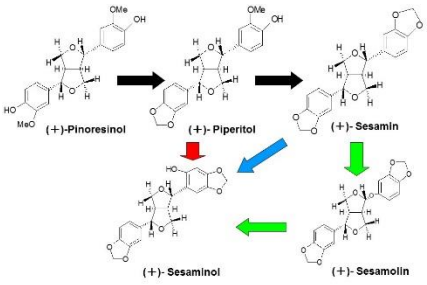
Research Area: Biological Molecular Chemistry
Research Specialization: Forest Biomass Chemistry
Name: KATAYAMA, Takeshi

Keywords: Wood, Lignan, Suberin, Bioactivity, Organic chemistry

Recent Research

1. Stereochemistry and Biosynthesis of Lignans

Lignans and neoolignans are dimers of phenylpropanes and generally have optical activity. They are present in the heartwood, bark, roots, leaves, and seeds of higher plants. They have various bioactivities and are attracting attention as medicines and health foods. We study the stereochemistry and biosynthesis of neolignans of *Eucommia ulmoides* and *Saururus chinensis* and functional lignans of sesame seeds (right figure).



Proposed biosynthetic pathway of sesaminol

2. Chemistry of Suberin in Outer Bark

Suberin is the main component of the cork tissue in outer bark (right picture) and of the wound-healing layers of potato tubers. It contributes to their functions (prevention of evaporation of water, protection against injury and pathogens, etc.). Its chemical structure is a complex three-dimensional heteropolymer composed of an aliphatic domain and an aromatic domain. The latter structure is much more unclear than that of the former, especially the structure of the outer bark is poorly studied. We focus on the fact that the suberin aromatic domain has a ferulic acid ester structure, unlike lignin.

3. Bioactive Components from Tropical Forest

A wide variety of tropical trees contain a wide variety of extractives. From these, we are exploring ingredients that have biological activities such as antioxidant and antifungal. Antioxidant lignans were obtained from seeds of Jatropha (right picture), a plant for biodiesel fuel.

4. Biomass Utilization of Indonesian Fast-growing Trees

In Southeast Asia, fast-growing trees such as falcata (right picture), eucalyptus, acacia, etc. are planted and supplied to the production of wood-based materials and paper. Using falcata waste wood, we are studying liquefaction and subsequent plasticisation, and pretreatment for bioethanol / biobutanol production.

Publications

・Syahidah, Katayama T., Suzuki, T., Asada, Y., Ohtani, Y., and Ohmura, W.: Antitermite and antifungal activities of *Vitex cofassus* heartwood. *Journal of the Forest Biomass Utilization Society*, **10** (2), 55-61, 2015.

・Andrianto, D., Katayama, T., and Suzuki, T.: Screening of Antioxidant and Antihyperlipidemic Potencies of Indonesian Underutilized Fruits. *Journal of the Forest Biomass Utilization Society*, **10** (1), 19-25, 2015.

・Lourith, N. Katayama T., Suzuki, T.: Biosynthesis of a syringyl 8-*O*-4' neolignan in *Eucommia ulmoides*: formation of syringylglycerol-8-*O*-4'-(sinapyl alcohol) ether from sinapyl alcohol. *Journal of Wood Science* **51**, 379-386.

Research Area: Bioresource & Functional Chemistry
Research Specialization: Plant Biochemistry
Name: KATO Hisashi

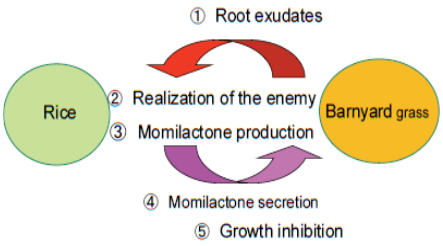
Keywords：**Allelopathy**，**Allelochemical, Tropical and subtropical plants**

Research topics: Allelopathy

The negative impacts of commercial herbicide use on the environment make it desirable to diversify weed management options. Many investigations have been attempted to exploit allelopathy of plants for weed control purposes in a variety of agricultural settings, since allelopathy is regarded as the direct influence of an organic chemical released from one living plant on the growth and development of other plants.

