



Nuclear mechanobiology: a brief history and five unresolved questions

Jan Lammerding , Jorine Eeftens , Gregg G. Gundersen , Megan C. King ,
Tanmay P. Lele , Song Li , Gant Luxton, G. W. , Ohad Medalia , Matthieu Piel ,
Pere Roca-Cusachs , Jörg Renkawitz , Kyle Roux , Daniel A. Starr , Amy R.
Strom , Hawa Racine Thiam , Sara A. Wickström & Howard J. Worman

To cite this article: Jan Lammerding , Jorine Eeftens , Gregg G. Gundersen , Megan C. King ,
Tanmay P. Lele , Song Li , Gant Luxton, G. W. , Ohad Medalia , Matthieu Piel , Pere Roca-
Cusachs , Jörg Renkawitz , Kyle Roux , Daniel A. Starr , Amy R. Strom , Hawa Racine Thiam , Sara
A. Wickström & Howard J. Worman (2026) Nuclear mechanobiology: a brief history and five
unresolved questions, *Nucleus*, 17:1, 2709894, DOI: [10.1080/19491034.2026.2709894](https://doi.org/10.1080/19491034.2026.2709894)

To link to this article: <https://doi.org/10.1080/19491034.2026.2709894>



© 2026 The Author(s). Published by Informa
UK Limited, trading as Taylor & Francis
Group.



Published online: 24 Aug 2026.



Submit your article to this journal [↗](#)



Article views: 1957



View related articles [↗](#)



View Crossmark data [↗](#)

Nuclear mechanobiology: a brief history and five unresolved questions

The nucleus has long been recognized as the repository of the cell's genomic information, providing the blueprints for assembling the cell's structures and carrying out its functions. Over the past three decades, however, it has become abundantly clear that cellular structure and function are not only governed by the genome's sequence, but also the physical structure and mechanical properties of the nucleus [1]. Furthermore, nuclear structure and mechanics are not fixed properties but respond dynamically to physical and biochemical cues from inside and outside the cell, thereby enabling cells to sense and adapt to their environment [2–4]. This intriguing interplay of how nuclear structure and mechanics modulate cellular functions, and how mechanical forces acting on the nucleus affect its structure and function is now commonly referred to as 'nuclear mechanobiology.'

Some of the earliest work motivating the study of nuclear mechanobiology includes the recognition that compression of cartilage induces severe changes in nuclear shape and volume [5], and the elegant demonstration that extracellular forces are rapidly transmitted to the nucleus via the cytoskeleton, inducing intranuclear deformation [6]. This led to the hypothesis that the nucleus plays a central role in cellular mechanosensing. Since then, nuclear mechanobiology has grown into a rapidly expanding, interdisciplinary research area spanning cell and molecular biology, genomics, physics, engineering, and, increasingly, translational science and medicine. Subsequent studies have (i) shed light on how nuclear envelope proteins such as lamins and emerin, along with chromatin and intranuclear condensates, determine the physical properties of the nucleus [7–11], (ii) described characteristic changes in nuclear mechanics during differentiation and in response to the cellular physical environment [2,12], (iii) identified the molecular components involved in physically coupling the nucleus to the cytoskeleton, including the aptly named Linker of

Nucleoskeleton and Cytoskeleton (LINC) complex [13–17], and (iv) demonstrated that the association and dissociation between the nuclear lamina and chromatin can drive chromatin remodeling [18–20]. These studies have laid the foundation for the discovery that the nucleus, and particularly the nuclear envelope, plays crucial roles in cellular mechanotransduction (i.e., the translation of mechanical cues into biochemical signals and changes in gene expression), both through structural reorganization and via biochemical signaling processes, thereby modulating cell differentiation, fate and survival [3,4,7,21–31].

Other studies have focused on how the physical properties of the cell nucleus, including its size, shape, and stiffness, modulate diverse cellular functions. Two areas of particular interest are the role of nuclear mechanobiology in (i) cell migration through confined spaces, e.g., during development, inflammation, and metastatic spreading of cancer cells, and (ii) diseases caused by mutations in genes encoding nuclear envelope proteins that affect skeletal and cardiac muscle and other mechanically active tissues. We now know that migration through tight spaces is limited by the deformability of the nucleus [32–38], that the nucleus can guide cells to find their path through complex 3D environments [39], and that the physical stress on the nucleus during confined migration can cause nuclear envelope rupture, DNA damage, altered chromatin organization, and changes in gene expression [40–48]. Mechanically induced nuclear damage has also emerged as an important disease driver in at least a subset of muscular dystrophies and cardiomyopathies caused by mutations in genes encoding nuclear envelope proteins such as lamins and emerin [7,49–53], with altered chromatin organization and transcription, in part resulting from perturbed tethering of chromatin to the nuclear periphery, likely serving as additional pathogenic mechanisms [54,55]. Intriguingly, reducing nuclear envelope rupture by disrupting the LINC complex has

been shown to dramatically slow disease progression and extend survival in preclinical models of these diseases [50,56–59]. A clinical trial leveraging this approach, scheduled to begin soon [60], showcases the potential of nuclear mechanobiology impact on patient care.

As interest in nuclear mechanobiology continues to grow, new insights and applications emerge. Recent examples include the opening of nuclear pore complexes in response to nuclear membrane tension [24,25,61–63], substrate stiffness-induced changes in chromatin compaction and/or accessibility [64,65], the bidirectional interplay between mechanical stress, nuclear mechanics, and DNA damage repair pathways [66–70], and the role of nuclear mechanics in immune cell function [71–73]. We are excited to highlight and discuss the current knowledge in many of these research areas in a *Special Issue on Nuclear Mechanobiology*. The special issue includes reviews on nuclear mechanobiology confined migration [74], immune cell function [75], mechanotransduction at the nuclear envelope [76], the role of chromatin in nuclear mechanics [77], nuclear movement and migration [78], integration between nuclear mechanosensing and integrin adhesions [79], muscle aging [80], and novel tools to image nuclear structure by cryo-electron tomography [81] or study mechanical regulation of chromatin [82].

Nevertheless, even as the field of nuclear mechanobiology has made extensive progress, many open questions remain, and new questions continue to arise. To kick off this special issue, we reached out to top experts in nuclear mechanobiology and asked them to list what they consider the most pressing open research questions in the field today. More than 15 experts responded and agreed to serve as coauthors for this editorial. We then consolidated their input into five central open questions in nuclear mechanobiology. We recognize that such a list cannot be comprehensive and offers only a single snapshot of prevalent thoughts and ideas in the field, and we encourage readers to add and ponder additional questions. We hope that the following questions will inspire and motivate further research into the mechanobiology of the nucleus, so that we gain further insights into the fascinating interplay between nuclear

structure, mechanics, and cellular functions. There is still so much to learn about mechanobiology and the nucleus!

Five central open questions in nuclear mechanobiology

The molecular basis of nuclear mechanics: which ultrastructural components and connections determine nuclear structure and stiffness, and how are they regulated?

Wide-ranging studies aimed at measuring nuclear biomechanics, using intact cells and isolated nuclei, have produced an extensive list of molecules that contribute to the mechanical properties of the nucleus. These contributors include various nuclear envelope proteins, such as lamins, emerin, LAP1, LAP2 β , LBR, and LEMD2, as well as chromatin and histone modifications [7,9,19,83–91]. However, exactly how these molecules contribute to nuclear mechanics, including their ultrastructural organization and their interplay that gives rise to emergent properties, remains largely undetermined. For example, lamins and many other nuclear envelope proteins can directly interact with each other and with chromatin but can also form discrete networks and complexes [92–94]. We still lack a complete understanding of the composition, structure, and function of these protein complexes at the nuclear envelope, as many of the nuclear envelope proteins include intrinsically disordered domains that are challenging to resolve with current methods. Furthermore, elegant work in yeast showed that untethering chromatin from the nuclear envelope results in increased nuclear deformability [11]. However, the effect of interactions between chromatin and the nuclear lamina, nuclear pore complexes, and nucleoskeletal structures on nuclear mechanics in mammalian cells has proven difficult to untangle from the intrinsic mechanical properties of chromatin and its role in gene expression. New approaches to ‘visualize’ the nuclear lamina structure and chromatin organization, including both imaging techniques and molecular biology assays, will be needed to paint an accurate picture of nuclear ultrastructure and dynamics.

Even when focusing on individual molecules, numerous questions remain. For example, despite very similar structure and biochemical properties,

A-type and B-type lamins differ substantially in their effect on nuclear deformability [85,92], but the molecular features responsible for this difference have yet to be determined. Additionally, many small nuclear envelope proteins such as emerin and short nesprin isoforms can be found both at the inner and outer nuclear membrane; how their intracellular localization affects their contribution to nuclear mechanobiology is only beginning to emerge [26].

