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Special Issue: The Magic of the Sugar Code

The magic of the sugar code

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'To an observer trying to obtain a bird's eye view of the present state of biochemistry, life may until very recently have seemed to depend on only two classes of compounds: nucleic acids and proteins', and Figure S1 (see the supplementary material online) is an illustration of Nathan Sharon's introductory statement to his lectures on complex carbohydrates [1]. This very special class of biomolecules with its unsurpassed capacity for information coding can now definitely be entered into the scheme (in red), to reflect our recent insights into the enormous functional versatility of glycans [2]. However, high-density coding comes at a price when scientific recognition is a measure, as Saul Roseman so clearly explains: 'in this remarkable age of genomics, proteomics, and functional proteomics, I am often asked by my colleagues why glycobiology has apparently lagged so far behind the other fields. The simple answer is that glycoconjugates are much more complex, variegated and difficult to study than proteins or nucleic acids' [3]. Building on a previous Feature Review in this journal [4], this issue is designed to introduce readers to the amazing (magical) virtues of coding by sugars, starting with an overview of bacterial glycosylation.

Glycan production in bacteria, as crucial as it was to track down DNA as genetic material by Oswald T. Avery and colleagues in 1944 (in an era when interest in nucleic acids was rather limited) [5], means much more than establishing a rigid wall or a protective cell coating, and Figure S2 gives a flavor of what to expect from the respective review [6]. *Mutatis mutandis*, the next two reviews let us understand the principles of eukaryotic protein glycosylation [7,8]. Even more, the intimate connection between basic research on N-glycan biosynthesis and clinical medicine will be made clear by illustrations that it has now become possible to pinpoint the molecular basis of congenital disorders of glycosylation (Figure S3 in the supplementary material online) [7,8]. Indeed, biomedical implications reach far beyond this class of diseases and glycoproteins. Lipid-presented glycans, such as the pentasaccharide illustrated in Figure S4 (top part) and also on the front cover, likewise are being unveiled as functionally pivotally active in many aspects [9,10]. Individual glycan determinants, presented by proteins and/or lipids, have already reached the status of being familiar to a wide community, albeit under a different name – that is, as the CD (cluster of differentiation) code. Examples are Lewis^x as CD15 and the Tn antigen as CD175. Not only immunologists but readers in general will find our dictionary of the glycobiology of the CD system, flanked by illustrations of the respective glycans and receptors (lectins; see Figure S4) useful [11]. Additionally, to address the question of the origin of the selectivity and specificity of lectin–glycoconjugate recognition, an illustrated primer to a six-level concept is shown as an 'appetizer' in Figure S4 (bottom) [11].

To tie this concept to an actual example for physiological function, Figure S5 depicts the connection between a glycolipid (sulfatide), an endogenous lectin (galectin-4), and growth of axons (for an overview of glycans as postal codes for routing and delivery in neurobiology, see [12]). Evidently, what Jean Montreuil concluded about glycoprotein research and indicated by his statement that 'we are discovering, filled with wonder, fascinating secrets. We have entered the golden age of glycoconjugates' [13] still holds true for the entire realm of glycosciences: hence the use of the theme of a fairy tale (see the front cover and accompanying text) as an illustrative introduction to this Special Issue.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tibs.2015.04.003.

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