

A Giant of Matrix Biology A celebration of Dick Heinegård's Life

When I heard the news of Dick's sudden passing, I immediately felt a sense of loss: a giant has left us. Indeed, the definition of "giant" in the field of matrix biology is truly appropriate, as Dick Heinegård possessed prodigious scientific output and strength. Dick was extremely productive and contributed not only to the field of cartilage and bone biology, but also to SLRP biology (his lab cloned and characterized several SLRPs) and to human diseases such as osteoporosis and arthritis. One of Dick's best qualities was his uncanny ability to see the "big picture". He was able to connect various interactions of matrix constituents to functional and biological properties that made sense. He was ahead of his times as he was already doing "Systems Biology" of the extracellular matrix before the arrival of supercomputers. His biggest influence to me came from his paper of 1984 with Kate Vogel where they described, for the first time, that the small proteoglycans of tendon, now known as SLRPs, inhibit *in vitro* fibrillogenesis of both collagens type I and II. This implicated the SLRPs as key regulators of both soft tissues (dermis, interstitial tissue etc.) and hard tissues (cartilage/bones). This seminal observation was subsequently confirmed by several investigators and then by the decorin null mice, which showed abnormal collagen fibrillogenesis *in vivo*. These observations were confirmed by the biglycan, fibromodulin and lumican deficient mice, which showed abnormal collagen phenotypes, thus validating his observations of more than a decade earlier. In more recent years, Dick has worked on so many aspects of matrix biology that is impossible to summarize them all in a few lines. I should mention that Dick has contributed to the structural and functional characterization of many, now famous, molecules including COMP, osteopontin, fibromodulin, decorin, biglycan, chondroadherin, osteoadherin, PRELP, aggrecan, link protein, and many others. Dick has published over 425 papers with 65 papers in JBC and 36 in BJ, an astonishing output (most of the papers are from his laboratory) equivalent to the productivity required by four full professors to reach tenure!



Anyone who joins our famous Proteoglycan Gordon Research Conference is surprised at our collegiality, friendship and vitality. We are able to have great fun and are proud of our community of scientists. Dick Heinegård was an intrinsic part of this community. I met him at the first PG Gordon in 1984 when I was starting my career at Penn. I was introduced to Dick by Vince Hascall and I thought that I finally joined the 'PG circle of trust'. I never left the circle and neither did Dick. He always participated in the scientific program and took part in the interesting and lively discussion. The best personal memories I have of Dick are during the time we spent together talking about science in the green lawn of Proctor Academy, especially during the interminable baseball and cricket games. I wanted to celebrate his life by inviting several of Dick's friend and colleagues to express their feelings and thoughts about him. I like to remember him as a happy, sensitive, mild-mannered and highly-creative human being with a great sense of humor. The photo (Fig. 1) shows Dick at the traditional Thursday evening lobster banquet of the PG Gordon held in 2010.

We will greatly miss you.

Renato V. Iozzo, Philadelphia

"I have been looking for a photograph of Dick Heinegård from one of the many times we were together, but I have been unable to find one that I think is good enough. Good enough in the sense of really reminding us what he was like. So what is the picture of Dick my mind's eye is looking for? I see him as the superb biochemist methodically teasing extracellular matrices apart to reveal their fundamental building blocks. I see him as the speaker at numerous meetings explaining what new components he has discovered and new ideas about how they work, as he did in the opening talk at an April symposium in Boston two years ago. In my mind's eye I see him next to me as we are walking along the beach in Skåne planning the 2009 Gordon Research Conference on Cartilage. I see him and hear him talk, full of ideas and plans, in his office, in his lab and in his apartment in Lund. But dearest of all is my picture of him as the generous host on his farm, in May, taking his American guests on a walk through the forest, seeing, smelling, listening and feeling life return after winter. This is my picture of Dick Heinegård. He was a great extracellular matrix biologist and scientist, but, above all, a real "Mensch" who enriched the life of those he touched."

