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Meet the Board of *ChemistryOpen*: Antony J. Fairbanks

Antony J. Fairbanks*[a]

Antony J. Fairbanks is a Professor in the Department of Chemistry at the University of Canterbury in New Zealand. The research of his group focuses on the broad areas of organic synthesis, particularly applied to carbohydrates. He currently serves as an active Editorial Board member for *ChemistryOpen*.

What is your current research focus and why it is important?

My group works on carbohydrate chemistry and chemical biology, and, although in the past our research had been quite diverse, we currently have two main focuses.

The first is the application of endo-β-N-acetylglucosaminidase enzymes (ENGases)[1] as biocatalysts for the production of homogenous N-linked glycopeptides[2] and glycoproteins.[3] This is a field that we have been involved in for a long time—indeed the first research proposal I wrote on the topic (which was of course not funded!) was as far back in 1998. The major problem here is that glycoproteins are expressed naturally as inseparable heterogeneous mixtures of materials—termed "glycoforms". This means that all glycoproteins produced by cellular expression are in fact complex mixtures of compounds, the different forms of which may have significantly different biological activities. "So what?" you may well think. Well, a quick scan of the world's best-selling drugs reveals that many of them are glycoproteins; monoclonal antibodies (mAbs) are glycoproteins with two sugars attached to asparagines in the Fc regions. Indeed, the global use and market for protein drugs is enormous, estimated at approximately US$ 175 billion in 2015 and growing fast (CAGR of 7.3%); 70% of these protein drugs are glycoproteins. So, developing a way to produce them in homogenous and structure-optimised form is clearly a very important scientific objective.

The second major area of research for us at the moment is the development of new protecting-group-free reactions of sugars in aqueous solutions. Until 2009, hardly any work was going on in this area until Prof. Shoda from Tohoku University in Japan developed some amazingly effective synthetic transformations.[4] We are now one of the leading groups building on these initial ground-breaking studies, with the objective of developing mild aqueous reaction conditions for a wide range of transformations of completely unprotected sugars of all sizes; that is, from monosaccharides up to large oligosaccharides isolated from natural sources.[5] Our real objective here is to develop the sort of new synthetic chemistry than anyone (i.e. non-carbohydrate specialists) will be able to perform—usually single (or perhaps two or three) steps, and not involving any protecting group manipulations.

What are the critical issues and what are the future perspectives that need to be addressed for the field to progress?

There are two areas where the field has been struggling to make significant progress.

The first is widespread access to very complicated oligosaccharides. Traditional multi-step organic synthesis of oligosaccharides is always going to suffer from inherent logistical problems, which mean that only very few research groups will have access to them and, even then, in only very limited quantities. Although long-promised as a solution, automated solid-phase synthesis of oligosaccharides has yet to have any significant widespread impact. Personally, I think the establishment of procedures for the production of many more pure mammalian oligosaccharides, either by isolation from natural sources, or by the establishment of cell factories to make them, would really help the field progress.

The second area is access to carbohydrate-processing enzymes, particularly for use in synthesis. Though many enzymes have been cloned an expressed, their availability is limited beyond the research groups that originally produced them. Additionally, many more new enzymes are needed for wider biocatalytic applications; in particular, chemoenzymatic approaches have not yet even started to address the O-linked glycosylation of proteins.

What is, in your personal opinion, most critical to teach students in university chemistry courses?

The most important thing to teach students is the importance of a mechanistic understanding for the chemistry they are performing. For me, this really is the difference between doing chemistry as simply "cooking"—that is, "if I mix compound A and compound B, that gives me compound C", and a true scientific rationalisation of the subject. Chemistry is the molecular science and, in order to understand chemistry, students must be able to correlate reactivity with molecular structure in a rational and predictive manner.

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