The nuclear interior poses many of its own questions. For example, how does biomolecular condensation influence nuclear mechanical properties and function, and conversely, how do mechanical forces on the nucleus—or generated within the nucleus during DNA replication, transcription, or loop extrusion—shape intranuclear architecture and condensate formation [95,96]? And how does macromolecular crowding, which can be affected by physical and biochemical cues [97,98], alter nuclear mechanics, function, and ultimately cell fate? Molecular crowding is emerging as an important mechanobiology variable [97,99,100], yet how mechanical forces alter local crowding, and how crowding modulates nuclear and cytoplasmic functions, remains largely unmapped.

Gaining further insights into the molecular and biophysical details governing nuclear mechanics will provide a deeper understanding of fundamental biological functions but might also reveal new clues into pathogenic processes and new therapeutic strategies.

The adaptability of nuclear structure and mechanics: how do mechanical stimuli and other signals modulate nuclear mechanics?

Increasing evidence suggests that the mechanical properties of the nucleus are not static, but can change dynamically, for example, during confined migration [101], in response to acute force application [21], changes in substrate stiffness [2], or cell differentiation [2,12, 97, 98, 102, 103]. In some cases, the changes in nuclear mechanics can be attributed to altered lamin expression or chromatin organization [2,12,102,103], although the upstream mechanisms largely remain to be determined. In many other scenarios, it is still unclear how intra- and extranuclear cellular processes modulate nuclear organization and mechanical properties, for example, by altering

macromolecular crowding, assembly of macromolecular complexes, and/or nuclear condensates. Similarly, it remains to be explored to what extent changes in nuclear mechanics result from direct mechanically induced protein conformational changes that affect protein–protein and protein–nucleic acid interactions, or downstream biochemical and signaling pathways. Additionally, the timescales required for such changes to occur or be reversed, and to what extent such changes can result in local variations in nuclear mechanics and function within the nucleus [104], are yet to be fully defined.

The simple fact that cells can rapidly ‘adjust’ their lamin levels to the substrate stiffness and viscoelasticity [2,31,105], yet different cell types retain the characteristic lamin levels of their tissue of origin in culture, even after numerous passages on stiff tissue culture plastic [2], indicates that there is still much to be learned about the dynamic regulation of nuclear mechanics. This includes cell cycle-dependent changes in nuclear mechanics, and the question whether nuclear mechanics are primarily determined during early post-mitotic events, e.g., nuclear envelope re-assembly and chromatin decondensation, or also later in the cell cycle. A fundamental question is how nuclear mechanical properties change over longer time periods, for example, during development or aging, and how such changes functionally contribute to both physiological and pathological processes.

Lastly, individual nuclei often display variability in chromatin compaction, nuclear body organization, and mechanical stiffness—regardless of whether studied *in vitro* or *in vivo*—but the origins and consequences of this heterogeneity are still not well understood. Answering this question might provide not only further clues into the factors that govern nuclear shape and function, but also how tissues and organs maintain robust function despite or because of this heterogeneity.

Nuclear mechanosensing: how are mechanical forces on the nucleus translated into changes in gene expression and cellular signals?

The nucleus has long been proposed to serve as a cellular mechanosensor, but experimental data unequivocally documenting that forces or

deformations applied to the nucleus are sufficient to activate cellular signaling pathways and expression of mechanoresponsive genes are still quite sparse. For example, whereas recent studies provided clear evidence that nuclear deformation triggers increased cell contractility, mediated by cPLA2 responding to changes in nuclear membrane tension [3,4,23,76,106], in many other cases it remains unclear whether observed changes in chromatin organization or gene expression result from mechanosensing events within the nucleus or downstream of mechanotransduction processes at the plasma membrane or in the cytoplasm. Thus, it largely remains to be resolved if, how, and to what extent, forces transmitted to the nucleus are transduced into changes in chromatin organization, gene expression, and epigenetic modifications, and which molecules and molecular pathways are involved in the associated processes. For example, are physical forces and deformations sufficient to induce chromatin opening, conformational changes in nuclear proteins, or alter intermolecular interactions (e.g., protein–protein binding, condensate formation, or protein–nucleic acid binding) under physiological conditions, thereby modulating transcriptional regulation? Or do the observed transcriptional changes require intermediate messengers and effectors, such as specific transcription factors, histone modifiers, or kinases, which could provide a mechanism to modulate the expression of specific genes? In the latter case it remains to be resolved how these modifiers are activated by mechanical stimuli, how such stimuli can achieve specificity, and whether these mechanoresponses employ mechanisms distinct from those associated with biochemical stimuli? Although recent studies support various putative mechanisms of nuclear mechanosensing [1,2,18,27,30,47,107], further work is needed to fully elucidate the underlying processes and identify the associated molecular players. It is also unclear whether nuclear tension, compression, and other deformations are sensed through the same or distinct mechanisms, and how such mechanical stimuli are integrated with cytoplasmic mechanotransduction pathways and input from other signals, such as biochemical stimulation, to inform cellular decision-making.

One illustrative example is the modulation of nucleo-cytoplasmic trafficking by nuclear membrane tension-mediated changes in the diameter of the nuclear pore complexes [24,25]. Based on cryo-

electron tomography imaging, the nuclear pore complex central channel increases from 43 nm to 57 nm when comparing isolated, tension-free nuclear envelope samples with nuclear pores *in situ* in fixed HeLa cells [108]. Smaller, but still significant changes in the nuclear pore diameter can also be detected in response to osmotic shock [61], or when cells are grown on soft versus stiff substrates [24,25], the latter of which cause nuclear flattening and increase membrane tension, and these changes are associated with increased nuclear transport. However, since numerous other factors also regulate nuclear transport of specific cargoes, including their posttranslational modifications, association with importins and exportins, the availability of co-transporters such as G-actin, retention by cytoplasmic or nuclear binding partners, and the intracellular Ran-GTP gradient [109,110], which can all be affected by the cell's physical environment, parsing out the contributions from nuclear membrane tension and changes in nuclear pore complex diameter versus other factors remains extremely challenging. Besides the mechanism of nuclear mechanosensing, other open questions revolve around the mechanical memory. This memory includes altered nuclear structure and cellular behavior that persists after the initial mechanical stimulus has been removed, along with how such mechanical memory is implemented, maintained, and, in many cases, eventually erased.

Answering these questions is made more challenging by the growing realization that many methods to disrupt nucleo-cytoskeletal force transmission, such as depletion of LINC complex components or LINC complex disruption using dominant-negative constructs, also affect nuclear and cytoskeletal organization, along with various signaling pathways, such as Wnt signaling [111–117]. For this reason, it is difficult to unambiguously distinguish between true nuclear mechanotransduction and other pathways.

Force transmission across the nuclear envelope: do we understand the structure and function of the LINC complex correctly, and how is the mechanical coupling between the cytoskeleton and nucleus regulated?

The LINC complex is comprised of KASH domain proteins, called nesprins in mammals, in the outer nuclear membrane that connect to SUN domain

protein trimers embedded in the inner nuclear membrane [13]. Since nesprins simultaneously interact with various cytoskeletal structures in the cytoplasm, and SUN proteins with lamins, nuclear pore complexes, and chromatin at the nuclear interior, this connection enables a physical link across the nuclear envelope. Consequently, over the past 20 years, the LINC complex has emerged as a central structure in mediating force transmission between the nucleus and cytoskeleton [13,114,118]. However, just as focal adhesions, adherens junctions, and desmosomes that mediate force transmission at the cell surface are not static mechanical connections but instead operate like a clutch that is responsive to inputs from inside and outside the cell, the interaction of nesprins and SUN proteins, along with their interaction with other binding partners, must be dynamically regulated to produce specific cellular outcomes. For example, cytoskeletal forces result in nuclear movement in some cases, while the nucleus can be anchored in place and resist movement in other cases, and in specific scenarios, such as meiosis, move chromosomes within the nucleus. Although recent imaging, modeling, and functional studies have shed some light on the interactions between nesprins and SUN proteins at the nuclear envelope [119–127], how this interaction is regulated, including the identity of relevant cellular signals and other molecules involved in the regulation [128], is still largely unknown. This is in part because the large size, flexible structure, and numerous isoforms of nesprins present substantial challenges in mapping their structure and function at the nuclear envelope.