We have been extensively studied with respect to plant allelopathy as part of a strategy for sustainable weed management. We have already found and isolated several allelopathic substances from various plant sources and determined their chemical structures. We also try to understand the mode of action of the allelopathic substances for their biological activities by biochemical techniques such as protein, enzyme and gene levels.

We isolated new allelopathic substances



The chemical-cross talk between rice and barnyard grass

One of our students got the best oral presentation award on International Conference.

Publications

- Kato-Noguchi, H., Nakamura, K., Ohno, O., Suenaga, K., and Okuda, N.: Asparagus decline: autotoxicity and autotoxic compounds in asparagus rhizomes. Journal of Plant Physiology 213: 23–29 (2017).
- Kato-Noguchi, H.: Allelopathic chemical interaction of bryophytes with vascular plants. Mini-Reviews in Organic Chemistry 13: 422 - 429 (2016).
- Kato-Noguchi, H., Saito, Y., Ohno, O. and Suenaga, K.: A phytotoxic active substance in the decomposing litter of the fern *Gleichenia japonica*. Journal of Plant Physiology 176: 55-60 (2015).
- Kato-Noguchi, H., Salam, M.A., Ohno, O. and Suenaga, K.: Nimbolide B and nimbic acid B, phytotoxic substances in neem leaves with allelopathic activity. Molecules 19: 6929-6940 (2014).
- Kato-Noguchi, H., Ai Kobayashi, A., Ohno, O., Kimura, F., Fujii, Y. and Suenaga, K.: Phytotoxic substances with allelopathic activity may be central to the strong invasive potential of *Brachiaria brizantha*. Journal of Plant Physiology 171: 525-530 (2014).
- Kato-Noguchi, H. and Peters, R.J.: The role of momilactones in rice allelopathy. Journal of Chemical Ecology 39:175-185 (2013).

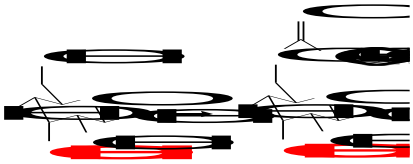
Research Area: Biological Molecular Science
Research Specialization: Synthetic Organic Chemistry
Name: KAWANAMI, Yasuhiro

Keywords: rare sugar, biological activity, asymmetric catalyst, aplysiatoxin, anti-cancer

Recent Research

1. Synthesis and Biological Evaluation of Rare Sugar Derivatives

Rare sugar is a monosaccharide that exists only in trace amounts in nature and has been shown to have various biological activities by our research on rare sugars. In order to further improve the biological activity of D-allose, which is an epimer at the C-3 position of D-glucose, we have synthesized D-allose fatty acid esters having a hydrophobic linear alkyl group from hydrophilic D-allose and are studying on structure-activity relationship of their plant growth inhibitory activity and cancer cell proliferation inhibitory activity.



2. Synthesis of optically active alcohols using asymmetric catalyst derived from amino acid

So far we have synthesized a natural amino acid derivative and developed an asymmetric borane reduction reaction of ketone using them as an asymmetric catalyst and demonstrated that the reaction proceeds with high stereoselectivity in asymmetric reduction of many aromatic ketones. At present, we are working on asymmetric reduction of trifluoromethyl ketone with low stereoselectivity due to high reactivity.

3. Function-Oriented Synthesis of Aplysiatoxin Simplified Analogs

Marine natural products, aplysiatoxin has tumor-promoting activity and cancer cell proliferation inhibitory activity. To develop novel anti-cancer agents with reduced side effects, we designed simplified analogs that eliminate tumor-promoting activity and evaluate their binding ability with kinase C playing an important role in intracellular signal transduction.

Publications

Synthese and biological activities of deoxy-D-alloses fatty acid ester analogs, *Biosci. Biotechnol. Biochem*., **88** (4), 676-681, 2016, Chowdhury, M. T. I., Naito, M., Yanagita, R. C., Kawanami, Y.

Binding mode prediction of aplysiatoxin, a potent agonist of protein kinase C, through molecular simulation and structure-activity study on simplified analogs of the receptor-recognition domain, *Bioorg. Med. Chem*., **24**, 4218-4227, 2016, Ashida, Y., Yanagita, R. C., Takahashi, C., Kawanami, Y., Irie, K.

