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How does a medical doctor become a glycobiologist?

The recent descriptions of novel disorders of glycosylation and the increasing awareness for CDGs in the biomedical community are the fruits seeded by committed scientists with a strong medical background and a profound knowledge of glycobiology. However, this combination of skills and expertise is far from being obvious in the current context of compartmentalized life sciences.

Accordingly, we will certainly not see glycobiology courses in the curriculum of medical students for a long time. Then, how does it happen that a medical doctor becomes interested in glycobiology, while many mainstream topics promise more research funding and celebrity? The recent successes in CDG research certainly contribute to raising the medical interest for this family of diseases. So, how about those medical doctors, who fancied glycobiology at a time when no disorders of glycosylation were known? Those early glycobiologists with a medical background can be qualified as pioneers as they paved the way to the recent achievements in CDG research. My good colleague Eric Berger definitively belongs to these pioneers and his commitment to the field contributed to the discovery of many disorders of glycosylation.

Eric Berger's interest for glycoconjugates was first raised by the work of Max Burger on the agglutination of cancer cells by lectins [1]. The idea that carbohydrates structures may affect the proliferation of tumor cells was fascinating in many respects. Along this line, the work of Georg Springer on the T-antigen in cancer was also of great inspiration in those years [2]. Many reports focused on the role of glycans as oncofetal antigens and the young field of glycobiology was busy at working out the mechanisms regulating the expression of glycans in the context of cancer. A galactosyltransferase enzyme had been claimed to be a reliable cancer marker [3] and galactosyltransferase activity was also involved in the regulation of the T-antigen [4]. Considering the importance of this activity in cancer, Eric Berger decided to work towards the purification and characterization of the galactosyltransferase enzyme. In a masterpiece of protein chemistry, the medical doctor succeeded at purifying the protein and at generating antibodies to the galactosyltransferase. These antibodies enabled the first visualization of the Golgi apparatus by immunofluorescence microscopy [5]. In addition, these antibodies have turned out to be instrumental in many instances, such as in establishing the localization of new intracellular proteins [6] and in determining the cellular action of antibiotics such as monensin [7] and brefeldin-A [8]. Note worthily, brefeldin-A is now used in a screening assay to detect potential defects of glycosyltransferase trafficking, such as encountered in deficiency of the COG complex.

The contribution of Eric Berger to the field of medical glycobiology is also evident when looking at his work on the Tn-syndrome, where O-GalNAc is abnormally exposed on erythrocytes. Eric Berger wondered whether a galactosyltransferase deficiency did account for the abnormal exposure of the

Tn-antigen. Indeed, the testing of galactosyltransferase activity in the erythrocyte membrane of Tn-syndrome patients confirmed this hypothesis. With this experiment, the first disease of glycosylation was established [9].

As a colleague, I particularly enjoyed the discussions with Eric Berger around a cup of coffee. Besides learning a lot from his encyclopedic knowledge of medicine and cell biology, I always took pleasure at our attempts to rebuild the world of glycobiology. I remember one of these discussions, when complaining that we glycobiologists are little appreciated at our department of Physiology, Eric commented at “what it does take to bring it to the next level”. Glycobiology has always been and is still at many institutions a niche outside of mainstream interest. The conclusion of Eric was that the future of glycobiology may be brighter if glycobiologists would join forces with other specialists, like geneticists, clinical chemists, and especially with clinicians. Fortunately, this discussion did not remain theoretical. Eric Berger pushed his first idea of a European network dedicated to the research on glycosylation disorders through his contacts to various European groups. Thank to Eric’s initial networking, clinicians and glycobiologists across Europe were brought together, which ultimately lead to the characterization of multiple glycosylation disorders over the last decade.

Eric Berger has retired last summer from his faculty position. Typical for Eric Berger, his farewell lecture was entitled “Perspectives of a Second Fiddle”, which is a much too modest statement regarding his achievement. Through his vision, perseverance, and diplomacy, Eric has played a key role in CDG research. It is with great pleasure that I join the other authors to dedicate the present issue of BBA to Eric Berger, a medical doctor who became a glycobiologist. May his example inspire many to follow!

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