Bjorn R. Olsen, Boston

“Dick worked in Helen Muir’s lab with Tim Hardingham (Fig. 2) before I met him in 1971 at the Mucopolysaccharide Gordon Conference. He had arranged to come to Ann Arbor after the conference. I had been told by Dr. Dziewiatkowski (Dr. Jay), who had recruited me to the University of Michigan, that Dick was considering coming to Ann Arbor to do a sabbatical, and that I should impress him. Dick did not seem very impressed, and after showing him our amino acid analyzer with his response “We have a better one”, I asked if he was really interested in doing a sabbatical in our lab. With a somewhat surprised look, he said “No, we would like you to come to Lund for a sabbatical.” It took about 10 seconds for me to say “Yes”, one of the most important decisions I have ever made. A year later my family and I began our Swedish adventure and the establishment of a lifetime friendship for me. It was not always easy at first to get past Dick’s reserve, but once there it was delightful, both in and out of the lab. During the year, we met Tim Hardingham and learned of his work on hyaluronan with Helen Muir. This led to a series of experiments that resolved the structure of the cartilage proteoglycan aggregates, introducing the role of the link proteins. Our excitement about the final key experiment went way into the morning hours as we sipped some Danish beer and watched the scintillation counter count out all the vials. Dick returned the sabbatical favor by spending another productive year in my lab in 1976 shortly after I moved to NIH.



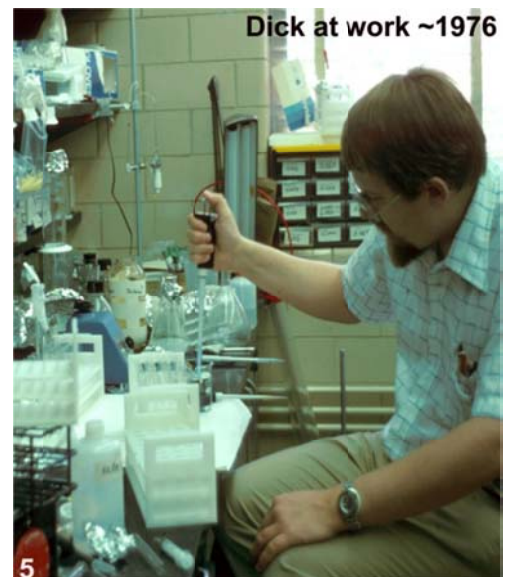
My picture of him on the Royal Gorge Bridge during a Colorado vacation (Fig. 3) epitomizes Dick. Dick would look at the extreme depth of the problem from the bridge and still go fishing. It is hard to imagine how many new macromolecules he pulled out of extracellular matrices with his talented colleagues. It was a delight to see his matrix model grow year after year in his wonderful talks, regretfully the last time during his visit to Cleveland last fall. Figure 4 shows the shoulder he always leaned on, his wonderful wife and companion, Lean, whom I was fortunate to get to know in Lund and in Bethesda. Visits to their farm were always a delight, and Dick’s persona was always curiosity driving forward to solve the next riddle in his ever expanding matrix research interests. My heart goes out to Lean and their family, and Dick will remain



my dear research brother as long as my memory lasts.”

Vincent Hascall, Cleveland

We first met in the early 1970ies in Lund, more than 40 years ago. Dick was one of Sven Gardell’s PhD students, running liquid chromatography columns, columns and columns, while drinking his Lapsang Souchong tea. I was a green PhD student at the Karolinska Institute coming down to the lab in Lund to learn mucopolysaccharide and later proteoglycan purification and chemistry. We didn’t interact much the first years, but once I graduated to the proteoglycan level we published together from 1975 to 2010. It is one of those coincidences that spread like rings on the water that Dick and Vince Hascall then started to work together, first in Lund, then in Bethesda. Dick knew me and my PhD work, and encouraged me to get in touch with Vince and to come over to Bethesda to visit the lab at NIDR where Dick was working in 1976 (Fig. 5). The Heinegård, the Hascalls and the Lohmanders then spent a memorable summer vacation together in the Colorado Rocky Mountains. Looking at the old Kodachrome slides brings back smiling memories of us all on midsummer eve, hiking back down from Longs Peak in a snowstorm with thunder and lightning. I guess we passed the test since I was invited to spend a year in Vince’s lab in Bethesda, a true game changer in my own career. On returning to Sweden, we soon moved down to Lund, where Dick’s support privately and professionally was again critical in building up my own lab and research group in parallel with a clinical training and