Effect of BF_3 on the enantioselective reduction of trifluoromethyl ketones using a chiral lactam alcohol with borane, *Terahedron: Asymmetry*, **26**, 333-337, 2015, Harauchi, Y., Takakura, C., Furumoto, T., Yanagita, R. C., Kawanami, Y.

Anti-proliferative Activity of 6-*O*-Acyl-D-Allose against the Human Leukemia MOLT-4F Cell Line, *Biosci. Biotechnol. Biochem*., **78** (2), 190-194, 2014, Yanagita, R. C., Kobayashi, K., Ogawa, C., Ashida, Y., Kawanami, Y.

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Research Area: **Biological Molecular Chemistry**
Research Specialization: **Bioactive Natural Products Chemistry**
Name: **SATO, Masashi**

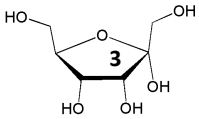
Keywords: Biologically active substance, *C. elegans*, Rare sugar, Anti-aging

Recent Research

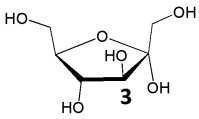
1. Exploration of anti-aging rare sugars

Restriction of calorie intake is known to prolong the life span of various experimental animals. Even in humans, calorie restriction retards the onset of age-related diseases such as diabetes and cancer, and as a result it is thought to prolong life span. We thought that rare sugars having a metabolic suppression effect would make the body calorie restricted and prolong the life of the animal. We conducted the research using the nematode *Caenorhabditis elegans*, a model animal of aging research, and have reported that the rare sugar D-allulose (a stereoisomer of D-fructose) extended the lifespan of *C. elegans*. Currently, we are working on searching for novel anti-aging substances from over 50 kinds of rare sugars and their derivatives, and are developing screening methods to find active substances conveniently and quickly.

C. elegans



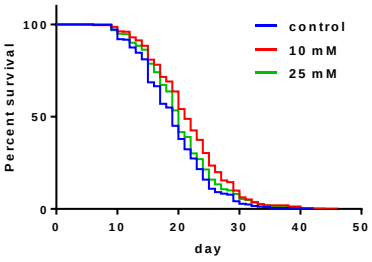
D-Allulose



D-Fructose

2. Mechanism of the anti-aging effect of rare sugars

We are working on elucidating the mechanism of action of rare sugar anti-aging effect by biochemical, molecular biological techniques, and bio-organic chemical approaches such as derivatives synthesis.



Lifespan extending effect of D-allulose

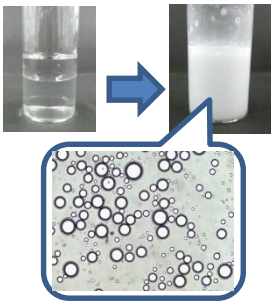
- Sato, M. et al.: Potential anthelmintic: D-psicose inhibits motility, growth and reproductive maturity of L1 larvae of *Caenorhabditis elegans*. J. Nat. Med.,62, 244-246, (2008).
- Sato, M. et al.: D-Ribose competitively reverses inhibition by D-psicose of Larval growth *in Caenorhabditis elegans*. Biological and Pharmaceutical Bulletin 32, 950-952 (2009) .
- Sato, M., et al.: Structural characteristics for superoxide anion radical scavenging and productive activities of green tea polyphenols including proanthocyanidin dimers. Chemical and Pharmaceutical Bulletin 58, 98-102 (2010).
- Sakoguchi, H. et al.: Growth inhibitory effect of D-arabinose against the nematode *Caenorhabditis elegans*: Discovery of a novel bioactive monosaccharide, Bioorg. Med. Chem. Lett., 26 726-729 (2016).
- Sakoguchi, H. et al.: Screening of biologically active monosaccharides: growth inhibitory effects of D-allose, D-talose, and L-idose against the nematode *Caenorhabditis elegans*, Biosci. Biotechnol. Biochem., 80 1058-1061 (2016).

