Curriculum Vitae



Name: Ichiro Hirao

Position: Chief Scientific Officer

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Biography

Ichiro Hirao is Chief Scientific Officer of Xenolis Pte. Ltd. He obtained his Ph.D. from the Chemistry Department at Tokyo Institute of Technology in 1983. From 1984, he worked at the University of Tokyo as a research associate. In 1992, he became an associate professor at Tokyo University of Pharmacy and Life Sciences. In 1995, he moved to Dr. Andrew Ellington's laboratory at Indiana University. Dr. Ellington is a pioneer of nucleic acid aptamers. In 1997, he joined the Japan Science and Technology Agency (JST) as a group leader, to start a new project for genetic alphabet expansion technologies. In 2002, he continued his work as a professor at The University of Tokyo. From 2006 to 2015, he managed a synthetic biology team at RIKEN, where his team established a genetic alphabet expansion technology and a high-affinity DNA aptamer generation method. In 2015, he moved to IBN (IBB), A*STAR in Singapore, with his team member. From 2018 to 2021, he served as the covering executive director at IBN. In April 2022, he founded a startup company, Xenolis Pte. Ltd., in Singapore, together with Michiko Hirao (Kimoto), to commercialize their novel DNA aptamer and unnatural base pair technologies.

Education:

1978 B.Eng.	Department of Industrial Chemistry, Faculty of Engineering, Shizuoka University.
1983 Ph.D.	Department of Chemistry, Faculty of Science, Tokyo Institute of Technology.

Occupation:

1984-1993	Assistant professor, Department of Industrial Chemistry, Faculty of Engineering, The University of Tokyo.
1993-1996	Associate professor, Laboratory of Pharmaceutical Chemistry, Tokyo University of Pharmacy and Life Science.

1995-1997	Associate Scientist, Department of Chemistry, Indiana University
1997-2001	Group Leader, Yokoyama CytoLogic Project, ERAO, Japan Science and Technology Corporation.
2001-2002	Team Leader, Protein Preparation/NMR Facilities, RIKEN Genomic Sciences Center.
2002-2006	Professor, Research Center for Advanced Science and Technology, The University of Tokyo.
2002-2006	Senior Visiting Scientist, Protein Research Group, RIKEN Genomic Science Center.
2006-2007	Team Leader, Protein-Regulating Macromolecules Research Team, Protein Preparation/NMR Facilities, RIKEN Genomic Sciences Center.
2007-2015	President & CEO, TagCyx Biotechnologies
2007-2015	Visiting Professor, Graduate School of Chemical Sciences and Engineering, Hokkaido University
2008-2013	Team Leader, Nucleic Acid Synthetic Biology Research Team, Systems and Structural Biology Center, Yokohama Institute, RIKEN
2012-2015	Visiting Professor, Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology
2013-2015	Team Leader, Synthetic Molecular Biology Team, RIKEN Center for Life Science Technologies
2013-2015	Visiting Professor, Graduate School of Medical Life Science, Yokohama City University
2013-2020	Faculty of 1000, F1000Prime Faculty Member
2015-2021	Team Leader and Principal Research Scientist, Institute of Bioengineering and Nanotechnology (IBN), A*STAR, Singapore
2016-2022	Scientific Reports, Editorial board member in the Chemical Biology region
2018-2020	Covering Executive Director, Institute of Bioengineering and Nanotechnology (IBN), A*STAR, Singapore
2021-2022	Senior Group Leader and Principal Research Scientist, Institute of Bioengineering and Bioimaging (IBB), A*STAR
2022-present	Chief Scientific Officer, Xenolis Pte. Ltd.

Research Interests:
Xenobiology, Chemical Biology, Bioorganic Chemistry, Molecular Biology, Molecular Evolution, Structural Biology, Nucleic acid chemistry and biology

Publications: 116 journal papers, *h*-index: 47 (by Google Scholar Citation)

Main Publication List:
Structural basis of transcription recognition of a hydrophobic unnatural base pair by T7 RNA polymerase. J. Oh, M. Kimoto, H. Xu, J. Chong, **I. Hirao**, D. Wang, *Nat. Commun.,* 14, 195 (2023).

High-affinity five/six-letter DNA aptamers with superior specificity enabling the detection of dengue NS1 protein variants beyond the serotype identification. K. Matsunaga, M. Kimoto,

V.W. Lim, H.P. Tan, Y.Q. Wong, W. Sun, S. Vasoo, Y.S. Leo, **I. Hirao**, *Nucleic Acids Res.*, in press selected as a Breakthrough Article (2021). doi.org/10.1093/nar/gkab515

Genetic Alphabet Expansion Technology by Creating Unnatural Base Pairs.
M. Kimoto, **I. Hirao**, *Chem. Soc. Rev.*, 49, 7602-7626 (2020).

Creation of unnatural base pairs for genetic alphabet expansion toward synthetic xenobiology.
K. Hamashima, M. Kimoto, **I. Hirao**, *Curr. Opin. Chem. Biol.*, 46, 108-114 (2018).

