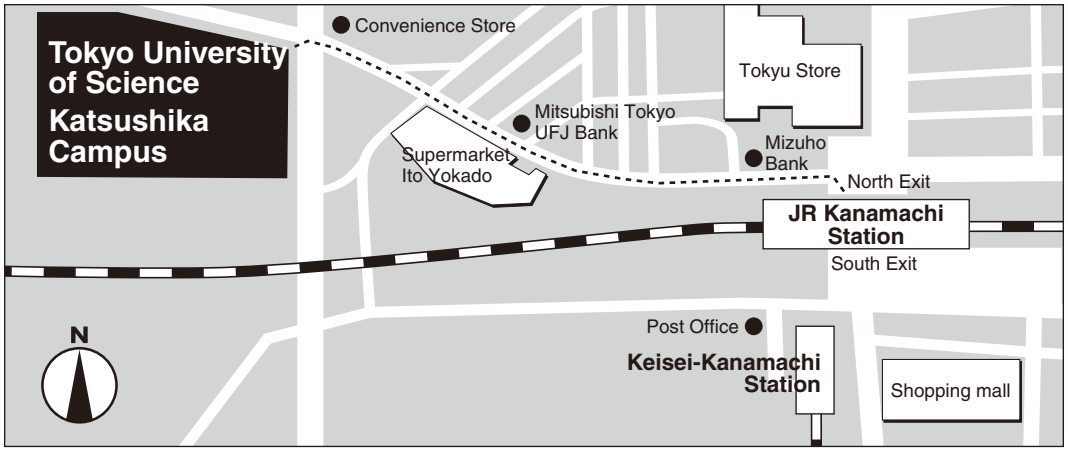
■ From Tokyo Station

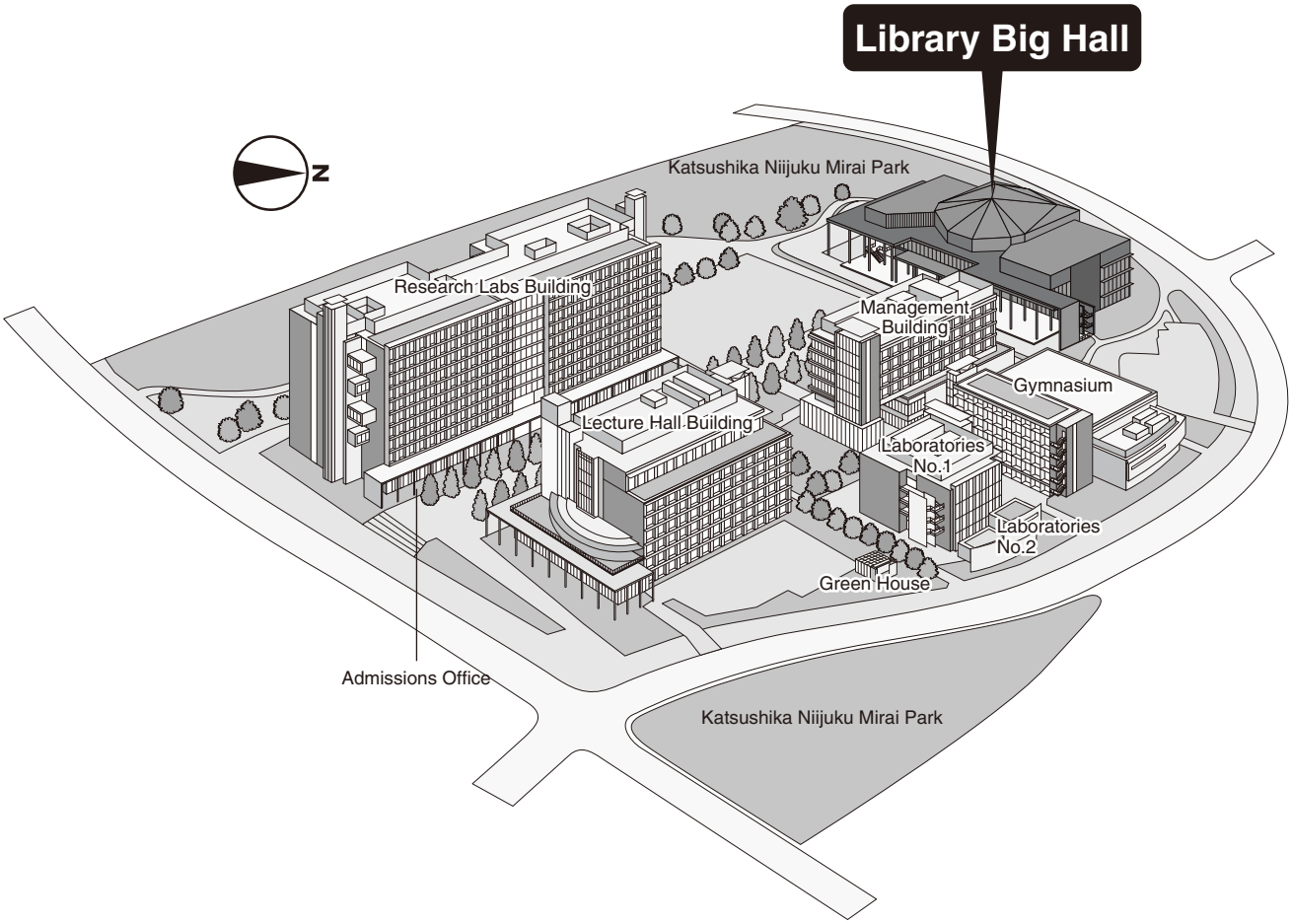
Take the JR Yamanote Line / Keihin-Tohoku Line to Nishi-Nippori Station.
Transfer to the Tokyo Metro Chiyoda Line and take it to Kanamachi Station.
Travel time : about 33 minutes.

