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Cosmetics for the matrix: An attractive new style for Matrix Biology.

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Commentary

Cosmetics for the matrix: An attractive new style for *Matrix Biology*

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This is a very special and historical issue for *Matrix Biology*. It is the inaugural issue that incorporates the new style and formatting that is commensurate for the next generation of Matrix Biologists. We hope you greatly enjoy the more contemporary and aesthetically-pleasing format of the new *Matrix Biology*.

These exciting changes include an overhauled approach for the citations. Effective immediately, all citations provided for original research articles and reviews are now fully hyperlinked and will link out to the source article upon clicking the desired title in blue font. Moreover, citations and in-text references have now been streamlined and appear in numerical order. This prevents distractions that are caused by reading over lengthy names with dates and, in turn, provides an unadulterated flow and unbridled experience for the reader. Moreover, the typeface has been changed to Arial, which undoubtedly increases reader fluidity and understanding while concurrently decreasing reader eyestrain and fatigue. This ultimately culminates in an uncluttered comprehension of the material. Finally, images will be more reproducible as they will be printed with the guaranteed standard of being at least 300 dpi.

This issue starts with the spotlight cast on two outstanding articles as provided by the *Matrix Biology Highlights* followed by a nice collage of photos depicting *Matrix Biologists in Action*. As many of you are aware, this past summer played host for the biennial Proteoglycan Gordon Research Conference (PG-GRC) held at Proctor Academy in Andover, New Hampshire (06–11 July 2014). The PG-GRC was enriched with a multitude of diverse and exciting extracurricular activities and social events. Many moments have been forever captured and immortalized in the photos presented within the *Matrix Biologists in Action*. We hope you enjoy them.

This issue also contains three significant articles from established leaders in the field of *Matrix Biology*.

The first article by Iozzo and Schaefer is a large review reporting an extended and comprehensive classification of all the proteoglycan gene families. Three main criteria have been used to generate this nomenclature: 1) The cellular and subcellular locations of various proteoglycans, 2) The overall genomic and protein homology, and 3) The use of finite protein modules within their respective protein cores. These three bio-signatures were utilized to design four major classes of proteoglycans with distinct forms and functions: the intracellular, cell-surface, pericellular and extracellular proteoglycans. We hope that this large review, which contains 620 references, will be useful to investigators not familiar with the proteoglycan field, and, hopefully, it will represent a useful teaching tool for proteoglycan biologists.

The second article is from Bjorn Olsen's laboratory, at Harvard Medical School in Boston (Besschetnova, T.Y., Ichimura, T., Katebi, N., St. Croix, B., Bonventre, J.V., Olsen, B.R. 2015. Regulatory mechanisms of anthrax toxin receptor 1-dependent vascular connective tissue homeostasis). This comprehensive research paper deciphers the pathomolecular links underpinning the role of angiogenesis in promoting fibroproliferative disorders. Identified as the nexus in this matrix-centric pathway, is anthrax toxin receptor 1 (ANTXR1) also commonly known as tumor endothelial marker 8 (TEM8). ANTXR1/TEM8 deficiency results in hyperproliferative and permeable blood vessels within the skin due to a malformed vascular basement membrane. Moreover, cell type specific loss of ANTRX1/TEM8 in fibroblasts boosts the synthesis of fibrillar collagens that ultimately culminates in the development of a

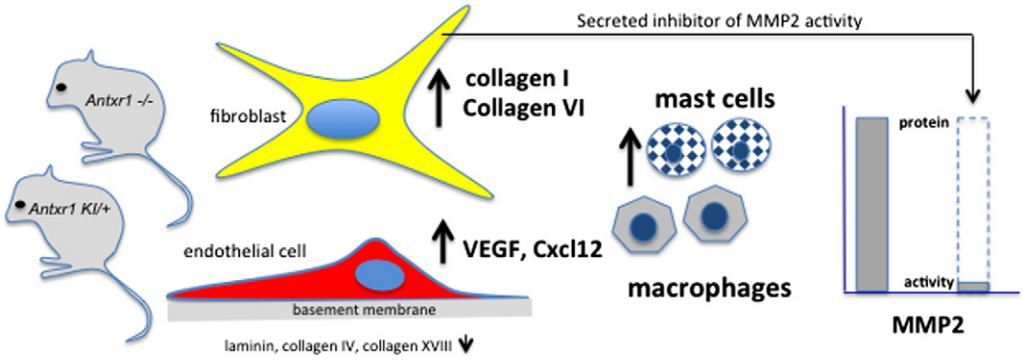

Fig. 1. Schematic representation depicting the interplay of the vascular and connective tissue compartments governed by the mechanism of ANTXR1/TEM8.
Figure provided by Bjorn Olsen.