High-Affinity DNA Aptamer Generation Targeting von Willebrand Factor A1-Domain by Genetic Alphabet Expansion SELEX (ExSELEX) using Two Types of Libraries Composed of Five Different Bases. K. Matsunaga, M. Kimoto and **I. Hirao**, *J. Am. Chem. Soc.*, 139, 324-334 (2017).

Structural basis for expansion of the genetic alphabet with an artificial nucleobase pair. K. Betz, M. Kimoto, K. Diederichs, **I, Hirao**, A. Marx, *Angew. Chem. Int. Ed. Engl.,* 56, 12000-12003 (2017).

Generation of high-affinity DNA aptamers using an expanded genetic alphabet.
M. Kimoto, R. Yamashige, K. Matsunaga, S. Yokoyama, **I. Hirao**, *Nat. Biotechnol.*, 31, 453-457 (2013).

Unnatural base pair systems toward the expansion of the genetic alphabet in the central dogma.
I. Hirao, M. Kimoto, *Proc. Jpn. Acad. Ser. B Phys. Biol. Sci.*, 88, 345-367 (2012).

Natural vs artificial creation of base pairs in DNA: origin of nucleobases from the perspectives of unnatural base pair studies.
I. Hirao, M. Kimoto, R. Yamashige, *Acc. Chem. Res.,*45, 2055-2065 (2012).

Site-specific fluorescent probing of RNA molecules by unnatural base-pair transcription for local structural conformation analysis.
Y. Hikida, M. Kimoto, S. Yokoyama, **I. Hirao**, *Nature Protocols*, 5, 1312-1323 (2010).

An unnatural base pair system for efficient PCR amplification and functionalization of DNA molecules.
M. Kimoto, R. Kawai, T. Mitsui, S. Yokoyama, **I. Hirao**, *Nucleic Acids Res.*, 37, e14 (2009).

An unnatural hydrophobic base pair system: site-specific incorporation of nucleotide analogs into DNA and RNA.
I. Hirao, M. Kimoto, T. Mitsui, T. Fujiwara, R. Kawai, A. Sato, Y. Harada, S. Yokoyama, *Nature Methods,* 3, 729-735 (2006).

An engineered *Escherichia coli* tyrosyl-tRNA synthetase for site-specific incorporation of an unnatural amino acid into proteins in eukaryotic translation and its application in a wheat germ cell-free system.
D. Kiga, K. Sakamoto, K. Kodama, T. Kigawa, T. Matsuda, T. Yabuki, M. Shirouzu, Y. Harada, H. Nakayama, K. Takio, Y. Hasegawa, Y. Endo, **I. Hirao**, S. Yokoyama, *Proc. Natl. Acad. Sci. USA*, 99, 9715-9720 (2002).

An unnatural base pair for incorporating amino acid analogs into proteins.
I. Hirao, T. Ohtsuki, T. Fujiwara, T. Mitsui, T. Yokogawa, T. Okuni, H. Nakayama, K. Takio, T. Yabuki, T. Kigawa, K. Kodama, T. Yokogawa, K. Nishikawa, S. Yokoyama, *Nature Biotechnology*, 20, 177-182 (2002).

Unnatural base pairs for specific transcription.
T. Ohtsuki, M. Kimoto, M. Ishikawa, T. Mitsui, **I. Hirao**, S. Yokoyama, *Proc. Natl. Acad. Sci. USA*, 98, 4922-4925 (2001).

Crystal structures of a series of RNA aptamers complexed to the same protein target.
S. Rowsell, N. Stonehouse, M. A. Convery, C. J. Adams, A. D. Ellington, **I. Hirao**, D. S. Peabody, P. G. Stockley, S. E. V. Philips, *Nature Structural Biol*., 5, 970-975 (1998).

Crystal structure of an RNA aptamer-protein complex at 2.8A resolution.
M. A. Convery, S. Rowsell, N. Stonehouse, A. D. Ellington, **I. Hirao**, J. B. Murray, D. S. Peabody, S. E. V. Phillips, P. G. Stockley, *Nature Structural Biol*., 5, 133-139 (1998).

Re-creating the RNA world.
I. Hirao, A. D. Ellington, *Current Biol*., **5**, 1017-1022 (1995).

Most compact hairpin-turn structure exerted by a short DNA fragment, d(GCGAAGC) in solution: an extraordinarily stable structure resistant to nucleases and heat.
I. Hirao, G. Kawai, S. Yoshizawa, Y. Nishimura, Y. Ishido, K. Watanabe, K. Miura, *Nucleic Acids Res.,* 22, 576-582 (1994).

