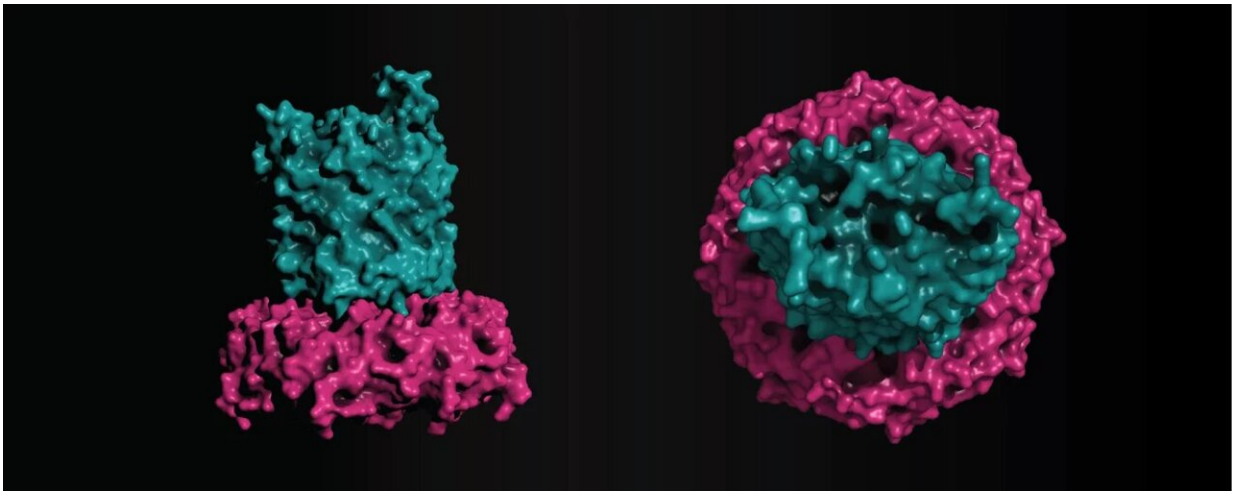
Scientists discover a new mechanism for bacterial polysaccharide export

August 29 2022



Structural model of the composite OPX/β-barrel translocon in the EPS pathway in Myxococcus xanthus consisting of a part… [more] Credit: Max Planck Institute for Terrestrial Microbiology/Schwabe

In Gram-negative bacteria, which include some of the most devastating human pathogens, just two mechanisms for the export of polysaccharides have been identified so far. Now a Max Planck research team led by Lotte Søgaard-Andersen has identified an entirely novel third mechanism for how polysaccharides are exported. These findings, published in *mBio*, pave the way toward a complete understanding of the mechanisms that mediate the protection, motility and interaction of many bacterial pathogens.

Bacteria not only thrive on sugar as a carbon and energy source—they also produce and secrete a wide variety of so-called polysaccharides. Polysaccharides are strings of sugars and are the most abundant biopolymers on earth. The long sugar chains play vital roles in free-living, commensal, and pathogenic bacteria. They are also crucial for bacterial protection, sheathing the cells against environmental stresses such as desiccation, immune effectors, and predators. In addition, their adhesive and structural functions contribute to surface colonization and biofilm formation. They are also important for the successful application of anti-bacterial vaccines. Thus, they hold the keys to understanding and controlling both beneficial and pathogenic human, animal- and plant-microbe interactions. And last but not least, polysaccharides are used in the food, pharmaceutical and medical industries.

Polysaccharide export is a major challenge because the molecules are chemically diverse and very large. In Gram-negative bacteria, only two mechanisms for export of polysaccharides have been known so far: an outer membrane OPX protein (in the so-called Wzx/Wzy- and ABC transporter-dependent pathways), and an outer membrane β-barrel protein (in the so-called synthase-dependent pathways). Yet there are examples of pathways that do not seem to follow these simple schemes: In particular, in some Wzx/Wzy-pathways, outer membrane β-barrel proteins were known to be important for polysaccharide export, for instance in Vibrio cholerae and Myxococcus xanthus, but the exact mechanism was unclear. In addition, other studies describe short OPX proteins that lack the part that integrates into the outer membrane. Here, it is unclear how these proteins could support polysaccharide export.

A research team at the Max-Planck-Institute for Terrestrial Microbiology led by Lotte Søgaard-Andersen was able to shed new light on these questions. Using experiments and computational structural biology, the scientists provide evidence for an entirely novel mechanism for how bacteria can export polysaccharides across the outer membrane.

Johannes Schwabe, a graduate student and lead author of the study, and Dr. María Pérez-Burgos say, "We started by taking a close look at the Wzx/Wzy-dependent pathway for the synthesis of a secreted polysaccharide called EPS in M. xanthus."

According to current knowledge, EPS would be secreted across the outer membrane by an OPX protein that is integrated into the membrane. However, the group found that an outer membrane β-barrel protein named EpsX is also important for EPS export. "Then, surprisingly, we discovered a corresponding periplasmic short OPX protein EpsY that completely lacks the part to span the outer membrane. Together with Dr. Timo Glatter, we also found that EpsX and EpsY directly interact."

Based on their observations and computational structural biology, the scientists propose that EpsX and EpsY represent a novel type of translocon for polysaccharide export across the outer membrane, where a β-barrel protein functions explicitly as the outer membrane-spanning part in a bipartite complex with an entirely periplasmic OPX protein.

According to Lotte Søgaard-Andersen, this detailed knowledge might open up new ways of controlling pathogenic bacteria. She explains, "Marco Herfurth, a graduate student in my research group, found using computational genomics that similar composite systems are widespread in Gram-negative bacteria.

"For instance, this new system explains how V. cholerae secretes its VPS polysaccharide, which is important for biofilm formation and virulence. Thus, our findings not only have significant implications for our understanding of polysaccharide export in M. xanthus but also profound implications for our understanding of polysaccharide export in general in Gram-negative bacteria."

More information: Johannes Schwabe et al, Evidence for a

Widespread Third System for Bacterial Polysaccharide Export across the Outer Membrane Comprising a Composite OPX/β-Barrel Translocon, *mBio* (2022). DOI: 10.1128/mbio.02032-22