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Glyco-Forum

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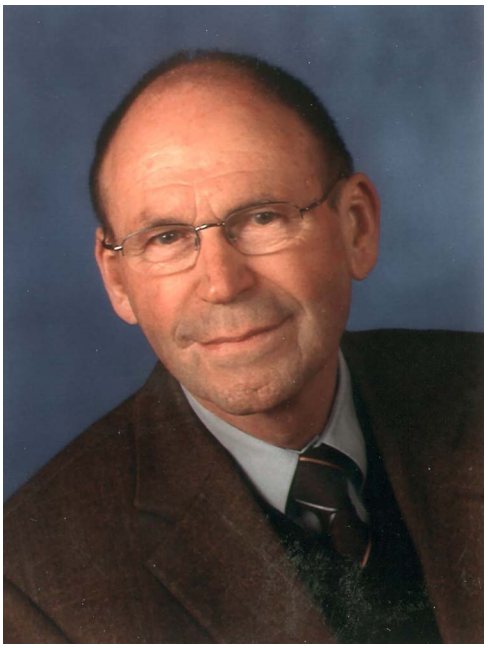

Roland Schauer (1936–2019): A tribute to "Mr. Sialic Acid"

For those interested in sialic acids, a major guiding light has been extinguished, but the afterglow lives on amongst numerous scientists he inspired and nurtured. Roland Walter Schauer was born at Stuttgart-Bad Cannstatt in Germany but was evacuated during World War II, because his parents' house was bombed. He then grew up in Schorndorf, where he experienced American soldiers moving in while taking children as hostages to make sure they would not be attacked. After school he would roam with his friends to explore nature, while making notes about the weather, a subject that became a life-long hobby, tracking the seasons, the start of flowers blooming, the start of birds singing and so on, combining with his expertise as a photographer. Following a brief stint learning chemistry in Stuttgart, Roland moved to Tübingen and obtained his medical degree in 1962. Right at that time, a new biochemistry curriculum was introduced in Tübingen, and Roland was one of the first students to finish this study with a diploma. Deciding that biochemistry was to be his passion (rather than a career in medicine), he applied for a position at the newly founded Ruhr-University in Bochum, where Hans Faillard, a student of Prof. E. Klenk (one of the early pioneers in sialic acids), was setting up his group. While in Tübingen, Roland also met his life-long partner Elfriede, and they married and went to Bochum in March 1967. Elfriede recounts that Roland once introduced her to Prof. Alfred Gottschalk (another pioneer in sialic acids), mentioning that this important person was working on projects involving slimy material that he would rather not touch himself. Not much later, Roland was the one to go to slaughterhouses to collect submandibular glands from cows, pigs and other animals! Following a postdoctorate at Bochum, he achieved Habilitation in 1970, with a thesis *Acylneuraminsäuren: Eigenschaften, Synthese und Biosynthese* under Faillard. After a stint as Associate Professor and Group Leader for Cell Chemistry at Bochum, Roland moved in 1976 to become Full Professor of Biochemistry and Director of the Institute of Biochemistry at the University of Kiel, where he spent the rest of his career.

From the early years of the discovery and characterization of sialic acids, it was evident that these 9-carbon backbone alpha-keto monosaccharides were frequently modified in various ways, often in a tissue- and/or species-specific manner. But given the diversity and complexity of these mostly labile modifications, they were frequently ignored or even destroyed during release and/or analysis of the underlying glycans. By the time, Roland began his independent career in the late 1960s, the original pioneers of the sialic acid field were retiring, and the mainstream of glycoscience research had begun to dismiss sialic acid diversity as species-specific curiosities that were too much trouble to work with. Fortunately, Roland was undeterred by these challenges and carried this torch almost single-handedly through the late 1960s and the early 1970s, focusing attention on the biosynthesis of sialic acids and their modifications using radioactive precursors and fresh slices of submandibular glands. Much of this early work was published in German in the classic journal *Hoppe-Seyler's Z Physiol Chem*, and therefore received less international attention. Beginning in the 1970s and through the early 1980s, Roland precisely defined many specific modifications of sialic acids in nature, in close collaborations with Kamerling and Vliegenthart in the Netherlands, a long-term friendship which began with the surprising discovery that what had long been assumed to be 8-O-acetyl esters on sialic acids, were in fact at the 9-position. By the end of the 1970s, Roland was authoring definitive reviews in *Methods in Enzymology*, and then edited the 1982 classic monograph *Chemistry, Metabolism, and Biological Functions of Sialic Acids*, which became the bible for the field in the 1980s. Besides leading the way in definitive identification and characterization of many sialic acid modifications, Roland was a pioneer in discovery of the enzymatic mechanisms for their biosynthesis and turnover.

