Abstract book

The 13th European Elastin Meeting

18-21 August 2026

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Speaker abstracts

Mechanisms of elastic lamellae in the aortic wall

Dieter P. Reinhardt, *McGill University, Montreal, Canada*

Elastogenesis is a fundamental process in the development and maintenance of elastic tissues, including blood vessels, skin, and lungs. Abnormalities in elastic fiber formation and function contribute significantly to both inherited and acquired diseases, leading to conditions such as aortic aneurysms, skin laxity, and pulmonary emphysema. In addition to elastin, elastic fiber assembly depends on several accessory proteins and matrix networks, including fibronectin, fibrillins, small fibulins, latent TGF-β binding protein 4 (LTBP4), and microfibril-associated glycoprotein 4 (MFAP4). While each of these components plays a critical role in elastogenesis, their precise molecular functions and interactions are only beginning to be understood. In this presentation, I will provide an overview of key molecular interactions and functional relationships that govern elastic fiber assembly and maintenance across diverse tissues and experimental models.

When the Matrix Fails: ECM Control of Aortic Wall Integrity

Hiromi Yanagisawa, *University of Tsukuba, Japan*

The extracellular matrix (ECM) is indispensable for maintaining aortic wall integrity by providing elasticity through elastic fibers and tensile strength through collagen fibers. Congenital or acquired defects in the ECM impair the ability of vascular smooth muscle cells to respond appropriately to mechanical stress, leading to progressive weakening of the aortic wall and aneurysm formation. We have previously demonstrated that the matricellular protein thrombospondin-1 acts as a mechanosensitive regulator of aortic wall homeostasis through the integrin–YAP signaling pathway.

In contrast, aortic dissection is characterized by acute separation of the medial layers, resulting in aortic rupture and organ malperfusion. It is a major cause of sudden death in connective tissue disorders such as Marfan syndrome, yet the molecular events that trigger dissection remain largely unknown. While aneurysm and dissection frequently coexist, the mechanisms that distinguish these two disease processes remain poorly understood.

In this talk, I will present our genetically engineered mouse models of aortic aneurysm and spontaneous aortic dissection, discuss the molecular mechanisms linking ECM dysfunction to disease initiation and progression, and introduce our recent findings suggesting that endothelial cells act as critical initiators of aortic dissection in response to ECM failure. Together, these studies provide new insight into how matrix dysfunction is translated into cellular responses that determine aortic wall integrity and may uncover new therapeutic opportunities for preventing aortic disease.

The elastin receptor complex: from a signaling receptor to a glyco-regulatory hub

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Elastin-derived peptides (EDPs), generated during extracellular matrix remodeling, have long been recognized as biologically active mediators involved in vascular aging, cardiovascular diseases, and numerous chronic disorders. Their biological effects are primarily mediated by the elastin receptor complex (ERC), a heterotrimeric receptor composed of the Elastin Binding Protein (EBP), Protective Protein/Cathepsin A (PPCA), and the sialidase Neu-1. The demonstration that Neu-1 provides the catalytic activity required for signal transduction profoundly reshaped the understanding of EDP-induced signaling and opened new perspectives on the biological functions of the ERC.

This presentation will retrace the major milestones that have shaped current knowledge of the elastin receptor complex, from its initial discovery to the emergence of its broader biological functions. The molecular mechanisms through which Neu-1 modulates the activity of multiple membrane receptors will first be reviewed, followed by recent evidence indicating that the role of the ERC extends far beyond the activation of canonical signaling pathways. Particular emphasis will be placed on the emerging role of the ERC in remodeling the membrane glycome and on the consequences of this process for the basal activity of inflammatory and metabolic pathways, as well as for the function of multiple membrane receptors.

Together, these advances support a major conceptual shift in which the elastin receptor complex can no longer be viewed solely as a signaling receptor activated by elastin-derived peptides, but rather as a genuine glyco-regulatory hub, capable of remodeling the membrane glycome and, consequently, modulating the signaling of numerous cell-surface receptors. This renewed perspective opens new avenues for understanding the contribution of extracellular matrix remodeling to age-related diseases, metabolic disorders, and, more broadly, to the understanding of membrane signaling mechanisms.

Tropoelastin as a driver of 3D complex architectures and cell performance

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Tissue elasticity is bestowed by the protein elastin, which in turn is predominantly assembled from the structural protein building-block tropoelastin. Tropoelastin is more than just an elastomer. We have found that tropoelastin can promote the repair many types of damaged tissues. Despite these critical abilities, and even though the tropoelastin gene is essential, paradoxically the production of tropoelastin drops precipitously with age.

This presentation will outline advances in our mechanistic understanding in the use of tropoelastin to deliver organized elastin in vascular walls during replacement-repair in vivo, promote heart muscle survival and recovery in an in vivo model of ischemic injury, and its ability to compress inflammatory signaling. Blended modified tropoelastin is used to rapidly seal interfaces with complex shapes, including damaged lung and heart. In vivo and model studies will be presented that show the value of using tropoelastin to modify cell performance in these cases, in order to help heal surgical wounds, repair arteries and modulate immunity while delivering synthetic tissue-materials for building 3D materials. The presentation will also show that tropoelastin incorporation enhances vascularization in a printable hydrogel with tissue-mimicking mechanics and supports the use of protein matrices to promote beneficial early vascularization in engineered tissue constructs.

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Structural basis for the contribution of latent TGFβ binding protein to TGFβ latency and activation

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Transforming growth factor-β (TGFβ) is a potent cytokine that controls all aspects of cellular behaviour, thus its activity is tightly regulated. TGFβ is secreted in complex with its prodomain that is covalently cross-linked to latent TGFβ-binding protein (LTBP)-1, which is required for normal tissue development and wound healing. This large latent TGFβ complex (LLC) with LTBP1 binds to the extracellular matrix via fibrillin and fibronectin which is required for integrin-mediated force activation. Previous studies have described the structure of TGFβ but how the large latent complex with LTBP1 influences the structure and activity of TGFβ is unknown. Here we report the cryo-EM structure of the LLC comprising the eight-cysteine domain of LTBP1 covalently bound to the TGFβ. The structure reveals a hydrophobic interface between the mature growth factor and LTBP1, which structure-guided mutation and signalling assays show is important for both the formation of the LLC and regulating TGFβ activity. Our structure supports a contralateral domain swapped architecture for TGFβ within the LLC, and simulations of force dependent activation show that this domain architecture requires increased force to overcome the barriers required for integrin-mediated TGFβ activation. Furthermore, the covalent attachment of TGFβ to LTBP1 distributes the force required for activation to reduce the unfolding force barriers. Together, our studies describe the contribution of LTBP1 to the formation of the LLC and its role in regulating TGFβ activity and activation, which is essential to understand how to target TGFβ therapeutically.

Elastin-Derived Bioresponsive Hydrogels for Targeted Drug Delivery in Inflammatory Skin Diseases

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Inflammatory skin diseases such as atopic dermatitis and psoriasis are characterized by cycles of flare-ups driven by immune dysregulation and elevated protease activity, including increased levels of matrix metalloproteinases such as MMP-9. To address the need for localized, inflammation-responsive therapies, we developed enzyme-sensitive hydrogels incorporating elastin-derived peptide linkers designed for selective MMP-mediated degradation.[1,2.] The hydrogels were synthesized via thiol-norbornene step-growth photopolymerization using multi-arm PEG macromers and peptide crosslinkers optimized for controlled enzymatic cleavage, and subsequently loaded with the anti-inflammatory drug tofacitinib citrate. Their physicochemical properties, including swelling behavior, mechanical characteristics, and degradation kinetics, were evaluated, and drug release was assessed under simulated inflammatory conditions using MMP-9 exposure. Biocompatibility and functional anti-inflammatory activity were examined in fibroblast and keratinocyte cultures, as well as in two complementary inflammatory assays involving T-cell and keratinocyte activation.

The hydrogels showed clear MMP-dependent degradation, with release rates modulated by crosslinker architecture and PEG composition. Swollen networks exhibited elasticity comparable to soft dermal tissue, supporting their suitability for topical or intradermal delivery. Cytotoxicity remained minimal across all tested cell types, confirming good biocompatibility. In inflammatory assays, drug-loaded hydrogels significantly reduced pro-inflammatory signaling, demonstrating effective release and biological activity of the encapsulated therapeutic. These findings highlight the potential of elastin-inspired, enzyme-responsive hydrogels as targeted drug delivery platforms for inflammatory skin diseases, enabling site-specific, inflammation-triggered release while maintaining stability under non-inflammatory conditions. This approach offers a promising strategy for improving the management of chronic inflammatory skin disorders, where protease activity is a key pathological driver.

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1. Noddeland HK, Lind M, Jensen LB, Petersson K, Skak-Nielsen T, Larsen FH, Malmsten M, Heinz A. Design and characterization of matrix metalloproteinase-responsive hydrogels for the treatment of inflammatory skin diseases. Acta Biomater. 2023. 157:149-161. doi: 10.1016/j.actbio.2022.12.015.
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Influence of developmental cell origin on aneurysm formation in lysyl oxidase deficiency

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This abstract is not available online at the author's request.