■ From Ueno Station

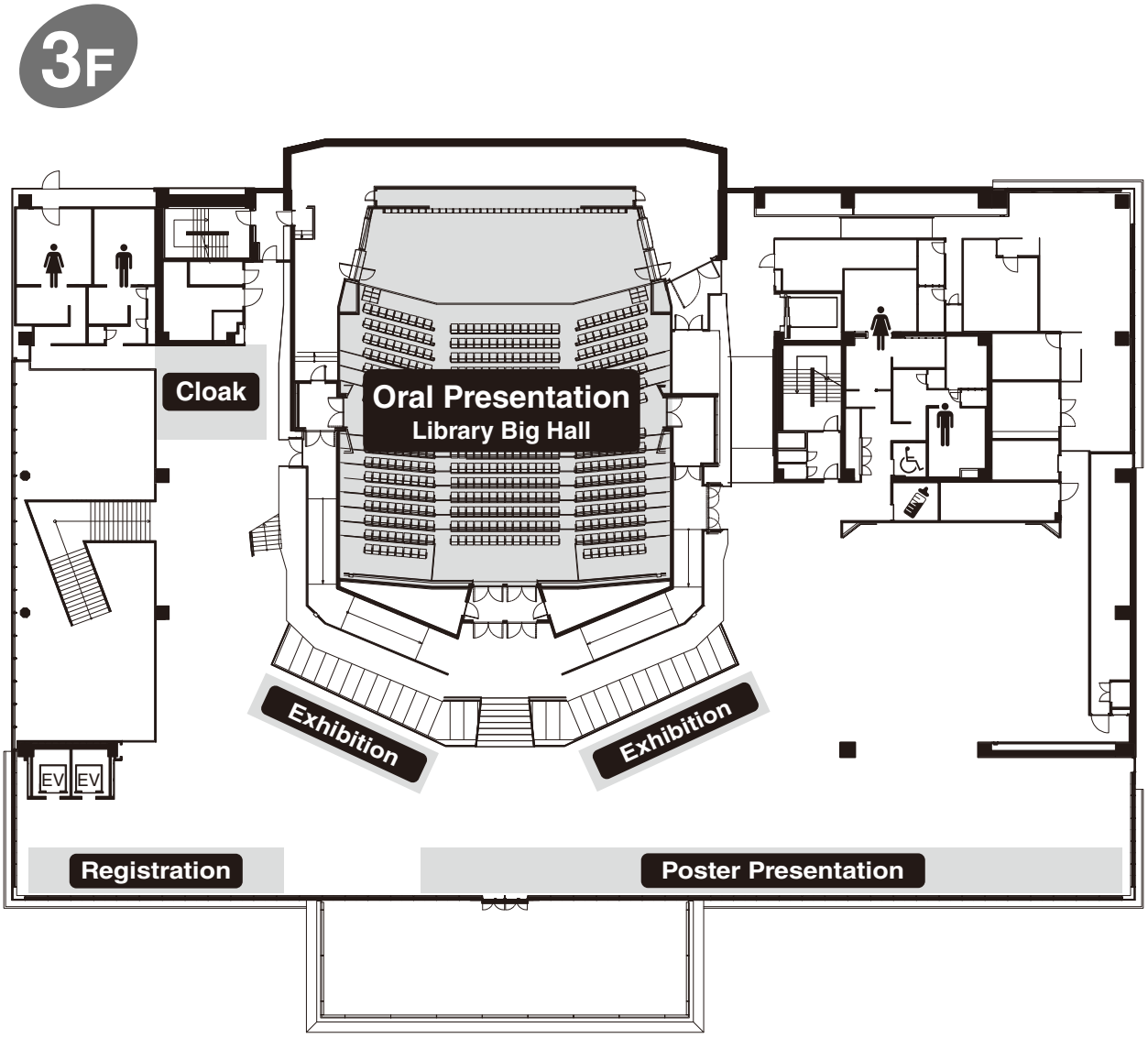
Take the JR Joban Line (rapid service) to Kita-Senju Station.
Transfer to the JR Joban Line (local service) and take it to Kanamachi Station.
Travel time : about 30 minutes.

Map of the Venue





Library, Tokyo University of Science



Program

Day 1: November 2 (Wed)