Main patents

Application: High-Affinity and High-Specificity Unnatural-Base DNA Aptamers that Bind Specifically to Dengue NS1 Proteins and their Application in the Detection of Desease-Related IgG antibodies, PCT/SG2020/050342, IBN/P/11210/00/SG (IBN-538 and IBN-539), 13 March 2020.
Inventor: I. Hirao, K. Matsunaga, M. Hirao, W. Sun, Y.S. Leo
Applicant: A*STAR and TTSH

Application: DNA Sequencing Method Including Unnatural Bases for DNA Aptamer Generation by Genetic Alphabet expansion, PCT/SG2019/050597, IBN/P/11087/00/SG (IBN-536), 5 July 2019.
Inventor: I. Hirao, K. Hamashima, M. Hirao,
Applicant: A*STAR

Application: DNA aptamer binds to cancer cell, PCT/JP2016/081517 (2016/10/25): JP
Inventor: Kazunobu Futami, Ichiro Hirao, Michiko Hirao
Applicant: A*STAR (from TAGCyx): IBN/P/12025

Application: DNA aptamer binds to vWF, PCT/JP2016/081518 (2016/10/25): JP
Inventor: Ichiro Hirao, Michiko Hirao, Ken-ichiro Matsunaga
Applicant: TAGCyx

Application: Method for stabilizing DNA aptamer, PCT/JP2016/056805 (WO2016/143700 A1): JP, US, EP, CN, SG
Inventor: Ichiro Hirao, Michiko Hirao, Ken-ichiro Matsunaga
Applicant: TAGCyx

Application: Nucleic acid base pair, PCT/JP00/04720: JP (3893075), US (7,101,992 / 7,667,031), EP (946311.8)
Inventor: Ichiro Hirao, Masahide Ishikawa, Tsuyoshi Fujihara, Shigeyuki Yokoyama
Applicant: TAGCyx

Application: Imidazopyridine derivative, PCT/JP2006/300502: JP (5002851), US (7,615,628), EP (1847546), CN (ZL200680002792.X), HK (1110079)
Inventor: Ichiro Hirao, Shigeyuki Yokoyama
Applicant: TAGCyx

Application: Novel artificial base pair and use thereof, PCT/JP2006/315479: JP, US (8212014), EP (1921141.0), SG (164429), CN (ZL200680029029.6), HK (1120292)
Inventor: Ichiro Hirao, Michiko Hirao, Shigeyuki Yokoyama
Applicant: TAGCyx

Application: Method for replication of nucleic acid and novel artificial base pair, PCT/JP2006/324484: JP (5146957), US (8030478), EP (1970445), KR, SG (167847), CN (200680052596-6), IN, AU (2006323745), HK (1121491)
Inventor: Ichiro Hirao, Shigeyuki Yokoyama
Applicant: TAGCyx

Application: Novel DNA capable of being amplified by PCR with high selectivity and high efficiency, PCT/JP2009/056718: JP (5424414), US (8426569), EP (9728695.9), AU (2009232716), CA, IN, KR, CN, HK
Inventor: Ichiro Hirao, Michiko Hirao, Shigeyuki Yokoyama
Applicant: TAGCyx/Riken

Application: Novel artificial fluorescent bases, PCT/JP2010/067989: JP (2011-535487, US (13/500.303), EP (10822158.1), HK (13101612.1), CN (201080055369.2), IN (3903/CHENP/2012)
Inventor: Ichiro Hirao, Michiko Hirao, Shigeyuki Yokoyama, Tsuneo Mitsui
Applicant: TAGCyx/Riken (CN and IN are in waiver of patent right)

Application: Artificial base pair capable of forming specific base pair, PCT/JP2010/067560: JP (2011-535429), US (8895712, EP (10822055.9), CN (201080055375.8), IN (3857/CHENP/2012)
Inventor: Ichiro Hirao, Michiko Hirao, Shigeyuki Yokoyama
Applicant: TAGCyx/Riken (CN and IN are in waiver of patent right)

Application: Nucleic acid base analog with quenching characteristics and fluorescence and application thereof, PCT/JP2011/060343: JP (2012-511735), US (13/642111), EP (11772132.4), HK (13107136.5)
Inventor: Ichiro Hirao, Michiko Hirao, Shigeyuki Yokoyama, Tsuneo Mitsui, Rie Yamashige
Applicant: TAGCyx/Riken

Application: Method for preparing nucleic acid aptamer, PCT/JP2012/070188: JP (2013-528982), US (14/237645), EP (12824560.2), CA, AU, CN

Inventor: Ichiro Hirao, Michiko Hirao, Shigeyuki Yokoyama
Applicant: TAGCyx/Riken (CA, AU and CN are in waiver of patent right)

Application: Activation of functional nucleic acid by specific modification, PCT/JP2012/076911: JP (2013-539680), US (14/352884), EP
Inventor: Ichiro Hirao, Michiko Hirao, Shuang Liu, Iwao Nozawa
Applicant: TAGCyx/Riken

Application: Nucleic acid fragment binding to target protein, PCT/JP2012/079611: JP, US, EP, CN, HK, SG, CA, KR, AU
Inventor: Ichiro Hirao, Michiko Hirao, Shigeyuki Yokoyama, Rie Yamashige
Applicant: TAGCyx/Riken

Application: Aptamers for the detection of cytokines and their potential as cytokine inhibitors, JP (2015-045266)
Inventor: Ichiro Hirao, Michiko Hirao, Kenichiro Matsunaga
Applicant: TAGCyx