In the case of focal adhesions, more than five decades of research have produced a nanoscale understanding of the architecture of the over 300 proteins that make up focal adhesions [129–133] and their role in mechanical force transmission and mechanosensing. Yet much of this information is still lacking for the LINC complex and its associated proteins, including its 3D topological architecture on the surface of the nucleus and the structure, function, and composition of the macromolecular complexes at the inner nuclear membrane involved in transmitting forces to the nuclear interior. Notably, although most illustrations of the LINC complex still depict nesprins as

long radial elements spanning large distances from the nucleus, recent studies suggest a different organization. Nesprins contain numerous spectrin-like repeats, which are commonly associated with membrane-proximal scaffolds [134,135], and likely form highly connected networks at the surface of the nuclear envelope, rather than projecting radially from the nucleus as isolated linkers [136–141]. The traditional view of the LINC complex is further complicated by the fact that, although nesprins are typically considered outer nuclear membrane proteins, shorter nesprin isoforms localize to the inner nuclear membrane, where they interact with lamins and chromatin [136,138,142].

Besides the LINC complex, other nuclear envelope structures contribute to nucleo-cytoskeletal coupling and force transmission, including nuclear pore complexes [143,144], emerin [21,37,145,146], and NEMO [147], but the relative contributions of these structures to overall force transmission, and the specific context in which one structure might be favored over another, remain incompletely understood. In addition, it is still unclear how nuclear membrane tension, which can modulate transit through nuclear pore complexes, opening of stretch sensitive ion channels, and association between cPLA2 and nuclear membrane [3,4,23–25,27,76], is transmitted to and propagated through the nuclear envelope, and what roles the LINC complex, lamins, and other nuclear envelope proteins play in this context. Answering these questions will likely require advances in imaging of the nuclear envelope at nanoscale resolution, along with innovative experimental approaches to delineate the contribution of specific nuclear envelope proteins.

Nuclear mechanobiology meets the clinic: how well do 2D in vitro studies represent physiological and pathological 3D in vivo conditions, and how can we use insights from tissue culture studies to develop deeper insights and new therapies for human diseases?

Changes in nuclear organization and mechanics associated with aging and pathological conditions, such as during cancer progression, cardiovascular disease, and muscular dystrophies [148–150], have

long provided a strong motivation to study nuclear mechanobiology. Nonetheless, most studies on nuclear mechanics and nuclear mechanobiology are still being conducted on cultured cells or even isolated nuclei, owing to the relative ease of experiments compared to *in vivo* studies, the increased control over experimental conditions, and the easier interpretation of results given fewer confounding factors. However, both cellular and nuclear morphology and function differ substantially between 2D and 3D conditions, and between culture on rigid substrates such as glass or polystyrene cell culture surfaces (Young's modulus: 3–75 GPa) versus materials with physiological stiffness (0.1–100 kPa, i.e., almost 10^6 -times softer). For example, while many cell types cultured on rigid 2D substrates exhibit extensive cell spreading resulting in flattened, disc-shaped nuclei often only a few micrometers in height, the same cells cultured in 3D environments or imaged *in vivo* have substantially thicker, more spherical, and larger nuclei, which is likely to affect the forces acting on the nucleus, along with nuclear crowding, mechanics, and intranuclear organization [41,151–154]. Thus, it will be crucial to determine how well 2D tissue culture models represent cellular and nuclear structure, architecture, and function *in vivo*, and how well our understanding of nuclear mechanobiology relates to the condition of cells in tissues, organs, and whole organisms. The increasing use of 3D culture systems, organoids, and *in situ* systems that better reflect the natural environment of cells, plus the use of model systems that enable intravital imaging and functional measurements, such as zebrafish, *Drosophila*, and *C. elegans*, provide critical complements to the cell culture systems.

Lastly, beyond advancing our fundamental understanding of key biological processes, mechanobiology is increasingly beginning to inform clinical applications, including new therapeutic strategies and diagnostic assays [155]. Clinical applications in nuclear mechanobiology are slowly starting to emerge, with the first clinical trial using LINC complex disruption to treat dilated cardiomyopathy caused by pathogenic lamin A/C gene mutations recently approved by the United States Food and Drug Administration [60]. Other recent studies linked nuclear envelope mechanical stability,

mediated by lamin A/C and SUN2, to the therapeutic mechanism of paclitaxel [156,157], which is commonly used in chemotherapy. Thus, a central question moving forward will be how to harness insights from nuclear mechanobiology for clinical application. Answering this challenge could inspire new diagnostic and therapeutic breakthroughs across a broad spectrum of human diseases, spanning development, cancer, musculoskeletal disease, immune cell dysfunction, and aging. We are excited to follow the payoffs of nuclear mechanobiology over the coming decades!

Acknowledgments

We apologize to all authors whose work could not be cited due to space constraints.

All authors contributed to the conception of this article by submitting ideas and open questions to J.L., who then drafted the manuscript and made revisions based on feedback from the co-authors. All authors approved the final version of the manuscript.

Funding

This work was supported by awards from the Volkswagen Foundation [A130142] to J.L., the National Institutes of Health [R01 HL082792], [R35 GM153257] and [R01 AR084664] to J.L.; [R35GM134859] to D.A.S.; [R35 GM136403] to G.G.G.; [R01 HL159389] and [R01 AG064944] to G.G.G. and H.J.W.; [R01 GM143485] and [R01 NS130677] to S.L.; [R35 GM153474] to M.C.K.; [R01 AG075047], [R01 AR048997], and [R03 AG088752 to H.J.W.], the National Science Foundation [UR0L2022048] to J.L.; awards [2412520] and [2226157 to T.P.L.], the Paul G. Allen Frontiers group (to D.A.S. and G.W.G.L.), the Leducq Foundation [20CVD01] to J.L. and [24CVD03 to J. L. and O.M.], the Biohub, San Francisco, and the David and Lucile Packard Foundation to H.R.T.; Swiss National Foundation [320030 L-231406] to O.M.; the Max Planck Society (to S.A.W.), and the German Research Foundation (Priority Program SPP2332, project [492014049 to J.R.]). The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or other funding sources.

Author contributions

CRedit: **Jan Lammerding**: Conceptualization, Writing – original draft, Writing – review & editing; **Jorine Eeftens**: Conceptualization, Writing – review & editing; **Gregg G. Gundersen**: Conceptualization, Writing – review & editing; **Megan C. King**: Conceptualization, Writing – review & editing; **Tanmay P. Lele**: Conceptualization, Writing –

review & editing; **Song Li**: Conceptualization, Writing – review & editing; **Gant Luxton, G. W.**: Conceptualization, Writing – review & editing; **Ohad Medalia**: Conceptualization, Writing – review & editing; **Matthieu Piel**: Conceptualization, Writing – review & editing; **Pere Roca-Cusachs**: Conceptualization, Writing – review & editing; **Jörg Renkawitz**: Conceptualization, Writing – review & editing; **Kyle Roux**: Conceptualization, Writing – review & editing; **Daniel A. Starr**: Conceptualization, Writing – review & editing; **Amy R. Strom**: Conceptualization, Writing – review & editing; **Hawa Racine Thiam**: Conceptualization, Writing – review & editing; **Sara A. Wickström**: Conceptualization, Writing – review & editing; **Howard J. Worman**: Conceptualization, Writing – review & editing.

Data availability statement

Data sharing not applicable – no new data generated.