9:55-10:00	**Opening Remarks**		
10:00-10:15	**Oral Presentations** Chairman: Shigeori Takenaka Kyushu Institute of Technology	**1O-01**	Synthesis of phosphoramidites for 3'-amino linker modification of base-labile oligonucleotides Takashi Osawa[1)], Qin Ren[1)], Satoshi Obika[1)2)3)] 1) Graduate School of Pharmaceutical Sciences, Osaka University, 2) Institute for Open and Transdisciplinary Research Initiatives, Osaka University, 3) National Institutes of Biomedical Innovation, Health and Nutrition
10:15-10:30		**1O-02**	4'-C-aminoethoxy modification augments stability of RNAs and DNAs, exhibiting sustained gene silencing Akash Chandela[1)], Ryo Tsukimura[2)], Yuki Katsuzaki[2)], Ryohei Kajino[3)], Yoshihito Ueno[1)2)3)] 1) Faculty of Applied Biological Sciences, Gifu University, 2) Graduate School of Natural Science and Technology, Gifu University, 3) The United Graduate School of Agricultural Science, Gifu University
10:30-10:45		**1O-03**	Selective photo-catalytic proximity labeling of G4 DNA-interacting proteins for the interaction proteomes of G4 DNA Ahmed Mostafa Abdelhady[1)], Kazumitsu Onizuka[1)], Tatsuki Masuzawa[2)], Shinichi Sato[3)], Keita Nakane[3)], Takanori Oyoshi[2)], Fumi Nagatsugi[1)] 1) IMRAM, Tohoku University, 2) Graduate School of Science and Technology, Shizuoka University, 3) FRIS, Tohoku University
10:45-11:00		**1O-04**	New parameters for accurate prediction of RNA/DNA hybrid duplex stability and their advantage in CRISPR-Cas9 technique Dipanwita Banerjee[1)], Hisae Tateishi-Karimata[1)], Tatsuya Ohyama[1)], Saptarshi Ghosh[1)], Tamaki Endoh[1)], Shuntaro Takahashi[1)], Naoki Sugimoto[1)2)] 1) Frontier Institute for Biomolecular Engineering Research (FIBER), Konan University, 2) Graduate School of Frontiers of Innovative Research in Science and Technology (FIRST), Konan University
11:00-11:15	**Break**		
11:15-12:05	**Invited Lecture 1** Chairman: Naoki Sugimoto Konan University	**IL-01**	Flex-nucleosides – a strategic approach to broad-spectrum antiviral therapeutics Katherine L. Seley-Radtke Professor, Department of Chemistry & Biochemistry, University of Maryland
12:05-13:25	**Lunch Break**		
13:25-15:25	**Poster Presentations (1P-01～1P-67)**		
15:25-15:40	**Oral Presentations** Chairman: Takashi Morii Kyoto University	**1O-05**	Crystallographic studies of ruthenium polypyridyl complexes bound to G-quadruplexes: Towards design, specificity, and function Kane McQuaid[1)], David Cardin[1)], James Hall[2)], Neil Paterson[3)], Shuntaro Takahashi[4)], Naoki Sugimoto[4)], Christine Cardin[1)] 1) Department of Chemistry, University of Reading, UK., 2) Department of Pharmacy, University of Reading, UK, 3) Diamond Light Source Ltd., Didcot, UK, 4) FIBER, Konan University, Kobe, Japan