pro-fibrotic phenotype that permeates throughout the body (Fig. 1). Simultaneously, loss of ANTRX1/TEM8 results in a marked increase in secreted VEGF and CXCL12 (Fig. 1). Clinically, the insights gleaned from these studies are directly applicable to various pathologies involving the vascular and connective tissue interfaces, such as the multisystem disorder that is collectively known as GAPO syndrome. Loss of function/mutations present in ANTRX1/TEM8 causes GAPO syndrome in part due to compromised crosstalk between ANTRX1/TEM8 impaired endothelial and fibroblast cells that result in a reduction of MMP2 activity (Fig. 1).

The third article is an original research from Tom Wight's group, Benaroya Research Institute in Seattle, WA (Evanko, S.P., Potter-Perigo, S., Petty, L.J., Workman, G.A., Wight, T.N. 2015. Hyaluronan controls the deposition of fibronectin and collagen and modulates TGF-β1 induction of lung myofibroblasts). Hyaluronan (HA) is critically responsible for regulating collagen type I and fibronectin deposition as well as for the induced myofibroblast phenotype via TGF-β1 signaling. Despite the fact that HA and fibronectin physically bind, the implications for the overall synthesis and assembly of the surrounding pericellular matrix during the fibroblast/myofibroblast

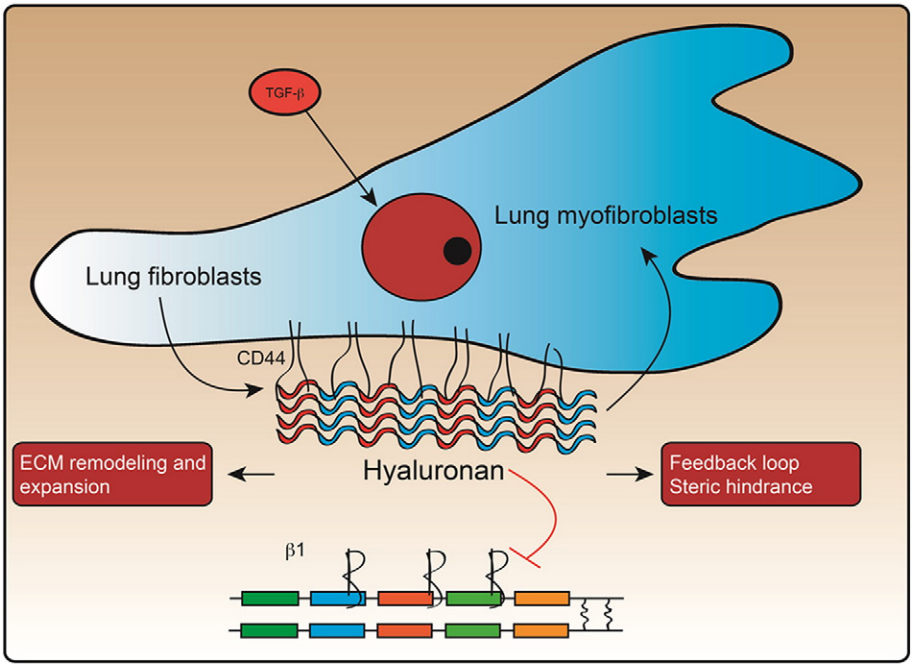

Fig. 2. Schematic representation of hyaluronan-dependent control of extracellular matrix dynamics during the transition of a fibroblast to a myofibroblast.
Image provided by Tom Wight.

transition remain highly elusive. Intriguingly, the authors discovered that pharmacological (e.g. 4-MU, HA oligosaccharides) or enzymatic (e.g. hyaluronidase) inhibition of HA synthesis in TGF-β1-induced lung myofibroblasts augmented myofibroblast morphology, increased collagen and fibronectin accumulation, and elevated *ACTA2* and *HAS2* mRNA. Moreover, CD44 and HA were excluded from incorporation into focal adhesion complexes and instead were found to be significantly co-localized with the cell's cortical actin network. As such, HA/CD44 binding modulates the attachment of the membrane and the cortical actin between focal contacts. Importantly, this is seemingly and mechanistically disparate from the role of fibronectin and the β1 integrin in mediating focal adhesion.

Moreover, labeled HA bound to fibronectin at regularly-spaced intervals and preferentially co-distributed with β1 integrin, and less with CD44. Thus, HA can act as a steric hindrance and can prevent the assembly of higher-order fibrillar ECM organization. This, in turn, can feedback via mechano- and TGF-β1-dependent pathways for myofibroblast reprogramming (Fig. 2).

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