

MUCIN GLYCANS AS REGULATORS OF PATHOGEN VIRULENCE

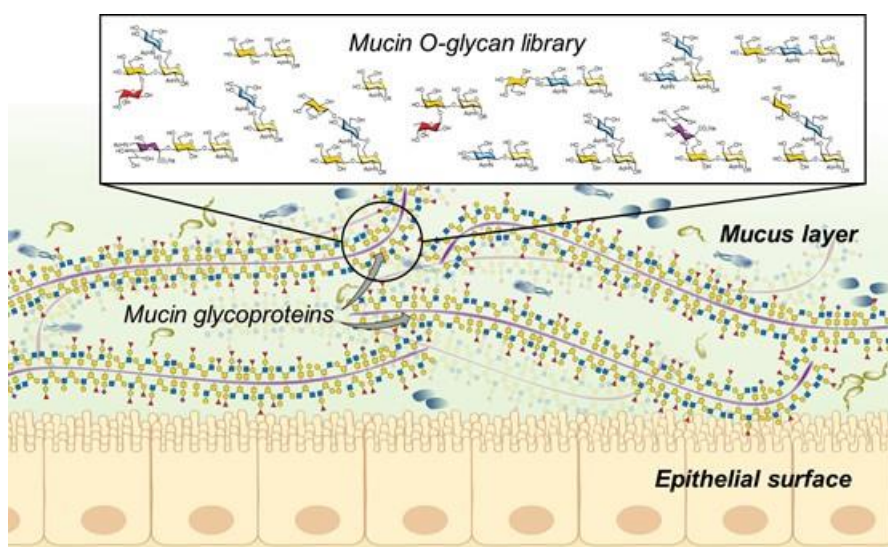
Rachel Hevey, Alem Storani, Carmen R. Cori, Victoria Susan, Haris Majstorović

Dept. Pharmaceutical Sciences, University of Basel, Klingelbergstrasse 50,
4056 Basel, Switzerland
rachel.hevey@unibas.ch

The mucosal barrier is well-established to play an important role in microbiome development and as a first line of host defense. Although this has traditionally been attributed to the physicochemical properties of mucus, several recent reports indicate that mucin glycoproteins and their associated glycans can regulate gene expression and are capable of attenuating virulence in diverse, cross-kingdom pathogens, including Gram-positive bacteria, Gram-negative bacteria, and fungi.

With mucins displaying several hundred distinct glycan structures, we sought to identify specific glycans responsible for this novel gene regulation. Individual mucin O-glycan structures are not commercially available, are not amenable to automated synthesis, and given their overlapping physical and chemical properties cannot be isolated as pure compounds from natural sources using current technologies.

Therefore, we have been developing routes [1,2] to obtain a library of individual mucin glycan structures in sufficient quantity (>30 mg) for extensive functional analysis (see Figure; adapted from [2]). With a diverse mucin glycan library in-hand, we have been working with collaborators to identify specific structures with anti-virulence activity [3,4], and in more recent work have begun to elucidate their discrete mechanisms-of-action.



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