15:40-15:55		**1O-06**	Liquid to solid phase transition of short RNA promoted by RNA structure in neurodegenerative diseases Shiyu Wang, Yan Xu Department of Medical Sciences, Faculty of Medicine, University of Miyazaki
15:55-16:10		**1O-07**	In quasi-cell evolution of an RNA-cleaving ribozyme using droplet screening integrated devices Shigeyoshi Matsumura, Tomoe Imai, Motochika Ehara, Yuka Nishiyama, Yoshiya Ikawa Graduate School of Science and Engineering, University of Toyama
16:10-16:25		**1O-08**	Toehold-mediated DNA hairpin circuits augmented by cationic copolymer Jun Wang, Naohiko Shimada, Atsushi Maruyama Department of Life Science and Technology, Tokyo Institute of Technology
16:25-16:40	**Break**		
16:40-17:30	**Invited Lecture 2** Chairman: Shuntaro Takahashi Konan University	**IL-02**	Advances and Future Perspectives of NIR Fluorescence Paradigms in Cutting-edge Theranostic Bio-applications Bengang Xing[1)], Thang Do Cong[2)], Caixia Sun[2)], Songhan Liu[2)] 1) Professor, Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, 2) School of Chemistry, Chemical Engineering, and Biotechnology (CCEB) Nanyang Technological University (NTU), Singapore
17:30-17:45	**Oral Presentations** Chairman: Daisuke Miyoshi Konan University	**1O-09**	Chemical communication between microdroplets using cell-free riboswitches Takeshi Tabuchi, Yohei Yokobayashi Nucleic Acid Chemistry and Engineering Unit, Okinawa Institute of Science and Technology Graduate University
17:45-18:00		**1O-10**	Stereoselective synthesis of dinucleoside phosphorothioates using chiral phosphoric acid salts as activators Natsuhisa Oka[1)2)], Tomoki Sakai[1)], Kensuke Ori[1)], Naoki Seo[1)], Kosuke Suzuki[1)], Takuya Otsuji[1)], Yuya Shibata[1)], Kaori Ando[1)] 1) Department of Chemistry and Biomolecular Science, Faculty of Engineering, Gifu University, 2) Institute for Glyco-core Research (iGCORE), Gifu University
18:00-18:15		**1O-11**	Complete Chemical Synthesis of mRNA by Chemical Capping Reaction Yasuaki Kimura[1)], Naoko Abe[1)], Akihiro Imaeda[1)], Masahito Inagaki[1)], Fumitaka Hashiya[1)], Satoshi Uchida[2)], Hiroto Iwai[3)], Masakazu Honma[3)], Junichiro Yamamoto[3)], Hiroshi Abe[1)4)] 1) Department of Chemistry, Graduate School of Science, Nagoya University, 2) Graduate School of Medicine, Kyoto Prefecture University of Medicine, 3) Kyowa Kirin Co., Ltd, 4) Institute for Glyco-core Research (iGCORE)
18:15-18:30		**1O-12**	Novel Strategy of Enhancement of RNase H Mediated Target RNA Digestion Activities by DNA-Artificial Nucleic Acid Chimera with Site Selective Cleavage Toward Application of COVID-19 Therapeutics Takehiko Wada[1)], Nozomu Ishiwata[1)], Kazutoshi Fujita[1)], Masahito Inagaki[3)], Hironori Hayashi[2)], Yuto Horiuchi[1)], Ryota Azuma[1)], Masaki Nishijima[1)], Yasuyuki Araki[1)], Eiichi Kodama[2)] 1) IMRAM, Tohoku University, 2) IRDeS, Tohoku University, 3) Graduate School of Science, Nagoya University

