## 理工学研究所 国際交流・公開研究セミナー

Prof. SHING Tony Kung Ming (香港, The Chinese University of Hong Kong)が来日される機会に、最近その応用が注目されている移送たんぱく質阻害剤について、基礎となる糖類の性質と天然物化学に関してご講演をお願いしました。是非ご参集ください。

題 目: From Sugars to Carbocyclic SGLT2 Inhibitors

講演者: Prof. SHING Tony Kung Ming

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日 時: 2018年07月24日(火曜) 16:30-18:00

場 所: 中央大学 後楽園キャンパス 6号館 4階 6429 号室

## アブストラクト:

Type 2 diabetes mellitus (T2DM) or noninsulin-dependent DM, is the most common type of diabetes. The number of patients suffering from T2DM is expected to be 380 million by2025. Unfortunately, current therapeutic agents are not so effective that only less than 36% of the patients have been treated satisfactorily. Selective inhibition of the transporter protein sodium-glucose cotransporter 2 (SGLT2) has emerged as a promising way to control blood glucose level in diabetes patients. Thus, novel small-molecule carbohydrate mimics as potential antidiabetic agents to supplement the existing medication has been investigated by us and others. In this lecture, the design, syntheses, and structure-activity relationship (SAR) studies of a novel class of transporter protein inhibitors will be presented. They are carbasugars, readily available from inexpensive D-gluconolactone, which contain a metabolically stable "glycosidic" C-O bond. We also prepared

their aza-analogues (with a C-N bond) to provide important insights into the structure-activity relationship (SAR) of these inhibitors, thereby aiding the development of carbasugar SGLT2 inhibitors as potential antidiabetic and antitumor agents. Target oxygen-carbasugars and amino-carbasugars, the carbocyclic analogues of sergliflozin and dapagliflozin, contain a C-O and C-N bond, respectively, were accessed via a key stereoselective palladium or ruthenium catalyzed allylic substitution or arylation.

Potential antidiabetic agent

OMe

Allylic substitution

HO

OH

OH

Pseudo-sergliflozin

IC<sub>S0</sub> (SGLT1) = >500000 nM
IC<sub>S0</sub> (SGLT2) = 2.45 nM

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