career. We were young newcomers to Lund, but Dick and his family generously included us among their friends on many visits to their home, island and farm.

We've stayed in touch since then as friends and colleagues for our entire careers, and into 'retirement' as senior professors. Dick was always there, even when traveling, always ready for a discussion, always the generous encyclopedia of matrix knowledge, a true giant in our field. "Ask Dick", were often used words in my discussions with my students, and in time, with their own students. Dick was always curious, always looking around the corner, always thinking forward, and never discarding any piece of information. He was competitive, but would always give you sound advice when asked. His extraordinary global network of friends and collaborators was an asset that we all could tap into when needed. We can't "ask Dick" any longer, but his legacy will live not only in his scientific production, but also in the bright memories of those of us fortunate to have known him.

Stefan Lohmander, Lund

"Dick enjoyed his weekends on his farm in the countryside in peaceful surroundings with his wife Lean. I had the privilege of staying a few days with him at his house in Lund a decade ago (affectionately named "Hotel Heinegård" by his lab, owing to the numerous visitors he hosted there) and spending the weekend with them at their farm. I enjoyed very much the delight that he took in riding his little tractor around (Fig. 6) and strolling the woods ax in hand, looking for something to cut down. Looking back now, I appreciate very much his kindness and generosity to a relative stranger, and the opportunity to have known him not only as a monumental figure in matrix/cartilage biology, but also as a very likeable, unpretentious human being. He was, and remains, an inspiring role model for my generation of matrix biologists".

Suneel Apte, Cleveland



I met Dick when I started my first post doc job in Helen Muir's lab at the Kennedy Institute in London. Dick was on a year's study in London with Helen, so we had chance to interact on lots of challenges presented by understanding proteoglycans in cartilage. Dick worked "Swedish hours", arrived about lunch and worked till midnight (or beyond). In the lab he wore clogs, smoked a pipe and drank lapsang souchong tea (very strong). Even then he was a fund of information and a stickler for attention to detail and systematic approach to problems. We continued contact when he was back in Lund and then when he subsequently went to NIH to work with Vince Hascall (and took the lapsang habit with him). I also spent a year with Vince shortly after Dick and the three of us maintained contact and friendship from that time on. In fact as recently as 2006, the three of us shared a holiday in Japan together, with wives and friends. There was a close family of proteoglycan researchers that developed at the time Dick was establishing himself and he was an essential part of that family. There was still rivalry and competition, but there was so much unknown, that sharing information, data and reagents was the norm. Dick was a leader from these early days and he has carried the flag for matrix biology over the past 40 years. It is difficult to think of this field without him there.

Tim Hardingham, Manchester



I first had the honor and pleasure of meeting Dick in 1976 in Birmingham, Alabama, USA where, ironically, in that same year I also met and befriended for the 2 other infamous "H's" in cartilage matrix biology (i.e. Vince Hascall & Tim Hardingham). From my very first meeting with Dick, I was amazed at his incredible depth of knowledge of basic science, wet lab experimentation and clinical medicine, particularly as they applied to connective tissue research and matrix biology. For the past 37 years I have had the pleasure of meeting up with Dick, usually at numerous meetings in different countries around the world. At these meetings I would take advantage of his huge knowledge base as 'the Encyclopedia

of Matrix Biology' to fearlessly discuss any new/mad thoughts and ideas that I might have but more importantly to find out the very latest of what was going on elsewhere in the ever changing world of matrix biology. Dick was an incredibly hard worker with most of his time in any given day or week being spent in his lab, his office at work, or in his basement at home. For many years, for his holidays, he chose to take up a medical position in the north of Sweden to keep his medical qualifications up to date; i.e. his dedication to medicine & research was second to none and clearly the envy of most of us working in matrix biology.

