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Sulfated lipopolysaccharides from marine gram-negative bacteria: structure and biological activity

Key words: lipopolysaccharide, O-polysaccharide, marine bacteria; biological activity

Gram-negative bacteria are an important component of marine ecosystems where they occupy diverse habitats including deep-sea and hydrothermal vents, sea ice as well as open and coastal water areas. Lipopolysaccharides (LPS) are the major component of the outer membrane of gram-negative bacteria. These characteristic and vital molecules maintain the contact between the bacterial cell and the surrounding environment; therefore, it is plausible that many of the functional changes induced by the harsh habitats can target LPS structure. One of the major interests to study marine gram-negative bacteria is their ability to produce biologically active compounds, such as antibiotics, toxins, endotoxins (LPS), anti-tumor and antibacterial agents having pharmacological and biotechnological potential.

In the last few years, we have studied the O-polysaccharides (OPS) and lipids A of LPS from some marine gram-negative bacteria that belong to genera *Cobetia*, *Idiomarina* and *Poseidonocella*. The chemical structure of the carbohydrate moiety of LPS of these marine gram-negative bacteria is diverse and includes rare monosaccharides and non-carbohydrate substituents. Several new sulfated polysaccharides were found.

In detail, bacteria of genus *Cobetia* (*C. pacifica* KMM 3789^T and KMM 3878) produce sulfated OPS composed of trisaccharide repeating units. The type strain contains D-glucose 3-sulfate and D-galactose 3-sulfate. A distinctive feature of the OPS of KMM 3878 is the presence of D-galactose 2,3-disulfate. The OPS of marine bacterium *C. litoralis* KMM 3880^T consists of trisaccharide repeating units and includes 2-keto-3-deoxy-D-manno-octanoic acid 5-sulfate. The same sugar residue was found in the disacharide repeating unit of OPS from *Poseidonocella pacifica* KMM 9010^T. Besides eight-carbon sugar, this polysaccharide includes D-rhamnose 2-sulfate. The OPS of another bacterium of genus *Poseidonocella* − *P. sedimentorum* KMM 9023^T, also consists of disacharide repeating units and contains 2-keto-3-deoxy-D-glycero-D-galacto-nononic and D-glucoronic acid 2-sulfate. One more sulfated OPS was found in the LPS of deep-sea marine bacterium *I. abyssalis* KMM 227^T. It consists of pentasaccharide repeating units and includes 3-(4-hydroxybutyramido)-3,6-dideoxy-D-glucose 2-sulfate.

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The LPS of bacteria of genus *Cobetia* were shown to exhibit a heterogenous lipids A, with hexa-, penta- and tetra-acylated species. Two penta-acylated lipid A species have been detected, differing in the acylation pattern. One lipid A form was found to be decorated by four (R)-12:0 (3-OH) and one 12:0 acyl moieties, whereas the other was decorated by three (R)-12:0 (3-OH), one 10:0 and one 12:0.

From biological point of view, we demonstrated that the LPS and O-deacylated LPS from *C. litoralis* KMM 3880^T, *C. pacifica* KMM 3789^T and KMM 3878, *P. pacifica* KMM 9010^T and *P. sedimentorum* KMM 9023^T inhibit colony formation of different human cancer cell lines, including melanoma SK-MEL-5 and SK-MEL-28, colorectal carcinoma HT-29 and HCT-116 and breast adenocarcinoma MCF-7. We showed that sulfated OPS retain anticancer properties that open up new prospects for studying the antitumor activity of sulfated LPS and OPS from marine gram-negative bacteria. In addition, the immunological studies demonstrated the very weak capability of marine Gram-negative bacteria LPS to elicit an immune response, as shown by the significantly lower release of pro-inflammatory cytokines in murine and human model systems compared to the potent immunostimulant *E. coli* LPS.