Research Area: Biological Molecular Chemistry
Research Speciality: Biophysical Chemistry & Colloid Science
Name: FUKADA, Kazuhiro

Key words : surfactant, emulsion, bio-colloids, phase transition, rare sugar

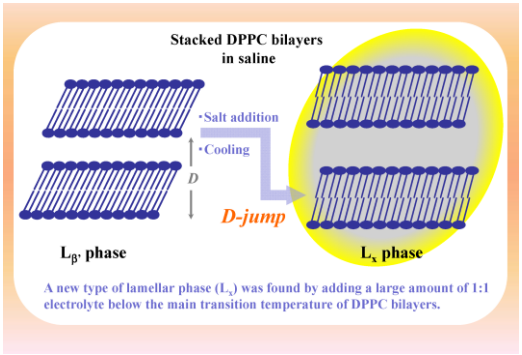
Recent Research

1. Protein-based O/W emulsions



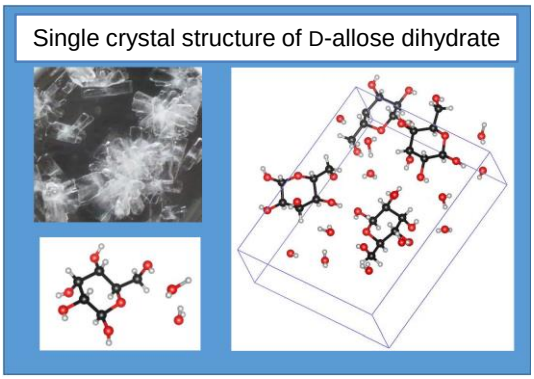
The oil-in-water (O/W) emulsions are aqueous liquids containing dispersed small oil droplets (usually < 10 μm diameter) . A large variety of industrial products such as processed-foods, medicines, pesticides, and cosmetics are produced as O/W emulsions. To prepare fairly stable emulsions, it is crucial to add some amphiphilic material as an emulsifier. We are studying on emulsifying properties of proteins (whey or egg white proteins, casein, and so on) to understand formation and stabilization mechanisms of small oil droplets in protein solutions by the emulsification processes.

2. Molecular assemblies of aqueous amphiphiles



When amphiphilic materials such as surfactants or phospholipids are mixed with water, they spontaneously form molecular assemblies, i.e., micelles or multi-lamellar vesicles, both of which are classified as associate colloidal system. In our laboratory, physico-chemical aspects on these colloids are studied focusing on the geometry of the molecular assemblies and effects of temperature and additives (salts, alcohols, and sugars) for the formation of assemblies.

3. Physico-chemical properties of rare sugars



Rare sugars are monosaccharides rarely existing in nature. Some of rare sugars, for example D-allulose, are recently found to have biological activities with benefit, and broad range of studies including molecular structure and rheological, spectroscopic, and thermodynamic properties in solution have been in progress. We are studying on basic phsico-chemical properties of rare hexoses to understand why living organisms did not select rare hexoses, but D-glucose and D-fructose, in their metabolisms.

Click here for more information

Publications

- A. Yoshihara, M. Sato, K. Fukada. Evaluation of the Equilibrium Content of Tautomers of Deoxy-ketohexoses and their Molar Absorption Coefficient of the Carbonyl Group in Aqueous Solution. *Chem. Lett.*, **45**, 113-115 (2016).
- T. Kozakai, K. Fukada, R. Kuwatori, T. Ishii, T. Senoo, K. Izumori. Aqueous Phase Behavior of the Rare Monosaccharide D-Allose and X-ray Crystallographic Analysis of D-Allose Dihydrate. *Bull. Chem. Soc. Jpn.*, **88**, 465-470 (2015).
- K. Fukada. Effects of Addition of Amphiphilic Molecules on the Dispersion Stability of Colloidal Systems. *Oleoscience*, **16**, 51-56 (2016). (in Japanese)
- N. Cheetangdee, K. Fukada, Emulsifying activity of bovine β-lactoglobulin conjugated with hexoses through the Maillard reaction. *Colloids Surfaces, A*, **450**, 148-155 (2014).