Through the years Dick has received numerous awards in recognition of his achievements and contributions to matrix biology research worldwide. When there were matrix biology meetings in or close to Sweden he very often invited many of the overseas participants to his summer island residence or his farm just outside of Lund. These wonderful 'hospitality extras' that he provided afforded many of us yet another opportunity to pick his brain, meet his wonderful family & friends enjoy matrix biology in a very social & convivial environment. In my opinion, the current knowledge that we have all lost with Dick's sudden and unexpected death is irreplaceable. However, because of his enormous set of achievements and contributions to matrix biology it will be almost impossible for any of us to forget the name Dick Heinegård when we do our research, or just remember wonderful past times. Dick was an incredible person and one whom we all will sorely miss.

Bruce Caterson, Cardiff



"In 1982 I was a young Assistant Professor at The University of New Mexico. I had taught myself how to study radioactive glycosaminoglycans in fibroblast cultures, but I wanted to actually see proteoglycans. Of course I chose to go to Sweden, the home of proteoglycan research. Thus, thanks to Dick's gracious invitation and a Research Career Development Award from the NIH, my husband and I, along with our two daughters, ages 9 and 12, headed off to Lund for a year. Wow, what a year it was! Our girls went straight into the local schools and quickly learned Swedish. Al did his sabbatical work at the Univ. of Lund Hospital, and I started isolating proteoglycans in Dick's lab. Our first decision was to choose a tissue. Because everybody was working in cartilage at that time I wanted something else. We chose tendon because it was the most fibrous tissue I could think of and because we didn't believe anybody had previously sought tendon proteoglycans. We got some cow feet, dissected out the flexor tendons, and I started learning protein chemistry under Dick's exacting guidance. Every step took so long it was tempting to take shortcuts ("Do I really have to dialyze for three days with changes every 12 hours?") but Dick's unforgettable lesson, in his delightfully colloquial English, was "don't get greedy." After months of work I had finally produced a small amount of purified small tendon proteoglycan (the molecule later named decorin) at which point, to my horror, Dick insisted that we inject most of this into a rabbit! But it all worked out well. By the end of that year we had characterized the tendon proteoglycans, produced an excellent antiserum, and shown that the core protein of the small proteoglycan interacted with collagen. I was started down a research path that would consume most of my career. For all of this, I thank Dick Heinegård.

During my year in Dick's lab we shared an office and a telephone.

Of course nobody called me, but in those days, before answering machines, I quickly learned that when Dick was not there I shouldn't just say "hello", because that would generate long sentences in rapid Swedish that I could never understand. Instead, with exaggerated slow diction I would pick up the telephone and say, "Hello. This is Kathryn Vogel." The surprised caller would usually mumble an apology and hang up. But occasionally I'd take a message and then I could tell Dick that while he was gone, "Stockholm called." I loved telling him that, and I wish the big call from Stockholm had really happened."

Kate Vogel, Aspen



"It is with great sadness that we learned about the passing of Dick Heinegård. Since the early days of my research program on extra-cellular matrix and then on small proteoglycans, Dick has been a role model to me for research innovation and excellence. He was a true leader in the field and at the same time devoted to community service and in helping to train and encourage our up and coming matrix scientists. He served on countless committees giving sound and fair advice. He participated enthusiastically in numerous venues for scientific exchange including Gordon Conferences, OARSI, ORS and more. Dick had both solid scientific rigor and a keen sense for important research topics. His contributions are too numerous to count having discovered and characterized key matrix components that included the SLRPS, the SIBLINGS and other collagenous and non-collagenous proteins such as COMP, now considered a marker of osteoarthritis. Dick kept clear his focus on bone and cartilage and on the biochemical parameters related to diseases affecting these tissues. His work took basic research findings to important and practical translational applications that impacted diseases caused by mineralized tissue abnormalities. It is not a surprise that Dick was a coveted speaker and discussion leader for professional scientific forums that presented new findings in the field of skeletal biology and pathology. In addition to all of this, Dick enjoyed life. Those of us in the proteoglycan field know how much camaraderie and good times matter to our community and Dick was always in the forefront participating scientifically and socially. Dick, you will dearly be missed!



