

## Insights from Mannatech's Research & Development Department

## The Language Of Life

When you eat, how does your digestive tract know which food components to grab and send into the blood stream and which ones to allow to pass through? How do the filters in your kidneys choose the correct molecules to expel? Unlike machines, living organisms are coded to perform many complex "involuntary" functions. The more complex the organism, the more such functions it must perform to live and thrive.

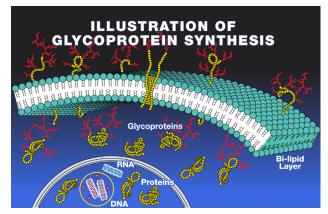
Science and medicine have long tried to break the biocodes by which the cells of the body communicate with each other so these complex functions can occur. These mysterious codes are truly the language of life. Biochemistry, the chemistry of life, is the science of the various molecules found in living cells and organisms and their chemical reactions. The aim of biochemistry is to explain the chemical processes of living cells.

The four major classes of biomolecules are proteins, nucleic acids (DNA and RNA), lipids (fats) and carbohydrates. For many years, scientists focused on proteins as key communication molecules. Eventually it became clear, however, that there were not enough possible protein configurations to provide all the messages needed to run the body. Another code was required.

# Research On Glycoproteins And The Code Of Life

In the 1960s, research began to be conducted on glycoproteins, protein molecules bound with sugar molecules. ("Glyco" means "sweet" and refers to sugars, or carbohydrates. These terms can be regarded as interchangeable.) Glycoproteins coat the surface of every cell with a nucleus in the human body. Glycolipids, fats bound with sugars, are another kind of glycoform, or glycoconjugate, found on cell surfaces. In Figure A the hairlike strands protruding from the section of the cell surface are glycoproteins. The gold component represents protein molecules; the red component represents carbohydrate molecules.

#### FIGURE A



This Figure is drawn after the 1996 cover of *Glycobiology: Official Journal of the* Society of *Glycobiology*, Oxford University Press. The journal acknowledged permission to reprint the original illustration from Oxford GlycoSystems, Ltd.

We now know that nature uses the sugars on cell surface glycoconjugates as communication (or recognition) molecules. Carbohydrates are much more structurally complex than the simpler proteins. Many more molecular configurations are possible with a six-carbon sugar (e.g., glucose), which has two isomeric forms and six binding sites. For example, while only 24 oligopeptide configurations are possible with four peptides (proteins), more than 1000 different oligosaccharide configurations are possible with four simple sugars.<sup>1</sup> So, sugars provide more specific forms of biological information for the code of life.

Since the 1960s, the study of glycoconjugates has grown exponentially as the technological means to conduct the studies have been developed. By 1996 scientists had identified, in <u>Harper's Biochemistry</u>, eight sugars found on human cell surface glycoforms involved in cellular recognition processes (from the roughly 200 sugars occurring naturally in plants).<sup>2</sup>

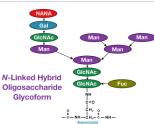
To illustrate, molecular communication codes can be compared with our own written language. Just as four different shapes can combine to make many letters, and these letters can combine to make many words, the different sugars combine within our bodies to make many cellular recognition "words" (Figure B). These precisely shaped "words" protrude from cell surfaces and are recognized and understood (or not understood) by neighboring cells through a sort of "sense of touch".

FIGURE B



Eight Essential Saccharides Required for Glycoprotein Synthesis Glucose (Glu) Galactose (Gal) Mannose (Man) Fucose (Fuc) Xylose (Xy) N-Acetylglucosamine (GlcNAc) N-Acetylglactosamine (GalNAc)



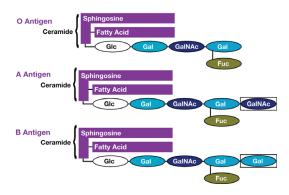


# Significance Of The Sugar Code On Glycoproteins

The significance of sugar components of glycoproteins is wellillustrated by our different blood types. Figure C shows terminal glycoproteins in the various human blood groups. The only difference between Type O and Types A and B blood is that Types A and B contain an additional sugar. Types A and B differ only in their terminal sugar. Type A contains N-acetylgalactosamine (GalNAc), while type B contains galactose (Gal). Yet such a seemingly minor distinction is the difference between life and death for a person given the wrong blood type.<sup>3</sup>

#### FIGURE C

### Human Blood Groups



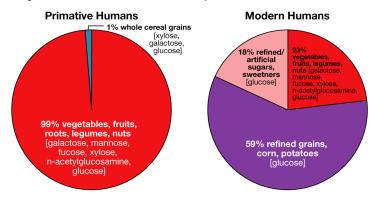
## Dietary Sources Of Sugars Used For Glycoprotein Synthesis