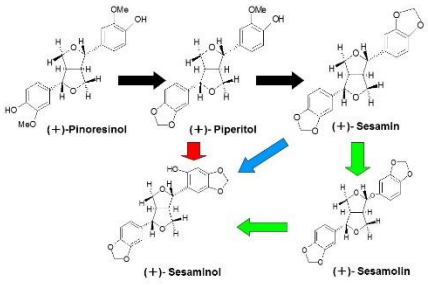
Research Area: Biological Molecular Chemistry
Research Specialization: Biomass Chemistry
Name: SUZUKI, Toshisada

Keywords：**Wood, Extractives, Bioactive substances, Biomass, Chemistry**

Resent research

1. Stereochemistry and Biosynthesis of lignans

Lignan exists to conifer and broadleaf tree heartwoods. It has the C6-C3-C3-C6 frame which consist of two phenyl propane unit (C6-C3) bounds. They are often exist as the glucoside in plants and shows optical activities. In the medical field, some of them are paid attention as bioactive substances. We investigate stereochemistry and biosynthesis of sesamin in sesame seeds, and lignans contained in *Eucommia ulmoides* and *Saururus chinensis.*



Proposed biosynthetic pathway of sesaminol

2. Chemistry of bark compounds

Suberin is one of the main components in outer bark of woody plants, wound surface of higher plants and periderm of underground organs. The plant biopolymer provides resistance against water loss, and is proposed to be a defensive barrier against invasion by bacteria, fungi and insect. The structure of suberin is expected to be composed of an aliphatic domain and an aromatic domain. While the structure and composition of the aliphatic domain are well investigated, those of the aromatic domain are unclear. We investigate the chemical structure and biosynthesis of the aromatic domain of suberin in outer bark of woody plants.

3. Bioactive substances of tropical trees

In tropical and subtropical regions, wide variety of plants are valuable genetic resources to provide bioactive constituents. Our current studies on isolation and identification of extractives of some Indonesian trees and their biological activity have been conducted in collaboration with some Indonesian researchers.

4. Fast-growing trees in Indonesia

In Indonesia, fast-growing trees such as falcata, acacia and eucalyptus have been planted for production of wood-based materials, pulp and paper. We investigate on effective utilization of waste wood and bark of the fast-growing trees.

Publications

Suzuki, *et al.*: Antioxidative catechol lignans/neolignans isolated from defatted kernel of *Jatropha curcas*. *Journal of Wood Science* 62, 339-348 (2016)

Suzuki, *et al.*: Extractives from Spanish Cherry and their Antioxidant Activity. *Journal of the Forest Biomass Utilization Society* 9, 57-60 (2014)

Suzuki, *et al.*: Furanoditerpenes from *Arcangelisia flava* (L.) Merr. and their antifungal activity. *Phytochemistry Letters* 4, 333-336 (2011)

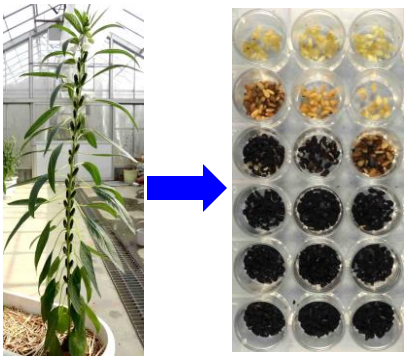
Research Area: Biological Molecular Chemistry
Research Specialization: Functional Phytochemistry
Name: FURUMOTO, Toshio

Key words: natural product chemistry, plant, chemical structure, biosynthesis, bioactivity

- ## Recent research

- ## 1. Secondary metabolites produced by plants

- Plants possess the ability to produce a variety of secondary metabolites (natural products). Our laboratory has carried out the isolation, structure determination, quantitative analysis, research for biosynthetic pathway and production mechanism, etc., about several plat secondary metabolites.
- For example, sesame seeds have been considered a valuable health food, and it is assumed that black seeds are more effective as health food than white seeds in Asia. Assay-guided fractionation of the extract from black seeds led to the isolation of a characteristic antioxidant that had a potent radical scavenging activity. Quinones are characterized by two carbonyl groups on a fully unsaturated ring and have various biological activities and wide utility. We isolated and elucidated the structures of many naphthoquinone and anthraquinone derivatives in *Sesamum indicum* roots and hairy roots. Moreover, the biosynthetic relationship among these quinone derivatives is under investigation.