Perhaps his most remarkable discovery was the completely counterintuitive mechanism for the biosynthesis of the sialic acid

N-glycolylneuraminic acid. A reasonable assumption was that this molecule was the product of an amino-acylation reaction involving a donor like glycolyl-CoA. Instead, coming in one Christmas day because the deep freezers did not work, Roland found that *N*-acetyl group of [1-^{14}C-*acetyl*]*N*-acetylglucosamine was partly metabolized to [1-^{14}C-*glycolyl*]*N*-glycolylneuraminic acid in cultured slices of porcine submandibular glands. This surprising finding allowed his prediction of a direct enzymatic hydroxylation of a sugar *N*-acetyl group, a transformation that would be a challenge even today to a synthetic chemist. Roland then found that this novel reaction occurred not during any step of sialic acid biosynthesis, but instead at the CMP-nucleotide sugar level. This work paved the way for the cloning of the *CMAH* gene that encodes the hydroxylase, and the later discovery of its inactivation in the human lineage. He also left behind many other fascinating avenues for future exploration, such as 9-O-lactyl-sialic acids. The mass spectral data for this modification was convincing and was verified several times, but its functions and biosynthesis remain a mystery. Only recently has lactyl-CoA (which he predicted) been described as a donor for lactylation of proteins.

Since Roland was one of my scientific godfathers, I have taken the liberty to tell a personal anecdote that exemplifies much that was special about him. When I was a postdoc in Stuart Kornfeld's lab from 1978 to 1982 elucidating lysosomal enzyme targeting by Man6P on N-glycans and the defect in I-cell disease, a side project lead me to find high O-acetylation of murine erythrocyte sialic acids, and its functional impact on the alternate complement pathway. This work would not have been possible without new methodologies I found in Roland's contemporaneous publications. It turned out that I was competing directly with the Schauer group and I even partly scooped them. When I started my independent position in San Diego, I chose not to continue work on Man6P and instead decided to study these fascinating sialic acid modifications, and sought career advice from Roland, even though I'd never met him in person. Rather than brushing off this upstart young physician-scientist from India with limited knowledge who was barging into his field, Roland invited me to visit his lab for a week, while he and Elfriede hosted me in their own home. And from that time on Roland nurtured me professionally even during friendly competitions, always humble and open-minded, despite his towering stature and achievements. Such stories about Roland are commonplace, as he took care of his associates or others, helping them to overcome obstacles and move ahead. In his own group, he guided >40 Diploma students, >50 PhD students and 5 habilitations, while also hosting guest researchers from over 20 different countries. He cherished contacts with colleagues from around the world and always had an interest in their culture, beyond the science aspects. Long before gender disparity awareness became popular Roland insisted that there were female scientists in his team, believing that encouraging young women scientists was very important. Always respected as a kind and honest person, his empathy and tactfulness were well known. Indeed, he always controlled himself when asked for opinions, so that nobody should ever be hurt by his remarks. He also graciously accepted corrections of his own writings, such as the discovery that sialic acids were not invented in the Deuterostome lineage, as he had suggested. He instead advised us about how to redefine the broader evolutionary distribution of sialic acids and the even more ancient family of their likely precursors, the prokaryotic nonulosonic acids.

During his lifetime, Roland Schauer published ~400 original papers and reviews, mainly concerning the chemistry, metabolism and biological functions of sialic acids, gave more than 200 invited lectures, was involved intimately in the organization of International symposia on sialic acids, ten Sialic Acid Workshops in Kiel and served on the Editorial Boards of the *Glycoconjugate Journal*, and *Trends in Glycoscience and Glycotechnology*. In 2009, he was recognized with the Rosalind Kornfeld Award for Lifetime Achievement by the Society for Glycobiology. Roland and Elfriede also established the Roland and Elfriede Schauer Foundation, "to promote science and research in the field of glyco-biochemistry with a focus on sialic acids." Fittingly, a citation of Max Planck (also once a Professor in Kiel) appeared above Roland's death notice: *Wem as vergönnt ist, an dem Aufbau der exakten Wissenschaften mitzuarbeiten, der wird sein Genügen und sein innerliches Glück finden in dem Bewusstsein, das Erforschliche erforscht zu haben und das Unerforschliche ruhig zu verehren* (Those who are granted the privilege to work on building up the exact sciences will find their satisfaction and inner happiness in the awareness that they have researched the researchable and calmly worship the unexplored).

Roland's final overview on sialic acids written with Hans Kamerling in 2018 lists more than 70 variations of sialic acids in nature, using the short form nomenclature he originally invented, and which has been adopted by IUPAC and by the NCBI-based Symbol Nomenclature for Glycans (SNFG). Largely based on his discoveries, the SNFG discussion group agreed to assign a red diamond as a symbol for "unspecified sialic acid." From now on, whenever you see a glycan structure with a symbol for Neu5Ac (purple diamond) as a "default sialic acid," insist that unless this was rigorously proven on the native structure, a red diamond be used instead. I propose that we dedicate this red diamond symbol to Roland Schauer. That way, every time we see a glycan structure with a red diamond, we will be reminded of his remarkable contributions to sialobiology.

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