References

- [1] Kalukula Y, Stephens AD, Lammerding J, et al. Mechanics and functional consequences of nuclear deformations. *Nat Rev Mol Cell Biol*. 2022;23(9):583–602. doi: [10.1038/s41580-022-00480-z](https://doi.org/10.1038/s41580-022-00480-z)
- [2] Swift J, Ivanovska IL, Buxboim A, et al. Nuclear lamin-A scales with tissue stiffness and enhances matrix-directed differentiation. *Science*. 2013;341(6149):1240104. doi: [10.1126/science.1240104](https://doi.org/10.1126/science.1240104)
- [3] Lomakin AJ, Cattin CJ, Cuvelier D, et al. The nucleus acts as a ruler tailoring cell responses to spatial constraints. *Science*. 2020;370(6514):eaba2894. doi: [10.1126/science.aba2894](https://doi.org/10.1126/science.aba2894)
- [4] Venturini V, Pezzano F, Català Castro F, et al. The nucleus measures shape changes for cellular proprioception to control dynamic cell behavior. *Science*. 2020;370(6514):eaba2644. doi: [10.1126/science.aba2644](https://doi.org/10.1126/science.aba2644)
- [5] Guilak F. Compression-induced changes in the shape and volume of the chondrocyte nucleus. *J Biomech*. 1995;28(12):1529–1541. doi: [10.1016/0021-9290\(95\)00100-x](https://doi.org/10.1016/0021-9290(95)00100-x)
- [6] Maniotis AJ, Chen CS, Ingber DE. Demonstration of mechanical connections between integrins, cytoskeletal filaments, and nucleoplasm that stabilize nuclear structure. *Proc Natl Acad Sci USA*. 1997;94(3):849–854. doi: [10.1073/pnas.94.3.849](https://doi.org/10.1073/pnas.94.3.849)
- [7] Lammerding J, Schulze PC, Takahashi T, et al. Lamin A/C deficiency causes defective nuclear mechanics and mechanotransduction. *J Clin Invest*. 2004;113(3):370–378. doi: [10.1172/JCI200419670](https://doi.org/10.1172/JCI200419670)
- [8] Dahl KN, Kahn SM, Wilson KL, et al. The nuclear envelope lamina network has elasticity and a compressibility limit suggestive of a molecular shock absorber. *J Cell Sci*. 2004;117(20):4779–4786. doi: [10.1242/jcs.01357](https://doi.org/10.1242/jcs.01357)
- [9] Stephens AD, Banigan EJ, Adam SA, et al. Chromatin and lamin a determine two different mechanical response regimes of the cell nucleus. *MBoC*. 2017;28(14):1984–1996. doi: [10.1091/mbc.e16-09-0653](https://doi.org/10.1091/mbc.e16-09-0653)
- [10] Strom AR, Kim Y, Zhao H, et al. Condensate interfacial forces reposition DNA loci and probe chromatin viscoelasticity. *Cell*. 2024. doi: [10.1016/j.cell.2024.07.034](https://doi.org/10.1016/j.cell.2024.07.034)
- [11] Schreiner SM, Koo PK, Zhao Y, et al. The tethering of chromatin to the nuclear envelope supports nuclear mechanics. *Nat Commun*. 2015;6():7159. doi: [10.1038/ncomms8159](https://doi.org/10.1038/ncomms8159)
- [12] Pajerowski JD, Dahl KN, Zhong FL, et al. Physical plasticity of the nucleus in stem cell differentiation. *Proc Natl Acad Sci USA*. 2007;104(40):15619–15624. doi: [10.1073/pnas.0702576104](https://doi.org/10.1073/pnas.0702576104)
- [13] Crisp M, Liu Q, Roux K, et al. Coupling of the nucleus and cytoplasm: role of the LINC complex. *J Cell Biol*. 2006;172(1):41–53. doi: [10.1083/jcb.200509124](https://doi.org/10.1083/jcb.200509124)
- [14] Haque F, Lloyd DJ, Smallwood DT, et al. SUN1 interacts with nuclear lamin a and cytoplasmic nesprins to provide a physical connection between the nuclear lamina and the cytoskeleton. *Mol Cell Biol*. 2006;26(10):3738–3751. doi: [10.1128/MCB.26.10.3738-3751.2006](https://doi.org/10.1128/MCB.26.10.3738-3751.2006)
- [15] Starr DA, Han M. Role of ANC-1 in tethering nuclei to the actin cytoskeleton. *Science*. 2002;298(5592):406–409. doi: [10.1126/science.1075119](https://doi.org/10.1126/science.1075119)
- [16] Starr DA, Fridolfsson HN. Interactions between nuclei and the cytoskeleton are mediated by SUN-KASH nuclear-envelope bridges. *Annu Rev Cell Dev Biol*. 2010;26(2010):421–444. doi: [10.1146/annurev-cellbio-100109-104037](https://doi.org/10.1146/annurev-cellbio-100109-104037)
- [17] Luxton GWG, Gomes ER, Folker ES, et al. Linear arrays of nuclear envelope proteins harness retrograde actin flow for nuclear movement. *Science*. 2010;329(5994):956–959. doi: [10.1126/science.1189072](https://doi.org/10.1126/science.1189072)
- [18] Song Y, Soto J, Chen B, et al. Transient nuclear deformation primes epigenetic state and promotes cell reprogramming. *Nat Mater*. 2022;21(10):1191–1199. doi: [10.1038/s41563-022-01312-3](https://doi.org/10.1038/s41563-022-01312-3)
- [19] Lewis R, Sinigiani V, Maziak N, et al. LBR and LAP2 mediate heterochromatin tethering to the nuclear periphery to preserve genome homeostasis. *Nat Cell Biol*. 2026;28(3):536–552. doi: [10.1038/s41556-025-01822-7](https://doi.org/10.1038/s41556-025-01822-7)
- [20] Buchwalter A, Kaneshiro JM, Hetzer MW. Coaching from the sidelines: the nuclear periphery in genome regulation. *Nat Rev Genet*. 2019;20(1):39–50. doi: [10.1038/s41576-018-0063-5](https://doi.org/10.1038/s41576-018-0063-5)
- [21] Guilluy C, Osborne LD, Van Landeghem L, et al. Isolated nuclei adapt to force and reveal a mechanotransduction pathway in the nucleus. *Nat Cell Biol*. 2014;16(4):376–381. doi: [10.1038/ncb2927](https://doi.org/10.1038/ncb2927)
- [22] Carley E, Stewart RM, Ziemann A, et al. The LINC complex transmits integrin-dependent tension to the nuclear lamina and represses epidermal differentiation. *Elife*. 2021;10:e58541. doi: [10.7554/eLife.58541](https://doi.org/10.7554/eLife.58541)
- [23] Enyedi B, Jelcic M, Niethammer P. The Cell nucleus serves as a mechanotransducer of tissue