Day 2: November 3 (Thu)

10:00-10:15	**Oral Presentations** Chairman: Atsushi Maruyama Tokyo Institute of Technology	**2O-01**	A Fluorescence Probe ANP77 for Sensing RNA Internal Loops and Their Binding Molecules Bimolendu Das[1)], Asako Murata[1)2)], Kazuhiko Nakatani[1)] 1) Department of Regulatory Bioorganic Chemistry, SANKEN, Osaka University, 2) Department of Material Sciences, Faculty of Engineering Sciences, Kyushu University, Japan
10:15-10:30		**2O-02**	Base-pair opening dynamics and interactions with ligands of nucleic acids in living human cells studied by in-cell NMR Yudai Yamaoki[1)2)], Omar Eladl[2)], Keiko Kondo[1)], Tomoki Sakamoto[2)], Takashi Nagata[1)2)], Masato Katahira[1)2)] 1) Institute of Advanced Energy, Kyoto University, 2) Graduate School of Energy Science, Kyoto University
10:30-10:45		**2O-03**	A strategy to control the affinity to the target cells using functional oligonucleotides Tatsuya Nishihara, Risa Yamada, Daichi Oka, Kazuhito Tanabe College of Science and Engineering, Aoyama Gakuin University
10:45-11:00		**2O-04**	Interaction of peptide-linked cyclic naphthalene dimides with G-quartet cluster Shigeori Takenaka, Kentarou Ono, Shinobu Sato Department of Applied Chemistry, Kyushu Institute of Technology
11:00-11:15	**Break**		
11:15-12:05	**Invited Lecture 3** Chairman: Masato Katahira Kyoto University	**IL-03**	Diversity of G-quadruplexes and their interaction with proteins Anh Tuân Phan Professor, Division of Physics & Applied Physics, School of Physical and Mathematical Sciences, Nanyang Technological University
12:05-13:25	**Lunch Break**		
13:25-15:25	**Poster Presentations (2P-01～2P-67)**		
15:25-15:40	**Break**		
15:40-16:10	**Special Lecture 1** Chairman: Kazuhiko Nakatani Osaka University	**SL-01**	Studies on the regulation of DNA structure and function Hiroshi Sugiyama Professor, iCeMS, Kyoto University
16:10-16:40	**Special Lecture 2** Chairman: Mitsuo Sekine Emeritus Professor, Tokyo Institute of Technology	**SL-02**	Creation of genetic alphabet expansion technologies Ichiro Hirao Chief Scientific Officer, Xenolis Pte. Ltd
16:40-16:50	**Break**		
16:50-18:00	**JSNAC General Meeting**		