Young Investigators

Modifier role of perlecan in renal microvascular dysfunction in a Marfan syndrome mouse model.

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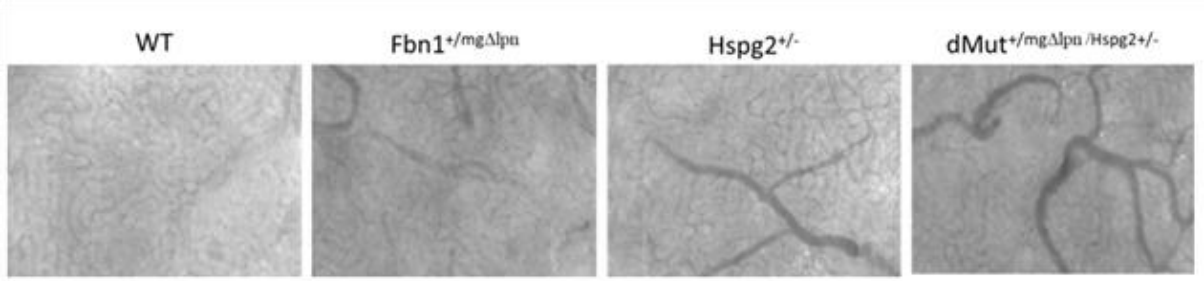
Introduction: Elastic fibers (EFs) are essential components of connective tissue, providing structural integrity and elasticity. They are primarily composed of tropoelastin and fibrillins, and their assembly is supported by extracellular matrix molecules such as perlecan. Marfan syndrome (MFS) is caused by mutations in the FBN1 gene, leading to disruption of elastic fibers and affecting multiple organ systems. In addition to classical cardiovascular, skeletal, and ocular manifestations, other organs, including the kidney, may also be involved. Clinical variability in MFS suggests the contribution of modifier genes; recently, the HSPG2, which encodes perlecan, was associated as a modifier gene. In the kidney, elastic fiber components range from fibers lacking tropoelastin to fully mature elastic fibers, distributed within microvessels, glomeruli, and the peritubular extracellular matrix. The Fbn1mgΔlpn/+ mouse model reproduces key features of MFS and exhibits alterations in renal elastic fibers. Aim: This study aimed to investigate the influence of perlecan in the organization of kidney structures in the Fbn1mgΔlpn/+ model. Methods: Twenty-nine 3-month-old female C57Black6N mice were analyzed: wild-type (WT, n=10), Fbn1mgΔlpn/+ (n=7), Hspg2+/- (n=7), and dMut-Fbn1mgΔlpn/+;Hspg2+/- (dMut, n=5). In vivo microcirculation was assessed using Sidestream Dark Field imaging (SDF), and kidney morphology was evaluated in historesin sections. Results: SDF imaging revealed a significant increase in microvessels with diameters higher than 13µm in dMut group when compared to WT and Fbn1mgΔlpn/+, whereas no differences were observed between WT and Fbn1mgΔlpn/+. Capillary analysis showed a reduction in vessels (3.35µm–5.02µm) and decreased blood flow velocity in dMut group when compared to WT and Fbn1mgΔlpn/+. Capillaries between 5.03µm–6.70µm were reduced in dMut and Hspg2+/- mice without changes in flow velocity when compared to WT group. Glomerular area and urinary space were increased in dMut and Fbn1mgΔlpn/+ mice when compared to WT and Hspg2+/- groups. Conclusion: These findings indicate that perlecan reduction in Fbn1mgΔlpn/+ mice, can contribute to modulating renal microvascular structure and capillary hemodynamics, whereas glomerular alterations are primarily associated with fibrillin-1 alteration rather than perlecan reduction at 3months.



Bioinspired elastin-like polypeptides as a versatile platform for hydrogel formation

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Elastin-like polypeptides (ELPs) are sequence-defined protein polymers composed of (Val-Pro-Gly-Xaa-Gly) repeats. Their intrinsic biocompatibility and thermoresponsive behavior make them highly attractive for advanced biomaterials, particularly in hydrogel design. Recombinant production enables tight control over molecular weight and composition, while optimized expression systems (e.g., ECPM1) provide high yields and scalability. In addition, their lower critical solution temperature (LCST) transition offers a powerful lever to control solubility, chain interactions, and pre-organization prior to network formation.

In this work, we developed a family of tyrosine-containing ELPs designed as versatile precursors for enzymatically crosslinked hydrogels. By incorporating tyrosine residues at defined positions along the sequence, we enable oxidative coupling into dityrosine crosslinks under mild conditions. Gelation is triggered using oxidative enzymes such as horseradish peroxidase (HRP) or laccase, which catalyze the formation of covalent networks in aqueous media without the need for synthetic crosslinkers or harsh reagents. The resulting networks can be adjusted by varying parameters such as tyrosine content, enzyme concentration, and oxidant levels, which influence gelation behavior and final material properties. The thermoresponsive character of ELPs may also contribute to the organization of the polymer chains before crosslinking, providing an additional level of control.

By combining sequence precision and enzymatic specificity, this work establishes a versatile platform for the design of fully protein-based hydrogels with tunable properties. These materials are particularly promising for applications requiring mild processing conditions and tunable mechanics, such as injectable systems, cell encapsulation, and biomimetic scaffolds.

A Novel, Preclinical Model of Patient-Specific Fbn1 Exon 30 Deletion Recapitulates Neonatal Marfan Syndrome

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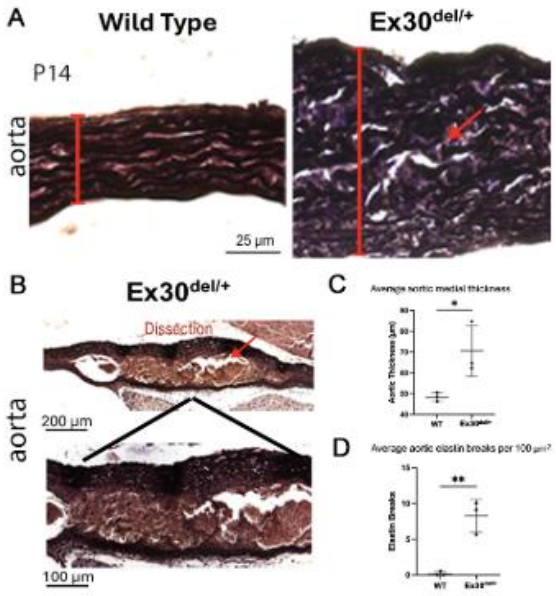
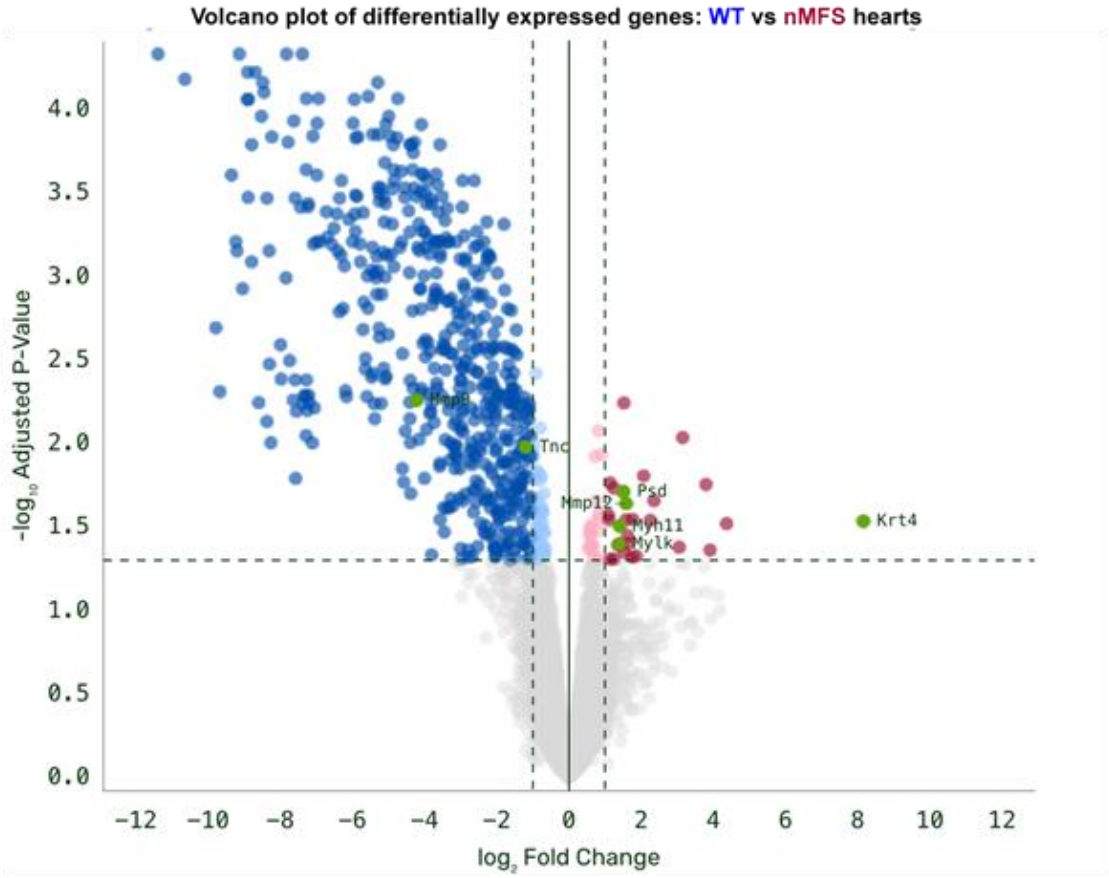
Neonatal Marfan syndrome (nMFS) is a severe, early-onset form of Marfan syndrome, a connective tissue disorder caused by mutations in fibrillin-1 (FBN1). nMFS is diagnosed at birth, as affected individuals are born with distinct cardiovascular and skeletal manifestations that continue to progress rapidly, with 95% of patients dying within 1-2 years. The most serious complications are cardiovascular and include congestive heart failure, heart valve dysfunction, and aortic aneurysms with risk of dissection. nMFS is associated with mutations within exons 23-32 of FBN1. Specifically, two patients diagnosed with nMFS had deletion of exon 30. Based on these clinical findings, and the lack of nMFS preclinical models, we generated a conditional Fbn1 exon 30 allele that was ubiquitously deleted via Cmv-Cre. Fbn1 exon 30 deleted heterozygous mice (ex30del/+) display phenotypic abnormalities associated with nMFS starting as early as postnatal day 0 (P0), with 97% dying within 24 days. qPCR analysis validated exon 30 Fbn1 reduction in ex30del/+ hearts compared to age matched controls. Whole mount imaging displayed smaller body size and aortic aneurysm in ex30del/+ mice. Elastin staining revealed increased elastic fiber breakage and disorganization, and enlarged wall thickness and dissections in ex30del/+ aortas. Movat pentachrome staining of ex30del/+ hearts revealed myxomatous valves. To understand the molecular significance of Fbn1 exon 30 deletion, bulkRNA-seq of P0 hearts was utilized to uncover genes involved in its manifestation. Transcriptomic data revealed downregulated genes in ex30del/+ hearts such as Tnc, and Mmp9, and upregulated genes such as Myh11, Mmp12 and Mylk. Additionally, Ingenuity Pathway Analysis analysis revealed upstream pathways involved in regulation of Fbn1 exon 30, such as EGFR, WNT and TGF-β. Therefore, we have successfully generated a preclinical model that phenocopies nMFS patient characteristics and have identified potential genes and pathways involved in its manifestation, that will ultimately be utilized to uncover therapeutic interventions.