- damage-induced inflammation. *Cell*. 2016;165(5):1160–1170. doi: [10.1016/j.cell.2016.04.016](https://doi.org/10.1016/j.cell.2016.04.016)
- [24] Elosegui-Artola A, Andreu I, Beedle AEM, et al. Force triggers YAP nuclear entry by regulating transport across nuclear pores. *Cell*. 2017;171(6):1397–1410.e14. doi: [10.1016/j.cell.2017.10.008](https://doi.org/10.1016/j.cell.2017.10.008)
- [25] Andreu I, Granero-Moya I, Chahare NR, et al. mechanical force application to the nucleus regulates nucleocytoplasmic transport. *Nat Cell Biol*. 2022;24(6):896–905. doi: [10.1038/s41556-022-00927-7](https://doi.org/10.1038/s41556-022-00927-7)
- [26] Le HQ, Ghatak S, Yeung CYC, et al. mechanical regulation of transcription controls polycomb-mediated gene silencing during lineage commitment. *Nat Cell Biol*. 2016;18(8):864–875. doi: [10.1038/ncb3387](https://doi.org/10.1038/ncb3387)
- [27] Nava MM, Miroshnikova YA, Biggs LC, et al. Heterochromatin-driven nuclear softening protects the genome against mechanical stress-induced damage. *Cell*. 2020;181(4):800–817.e22. doi: [10.1016/j.cell.2020.03.052](https://doi.org/10.1016/j.cell.2020.03.052)
- [28] Iyer KV, Pulford S, Mogilner A, et al. mechanical activation of cells induces chromatin remodeling preceding MKL nuclear transport. *Biophys J*. 2012;103(7):1416–1428. doi: [10.1016/j.bpj.2012.08.041](https://doi.org/10.1016/j.bpj.2012.08.041)
- [29] Alisafaei F, Jokhun DS, Shivashankar GV, et al. Regulation of nuclear architecture, mechanics, and nucleocytoplasmic shuttling of epigenetic factors by cell geometric constraints. *Proc Natl Acad Sci USA*. 2019;116(27):13200–13209. doi: [10.1073/pnas.1902035116](https://doi.org/10.1073/pnas.1902035116)
- [30] Tajik A, Zhang Y, Wei F, et al. Transcription upregulation via force-induced direct stretching of chromatin. *Nat Mater*. 2016;15(12):1287–1296. doi: [10.1038/nmat4729](https://doi.org/10.1038/nmat4729)
- [31] Wu Y, Song Y, Soto J, et al. Viscoelastic extracellular matrix enhances epigenetic remodeling and cellular plasticity. *Nat Commun*. 2025;16(1):4054. doi: [10.1038/s41467-025-59190-7](https://doi.org/10.1038/s41467-025-59190-7)
- [32] Wolf K, Te Lindert M, Krause M, et al. Physical limits of cell migration: control by ECM space and nuclear deformation and tuning by proteolysis and traction force. *J Cell Bio*. 2013;201(7):1069–1084. doi: [10.1083/jcb.201210152](https://doi.org/10.1083/jcb.201210152)
- [33] Harada T, Swift J, Irianto J, et al. Nuclear lamin stiffness is a barrier to 3D migration, but softness can limit survival. *J Cell Bio*. 2014;204(5):669–682. doi: [10.1083/jcb.201308029](https://doi.org/10.1083/jcb.201308029)
- [34] Rowat AC, Jaalouk DE, Zwerger M, et al. Nuclear envelope composition determines the ability of neutrophil-type cells to passage through micron-scale constrictions. *J Biol Chem*. 2013;288(12):8610–8618. doi: [10.1074/jbc.M112.441535](https://doi.org/10.1074/jbc.M112.441535)
- [35] Davidson PM, Denais C, Bakshi MC, et al. Nuclear deformability constitutes a rate-limiting step during cell migration in 3-D environments. *Cell Mol Bioeng*. 2014;7(3):293–306. doi: [10.1007/s12195-014-0342-y](https://doi.org/10.1007/s12195-014-0342-y)
- [36] Thiam HR, Vargas P, Carpi N, et al. Perinuclear Arp2/3-driven actin polymerization enables nuclear deformation to facilitate cell migration through complex environments. *Nat Commun*. 2016;7(1):10997. doi: [10.1038/ncomms10997](https://doi.org/10.1038/ncomms10997)
- [37] Liddane AG, McNamara CA, Campbell MC, et al. Defects in emerin-nucleoskeleton binding disrupt nuclear structure and promote breast cancer Cell motility and metastasis. *Mol Cancer Res*. 2021;19(7):1196–1207. doi: [10.1158/1541-7786.MCR-20-0413](https://doi.org/10.1158/1541-7786.MCR-20-0413)
- [38] Lautscham LA, Kämmerer C, Lange JR, et al. Migration in confined 3D environments is determined by a combination of adhesiveness, nuclear volume, contractility, and Cell stiffness. *Biophys J*. 2015;109(5):900–913. doi: [10.1016/j.bpj.2015.07.025](https://doi.org/10.1016/j.bpj.2015.07.025)
- [39] Renkawitz J, Kopf A, Stopp J, et al. Nuclear positioning facilitates amoeboid migration along the path of least resistance. *Nature*. 2019;568(7753):546–550. doi: [10.1038/s41586-019-1087-5](https://doi.org/10.1038/s41586-019-1087-5)
- [40] Raab M, Gentili M, De Belly H, et al. ESCRT III repairs nuclear envelope ruptures during cell migration to limit DNA damage and cell death. *Science*. 2016;352(6283):359–362. doi: [10.1126/science.aad7611](https://doi.org/10.1126/science.aad7611)
- [41] Denais CM, Gilbert RM, Isermann P, et al. Nuclear envelope rupture and repair during cancer cell migration. *Science*. 2016;352(6283):353–358. doi: [10.1126/science.aad7297](https://doi.org/10.1126/science.aad7297)
- [42] Irianto J, Xia Y, Pfeifer CR, et al. DNA damage follows repair factor depletion and portends genome variation in cancer cells after pore migration. *Curr Biol*. 2017;27(2):210–223. doi: [10.1016/j.cub.2016.11.049](https://doi.org/10.1016/j.cub.2016.11.049)
- [43] Shah P, Hobson CM, Cheng S, et al. Nuclear deformation causes DNA damage by increasing replication stress. *Curr Biol*. 2021;31(4):753–765.e6. doi: [10.1016/j.cub.2020.11.037](https://doi.org/10.1016/j.cub.2020.11.037)
- [44] Hsia CR, McAllister J, Hasan O, et al. Confined migration induces heterochromatin formation and alters chromatin accessibility. *iScience*. 2022;25(9):104978. doi: [10.1016/j.isci.2022.104978](https://doi.org/10.1016/j.isci.2022.104978)
- [45] Jacobson EC, Perry JK, Long DS, et al. Migration through a small pore disrupts inactive chromatin organization in neutrophil-like cells. *BMC Biol*. 2018;16(1):142. doi: [10.1186/s12915-018-0608-2](https://doi.org/10.1186/s12915-018-0608-2)
- [46] Gollosi R, Playter C, Freeman TF, et al. Constricted migration is associated with stable 3D genome structure differences in cancer cells. *EMBO Rep*. 2022;23(10):e52149. doi: [10.15252/embr.202052149](https://doi.org/10.15252/embr.202052149)
- [47] Zhao JZ, Xia J, Brangwynne CP. Chromatin compaction during confined cell migration induces and reshapes nuclear condensates. *Nat Commun*. 2024;15(1):9964. doi: [10.1038/s41467-024-54120-5](https://doi.org/10.1038/s41467-024-54120-5)
- [48] Bastianello G, Kidiyoor GR, Lowndes C, et al. mechanical stress during confined migration causes aberrant mitoses and c-MYC amplification. *Proc Natl Acad Sci USA*. 2024;121(29):e2404551121. doi: [10.1073/pnas.2404551121](https://doi.org/10.1073/pnas.2404551121)
- [49] Cho S, Vashisth M, Abbas A, et al. Mechanosensing by the lamina protects against nuclear rupture, DNA damage, and cell cycle arrest. *Dev Cell*. 2019;49(6):920–935.e5. doi: [10.1016/j.devcel.2019.04.020](https://doi.org/10.1016/j.devcel.2019.04.020)