Marian Young, Bethesda

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Below are several statements from e mails I received from our scientific community regarding Dick Heinegård:

"My memory of Dick is someone who was always filled with words of wisdom- a gentle intellectual giant!! The Matrix field has lost one of its pioneers and he will be deeply missed"

Thomas N. Wight, Seattle

"It is a very great loss. I regarded Dick as a mentor and admired his work and command of the field of matrix and cartilage biology"

Suneel Apte, Cleveland

"...always helpful and always positive. What a terrible loss for all of us.a giant in our field, and I am also sure that his family will appreciate the recognition and appreciation by all of us of his amazing scientific and human qualities"

Maurizio Pacifici, Philadelphia

"His contributions to our field have been unparalleled. It was a great bounty to be able to experience his magnanimous presence, usual grace and wisdom at OARSI last week. He was always encouraging. For him to tell you "That was clever" and to hear his appreciative laugh was high heartwarming praise. Words cannot express the extent to which he will be missed by us all"

Virginia Byers Kraus, Durham

"It is with great sadness that I heard of the passing of Dick Heinegård, he was a great scientist whom I've known for close to 30 years. Dick served as a member of the Scientific Advisory Board of the ICCBMT meeting that I organized in 1985 (I think), and attended all the board meetings that we had, and participated in the program. He later served as a consultant on my grant, providing me with proteoglycans and knockout animals, to use in my study of calcification mechanisms. More than his science, I remember his great sense of humor. He was a great man, and a great scientist, and I am sure we will all miss him."

Adele L Boskey, New York

I met Dick Heinegård for the first time in 1984 at a meeting organized by Klaus Kühn, Björn Olsen, and Raul Fleischmayer for the New York Academy of Sciences. Of course, I already knew about Dick's landmark discoveries - together with Vince Hascall - on aggrecan. Although I was under way myself in matrix biology already for several years, I was not really used to raising in my peers such an overwhelming interest in my findings. It was about collagen IX actually being a proteoglycan, something that appeared to be an unthinkable heresy at the time. Needless to say, Koji Kimata already had published exactly this iconoclasm with his JBC paper on PG-Lt which, moreover, turned out to be the same as collagen IX. So, the contribution of Lloyd Vaughan and myself to the advancement of science appeared rather modest to me.

Not to Dick, apparently. He came to my poster and introduced himself. I was awed by the encounter of such a famous colleague and even more by the kind of enthusiastic interest he showed. After about three seconds, however, I realized that I had met a friend rather than a fearsome authority. Dick had this rather rare gift of making patently evident his great respect for every conversation partner without hiding, at the same time, his immense talents. And we stayed friends for many years. I later had the privilege of many scientific communions with Dick, sometimes late into nights at his home or the farm house nearby where he enjoyed his "free" time with his wife Lean.

At the time in New York, he insisted in discussing with me the possibilities opened by a proteoglycan-collagen during the whole evening and also the conference dinner. Again, I do not need to mention that we still have only vague ideas about the significance of the dermatan sulphate chains of collagen IX even after thirty years. But Dick already then was thrilled by the union of the major subjects of interest of many matrix biologists, namely his own (proteoglycans) and that of e.g. the conference organizers (collagen). Dick's close familiarity with cartilage where this union takes place so obviously made him curious about our findings. It is easy to say for me that Dick was a scientific visionary and a lot of what we did in Zurich after that was actually stimulated by him.

Peter Bruckner, Münster