- ## 2. Plant growth regulators in rhizoshere

- Plants produce and accumulate many organic compound in the roots, and the substances secreted or released from the roots affect other living organisms. We recently isolated a novel germination stimulant for the seeds of root parasitic weeds from sunflower root exudates.

Publications

• Furumoto, T. et al. (2003). Anthrasesamones from roots of *Sesamum indicum*. Phytochemistry 64: 863-866.

• Furumoto, T. et al. (2011). Biosynthetic origin of 2-geranyl-1,4-naphthoquinone and its related anthraquinone in a *Sesamum indicum* hairy root culture. Phytochemistry 72: 871-874.

• Furumoto, T. et al. (2012). Effect of chloride ions on anthrasesamone C production in a *Sesamum indicum* hairy root culture and identification of the precursor for its abiotic formation. Biosci. Biotechnol. Biochem. 76: 305-308.

• Furumoto, T. et al. (2016). Identification of a characteristic antioxidant, anthrasesamone F, in black sesame seeds and its accumulation at different seed developmental stages. Biosci. Biotechnol. Biochem. 80: 350-355.

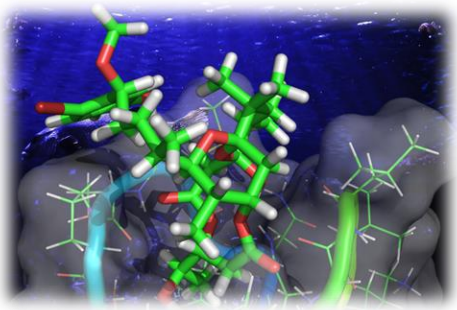
• Ueno, K. et al. (2014). Heliolactone, a non-sesquiterpene lactone germination stimulant for root parasitic weeds from sunflower. Phytochemistry 108: 122-128.

Research Area: Biological Molecular Chemistry
Research Specialization: Chemical Biology
Name: YANAGITA, Ryo C.

Keywords : Natural product, tumor promoter, analog synthesis

Recent Research

1. Development of simplified analogs of naturally-occurring tumor promoters



Tumor promoters are compounds which enhance tumorigenesis in cells initiated by a carcinogen. Recently, design and synthesis of simplified analogs of naturally-occurring tumor promoters with desirable therapeutic effects including anticancer effect have been reported.

We are currently studying on the development of simplified analogs of aplysiatoxin, a polyacetate isolated from sea hare, and thapsigargin, a sesquiterpene lactone isolated from Apiaceae plant, being synthetically accessible and having less side effect.

2. Screening of new protein kinase C ligands with anti-proliferative activity

Protein kinase C (PKC) is a family of serine/threonine kinase that involves in many cellular function, and are attracted as potential therapeutic target for the treatment of cancer, Alzheimer's disease, and AIDS.

We are searching for new PKC ligands from plant sources by an assay using synthetic PKC C1 peptides.

3. Development of biologically active derivatives of naturally-rare monosaccharide

Several of naturally-occurring monosaccharides are found to exhibit biological activities including anti-cancer activity. We currently focus our attention on the development of rare monosaccharide derivatives with "unnatural" moiety to improve their cell permeability and biological activities.

Publications

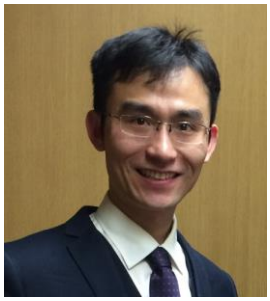
Ueno, S., *et al.* Identification and Biological Activities of Bryostatins from Japanese Bryozoan. *Biosci. Biotechnol. Biochem.* **2012**, *76*, 1041–1043.

Yanagita, R. C., *et al.* Effects of the methoxy group in the side chain of debromoaplysiatoxin on its tumor-promoting and anti-proliferative activities. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 4319–4323.

Yanagita, R. C., *et al.* Anti-proliferative activity of 6-*O*-acyl-D-allose against the human leukemia MOLT-4F cell line. *Biosci. Biotechnol. Biochem.* **2014**, 78, 190–194.