- [50] Earle AJ, Kirby TJ, Fedorchak GR, et al. Mutant lamins cause nuclear envelope rupture and DNA damage in skeletal muscle cells. *Nat Mater.* 2020;19(4):464–473. doi: [10.1038/s41563-019-0563-5](https://doi.org/10.1038/s41563-019-0563-5)
- [51] Zwerger M, Jaalouk DE, Lombardi ML, et al. Myopathic lamin mutations impair nuclear stability in cells and tissue and disrupt nucleo-cytoskeletal coupling. *Hum Mol Genet.* 2013;22(12):2335–2349. doi: [10.1093/hmg/ddt079](https://doi.org/10.1093/hmg/ddt079).
- [52] En A, Bogireddi H, Thomas B, et al. Pervasive nuclear envelope ruptures precede ECM signaling and disease onset without activating cGAS-STING in lamin-cardiomyopathy mice. *Cell Rep.* 2024;43(6):114284. doi: [10.1016/j.celrep.2024.114284](https://doi.org/10.1016/j.celrep.2024.114284)
- [53] Sikder K, Phillips E, Zhong Z, et al. Perinuclear damage from nuclear envelope deterioration elicits stress responses that contribute to LMNA cardiomyopathy. *Sci Adv.* 2024;10(19):eadh0798. doi: [10.1126/sciadv.adh0798](https://doi.org/10.1126/sciadv.adh0798)
- [54] Mattout A, Pike BL, Towbin BD, et al. An EDMD mutation in *C. elegans* lamin blocks muscle-specific gene relocation and compromises muscle integrity. *Curr Biol.* 2011;21(19):1603–1614. doi: [10.1016/j.cub.2011.08.030](https://doi.org/10.1016/j.cub.2011.08.030).
- [55] Cheedipudi SM, Matkovich SJ, Coarfa C, et al. Genomic reorganization of lamin-associated domains in cardiac myocytes is associated with differential gene expression and DNA methylation in human dilated cardiomyopathy. *Circ Res.* 2019;124(8):1198–1213. doi: [10.1161/CIRCRESAHA.118.314177](https://doi.org/10.1161/CIRCRESAHA.118.314177)
- [56] Chai RJ, Werner H, Li PY, et al. Disrupting the LINC complex by AAV mediated gene transduction prevents progression of lamin induced cardiomyopathy. *Nat Commun.* 2021;12(1):4722. doi: [10.1038/s41467-021-24849-4](https://doi.org/10.1038/s41467-021-24849-4)
- [57] Leong EL, Khaing NT, Cadot B, et al. Nesprin-1 LINC complexes recruit microtubule cytoskeleton proteins and drive pathology in *Lmna*-mutant striated muscle. *Hum Mol Genet.* 2023;32(2):177–191. doi: [10.1093/hmg/ddac179](https://doi.org/10.1093/hmg/ddac179)
- [58] Amiad Pavlov D, Heffler J, Suay-Corredera C, et al. Microtubule forces drive nuclear damage in LMNA cardiomyopathy. *Nat Cardiovasc Res.* 2025;4(11):1501–1520. doi: [10.1038/s44161-025-00727-w](https://doi.org/10.1038/s44161-025-00727-w)
- [59] Tan CY, Chan PS, Tan H, et al. Systematic in vivo candidate evaluation uncovers therapeutic targets for LMNA dilated cardiomyopathy and risk of lamin a toxicity. *J Transl Med.* 2023;21(1):690. doi: [10.1186/s12967-023-04542-4](https://doi.org/10.1186/s12967-023-04542-4)
- [60] Ng SR, Wang A, Tukijan F, et al. Abstract 4359043: NVC-001 – an AAV gene therapy functional cure for LMNA dilated cardiomyopathy. *Circulation.* 2025;152(Suppl_3):A4359043. doi: [10.1161/circ.152.suppl_3.4359043](https://doi.org/10.1161/circ.152.suppl_3.4359043)
- [61] Zimmerli CE, Allegretti M, Rantos V, et al. Nuclear pores dilate and constrict in cellulose. *Science.* 2021;374(6573):eabd9776. doi: [10.1126/science.abd9776](https://doi.org/10.1126/science.abd9776)
- [62] Lusk CP, Morgan KJ, King MC. Nuclear mechanics as a determinant of nuclear pore complex plasticity. *Nat Cell Biol.* 2025;27(10):1622–1631. doi: [10.1038/s41556-025-01768-w](https://doi.org/10.1038/s41556-025-01768-w)
- [63] Morgan KJ, Carley E, Coyne AN, et al. Visualizing nuclear pore complex plasticity with pan-expansion microscopy. *J Cell Biol.* 2025;224(9):e202409120. doi: [10.1083/jcb.202409120](https://doi.org/10.1083/jcb.202409120)
- [64] Heo SJ, Thakur S, Chen X, et al. Aberrant chromatin reorganization in cells from diseased fibrous connective tissue in response to altered chemomechanical cues. *Nat Biomed Eng.* 2023;7(2):177–191. doi: [10.1038/s41551-022-00910-5](https://doi.org/10.1038/s41551-022-00910-5)
- [65] Song Y, Soto J, Wong SY, et al. Biphasic regulation of epigenetic state by matrix stiffness during cell reprogramming. *Sci Adv.* 2024;10(7):eadk0639. doi: [10.1126/sciadv.adk0639](https://doi.org/10.1126/sciadv.adk0639)
- [66] Kidiyoor GR, Li Q, Bastianello G, et al. ATR is essential for preservation of cell mechanics and nuclear integrity during interstitial migration. *Nat Commun.* 2020;11(1):4828. doi: [10.1038/s41467-020-18580-9](https://doi.org/10.1038/s41467-020-18580-9)
- [67] Bastianello G, Porcella G, Beznoussenko GV, et al. Cell stretching activates an ATM mechano-transduction pathway that remodels cytoskeleton and chromatin. *Cell Rep.* 2023;42(12):113555. doi: [10.1016/j.celrep.2023.113555](https://doi.org/10.1016/j.celrep.2023.113555)
- [68] Shah P, McGuigan CW, Cheng S, et al. ATM modulates nuclear mechanics by regulating lamin A levels. *Front Cell Dev Biol.* 2022;10:875132. doi: [10.3389/fcell.2022.875132](https://doi.org/10.3389/fcell.2022.875132)
- [69] Kovacs MT, Vallette M, Wiertsema P, et al. DNA damage induces nuclear envelope rupture through ATR-mediated phosphorylation of lamin A/C. *Mol Cell.* 2023;83(20):3659–3668.e10. doi: [10.1016/j.molcel.2023.09.023](https://doi.org/10.1016/j.molcel.2023.09.023)
- [70] Joo YK, Black EM, Trier I, et al. ATR promotes clearance of damaged DNA and damaged cells by rupturing micronuclei. *Mol Cell.* 2023;83(20):3642–3658.e4. doi: [10.1016/j.molcel.2023.09.003](https://doi.org/10.1016/j.molcel.2023.09.003)
- [71] Thiam HR, Wong SL, Qiu R, et al. Netosis proceeds by cytoskeleton and endomembrane disassembly and PAD4-mediated chromatin decondensation and nuclear envelope rupture. *Proc Natl Acad Sci USA.* 2020;117(13):7326–7337. doi: [10.1073/pnas.1909546117](https://doi.org/10.1073/pnas.1909546117)
- [72] González-Granado JM, Silvestre-Roig C, Rocha-Perugini V, et al. Nuclear envelope lamin-A couples actin dynamics with immunological synapse architecture and T Cell activation. *Sci Signal.* 2014;7(322). doi: [10.1126/scisignal.2004872](https://doi.org/10.1126/scisignal.2004872)
- [73] Alraies Z, Rivera CA, Delgado MG, et al. Cell shape sensing licenses dendritic cells for homeostatic migration to lymph nodes. *Nat Immunol.* 2024;25(7):1193–1206. doi: [10.1038/s41590-024-01856-3](https://doi.org/10.1038/s41590-024-01856-3)
- [74] Patel H, Kaur S, Dickinson RB, et al. Nuclear mechanobiology in confined cell migration. *Nucleus.* 2026;17(1):2620879. doi: [10.1080/19491034.2026.2620879](https://doi.org/10.1080/19491034.2026.2620879)
- [75] Renkawitz J, Yesin A, Kroll J, et al. Nuclear mechanobiology rules immune cells' functions: from differentiation to

