Polysaccharide biosynthesis by membrane-integrated processive glycosyltransferases – lessons from cellulose and hyaluronan formation

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Polysaccharides are abundant biopolymers that perform a plethora of biological functions. On the cell surface, the polymers usually perform architectural functions by stabilizing cell walls, forming capsules, or mediating cell-to-cell adhesion. Cellulose, chitin and hyaluronan are linear polysaccharides synthesized by membrane-embedded processive glycosyltransferases. These fascinating enzymes couple the biosynthesis of high molecular weight polysaccharides with their translocation across the plasma membrane. Structural and functional analyses of cellulose synthase revealed the mechanistic and molecular basis of this coupled reaction. Further, oligomeric forms of plant cellulose synthase suggest how the simultaneous synthesis of multiple glucan chains may facilitate their alignment into microfibrils. These studies are expanded upon by analysis of hyaluronan biosynthesis. Hyaluronan (HA) is an abundant vertebrate glycosaminoglycan. It is a heteropolysaccharide of N-acetylglucosamine and glucuronic acid units synthesized by a single membrane-integrated enzyme, the HA synthase. Biochemical and structural analyses of HAS delineate critical steps of HA biosynthesis, from initiation of biosynthesis to secretion, substrate selectivity, and enzyme processivity. Combined, our research provides fundamental insights into the function and engineering potential of polysaccharide synthases.