Although current nutrition textbooks stress the importance of essential vitamins, minerals, proteins (amino acids) and fats in great detail, sugars are typically recognized only as a source of energy,<sup>4</sup> not as substances that can be used for glycoform production and thus for overall wellness. If these sugars are so important, what is the source of them for our cells? Ultimately, only plants can capture the sun's energy to produce the carbohydrates required by the body. Thus, the plants in our diet are the primary building blocks for the sugar portion of these molecules that are so vital to continued good health.

The carbohydrates in refined sugars, refined grains, corn, potatoes and yams provide an abundance of just one of the eight glycoprotein sugars named in <u>Harper's Biochemistry</u>, glucose. Those who drink milk will consume glucose and galactose and may consume very small amounts of N-acetylgalactosamine and N-acetylneuraminic acid. Additional sources of sugars can be found in fruits, vegetables, seeds and roots: mannose, fucose, N-acetylglucosamine and xylose.<sup>4,5</sup>

Are we consuming enough of these sugars? During much of human history and before the advent of farming, people consumed diets that were much richer in the kinds of foods rich in carbohydrates containing all of the glycoprotein sugars.<sup>6</sup> Today, few people consume enough of such foods. Our carbohydrate intake via a rich variety of plant foods has been reduced by an estimated 76%. And, food processing of plant foods can further reduce their monosaccharide sugar content.<sup>7,8</sup> The notable changes in our plant derived carbohydrate intake, and thus our glycoprotein sugar intake, are detailed in Figure D.

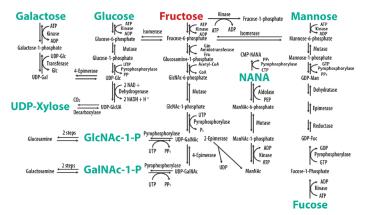
#### Figure D: Food Sources of Carbohydrates<sup>6</sup>



## Production Of Glycoprotein Sugars By The Human Body

If specific dietary sugars aren't available in our diets today, a healthy body can take an available sugar and convert it into other required sugars and then use those sugars to build glycoforms required for accurate cellular communication and resultant overall wellness. Enzymes are the tools the body uses to convert one sugar into another. Figure E illustrates the enzymes needed for such conversions. Note that 15 enzymatic conversions are required to change galactose to fucose.<sup>9</sup>

FIGURE E: Monosaccharide Interconversions



### Limitations Of Enzymatic Conversion To Build The Sugar Code

The effectiveness of the enzymatic conversion system to create the needed sugar molecules is not guaranteed. First, some individuals have inborn errors of metabolism, which means they may be missing one or more of the enzymes needed to make the conversions. The conversion process also requires specific vitamins at certain steps, and these vitamins may be missing. Finally, the conversion process requires time and energy. The more conversion steps required, the more energy is expended, and the speed at which a product is formed is proportional to available substrate. The more substrate provided, the fewer steps the enzymatic conversion system has to take and the more the system functions at optimal capacity. At high substrate concentrations the rate of the reaction is maximized.<sup>3</sup>

#### Benefit Of Nutritional Supplementation With Sugars Used For Glycoprotein Synthesis (Glyconutrients)

For most people today, intake of processed grains and refined sugars provides just a source of one glycoprotein sugar: glucose. Those who drink milk are also consuming some galactose very small amounts of N-acetylgalactosamine and N-acetylneuraminic acid. The remaining five sugars used to make cellular words must either be synthesized by the body through the the complex process described above, consumed via a diet markedly enriched with unprocessed plant foods, or obtained from dietary supplements.

Glyconutrient dietary supplements are designed to provide substrates for the body to use in building the glyco portion of glycoconjugates on cell surfaces. They are intended to make the necessary sugars available to the cells more quickly and in greater quantity. Since 1997, over three million people around the world have safely experienced the benefits of Mannatech's glyconutritional Ambrotose products. These products have been validated in peer-reviewed pre-clinical and clinical published research, including six gold-standard doubleblind, placebo-controlled human clinical trials. These studies indicate that they support cellular communication by impacting glycoprotein synthesis.<sup>10</sup> Ambrotose powders can improve immune system health<sup>11,12</sup> and have been shown to improve cognitive function, <sup>13,14,15,16,17</sup> and support gastrointestinal health and overall well-being.<sup>17\*</sup>



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\*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.