Day 3: November 4 (Fri)

10:00-10:50	**Invited Lecture 4** Chairman: Makoto Komiyama Emeritus Professor, University of Tokyo	**IL-04**	Circularization of ssDNA or ssRNA and its applications Ran An[1)2)], Hui Chen[1)], Mengqing Liu[1)], Zhe Sui[1)], Zhenzhu Gu[1)], Yixiao Cui[1)], Yaping Zhang[1)], Lin Li[1)], Qi Li[1)], Makoto Komiyama[1)], Xingguo Liang[1)2)] 1) College of Food Science and Engineering, Ocean University of China, Qingdao 266003, China, 2) Laboratory for Marine Drugs and Bioproducts, Qingdao National Laboratory for Marine Science and Technology, Qingdao 266235, China
10:50-11:05	**Break**		
11:05-11:20	**Oral Presentations** Chairman: Toshihiro Ihara Kumamoto University	**3O-01**	Characterization of High-Affinity Unnatural-Base DNA Aptamers Generated by Genetic Alphabet Expansion Technology Michiko Kimoto[1)], Ken-ichiro Matsunaga[1)], Hui Pen Tan[1)], Nur Afiqah Binte Mohd Mislan[1)2)], Ichiro Hirao[1)2)] 1) Institute of Bioengineering and Bioimaging, A*STAR, 2) Xenolis Pte. Ltd.
11:20-11:35		**3O-02**	Anti-idiotype aptamer against Bevacizumab and its affinity change depending on pH Kazunori Ikebukuro[1)], Taro Saito[1)], Yutaka Shimizu[1)], Kaori Tsukakoshi[1)], Ryutaro Asano[1)], Tomohiro Yamada[2)], Tatsuki Nakano[2)], Kodai Hara[3)], Hitoshi Hashimoto[3)], Kenichiro Todoroki[2)] 1) Department of Biotechnology and Life Science, Tokyo University of Agriculture and Technology, 2) Department of Analytical and Bio-Analytical Chemistry, School of Pharmaceutical Sciences, University of Shizuoka, 3) Department of Physical Biochemistry, School of Pharmaceutical Sciences, University of Shizuoka
11:35-11:50		**3O-03**	Efficient Ligation of Nicks in DNA Origami Arivazhagan Rajendran, Kirankumar Krishnamurthy, Eiji Nakata, Takashi Morii Institute of Advanced Energy, Kyoto University
11:50-12:05		**3O-04**	A novel strategy for the selective inhibition of membrane protein functions with DNA aptamers Ryosuke Ueki[1)], Junya Hoshiyama[1)], Shinsuke Sando[1)2)] 1) Department of Chemistry and Biotechnology, Graduate School of Engineering, The University of Tokyo, 2) Department of Bioengineering, Graduate School of Engineering, The University of Tokyo
12:05-	**Closing Remarks**		

List of Poster Presentations

Poster Presentations	1P numbers:	November 2 (Wed)	13:25 – 15:25
	2P numbers:	November 3 (Thu)	13:25 – 15:25

1P-01 Development of cancer cell-selective oligonucleotide therapeutics using weakly acidic microenvironment-responsive artificial nucleobase

Yui Nemoto, Kunihiko Morihiro, Akimitsu Okamoto
Graduate School of engineering, The University of Tokyo

1P-02 Development of artificial nucleic acids that enable to form triplex DNA for DNA sequences containing 5mCG base pair

Ryotaro Notomi[1)], Shigeki Sasaki[2)], Yosuke Taniguchi[1)]
1) Graduate School of Pharmaceutical Sciences, Kyushu University, 2) Faculty of Pharmaceutical Science, Nagasaki International University