Volcano plot of differentially expressed genes: WT vs nMFS hearts
-log10 Adjusted P-Value
log2 Fold Change
Mmp8
Tnc
Mmp12
Psd
Myh11
Mylk
Krt4

Targeting miR-29 through engineered tropoelastin mRNA formulated in lipid nanoparticles to restore ELN expression and limit pulmonary cellular senescence

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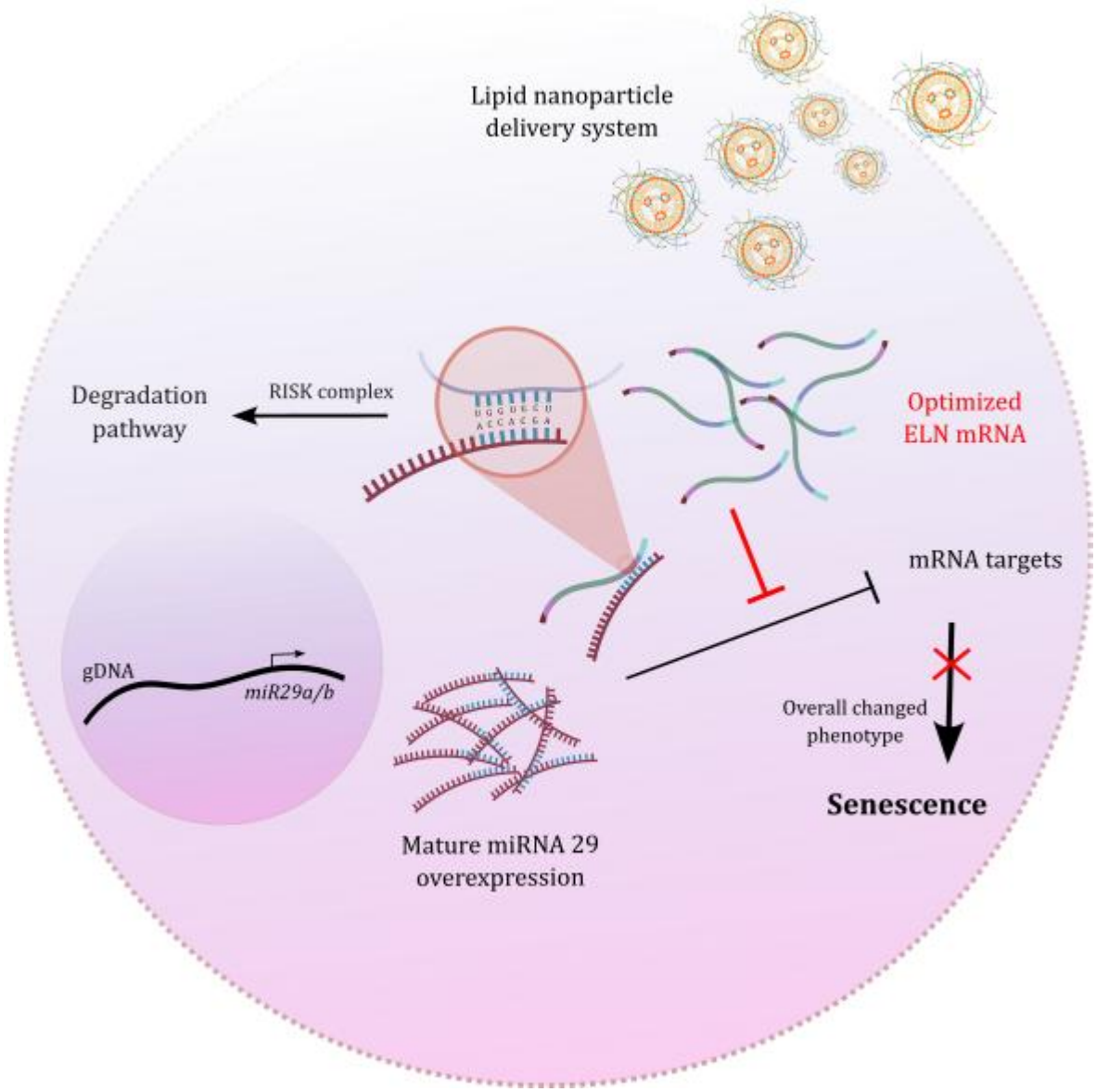
Cellular senescence is a central hallmark of premature tissue aging and contributes to the progression of numerous pathologies, including pulmonary emphysema. These conditions are also characterized by extracellular matrix (ECM) dysfunction, notably a reduction in tropoelastin (ELN) expression. A shared regulatory mechanism may underlie both processes through microRNA-29 (miR-29), which post-transcriptionally represses ELN by binding to MicroRNA Response Elements (MREs) in its 3'UTR, thereby inhibiting translation and promoting mRNA degradation. Importantly, miR-29 overexpression has been consistently associated with increased cellular senescence and tissue aging. To restore ELN expression while modulating miR-29 activity, an optimized ELN mRNA was engineered and formulated in lipid nanoparticles (LNPs) to function as a molecular sponge. This construct preserves the canonical mRNA architecture (5'UTR, coding sequence, 3'UTR, and polyA tail) and incorporates modifications to enhance stability and translational efficiency. These include an extended polyA tail (>100 adenines) and the incorporation of modified nucleotides (N1-methyl-pseudouridine and 5-methyl-cytidine), known to improve mRNA performance and reduce immunogenicity. To maximize miR-29 sequestration, the 3'UTR was redesigned to include tandem repeats of MRE sequences. Three variants were generated, containing 4, 8, or 12 MRE sites. The functionality of these constructs was assessed using electrophoretic mobility shift assays (EMSA) with fluorescently labeled miR-29, alongside reporter gene assays and gene/protein expression analyses in MRC5 and NHDF cells. EMSA analysis revealed a fluorescence shift proportional to the number of MRE sites, indicating increased interaction between miR-29 and engineered mRNAs. Reporter assays further demonstrated high specificity, as fluorescence recovery reached levels comparable to controls. Notably, the construct containing 8 MRE sites demonstrated optimal performance. Treatment with this variant led to a significant reduction in miR-29 levels after 24 hours in MRC5 cells and a concomitant increase in tropoelastin protein expression in NHDF cells following LNP delivery over one week without toxicity. Ongoing studies aim to evaluate the impact of these constructs on cellular senescence and ECM restoration. Overall, these engineered ELN mRNAs represent promising tools to investigate the interplay between miR-29, ELN expression, and senescence, and may provide a foundation for innovative therapeutic strategies restoring extracellular matrix integrity in senescence-associated conditions.

