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A tribute to Dick Heinegård

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Abstract

This issue of Matrix Biology commemorates the memory of Dick Heinegård and his exceptional contributions to identify extracellular matrix molecules and their interactions that form cartilage matrices. This tribute to him demonstrates the development of his cartilage matrix model and how this model relates to the articles in this Matrix Biology Cartilage issue.

Keywords

Dick Heinegård; Cartilage; Extracellular Matrix; Hyaluronan; Proteoglycan

1. Introduction to Matrix Biology Cartilage issue

This Matrix Biology issue commemorates the memory of Dick Heinegård, a pioneer in cartilage matrix biology. Fig. 1 (courtesy of Cahir McDevitt) shows Dick in 1970, wearing a tie, possibly after completing a chalk talk about collagen on the blackboard. At this time he was a student on leave from Lund working in Helen Muir's laboratory in London with Tim Hardingham (bearded) and Mike Bayliss (sleepy) who are also in the picture, and the predominant model for cartilage at that time was chondrocytes surrounded by a collagen network embedded in 'ground substance'. However, the pioneering work of Helen Muir and Maxwell Schubert had shown that cartilage was a good source for protein polysaccharides, renamed proteoglycans 2–3 years later.

We met at the Gordon Conference – Structural Macromolecules; Mucopolysaccharides – in 1971, which was the grandfather for the ongoing bi-annual Proteoglycan Gordon Conference initiated in 1984. Dick visited me at the University of Michigan after the meeting and invited me to do a sabbatical in his laboratory in Sven Gardell's Department at the University of Lund, which I gladly accepted. Our collaboration in 1972/73 established the model for cartilage proteoglycan aggregates [Heinegård and Hascall, 1974] and initiated its addition to his early model of cartilage matrix (Fig. 2).

This began Dick's lifelong career to identify cartilage matrix molecules and build them into his ever evolving model. Fig. 3 (courtesy of Pilar Lorenzo) shows the model that Dick used for his seminar at the Cleveland Clinic in October, 2012, sadly the last time we met. I have added dates to show the remarkable journey that brought Dick and his research colleagues to this dynamic model. In 1979, cartilage matrix protein (later re-named matrilin 1) was identified (Paulsson and Heinegård, 1979), and its interaction with biglycan/decorin and collagen II determined later (Wiberg et al., 2001). *P*rotein/arginine-*R*ich *E*nd *L*eucine-rich

repeat *P*rotein (PRELP) (territorial) and fibromodulin (interterritorial) arrived in the cartilage matrix in 1986 (Heinegård et al., 1986). Chondroadherin (CHAD) that interacts with integrins (Haglund et al., 2011) was identified in 1991 as a 36 kDa protein (Larsson et al., 1991). Cartilage Oligomeric Matrix Protein (COMP) that interacts with collagens was isolated in 1992 (Hedbom et al., 1992), and cartilage intermediate layer protein (CILP) followed a few years later (Lorenzo et al., 1998). The final component in Dick's model was added in 2001 as asporin, a name based on its polyaspartate stretch in its amino terminus (Lorenzo et al., 2001). The beautiful final model and the integration of its components into the cartilage matrix is an elegant demonstration of Dick's dedication and contribution to cartilage research.

Several of the articles in this Matrix Biology issue refer to relevant work that relates to aspects of this model. The article by Hsueh et al., which focuses on biomarker and proteomic analyses in osteoarthritis, has a treasure trove of citations co-authored with Heinegård, including 1 posthumously this year (Dakin et al., 2014), and proteomics was a major direction for Dick's laboratory in the years following the identification of asporin (Önnerfjord et al., 2012). The article by Loesser discussing chondrocyte matrix interactions with integrins features the 2011 study by Heinegård's laboratory showing that chondroadherin binds to α2β1 integrin, which initiates signaling pathways that maintain chondrocyte roundness and inhibits cell division (Haglund et al., 2011). The article by Hunziker et al. features an early study using rotary shadowing to analyze hyaluronan organization and aggrecan distribution in aggregates (Morgelin et al., 1995). The article by Wilutsz et al. features an article describing differences in cartilage pericellular matrix (territorial) and extracellular (interterritorial) matrix (Heinegård and Oldberg, 1989).