- cell trafficking and pathogen killing. *Nucleus*. 2026;17(1):2590843. doi: [10.1080/19491034.2025.2590843](https://doi.org/10.1080/19491034.2025.2590843)
- [76] Rajan SG, Roca-Cusachs P, Niethammer P. Mechanotransduction by nuclear envelope tension. *Nucleus*. 2026;17(1):2600901. doi: [10.1080/19491034.2025.2600901](https://doi.org/10.1080/19491034.2025.2600901)
- [77] Rodenburg WS, Strom AR, Eeftens JM. Heterogeneity as a feature: unraveling chromatin's role in nuclear mechanics. *Nucleus*. 2025;16(1):2545037. doi: [10.1080/19491034.2025.2545037](https://doi.org/10.1080/19491034.2025.2545037)
- [78] Gümüşderelioglu S, Gant Luxton GW, Starr DA. Nuclei on the move: LINC complex-dependent and -independent mechanisms of nuclear migration in development. *Nucleus*. 2026;17(1):2679812. doi: [10.1080/19491034.2026.2679812](https://doi.org/10.1080/19491034.2026.2679812)
- [79] Sandria S, King MC. Integration of nuclear mechanosensing with integrin-extracellular matrix adhesions. *Nucleus*. 2026;17(1):2677308. doi: [10.1080/19491034.2026.2677308](https://doi.org/10.1080/19491034.2026.2677308)
- [80] Esen O, Battey E, Stroud MJ, et al. The nucleus as a mechanobiological hub in muscle aging. *Nucleus*. 2026;17(1):2688584. doi: [10.1080/19491034.2026.2688584](https://doi.org/10.1080/19491034.2026.2688584)
- [81] Kechagia Z, Medalia O. High-resolution nuclear cell biology by cryo-electron tomography. *Nucleus*. 2026;17(1):2675754. doi: [10.1080/19491034.2026.2675754](https://doi.org/10.1080/19491034.2026.2675754)
- [82] Soto J, Origer N, Wu Y, et al. Nuclear mechanotransduction: tools for mechanical perturbation and chromatin characterization. *Nucleus*. 2026;17(1):2690847. doi: [10.1080/19491034.2026.2690847](https://doi.org/10.1080/19491034.2026.2690847)
- [83] Jung-Garcia Y, Maiques O, Monger J, et al. LAP1 supports nuclear adaptability during constrained melanoma cell migration and invasion. *Nat Cell Biol*. 2023;25(1):108–119. doi: [10.1038/s41556-022-01042-3](https://doi.org/10.1038/s41556-022-01042-3)
- [84] Caravia XM, Ramirez-Martinez A, Gan P, et al. Loss of function of the nuclear envelope protein LEMD2 causes DNA damage-dependent cardiomyopathy. *J Clin Invest*. 2022;132(22):e158897. doi: [10.1172/JCI158897](https://doi.org/10.1172/JCI158897)
- [85] Lammerding J, Fong LG, Ji JY, et al. Lamins A and C but not lamin B1 regulate nuclear mechanics. *J Biol Chem*. 2006;281(35):25768–25780. doi: [10.1074/jbc.M513511200](https://doi.org/10.1074/jbc.M513511200)
- [86] Lammerding J, Hsiao J, Schulze PC, et al. Abnormal nuclear shape and impaired mechanotransduction in emerin-deficient cells. *J Cell Biol*. 2005;170(5):781–791. doi: [10.1083/jcb.200502148](https://doi.org/10.1083/jcb.200502148)
- [87] Rowat AC, Lammerding J, Ipsen JH. mechanical properties of the Cell nucleus and the effect of emerin deficiency. *Biophys J*. 2006;91(12):4649–4664. doi: [10.1529/biophysj.106.086454](https://doi.org/10.1529/biophysj.106.086454)
- [88] Chen NY, Kim PH, Tu Y, et al. Increased expression of LAP2 β eliminates nuclear membrane ruptures in nuclear lamin-deficient neurons and fibroblasts. *Proc Natl Acad Sci USA*. 2021;118(25):e2107770118. doi: [10.1073/pnas.2107770118](https://doi.org/10.1073/pnas.2107770118)
- [89] Alabi Y, Aksenova V, Arnaoutov A, et al. Lamin B1 and LAP2 β resist cytoskeletal force to maintain lamin A/C meshwork organization and preserve nuclear integrity. *Mol Biol Cell*. 2025;36(9):ar111. doi: [10.1091/mbc.E25-02-0057](https://doi.org/10.1091/mbc.E25-02-0057)
- [90] Ross JA, Arcos-Villacis N, Battey E, et al. Lem2 is essential for cardiac development by maintaining nuclear integrity. *Cardiovasc Res*. 2023;119(11):2074–2088. doi: [10.1093/cvr/cvad061](https://doi.org/10.1093/cvr/cvad061)
- [91] Stephens AD, Liu PZ, Banigan EJ, et al. Chromatin histone modifications and rigidity affect nuclear morphology independent of lamins. *Mol Biol Cell*. 2018;29(2):220–233. doi: [10.1091/mbc.E17-06-0410](https://doi.org/10.1091/mbc.E17-06-0410)
- [92] Nmezi B, Xu J, Fu R, et al. Concentric organization of A- and B-type lamins predicts their distinct roles in the spatial organization and stability of the nuclear lamina. *Proc Natl Acad Sci USA*. 2019;116(10):4307–4315. doi: [10.1073/pnas.1810070116](https://doi.org/10.1073/pnas.1810070116)
- [93] Xie W, Chojnowski A, Boudier T, et al. A-type lamins form distinct filamentous networks with differential nuclear pore complex associations. *Curr Biol*. 2016;26(19):2651–2658. doi: [10.1016/j.cub.2016.07.049](https://doi.org/10.1016/j.cub.2016.07.049)
- [94] Shimi T, Kittisopikul M, Tran J, et al. Structural organization of nuclear lamins A, C, B1, and B2 revealed by superresolution microscopy. *Mol Biol Cell*. 2015;26(22):4075–4086. doi: [10.1091/mbc.E15-07-0461](https://doi.org/10.1091/mbc.E15-07-0461)
- [95] Negri ML, D'Annunzio S, Vitali G, et al. May the force be with you: nuclear condensates function beyond transcription control: potential nongenetic functions of nuclear condensates in physiological and pathological conditions. *Bioessays*. 2023;45(10):e2300075. doi: [10.1002/bies.202300075](https://doi.org/10.1002/bies.202300075)
- [96] Zhao JZ, Xia J, Brangwynne CP. mechanical regulation and activity of nuclear condensates. *Biophys J*. 2025;S0006-3495(25):00660–5. doi: [10.1016/j.bpj.2025.10.009](https://doi.org/10.1016/j.bpj.2025.10.009)
- [97] McCreery KP, Stubb A, Stephens R, et al. Mechano-osmotic signals control chromatin state and fate transitions in pluripotent stem cells. *Nat Cell Biol*. 2025;27(10):1757–1770. doi: [10.1038/s41556-025-01767-x](https://doi.org/10.1038/s41556-025-01767-x)
- [98] Elpers MA, Odell JD, Shu T, et al. Polarization increases nuclear stiffness in macrophages despite reduction in lamin A/C levels. 2025. doi: [10.1101/2025.11.22.689940](https://doi.org/10.1101/2025.11.22.689940)
- [99] Ding X, Hao H, Elnatan D, et al. Giant KASH proteins and ribosomes establish distinct cytoplasmic biophysical properties in vivo. *Sci Adv*. 2025;11(37):eadx0952. doi: [10.1126/sciadv.adx0952](https://doi.org/10.1126/sciadv.adx0952)
- [100] Elpers MA, Odell J, Henretta SJ, et al. Polarization increases nuclear stiffness in macrophages despite reduction in lamin A/C levels. *NPJ Biol Phys Mech*. 2026;3(1):8. doi: [10.1038/s44341-026-00038-6](https://doi.org/10.1038/s44341-026-00038-6)
- [101] Roberts AB, Zhang J, Raj Singh V, et al. Tumor cell nuclei soften during transendothelial migration. *J Biomech*. 2021;121:110400. doi: [10.1016/j.jbiomech.2021.110400](https://doi.org/10.1016/j.jbiomech.2021.110400)
- [102] Chalut KJ, Höpfner M, Lautenschläger F, et al. Chromatin decondensation and nuclear softening accompany Nanog