Supporting image on the next page


Lipid nanoparticle
delivery system
Degradation
pathway
RISK complex
Optimized
ELN mRNA
mRNA targets
gDNA
miR29a/b
Overall changed
phenotype
Senescence
Mature miRNA 29
overexpression

Cooperative Coupling of Hydrophobic Interactions and Crosslinking Reveals Atomistic Mechanisms of Tropoelastin Assembly

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Elastogenesis is a complex, multistep process involving the association, crosslinking, and deposition of tropoelastin molecules into functional elastic fibers. Numerous mechanisms have been proposed to describe how this process occurs and which molecular factors are involved. However, due to the highly disordered nature of tropoelastin and the rapid kinetics of coacervation, experimental characterization remains challenging, and many mechanistic details have yet to be fully elucidated at the molecular level.

Here, we employ molecular docking and molecular dynamics simulations to construct the first full atomistic-resolution model of tropoelastin dimers, both in the absence and presence of covalent crosslinks identified by mass spectrometry. We use these models to resolve the structural and dynamic features of tropoelastin association and to define step-by-step molecular mechanisms of assembly at high temporal and spatial resolution.

Our results demonstrate that strong hydrophobic interactions exist between tropoelastin monomers, contributing significantly to dimer stabilization. Upon crosslink formation, the monomer conformations within the dimer diverge into two distinct structural states, consistent with previous studies. Furthermore, we find that noncovalent hydrophobic interactions and covalent crosslinking act cooperatively to enhance self-assembly efficiency by modulating the exposure of hydrophobic regions and crosslinking sites.

Importantly, crosslinking plays a dominant role in shaping the energy landscape by regulating the sequestration of hydrophobic regions between monomers, thereby maximizing the availability of binding interfaces for additional tropoelastin molecules. At the same time, crosslinking helps overcome the energetic penalty associated with unfavorable hydrophobic exposure, facilitating continued assembly.

Together, these findings suggest that noncovalent hydrophobic interactions and covalent crosslinking are both necessary and cooperative in driving tropoelastin assembly during the early stages of elastogenesis. This contrasts with previous models proposing that crosslinking occurs only after coacervates are deposited onto microfibrils.

Overall, this work provides molecular-level insights into tropoelastin assembly. We establish a framework for investigating the kinetics of early-stage elastogenesis and offer a mechanistic basis for understanding how molecular interactions govern tropoelastin assembly and elastic fiber formation. We define principles for modulating tropoelastin assembly through targeted perturbation of hydrophobic interactions and crosslinking dynamics, which may help elucidate how disruptions contribute to disorders of impaired elastogenesis.

Elastin Proteomics – Developing LC-MS Workflows to Enhance Elastin Analysis

Jacob Heeckt, Nicoline Thorsen, Sara Jørgensen, Lasse Lorentzen, Luke Gamon, Andrea Heinz, Michael Davies

Liquid-chromatography-mass spectrometry (LC-MS/MS) is a powerful technique for unbiased examination of protein abundances and changes in tissues. A major bottleneck in studying elastin using this technique arises from the difficulty of digesting elastin with trypsin, the standard digestion enzyme used in bottom-up proteomic approaches, as cleavage sites are sparse and involved in crosslinking. Traditional methods to isolate elastin from tissue samples are laborious and typically do not permit comprehensive dual examination of elastin and non-elastin proteins in the same sample.

We have developed a new LC-MS workflow tailored to detect the insoluble, crosslinked elastin found in elastic fibers in different tissues including human skin and arteries. The core of this approach involves the sequential enzymatic digestion of tissue fragments that remain insoluble after trifluoroacetic acid (TFA) lysis as part of the well-established SPEED protocol. Multiple combinations of enzymes including trypsin, porcine pancreatic elastase and ProAlanase (a novel endopeptidase that cleaves elastin-like polypeptides) have been examined. Using recombinant tropoelastin, we have also generated a peptide library of possible cleavage products of elastin. This workflow achieves ~90% elastin sequence coverage in skin and artery and near-complete coverage of recombinant tropoelastin.

Current studies are examining age- and disease-drives changes in elastin from skin, where young and old donors are compared, and arteries where atherosclerotic plaques are compared with (supposedly) healthy control arteries. In the plaques, a shift of the broader proteome towards a disease state is detected. We believe that the simplicity and throughput of the developed workflow will allow elastin analysis to be incorporated into routine proteomic analyses of elastic tissues, systematically capturing changes that have been previously missed.

Investigating plaque specific degradation patterns of elastin and other ECM proteins in Atherosclerosis using N-terminal proteomics

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Atherosclerosis is the main underlaying cause of cardiovascular disease worldwide. It leads to a narrowing of the vessels with various degrees of lipid build up, immune cell infiltration and ECM remodeling in the vessel wall. Plaque phenotypes are highly diverse, and remodeling of the ECM plays an integral part of determining plaque stability, but how this remodeling occurs is still not well understood. We propose that differential proteolytic activity might be driving remodeling and stability of atherosclerotic plaques and that a better understanding of the process can potentially drive new therapeutic target and biomarker discovery.

75 carotid atherosclerotic plaques and 8 superior thyroid vessels obtained from patients underwent an N-terminal proteomics workflow. Proteins were extracted using SPEED (concentrated acid), cleaved by TrypN followed by enrichment using strong-cation-exchange material and analyzed using LC-MS. This workflow allows us to investigate the endogenously cleaved products found within the plaque environment and compare them with control vessels lacking plaque formation.

A total of ~17000 unique N-terminal peptides were identified across all samples. After filtering, a total of 7979 N-terminal peptides were used for continued analysis originating from 1082 genes. 4,287 peptides were shared between controls and plaques, whereas 2353 were unique to plaques and 1339 were unique to controls. ECM proteins contribute with 24% of the intensity signal in both the control and plaque samples; however, the subgroups of ECM proteins differ in their contribution. Elastin was identified with 52 fragments (142 before filtering) found in plaques and ranked no. 28 on most abundant protein based on fragment intensities in plaques vs. 12 fragments and a ranking of 171 in control vessels. Fragment sequences suggest MMP-12 and/or MMP-9 as the main responsible proteases for elastase degradation with the active neo-N-terminal of MMP-9 being detected in about half of all plaque samples.

Further investigation into the cleavage sites of ECM species might provide new information about substrate and proteolytic activity happening during remodeling in atherosclerotic plaques.

Elastin and Elastic Fibers: Structure, Assembly, and Function

Searching for the Evolutionary Origin of Tropoelastin

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We have previously shown that elements of both positional sequence and collective properties (sequence 'style') in tropoelastins are remarkably conserved across Amniotes, representing ~320 million years (myrs) of evolutionary separation. We now have evidence that such strong conservation extends to at least 450 myrs, back to the earliest known examples of tropoelastins in living species, including Elasmobranchs (true sharks, rays and skates) and Holocephali (elephant sharks).

While it is highly unlikely that tropoelatin appeared de novo ~450 myrs ago, simple searches using conserved positional sequence motifs of tropoelastins fail to identify convincing progenitor proteins, even in Cyclostomes (lampreys and hagfish), the closest ancestral species group situated near the vertebrate/invertebrate boundary. While some sequence motifs, most notably GGLGY/GGYGL-like tandem repeats, are present in structural proteins from a very wide range of species (including arthropods, lampreys and some domains of tropoelastins), these more likely reflect a process of convergent evolution. Identification of true tropoelastin progenitors may therefore require more subtle search strategies, which also take into account conserved collective, but non-positional sequence characteristics that appear to be essential for polymeric assembly and elastomeric functionality.

Using this approach, we have identified a protein forming the structural matrix of lamprey branchial cartilage as a likely Cyclostomal progenitor of tropoelastins. The gene for this protein contains 8 exons, including (as is the case for tropoelastins) a signal peptide comprising most of exon 1. Exons contain extensive regions of tandem repeats, and intron/exon boundary characteristics are identical to those in all tropoelastin genes. Most importantly, the protein shares significant sequence elements and collective characteristics with tropoelastins across the entire evolutionary range, including matrix formation through lysyl oxidase-generated cross-links.

Identification of this protein as a progentitor of tropoelastins also raises the possibility of a much deeper evolutionary relationship of tropoelastins to proteins containing polyQ-rich motifs, suggested by facile transition of such polyQ motifs to conserved tropoelastin-like motifs through a simple process of frame-shifting and single-base codon substitutions.