1P-03 Development of a new synthetic method of oligonucleotides using H-phosphonamidate derivatives

Taiki Tsurusaki, Takeshi Wada, Kazuki Sato
Department of Pharmacy, Faculty of Pharmacy, Tokyo University of Science

1P-04 Synthesis of peptide nucleic acid possessing dicationic cytosine derivative

Toru Sugiyama[1)], Shun-suke Moriya[1)], Misaki Yonezu[1)], Yuzu Kondo[1)], Yosuke Demizu[2)], Masaaki Kurihara[3)], Atsushi Kittaka[1)]
1) Faculty of Pharma-Sciences, Teikyo University, 2) Division of Organic Chemistry, National Institute of Health Sciences,
3) Faculty of Pharmaceutical Sciences, Shonan University of Medical Sciences

1P-05 Synthesis of P-modified DNA from boranophosphate DNA as a precursor via acyl phosphite intermediates

Yuhei Takahashi[1)], Takeshi Wada[1)], Kazuki Sato[1)], Yukichi Namioka[1)], Ayumi Igarashi[2)], Rintaro Iwata Hara[3)]
1) Department of Medicinal and Life Sciences, Faculty of Pharmaceutical Sciences, Tokyo University of Science,
2) Department of Medical Genome Sciences, Graduate School of Frontier Sciences, The University of Tokyo,
3) Department of Neurology and Neurological Science, Graduate School of Medicinal and Dental Sciences, Tokyo Medical and Dental University

1P-06 Development of 2-amino-7-deaza-6-vinylpurine-deoxyriboside as a U-selective cross-linker toward miRNA inhibition

Nadya Syahla Soemawisastra[1)2)], Hidenori Okamura[1)2)], Ahmed Mostafa Abdelhady[1)2)], Kazumitsu Onizuka[1)2)], Mamiko Ozawa[1)], Fumi Nagatsugi[1)2)]
1) Institute of Multidisciplinary Research for Advanced Materials, Tohoku University,
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1P-07 Development of a chemically-convertible nucleoside system toward enzymatic amplification of the minor-groove modified DNA

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1P-08 Synthesis and properties of 1'-C, 3'-O-butylene-bridged D-altritol nucleic acid

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Abstract

Invited Lecture

IL-01

Flex-nucleosides – a strategic approach to broad-spectrum antiviral therapeutics

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ABSTRACT

Over the past several decades nucleos(t)ides have maintained a prominent role as one of the cornerstones of antiviral and anticancer therapeutics and many approaches to nucleos(t)ide and nucleic acid drug design have been pursued. One such approach involves flexibility in the sugar moieties of nucleos(t)ides, for example, in the highly successful anti-HIV/HBV drug Tenofovir. In contrast, introduction of flexibility to the nucleobase has only more recently gained significance with the development of our fleximers. This has led to a significant increase in antiviral activity when the parent rigid nucleoside was totally inactive. A brief history of their development, as well as some of our most recent findings for this innovative class of nucleos(t)ides will be described.

INTRODUCTION

Nucleosides represent one of the most important classes of drugs for treating viral infections.[1, 2] For a number of years, the Seley-Radtke group has focused on developing flexible purine base nucleoside analogues termed "fleximers".[3-6] These nucleosides feature a purine ring that is "split" into the imidazole and pyrimidine moieties, with a single carbon-carbon bond between the C4 of the imidazole and the C5 of the pyrimidine (proximal fleximers), or the C5 of the imidazole and the C6 of the pyrimidine (distal fleximers). The analogues retain the hydrogen bonding and stacking elements necessary for nucleoside recognizing enzymes, while allowing for alternative interactions in the enzyme binding site. This inherent flexibility allows for free rotation around the carbon-carbon bond between the two heterocyclic rings, thereby increasing the rotational degrees of freedom and allowing the fleximer to interact with other binding site moieties that were previously unattainable by the parent purine nucleoside.

