

Glycobiology and the Skin: A New Frontier

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Glycobiology is a new frontier in molecular biology that is relevant to dermatology. The term was coined in 1988 by Rademacher et al¹ to describe the emerging field that combined the knowledge base of carbohydrate chemistry and biochemistry with cellular and molecular biology. There even is a journal that bears the name *Glycobiology*. Why is glycobiology relevant to dermatology? Glycans are important in the structure and function of the skin and provide a new target for cosmeceutical development.

Glycobiology examines sugar chains, or glycans, that are multifunctional. Many macromolecules carry a dense array of covalently attached sugars that mediate cell-cell and cell-matrix interactions. Protein-bound glycans are found in the nucleus and cytoplasm of the cell where they function as regulatory switches. Therefore, an understanding of glycobiology might provide insight on skin aging and dysfunction. This article examines glycobiology from a dermatologic perspective.²

Glycans

Glycans are composed of basic monosaccharide units. A monosaccharide is the simplest carbohydrate that cannot be hydrolyzed. It has a carbonyl group either at the end of the carbon chain or at an inner carbon, yielding 2 types of monosaccharides: aldoses and ketoses. Examples of monosaccharides include 6 carbon-neutral sugars, such as glucose, galactose, and mannose. Disaccharides also can be formed, such as lactose and sucrose. Monosaccharides can be formed into oligosaccharides, which are branched or linear monosaccharides attached via glycosidic linkages. Repeated oligosaccharides then are formed into

polysaccharides, such as glycogen, glycosaminoglycans, and proteoglycans. Thus the various structures of glycans can be used for energy storage in the cytoplasm, can function as coactivators of cell-membrane receptors, can build structural components of the extracellular matrix, and can enhance skin hydration.

Glycan Diversity and Glycomics

The study of glycans is extremely complex because of the many types of α and β linkages that can occur between monosaccharides and other molecules. Nucleotides and proteins are linear polymers that have specific linkages, thus diversity of linkages is not as great. The study of the 4 bases that form DNA—adenine, cytosine, guanine, thymine—is known as genomics. These bases can form 250 four-unit structures, providing the genetic code for humans. Proteins that are made from amino acids can yield 16,000 four-unit structures; the study of these proteins is known as proteomics. Amazingly, 16 million four-unit structures can be made from sugars, the study of which is known as glycomics. Because the field of glycomics is so vast, it has been hard for scientists to focus on any given area, thus it is still in its infancy and represents a new frontier for skin study.

Glycoconjugates

Glycan diversity is further complicated by the ability of sugars to bind to other structures. Glycoconjugates are carbohydrates, such as monosaccharides, that are covalently linked with other chemical species, such as amino acids or lipids. These glycoconjugates include glycoproteins, glycopeptides, peptidoglycans, glycolipids, and lipopolysaccharides. Glycoconjugates are important in cell-cell interactions, cell-cell recognition, and cell-matrix interactions.

There are several glycans that are especially important in the skin, including glycosaminoglycans, which are linear copolymers of acidic disaccharide-repeating units that each contain a hexosamine and a hexose or hexuronic acid. Examples of glycosaminoglycans include chondroitin or dermatin sulfate and hyaluronan.

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Glycan Functions

Glycans are sugars that perform a variety of functions in the body. Glycans located on the cell surface interact with proteins from bacteria, bacterial toxins, antibodies, and tumor antigens as a form of cellular communication. Glycans also play a role in the structure and biology of healthy skin. Thus there are 2 distinct functions of glycans. One function is involvement in structural and modulatory activities, while the second function is specific recognition of glycan structures by other molecules, such as receptor proteins or lectins. The specific recognition can be further divided into the recognition of endogenous receptors by the same organism and the recognition of exogenous agents.

Structural glycans can protect, organize, and stabilize the skin. Glycans that are attached to collagens and proteoglycans in the skin maintain tissue structure, porosity, and integrity. The external location of glycans on most proteoglycans provides a protective shield to recognition and binding of proteases or antibodies. Glycans also are important in maintaining the proper folding of polypeptides in the endoplasmic reticulum that is necessary for protein solubility and conformation.

Glycans also can function as protective storage depots for biologically vital molecules. Glycosaminoglycan chains are found in secretory granules that bind and protect the protein contents of the granule. Glycosaminoglycans in the skin also are necessary for holding water, controlling ion flux, and modulating complement regulatory proteins. Hyaluronic acid-based fillers are glycans that are used to fill folds and wrinkles of the face based on water-holding capabilities.

The dark side of glycans is their ability to function as receptors for the binding of viruses, parasites, and bacteria. Bacterial and plant toxins also can bind to human glycans. Alterations in surface glycans may account for some of the autoimmune diseases found in dermatology; however, glycans found on soluble glycoconjugates, such as secreted mucin, can function as decoys for microorganisms that prevent infection.

Glycans and Aging

The amount of glycans decreases with aging, which reduces the ability of cells to coordinate cellular function, as glycans are exposed on the cell's surface. Loss of

glycans also reduces skin architecture, creating the visible changes associated with skin aging. Stratum corneum-free mannose, galactose, N-acetylglucosamine, and N-acetylgalactosamine decrease with age, but glucose is the most affected. The theory that the loss of glycans may lead to aging and a poor appearance has encouraged cosmetic chemists to develop moisturizers that are designed to enhance glycan functioning, which has led to a new generation of antiaging products. The first glycan-based moisturizer was launched this past year.

Skin Glycation

Glycans function in many different ways in the body. When sugars bind to proteins, glycation occurs, which prematurely ages the body by decreasing the flexibility of proteins, leading to cataracts as well as decreased nerve and renal functioning and myocardial contractility. The process of glycation is damaging to the body, but glycans function positively on the cell surface to act as antennae, allowing efficient communication. Sugars are essential to human life, and their decrease with aging provides an interesting target for aging prevention. Glycans on the cell surface can be tagged to fluorescent substances and analyzed for changes in their distribution following cosmetic application, which provides a way of studying topical glycan modulation and improving appearance of aged skin.

Summary

Glycobiology is a new frontier in dermatology. We already are harnessing some of the science of glycobiology every time we inject hyaluronic acid fillers or botulinum toxin. Glycobiology is a broad field in dermatology that can provide a better understanding of skin hydration, cell-cell communication, skin barrier function, and skin structure. Certainly DNA and proteins are 2 important building blocks of the skin, but sugars are equally as important and many times more diverse in their activities and chemical structures. Cosmeceuticals based on glycobiology may hold new promise in antiaging science.

References

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