創価大学

糖鎖生命システム融合研究所 臨時コロキウム

Cell-based Mucin Array for Discovery and Characterization of Mucinase and Glycan-Binding Modules

講師

成松 由規 先生

デンマーク・

コペンハーゲン大学

日付：9 月 4 日（月）
時間：15時00分～16時30分
場所：E203 教室

講演概要

Mucins arguably represent the last frontier in the analytics of glycoproteins. Most mucins are extremely large and heterogeneous glycoproteins that are resistant to conventional glycoproteomics strategies dependent on proteolytic fragmentation and sequencing. Currently, there are no methods for obtaining human mucin molecules in reasonable purity with defined glycans, and this is a fundamental barrier and limitation for studies of mucins and their complex biology, particularly for the microbiome field. We therefore sought to capture the molecular cues contained in the tandem repeat regions (TRs) of human mucin and mucin-like *O*-glycodomains and enable molecular dissection of these cues by developing a glycoengineered cell-based platform for the display and production of representative mucin TRs with defined *O*-glycans. This cell-based mucin array enables molecular dissection of microbial interactions with the mucin TR sequence and the *O*-glycan structures attached independently. We discovered that mucin TR reporters with around 200 amino acids could be produced as rather homogeneous molecules with near full *O*-glycan occupancies and distinct custom-designed *O*-glycan structures, which enabled us to characterize these reporters (at least for the simplest glycoforms) by intact mass spectrometry. Display of these reporters on the cell surface provides the first cell-based display of the human mucins and we used this to probe and dissect the binding specificities of microbial adhesins, influenza virus as well as Siglecs. We discovered that these adhesins show highly distinct binding preferences for *O*-glycan patterns displayed on distinct mucin TRs, providing a new level of complexity and diversity to interactions with the mucin glycome. We showed that the mucin display platform is ideal for the discovery and exploration of mucin-degrading enzymes, and we discovered a small mucin-binding module X409 on the mucinase StcE. Probing the X409 module with the cell-based mucin TR display revealed that this module bound to select human mucin TRs and for example not to the MUC1 TR, and interestingly the binding to these mucin TRs was not dependent on particular *O*-glycan structures. The X409 mucin-binding module provides a novel concept for selective binding to mucins without requiring particular *O*-glycan structures.

問い合わせ先

伊藤和義：kazuyoshi★soka.ac.jp

研究所HP：https://www.soka.ac.jp/glycan/

メールアドレスの★を半角@に変えてください。