Fig. 4 (courtesy of Suneel Apte) shows Dick and his lovely wife Lean in 2012 at their farm near Lund, which was a favorite place to visit, relax and even work. Those of us who had the privilege to know and work with Dick will ever be grateful for his contributions to our lives and our research.

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Fig. 1.
Dick and his colleagues at the Kennedy Institute in Helen Muir's lab in 1970. Provided by Cahir McDevitt.

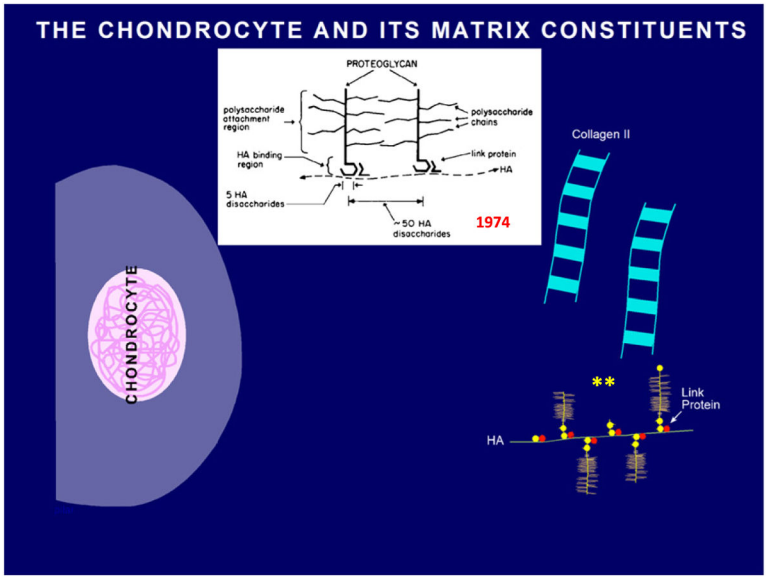

Fig. 2.

Dick's early model of cartilage matrix with the inserted model that placed hyaluronan into the proteoglycan aggregate.

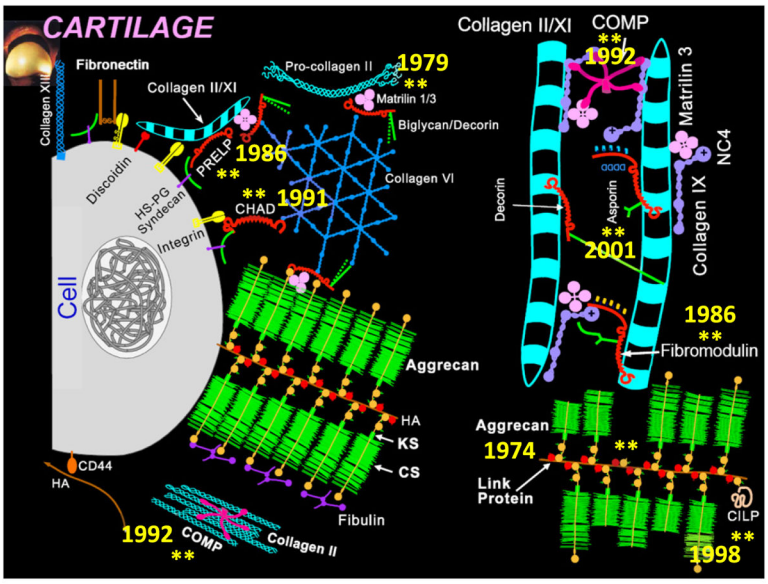

Fig. 3.

Dick's last model with dates for the addition of the different molecules from his laboratory. Provided by Pilar Lorenzo.

Fig. 4.
Dick and his wife Lean at their farm in 2012. Provided by Suneel Apte.