These studies not only illuminate the evolutionary history of elastin but also provide important information for manipulating biomimetic properties of elastin-like biomaterials.

Aging of the elastic extracellular matrix: from molecules to tissues

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This abstract is not available online at the author's request.

Multiscale Mechanics and Structural Integrity of Arterial Elastin in Aging

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Elastic fibers form a hierarchical network that provides elasticity, resilience, and long-term mechanical integrity to the arterial wall. From single elastic fibers and elastic laminae to interconnected elastin networks, these structures bear substantial mechanical loads and must withstand billions of loading cycles throughout life. Despite their critical biomechanical role, the mechanisms by which age-related structural deterioration alters elastin function across multiple length scales remain to be understood.

We performed a multiscale investigation of arterial elastin spanning the fiber, lamellar, and tissue levels using human arterial tissues. Mechanical behavior was quantified through tensile testing of individual elastic fibers, purified elastin fibers, isolated elastic laminae, and purified elastin networks. Structural organization and integrity were characterized using multiphoton microscopy, histology, scanning electron microscopy, and quantitative image analysis. In addition, elastin structures were imaged during mechanical loading to directly examine deformation mechanisms, fiber recruitment and engagement.

Across hierarchical levels, elastin exhibited strong structure-function relationships. Mechanical behavior was governed not only by the intrinsic properties of individual fibers but also by the organization, connectivity, and integrity of the network architecture. Aging increased the mechanical heterogeneity of elastin fibers, resulting in a broader distribution of fiber strengths and an increased prevalence of mechanically compromised fibers. Furthermore, aging was associated with progressive microstructural deterioration, including fiber fraying, fragmentation, loss of continuity, and disruption of network organization. These structural changes compromise fiber recruitment and load bearing during deformation, leading to impaired mechanical integrity at larger scales. Together, these results reveal how age-related elastin degradation propagates across the structural hierarchy to alter arterial mechanical function, providing a multiscale framework for understanding vascular aging.

Elastin in Vascular, Pulmonary, and Skin Aging and Disease & treatment options and therapeutic advances?

Conditional inactivation of Adamts6 increased longevity and improved aortic wall structure in Marfan syndrome

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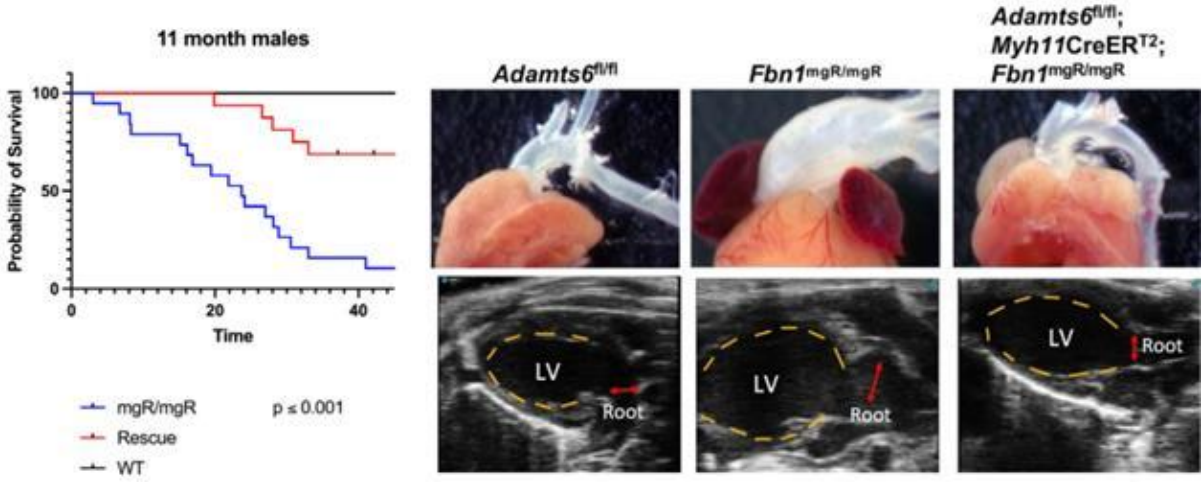
Marfan syndrome, a genetic connective tissue disorder, is characterized by aortic wall insufficiency in which aortic aneurysm and dissection can occur causing significant morbidity and mortality. This is caused, in part, by deficiency of fibrillin-1 microfibrils, which are necessary for aortic wall structure and function. We recently showed that purified fibrillin-1 bound to ADAMTS6 in a binary interaction assay and an ADAMTS6 cleavage site was subsequently identified in fibrillin-1 via N-terminomics. However, the impact of ADAMTS6 cleavage of fibrillin-1 is unknown during heart development and adult maintenance.

Mutant Adamts6 mice die at birth due to a myriad of congenital heart malformations. Therefore, we generated a conditional Adamts6 allele to delineate its role in the postnatal period, specifically in smooth muscle cells in a mouse model of Marfan syndrome (Fbn1mgR/mgR). This results in histologic improvement of aortic wall structure with statistically significant increased staining of fibrillin-1 microfibrils, decreased proteoglycan accumulation, diminished elastin breaks, increased aortic wall thickness, and increased longevity in Adamts6fl/fl;Myh11CreER;Fbn1mgR/mgR mice (termed rescue) in contrast to Fbn1mgR/mgR mice (termed MFS). Furthermore, echocardiogram showed that the rescue mice had comparable aortic root dimensions and E/A diastolic ratios to control as compared to MFS aorta. Single cell RNAseq showed increased contractile and decrease apoptotic smooth muscle cells in rescue aorta as compared to MFS aorta.

Together, the data herein suggests that ADAMTS6 regulation of fibrillin-1 microfibril and smooth muscle cell abundance is necessary for aortic wall maintenance. Moreover, it points to ADAMTS6 inhibition as a mediator of fibrillin-1 microfibril quantity in Marfan syndrome and the potential for therapeutic intervention to mitigate aortic aneurysms.



A genetic mouse model of cutis laxa reveals immune-driven descending and abdominal aortic aneurysms

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Aortic aneurysms (AAs) are a life-threatening manifestation of heritable connective tissue disorders such as cutis laxa, yet the influence of genetic background and the cellular mechanisms driving regional disease progression remain poorly understood. We studied a hypomorphic Fibulin-4 mouse model (Fibulin-4R/R) on an FVB genetic background to define aneurysm development and its underlying cellular pathology.

Fibulin-4 R/R mice showed reduced Mendelian birth frequency and early postnatal mortality, particularly in females, indicating perinatal lethality. Surviving mice exhibited congenital structural abnormalities of the thoracic aorta and developed progressive aneurysmal dilations with age that extended into the descending thoracic and abdominal aorta—regions for which genetically driven mouse models are scarce. Early vascular changes included medial thickening, elastin disorganization, and increased proteoglycan deposition, preceding overt aneurysm formation. Quantitative µCT and histological analyses confirmed site-specific aneurysm progression. Cardiac assessment revealed heterogeneous remodeling, characterized by increased left ventricular mass, induction of hypertrophic and extracellular matrix remodeling markers, and impaired function in a subset of animals.

To link vascular pathology to cellular mechanisms, we performed single-cell RNA sequencing of aneurysmal aortic tissue. This revealed pronounced smooth muscle cell (SMC) phenotypic switching, with the emergence of aberrant SMC populations displaying fibroblast-like, osteogenic-like, and inflammatory transcriptional profiles. These altered SMC states were associated with markers of cellular senescence, dysregulated TGF-β signaling, and increased p21 expression. In addition, substantial infiltration of immune cells, including $CD45^+$ populations, was observed, indicating an inflammatory vascular microenvironment.

In summary, this study identifies Fibulin-4 R/R mice on an FVB genetic background as a rare genetic model that develops not only congenital thoracic but also progressive descending thoracic and abdominal aortic aneurysms. By combining in vivo phenotyping with single-cell transcriptomics, we demonstrate that aneurysm progression in these regions is associated with pronounced smooth muscle cell phenotypic switching toward senescent and inflammatory states, together with robust immune cell infiltration. These findings uncover previously underappreciated immune involvement and regional vulnerability in Fibulin-4–associated aortopathy, providing new mechanistic insight into abdominal aneurysm development in cutis laxa and a platform to explore targeted therapeutic strategies.

Impact of Estradiol-Priming on Elastic Matrix Regenerative Properties of Stem Cell Extracellular Vesicles

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Abdominal aortic aneurysms (AAAs) are rupture-prone dilations resulting from chronic MMP-mediated elastic matrix proteolysis, carrying high surgical risk in older patients with no established drug therapies. AAA prevalence is 6-fold higher in males than pre-menopausal females, and estrogen (17β-estradiol, E2) may reduce AAA formation. E2-preconditioned mesenchymal stem cells (MSCs) show improved paracrine therapeutic effects mediated through extracellular vesicles (EVs). We investigated IV-injected MSC-EV biodistribution in a rat AAA model and assessed the effects of E2-primed male MSC-EVs on gene and protein expression in AAA regenerative repair.