RESULTS AND DISCUSSION

Due to these unique properties, we have recently applied the fleximer technology to several FDA-approved nucleoside inhibitors in order to create more potent analogues for antiviral therapeutics. For example, Acyclovir (ACV) is an FDA-approved acyclic nucleoside analogue used to treat herpes simplex virus and varicella zoster virus infections.[2] Acyclovir has no activity even up to 1000 mgs/kg against flaviviruses such as Dengue, Zika, and Yellow Fever, as well as against filoviruses such as Ebola and Marburg, or coronaviruses such as SARS-CoV-1 and MERS. In contrast, the analogous fleximers exhibit potent activity (from single digit micromolar to nanomolar levels) against all of those viruses.[3, 4, 7]

Current efforts are focused on SARS-CoV-2/COVID and other viruses. In that regard, we have designed a series of new analogues that are under investigation against a number of viruses as part of our role in the NIH's Antiviral Drug Discovery Centers for Pathogens of Pandemic Concern (AViDD) program.

Following on the success of the flex-acyclovir analogues, we have now designed a number of new scaffolds that further expand the potential of the fleximers to explore additional chemical space. The synthetic routes are based on a combination of literature procedures previously utilized, as well as new approaches developed in our laboratories. Preliminary testing results reveal activity against the aforementioned viruses as well as new viruses such as Epstein-Barr and enteroviruses.

CONCLUSION

Our studies have shown that flexibility in nucleoside drug design can lead to potent antiviral activity, including against unexpected viruses, not previously seen with the parent rigid nucleoside. Moreover, the ability to engage secondary amino acid residues not previously involved in the mechanism of action can allow the drug to maintain activity in the face of resistant mutations, a strategic property particularly in the face of emerging variants.

REFERENCES

1. Seley-Radtke, K. L.; Yates, M. K. The evolution of nucleoside analogue antivirals: A review for chemists and non-chemists. Part 1: Early structural modifications to the nucleoside scaffold. *Antiviral Research* **2018,** 154, 66-86.

2. Yates, M. K.; Seley-Radtke, K. L. The evolution of antiviral nucleoside analogues: A review for chemists and non-chemists. Part II: Complex modifications to the nucleoside scaffold. *Antiviral Research* **2019,** 162, 5-21.

3. Yates, M. K.; Raje, M. R.; Chatterjee, P.; Spiropoulou, C. F.; Bavari, S.; Flint, M.; Soloveva, V.; Seley-Radtke, K. L. Flex-nucleoside analogues - Novel therapeutics against filoviruses. *Bioorganic & Medicinal Chemistry Letters* **2017,** 27, 2800-2802.

4. Peters, H. L.; Jochmans, D.; de Wilde, A. H.; Posthuma, C. C.; Snijder, E. J.; Neyts, J.; Seley-Radtke, K. L. Design, synthesis and evaluation of a series of acyclic fleximer nucleoside analogues with anti-coronavirus activity. *Bioorganic & Medicinal Chemistry Letters* **2015,** 25, 2923-2926.

5. Seley-Radtke, K. Flexibility - not just for yoga anymore! *Antivir Agents Chem Chemother* **2018,** 26, 1-12.

6. Ku, T.; Seley-Radtke, K. Synthetic Approaches to the Fleximer Class of Nucleosides - A Historic Perspective. In 2018; pp 195-235.

7. Thames, J. E.; Waters, C. D., 3rd; Valle, C.; Bassetto, M.; Aouadi, W.; Martin, B.; Selisko, B.; Falat, A.; Coutard, B.; Brancale, A.; Canard, B.; Decroly, E.; Seley-Radtke, K. L. Synthesis and biological evaluation of novel flexible nucleoside analogues that inhibit flavivirus replication in vitro. *Bioorg Med Chem* **2020,** 28, 115713.

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