Ashida, Y., *et al*. Binding mode prediction of aplysiatoxin, a potent agonist of protein kinase C, through molecular simulation and structure–activity study on simplified analogs of the receptor-recognition domain. *Bioorg. Med. Chem*. **2016**, *24*, 4218–4227.

Research Area: Biological Molecular Chemistry
Research Specialization: Rare sugar organic chemistry
Name: KONG, Lingbing

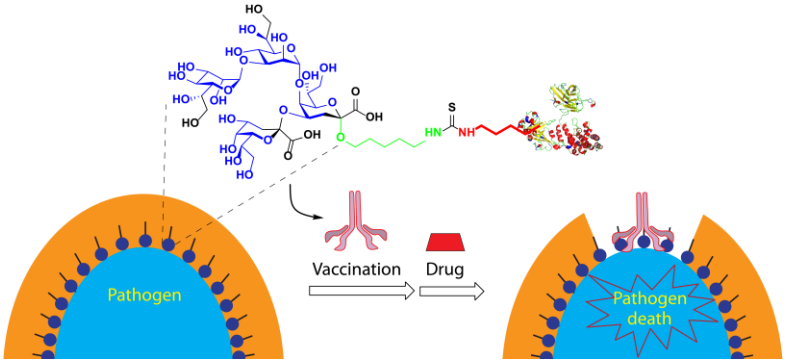


Keywords：sugars, rare sugars, organic chemistry, sugar transporters

Recent Research

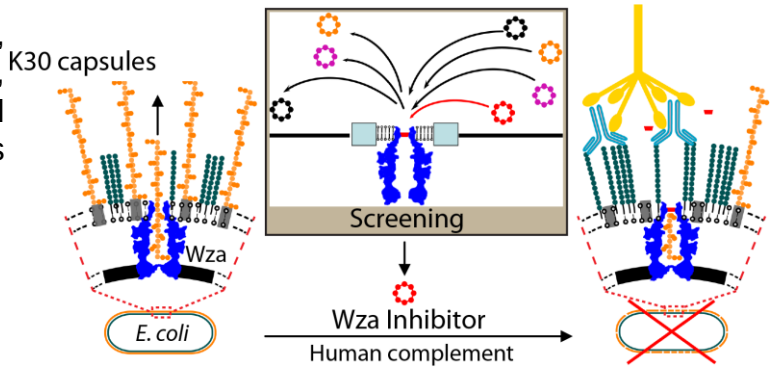
1. Rare sugar production

We use organic chemistry to strengthen rare sugar production with a combinational technology of sugar enzymology and sugar chemistry



2. Functional analysis of sugar transporters

We analyse sugar transporters, especially those related to rare sugars, with single-molecule electrical channel recording to allow functional analysis and development of novel therapeutics.



Publications

・A monodisperse transmembrane α-helical peptide barrel, *Nature Chemistry*, 9, 411-419, 2017, Kozhinjampara R. Mahendran, Ai Niitsu, **Lingbing Kong**, Andrew R. Thomson, Richard B. Sessions, Derek N. Woolfson and Hagan Bayley

・Chemical polyglycosylation and nanolitre detection system enables single-molecule recapitulation of bacterial sugar export, *Nature Chemistry*, 8, 461-469, 2016, **Lingbing Kong**, Andrew Almond, Hagan Bayley and Benjamin G. Davis

・An antibacterial vaccination strategy based on a glycoconjugate containing the core lipopolysacchride tetrasaccharide Hep_2Kdo_2, *Nature Chemistry*, 8, 242-249, 2016, **Lingbing Kong**, Balakumar Vijayakrishnan, Michael Kowarik, Jin Park, Alexandra N. Zakharova, Larissa Neiwert, Amirreza Faridmoayer and Benjamin G. Davis

・Single-molecule interrogation of a bacterial sugar transporter allows the discovery of an extracellular inhibitor, *Nature Chemistry*, 5, 651-659, 2013, **Lingbing Kong**, Leon Harrington, Qiuhong Li, Stephen Cheley, Benjamin G. Davis and Hagan Bayley.