EVs were isolated from male, E2-primed male, and female human bone marrow MSC supernatants via differential ultracentrifugation. To evaluate E2 priming effects, elastase-induced rat AAA smooth muscle cells (EaRASMCs) and rat AAA models were treated with EVs from male, E2-primed male, and female MSCs for 24 h, or weekly (25 µg IV) for three weeks. qPCR showed significantly higher TIMP2 gene expression with E2-primed male EVs versus non-primed male EVs, female EVs, and untreated controls. Western blot confirmed significantly higher TIMP2 protein with E2-primed male EVs versus female EVs. MMP2 gene and protein expression were significantly reduced in all EV-treated groups compared to untreated controls. Biodistribution was assessed in an elastase-injury rat model (male Sprague Dawley rats, 100–150g) using near-infrared labeled EVs (ExoGlow-Vivo) injected via tail vein at 21 days post-injury, tracked at 6 h, 24 h, 72 h, and 7 days. Lungs, heart, aorta, liver, kidneys, and spleen were harvested and imaged. Imaging revealed partial EV uptake at aneurysmal sites within 6–24 h with fluorescent EVs absent in healthy aortic segments and declining retention through day 7. Evs accumulated in non-target organs including liver, spleen, lungs, and kidneys. Quantitative morphometry of Modified-Harts-stained tissue sections showed marked improvement in elastic lamellar structure in E2-primed-EV-treated animals. Cytokine and MMP array-assessment of EV effects is ongoing.

IV-administered MSC-EVs demonstrate natural affinity for aneurysmal sites, while E2-primed male MSC-EVs show superior matrix remodeling effects, elevated TIMP2 and reduced MMP2, compared to non-primed male and female EVs. Weekly repeat dosing holds potential to maximize elastic matrix restoration and inflammatory modulation, supporting a stem cell-inspired, cell-free AAA treatment strategy.

Dill extract induces elastic fibers preservation/neosynthesis and improves the aortic function in adult and aged male and female mice

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Elastic fibers are extracellular matrix components made of elastin and microfibrils, only synthesized until the end of adolescence. They provide large arteries with elasticity, allowing for smoothing of the discrete/pulsatile blood flow and pressure generated by the heart, which is essential for appropriate tissue perfusion. During aging, elastin and elastic fibers are progressively degraded, without possibility of natural repair/resynthesis, leading to arterial stiffening and dysfunction. Dill extract (DE) was previously shown to stimulate elastin or elastic fiber neosynthesis: i) in vitro in human skin fibroblasts, derm equivalent models and ascending aorta vascular smooth muscle cells (VSMCs), and ii) in vivo in the ascending aorta of aged male mice, at 10% in drinking water for 3 months, with decreased aortic stiffness and unchanged blood pressure (while 5% DE decreased blood pressure). In male and female C57Bl6/J mice, in which physiological elastic fiber synthesis is physiologically stopped, we investigated the impacts of age (6- vs. 24-months-old) and sex on the cardiovascular effects, in particular the abdominal aorta structure-function (blood pressure, mechanics, histology), of a chronic DE treatment (5% v/v, in drinking water, for 3 months) and impact of 1-3% DE on elastin production by cultured aortic VSMCs. In all groups, DE reduced aortic elastic fiber ruptures and re-induced elastin and/or elastic fiber synthesis in the aorta, in cultured aortic VSMCs, and relative desmosine content of the carotid artery wall in females. DE treatment decreased aortic stiffness in animals of both ages (particularly in females) and shifted the stress-strain relation of aortae from aged mice of both sexes close to that found in corresponding untreated adults. Finally, DE treatment decreased blood pressure of aged animals and abolished the age-dependent increase in pulse pressure in both sexes, while it reversed the age-related cardiac hypertrophy in male mice, not in females. Our results suggest that DE presents a clear potential for arterial structure-function regeneration in elastic fiber-degrading diseases in adult animals or in an anti-aging perspective, even when treating already aged animals. Future structural studies using high resolution tomography should clarify the impact of DE on the 3D organization of elastic fiber networks in arteries.

Elastin-Related Signaling

Interaction of elastin-derived peptides with model lipid membranes

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Elastin-derived peptides (EDPs), generated during elastin fragmentation in aging and pathological conditions, are widely recognized for their biological activity through interactions with cell-surface receptors. However, despite their hydrophobic character and proximity to membrane-associated receptors, their capacity to directly interact with lipid bilayers has remained largely unexplored. In this study, we investigated the membrane-binding properties of representative elastin hexa and nonapeptides using a combination of molecular dynamics simulations, potential of mean force calculations, and synchrotron radiation circular dichroism spectroscopy. Our results reveal that the hexapeptide displays minimal membrane interactions while nonapeptides bearing the XGXPGXGXG consensus motif exhibit significant and dynamic membrane association. Cholesterol markedly reduces membrane affinity, indicating a strong dependence on membrane composition. Membrane interaction stabilizes β-turn conformations, particularly type II turns. Together, these findings demonstrate that certain elastin nonapeptides are capable of direct lipid-bilayer interactions, unveiling a previously underappreciated physicochemical dimension of EDP activity. This membrane-binding capability may contribute to their biological effects by modulating local membrane organization.

Acknowledgements. The authors thank Synchrotron SOLEIL for beamtime allocation under proposals 20230968 and 20241157.

Understanding the molecular mechanisms underlying the binding selectivity of human EBP toward elastin peptides and galactosugars

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The extracellular matrix (ECM) plays an important role in maintaining tissue function, integrity and homeostasis, and provides architectural support for cells. Elastic fibres, composed of the protein elastin, are the main components of the ECM and are abundant in tissues subject to high mechanical stress, such as the skin, lungs and arteries. Elastin derived peptides (EDPs), formed as a result of elastin degradation, have been shown to modulate key cellular processes through binding to the elastin-binding protein (EBP), yet the molecular basis underlying their differential activities remains unclear. In the present study, systematic molecular docking on a homology model of EBP with duplicate 1 µs molecular dynamics (MD) simulations were combined to characterize the binding modes and interaction networks of galactosugars, biologically active (LGTIPG, PGAIPG) and inactive (VVGPGA, VPVGGA, GGVPG) elastin-derived peptides (EDPs) within the V32 pocket of EBP. The observed results reveal two partially overlapping functional regions within the V32 pocket and make it possible to identify the interaction sites of the different ligands and to propose a model in which the active peptides and galactosugars share a common region, while the inactive peptides preferentially occupy an adjacent subregion that partially overlaps the first, thereby challenging the notion of entirely distinct EBP binding sites.

Detection and quantification of native and modified proteins in extracellular matrices

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Atherosclerosis is the major underlying cause of cardiovascular disease, and a leading cause of mortality worldwide. Destabilization and rupture of atherosclerotic plaques can result in limb ischemia, myocardial infarction and ischemic stroke. Data indicate plaque destabilization is associated with extracellular matrix (ECM) modification and remodelling, with instability potentially arising from the generation of oxidants and the activity of proteases. We hypothesized that plaques susceptible to rupture would contain different protein populations, and larger numbers of modified and fragmented species, when compared to stable plaques and control arteries.

Plaques from 76 patients who underwent carotid surgery following symptomatic carotid artery stenosis were examined. A small number of non-atherosclerotic superior thyroid artery segments (n=8) were also obtained. These were solubilized, digested, and analyzed by LC-MS. 7,343 parent proteins were identified at a 1% false-discovery rate, with 5,731 proteins subsequently quantified, including 354 ECM proteins. Fragment analyses yielded 35349 peptides, with 19543 being N-terminal species; of these, 6561 were subsequently quantified. Multidimensional scaling analysis and hierarchical clustering indicate the presence of three distinct clusters, and large numbers of differentially-abundant proteins, oxidation products and protein fragments. These clusters correlate with gross macroscopic morphology, ultrasound classification (echolucent/echogenic) and presence of hemorrhage/ulceration.

Major differences were identified in the complement of proteins and fragments between control arteries and plaques, and between plaque types. In contrast the pattern of oxidation products remained relatively constant between control versus diseases tissue, but the levels in plaques were considerably higher, and the proteins on which they were present differed.

Rupture-prone plaques contained higher levels of proteins from leukocytes, and those associated with inflammation, proteolysis and oxidant generation. Stable plaques showed higher levels of structural and ECM species. Sequence analysis provided data on the targets of oxidation and fragmentation, with these including elastin, together with data on the proteases responsible for fragment generation.

These studies therefore provide a large dataset on proteins, oxidative modifications and protein fragments present in plaques, with these being possible biomarkers for improved risk profiling. Furthermore, these studies provide mechanistic insights into remodelling processes, and biochemical processes that are active in stable versus rupture-prone plaques.

Elastin-Based Biomaterials for Tissue Regeneration

Photolabile elastin-like recombinamer hydrogels for dynamic modulation of cell-instructive microenvironments

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Dynamic changes in extracellular matrix (ECM) mechanics regulate fundamental cellular processes, yet most photoresponsive hydrogels either lack biological functionality or exhibit limited reproducibility. Here, we developed a fully recombinant photolabile elastin-like recombinamer (ELR) hydrogel capable of light-mediated modulation of its mechanical and structural properties while preserving high cytocompatibility.

Two ELR-based hydrogels were generated by catalyst-free strain-promoted azide–alkyne cycloaddition (SPAAC) using structural cyclooctyne-functionalized ELRs and RGD containing ELRs bearing either fully photolabile or mixed photolabile/stable nitrobenzyl crosslinkers. Photocleavage kinetics were analysed by NMR, while rheology and scanning electron microscopy (SEM) were used to characterize changes in stiffness and microstructure following

UV irradiation (365 nm). Human mesenchymal stromal cells (hMSCs) were encapsulated to evaluate cell viability and morphology. UV irradiation induced first-order photocleavage of nitrobenzyl crosslinkers, resulting in progressive hydrogel softening and pore enlargement. In fully photolabile hydrogels, the elastic modulus decreased from approximately 2.6 kPa to 1.0 kPa after 15 minutes of irradiation, whereas partially photolabile hydrogels softened from 1.6 kPa to 0.4 kPa. SEM analysis revealed a marked increase in pore size together with progressive network remodelling. Importantly, hMSC viability remained above 75% under all irradiation conditions. Matrix softening significantly altered cell behaviour, increasing the proportion of elongated cells from <10% in non-irradiated hydrogels to approximately 85–90% after 15 minutes of light exposure, indicating enhanced cell spreading and matrix invasion [1].

This recombinant ELR platform enables precise spatiotemporal control of hydrogel mechanics without compromising cell viability. The combination of dynamic mechanical tunability, intrinsic bioactivity, and recombinant reproducibility provides a versatile biomaterial for mechanobiology studies, organ-on-chip systems, bioprinting, and next-generation adaptive tissue engineering strategies.

References:

[1]. P. Rodríguez-Alonso, A. I. Montero-Toquero, S. Herrero-Fernández, L. Quintanilla Sierra, J. C. Rodríguez-Cabello, and M. Santos-García, "Photolabile Elastin-Like Recombinamer Hydrogels for Dynamic Modulation of Cell-Instructive Microenvironments," European Polymer Journal 254 (2026): 114828

Elastogenic compounds modulating extracellular matrix production in vitro

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This abstract is not available online at the author's request.

Electrospun Scaffold enriched with bioactive molecules as nanofibered medical devices.

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Chronic skin wounds affect approximately 37 million individuals worldwide and account for an estimated 35% of total healthcare expenditures related to wound management. Their incidence continues to rise particularly in patients with diabetes mellitus (DM), vascular disease, and advanced age. Nanotechnology enables the fabrication of materials with tailored architecture, controlled presentation of bioactive cues, and programmable drug release profiles, thereby providing advanced and effective strategies for tissue regeneration and wound healing. Representative systems include electrospun nanofibers (NFs) delivering bioactive substances such as angiogenic, and growth factors. In this work, bilayered electrospun scaffolds were engineered. They consist of a hydrophobic PDLLA and hydrophilic PVP layer that incorporate either native HA or semi-synthetic HA-Xxx-OH at concentrations of 1% and/or 3% w/w (Xxx=Gly, Arg). Glycine is the most abundant aminoacid in elastin and therefore the choice of Gly is aimed to being a model. L-Arginine a precursor of nitric oxide (NO), plays a key role in promoting angiogenesis, collagen synthesis, and re-epithelialization playing a key role in wound dressing. Generally, bilayer scaffolds electrospun on different days delaminated, while herein they maintained their integrity because they were electrospun on the same day. Sequential electrospinning enabled the bilayer structure characterized via Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM), and Youngs modulus measurements to assess morphology and mechanics. In vitro cytotoxicity and cell viability assays with fibroblast cells confirmed good biocompatibility for both the individual layers and the bilayer system. Among the tested formulations, the bilayer PDLLA/PVP–HA-Gly-OH 1% showed the most promising performance, attributed to the synergistic effects of HA and Gly-OH in promoting adhesion and proliferation.

Elastin-like recombinamer hydrogels as multiphase and mechanically active matrices for instructive tissue regeneration

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This abstract is not available online at the author's request.

Emerging Techniques to Study Elastin and Elastic Fibers

Revisiting Elastin Recoil: Shear-Driven Molecular Stretching in Hydrated Intact Fibres Revealed by Solid-State NMR

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Elastic properties of elastin arise from the its sequence. Lysine (Lys)-derived cross-links in hydrophilic domains form short α-helices, which enable structure-driven recoil. Hydrophobic domains, enriched in hydroxyproline (Hyp), form water-swollen aggregates with transient conformations (random coils, β-turns, and short polyproline II (PPII) helices) that interconvert rapidly, providing entropy-driven recoil. However, these findings are based on studies of isolated elastin or polypeptides and have not been validated in intact elastin fibres. Additionally, dehydration of elastin during extraction leads to a loss of elasticity; thus, elastin must be studied in hydrated tissue.

Therefore, we developed a vascular smooth muscle cell model which, after mild decellularisation, yielded elastin fibres within a preserved extracellular matrix (ECM), suitable for study by solid-state NMR (SSNMR). Using heteronuclear correlation (HETCOR), we examined conformational changes as water was partially removed by centrifugal force or reintroduced during a pause. This model mimics aspects of arterial pulsatile flow, which introduces shear stress within the vascular wall.

In hydrophobic domains, shear stress caused a chemical shift change for Hyp 13Cγ (70.5→70.8 ppm) and 1Hγ (4.4→4.7 ppm), as well as 13Cβ and 13Cδ broadening, consistent with pyrrolidine ring-puckering and a transition of some sequences from random coil to PPII helices. Hydrophilic domains were also affected: Lys in α-helical conformation showed changes in 13Cα (57 → 56.6 ppm) and 1Hα (4.15 → 4.3 ppm) . These chemical shift changes are consistent with slight molecular stretching, in which hydrogen bonds are extended but not broken. Lys in random coil conformation was also sensitive to shear stress, with shifts in 13Cα (53.6 → 53.1 ppm) and 1Hα (4.7 → 4.9 ppm), indicating a transition to β-turns or PPII helices. All spectral changes were fully reversed during the pause in centrifugation.

Thus, the recoil of intact elastin fibres depends not only on structurally disordered sequences but also on α-helices, which, under shear stress, undergo molecular stretching of hydrogen bonds and, at higher stress, may lead to bond rupture and loss of recoil ability associated with many diseases.

An integrative machine learning approach to classify cutis laxa syndromes, supported by electron microscopy

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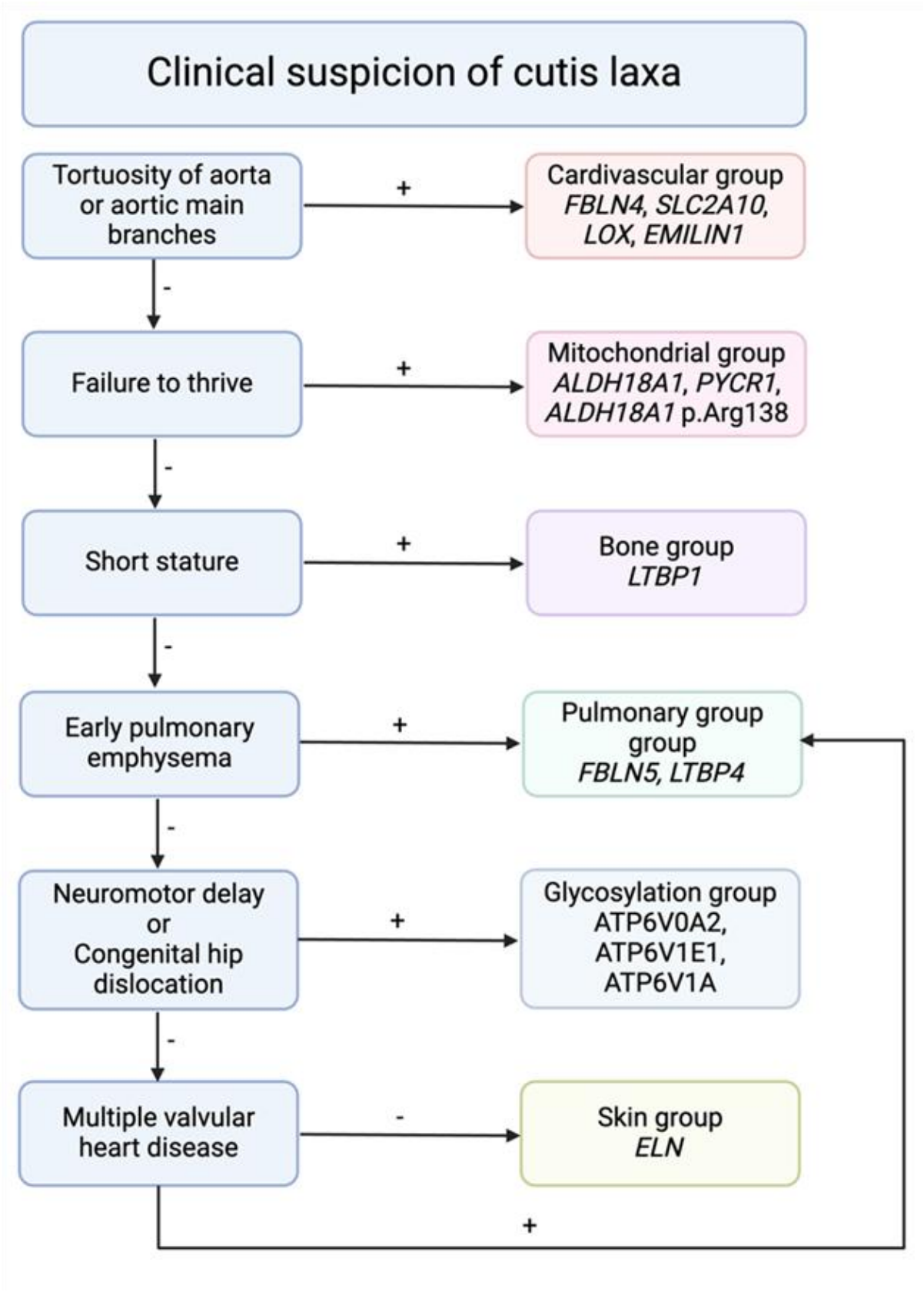
Background: Cutis laxa (CL) syndromes comprise a heterogeneous group of disorders characterized by loose redundant skin and variable systemic involvement. The current OMIM classification does not use clinical handles and fails to account for pathophysiological correlations

Objective: To develop a classification system for CL syndromes integrating clinical features, histopathology, and pathophysiology.

Methods: We retrospectively analyzed 192 in-house patients and conducted a systematic literature review including 577 patients. A CART algorithm was trained and tested on the in-house cohort to evaluate stratification into predefined clinically derived classes and externally validated on the literature cohort. Image-based classification of 203 cases used GestaltMatcher descriptors as input for a support vector machine (SVM) trained to distinguish six classes. Transmission electron microscopy (TEM) was performed on skin biopsies across subtypes.

Results: A six-step clinical flowchart achieved 91% accuracy (κ = 0.870) in the in-house cohort and 76.5% (κ = 0.684) in the literature cohort, with reduced performance mainly due to incomplete data. The SVM performed best for mitochondrial, glycosylation, and cardiovascular classes. TEM demonstrated subtype-specific and overlapping abnormalities of elastic fibers consistent with clinical groupings.
Conclusion: We propose a machine learning–based CL classification integrating clinical, molecular, and ultrastructural data. Image-based SVM analysis provides complementary support, offering a robust and clinically applicable framework for CL patient management.

Supporting images on the next page


Clinical suspicion of cutis laxa
Tortuosity of aorta or aortic main branches
+
Cardivascular group
FBLN4, SLC2A10, LOX, EMILIN1
-
Failure to thrive
+
Mitochondrial group
ALDH18A1, PYCR1, ALDH18A1 p.Arg138
-
Short stature
+
Bone group
LTBP1
-
Early pulmonary emphysema
+
Pulmonary group
group
FBLN5, LTBP4
-
Neuromotor delay or Congenital hip dislocation
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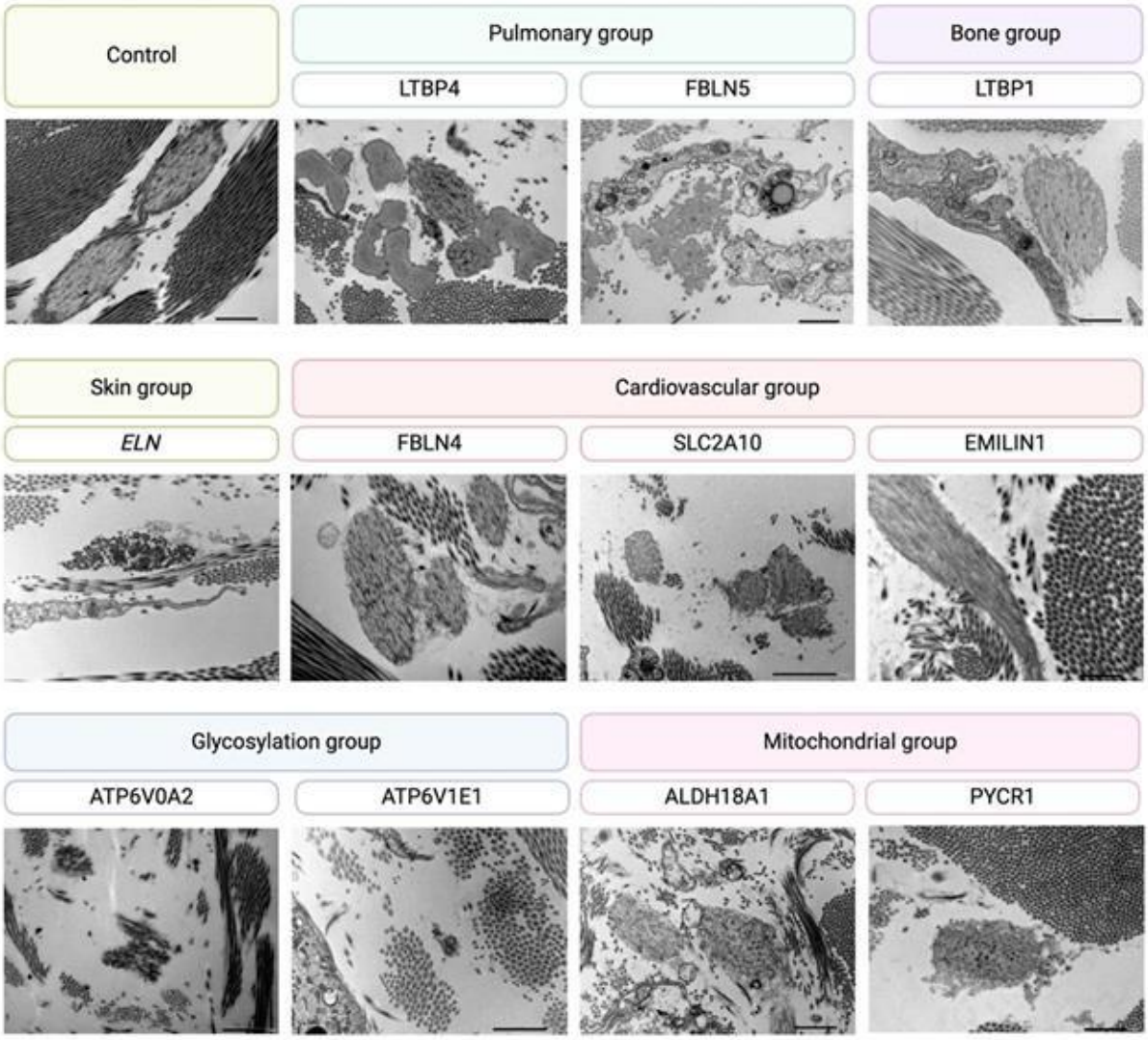
Glycosylation group
ATP6V0A2, ATP6V1E1, ATP6V1A
-
Multiple valvular heart disease
-
Skin group
ELN
+


Control
Pulmonary group
Bone group
LTBP4
FBLN5
LTBP1
Skin group
Cardiovascular group
ELN
FBLN4
SLC2A10
EMILIN1
Glycosylation group
Mitochondrial group
ATP6V0A2
ATP6V1E1
ALDH18A1
PYCR1

Biomechanical and extracellular matrix changes in young and menopausal forearm skin

Ozorun G[1], Santos M[2], Masen M[2], Irwin R[3], Bradley E[3], Farrar M[1], Langton A[1], Purohit K[1], Birtles T[1], Mistry K[1], Eckersley A[1], Swift J[1], Sherratt M[1]

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This abstract is not available online at the author's request.

Obesity-associated remodeling of the lung matrisome is linked to elastic fiber alterations and features of premature aging

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Obesity induces systemic tissue remodeling beyond classical metabolic organs, yet its impact on lung extracellular matrix homeostasis remains poorly understood. Here, we combined proteomics, lipidomics, single-cell transcriptomics, and histological analyses to characterize obesity-associated changes in the lung matrisome. We identified broad alterations in extracellular matrix composition, including disturbed elastic fiber architecture, changes in elastin-associated proteins, and an imbalance of protease-antiprotease pathways. Several of these alterations partially overlapped with signatures observed in the aging lung, suggesting features of premature tissue aging. Together, our findings indicate that obesity profoundly remodels the pulmonary matrisome and may compromise elastic fiber maintenance, potentially affecting tissue resilience and repair capacity.