- downregulation in embryonic stem cells. *Biophys J*. 2012;103(10):2060–2070. doi: [10.1016/j.bpj.2012.10.015](https://doi.org/10.1016/j.bpj.2012.10.015)
- [103] Heo SJ, Driscoll TP, Thorpe SD, et al. Differentiation alters stem cell nuclear architecture, mechanics, and mechano-sensitivity. *Elife*. 2016;5:e18207. doi: [10.7554/eLife.18207](https://doi.org/10.7554/eLife.18207)
- [104] Ihalainen TO, Aires L, Herzog FA, et al. Differential basal-to-apical accessibility of lamin A/C epitopes in the nuclear lamina regulated by changes in cytoskeletal tension. *Nat Mater*. 2015;14(12):1252–1261. doi: [10.1038/nmat4389](https://doi.org/10.1038/nmat4389)
- [105] Buxboim A, Swift J, Irianto J, et al. Matrix elasticity regulates lamin-A,C phosphorylation and turnover with feedback to Actomyosin. *Curr Biol*. 2014;24(16):1909–1917. doi: [10.1016/j.cub.2014.07.001](https://doi.org/10.1016/j.cub.2014.07.001)
- [106] Shen Z, Gelashvili Z, Niethammer P. Endoplasmic reticulum disruption stimulates nuclear membrane mechanotransduction. *Nat Cell Biol*. 2026;28(1):125–134. doi: [10.1038/s41556-025-01820-9](https://doi.org/10.1038/s41556-025-01820-9)
- [107] Booth-Gauthier EA, Alcoser TA, Yang G, et al. Force-induced changes in subnuclear movement and rheology. *Biophys J*. 2012;103(12):2423–2431. doi: [10.1016/j.bpj.2012.10.039](https://doi.org/10.1016/j.bpj.2012.10.039)
- [108] Schuller AP, Wojtynek M, Mankus D, et al. The cellular environment shapes the nuclear pore complex architecture. *Nature*. 2021;598(7882):667–671. doi: [10.1038/s41586-021-03985-3](https://doi.org/10.1038/s41586-021-03985-3)
- [109] Wing CE, Fung HY, Chook YM. Karyopherin-mediated nucleocytoplasmic transport. *Nat Rev Mol Cell Biol*. 2022;23(5):307–328. doi: [10.1038/s41580-021-00446-7](https://doi.org/10.1038/s41580-021-00446-7)
- [110] Kofler M, Kapus A. Nuclear import and export of YAP and TAZ. *Cancers (Basel)*. 2023;15(20):4956. doi: [10.3390/cancers15204956](https://doi.org/10.3390/cancers15204956)
- [111] Khatau SB, Hale CM, Stewart-Hutchinson PJ, et al. A perinuclear actin cap regulates nuclear shape. *Proc Natl Acad Sci USA*. 2009;106(45):19017–19022. doi: [10.1073/pnas.0908686106](https://doi.org/10.1073/pnas.0908686106)
- [112] Chancellor TJ, Lee J, Thodeti CK, et al. Actomyosin tension exerted on the nucleus through Nesprin-1 connections influences endothelial Cell adhesion, migration, and cyclic strain-induced reorientation. *Biophys J*. 2010;99(1):115–123. doi: [10.1016/j.bpj.2010.04.011](https://doi.org/10.1016/j.bpj.2010.04.011)
- [113] Neumann S, Schneider M, Daugherty RL, et al. Nesprin-2 interacts with α -catenin and regulates wnt signaling at the nuclear envelope. *J Biol Chem*. 2010;285(45):34932–34938. doi: [10.1074/jbc.M110.119651](https://doi.org/10.1074/jbc.M110.119651)
- [114] Lombardi ML, Jaalouk DE, Shanahan CM, et al. The interaction between nesprins and sun proteins at the nuclear envelope is critical for force transmission between the nucleus and cytoskeleton. *J Biol Chem*. 2011;286(30):26743–26753. doi: [10.1074/jbc.M111.233700](https://doi.org/10.1074/jbc.M111.233700)
- [115] Morgan JT, Pfeiffer ER, Thirkill TL, et al. Nesprin-3 regulates endothelial cell morphology, perinuclear cytoskeletal architecture, and flow-induced polarization. *Mol Biol Cell*. 2011;22(22):4324–4334. doi: [10.1091/mbc.E11-04-0287](https://doi.org/10.1091/mbc.E11-04-0287)
- [116] Stewart RM, Zubeck AE, Rosowski KA, et al. Nuclear-cytoskeletal linkages facilitate cross talk between the nucleus and intercellular adhesions. *J Cell Bio*. 2015;209(3):403–418. doi: [10.1083/jcb.201502024](https://doi.org/10.1083/jcb.201502024)
- [117] Shen KM, Shields EJ, Barka V, et al. The cytoskeleton contributes to abnormal genome-lamina interactions in LMNA-deficient cardiomyocytes. *J Cell Biol*. 2026;225(5):e202506137. doi: [10.1083/jcb.202506137](https://doi.org/10.1083/jcb.202506137)
- [118] Lee YL, Burke B. LINC complexes and nuclear positioning. *Semin Cell Dev Biol*. 2018;82:67–76. doi: [10.1016/j.semcdb.2017.11.008](https://doi.org/10.1016/j.semcdb.2017.11.008)
- [119] Sosa BA, Rothballer A, Kutay U, et al. LINC complexes form by binding of Three KASH peptides to domain interfaces of trimeric SUN proteins. *Cell*. 2012;149(5):1035–1047. doi: [10.1016/j.cell.2012.03.046](https://doi.org/10.1016/j.cell.2012.03.046)
- [120] Zhou Z, Du X, Cai Z, et al. Structure of Sad1-UNC84 homology (SUN) domain defines features of molecular bridge in nuclear envelope. *J Biol Chem*. 2012;287(8):5317–5326. doi: [10.1074/jbc.M111.304543](https://doi.org/10.1074/jbc.M111.304543)
- [121] Rothballer A, Schwartz TU, Kutay U. Lincing complex functions at the nuclear envelope: what the molecular architecture of the LINC complex can reveal about its function. *Nucleus*. 2013;4(1):29–36. doi: [10.4161/nucl.23387](https://doi.org/10.4161/nucl.23387)
- [122] Cruz VE, Esra Demircioglu F, Schwartz TU. Structural analysis of different LINC complexes reveals distinct binding modes. *J Mol Biol*. 2020;432(23):6028–6041. doi: [10.1016/j.jmb.2020.09.019](https://doi.org/10.1016/j.jmb.2020.09.019)
- [123] Lim SM, Cruz VE, Antoku S, et al. Structures of FHOD1-Nesprin1/2 complexes reveal alternate binding modes for the FH3 domain of formins. *Structure*. 2021;29(6):540–552.e5. doi: [10.1016/j.str.2020.12.013](https://doi.org/10.1016/j.str.2020.12.013)
- [124] Jahed Z, Shams H, Mofrad MRK. A disulfide bond is required for the transmission of forces through SUN-KASH complexes. *Biophys J*. 2015;109(3):501–509. doi: [10.1016/j.bpj.2015.06.057](https://doi.org/10.1016/j.bpj.2015.06.057)
- [125] Cain NE, Jahed Z, Schoenhofen A, et al. Conserved SUN-KASH interfaces mediate LINC complex-dependent nuclear movement and positioning. *Curr Biol*. 2018;28(19):3086–3097.e4. doi: [10.1016/j.cub.2018.08.001](https://doi.org/10.1016/j.cub.2018.08.001)
- [126] Gurusaran M, Davies OR. A molecular mechanism for LINC complex branching by structurally diverse SUN-KASH 6: 6 assemblies. *Elife*. 2021;10:e60175. doi: [10.7554/eLife.60175](https://doi.org/10.7554/eLife.60175)
- [127] Hennen J, Saunders CA, Mueller JD, et al. Fluorescence fluctuation spectroscopy reveals differential SUN protein oligomerization in living cells. *Mol Biol Cell*. 2018;29(9):1003–1011. doi: [10.1091/mbc.E17-04-0233](https://doi.org/10.1091/mbc.E17-04-0233)
- [128] King MC. Dynamic regulation of LINC complex composition and function across tissues and contexts. *FEBS Lett*. 2023;597(22):2823–2832. doi: [10.1002/1873-3468.14757](https://doi.org/10.1002/1873-3468.14757)
- [129] Kanchanawong P, Shtengel G, Pasapera AM, et al. Nanoscale architecture of integrin-based cell adhesions. *Nature*. 2010;468(7323):580–584. doi: [10.1038/nature09621](https://doi.org/10.1038/nature09621)

- [130] Kanchanawong P, Calderwood DA. Organization, dynamics and mechanoregulation of integrin-mediated cell-ECM adhesions. *Nat Rev Mol Cell Biol.* 2023;24(2):142–161. doi: [10.1038/s41580-022-00531-5](https://doi.org/10.1038/s41580-022-00531-5)
- [131] Zaidel-Bar R, Itzkovitz S, Ma'ayan A, et al. Functional atlas of the integrin adhesome. *Nat Cell Biol.* 2007;9(8):858–867. doi: [10.1038/ncb0807-858](https://doi.org/10.1038/ncb0807-858)
- [132] Horton ER, Byron A, Askari JA, et al. Definition of a consensus integrin adhesome and its dynamics during adhesion complex assembly and disassembly. *Nat Cell Biol.* 2015;17(12):1577–1587. doi: [10.1038/ncb3257](https://doi.org/10.1038/ncb3257)
- [133] Patla I, Volberg T, Elad N, et al. Dissecting the molecular architecture of integrin adhesion sites by cryo-electron tomography. *Nat Cell Biol.* 2010;12(9):909–915. doi: [10.1038/ncb2095](https://doi.org/10.1038/ncb2095)
- [134] Bennett V, Lorenzo DN. Spectrin- and ankyrin-based membrane domains and the evolution of vertebrates. *Curr Top Membr.* 2013;72:1–37. doi: [10.1016/B978-0-12-417027-8.00001-5](https://doi.org/10.1016/B978-0-12-417027-8.00001-5)
- [135] Machnicka B, Czogalla A, Hryniewicz-Jankowska A, et al. Spectrins: a structural platform for stabilization and activation of membrane channels, receptors and transporters. *Biochim Biophys Acta.* 2014;1838(2):620–634. doi: [10.1016/j.bbame.2013.05.002](https://doi.org/10.1016/j.bbame.2013.05.002)
- [136] Mislow JMK, Holaska JM, Kim MS, et al. Nesprin-1alpha self-associates and binds directly to emerin and lamin a in vitro. *FEBS Lett.* 2002;525(1–3):135–140. doi: [10.1016/s0014-5793\(02\)03105-8](https://doi.org/10.1016/s0014-5793(02)03105-8)
- [137] Lu W, Schneider M, Neumann S, et al. Nesprin inter-chain associations control nuclear size. *Cell Mol Life Sci.* 2012;69(20):3493–3509. doi: [10.1007/s00018-012-1034-1](https://doi.org/10.1007/s00018-012-1034-1)
- [138] Rajgor D, Shanahan CM. Nesprins: from the nuclear envelope and beyond. *Expert Rev Mol Med.* 2013;15:e5. doi: [10.1017/erm.2013.6](https://doi.org/10.1017/erm.2013.6)
- [139] Kutscheidt S, Zhu R, Antoku S, et al. FHOD1 interaction with nesprin-2G mediates TAN line formation and nuclear movement. *Nat Cell Biol.* 2014;16(7):708–715. doi: [10.1038/ncb2981](https://doi.org/10.1038/ncb2981)
- [140] Taranum S, Sur I, Müller R, et al. Cytoskeletal interactions at the nuclear envelope mediated by nesprins. *Int J Cell Biol.* 2012;2012:1–11. doi: [10.1155/2012/736524](https://doi.org/10.1155/2012/736524)
- [141] Ding X, Kumari S, Gregory E, et al. Muscular dystrophy-associated lamin variants disrupt cellular organization through a nucleolar-ribosomal axis controlling cytoplasmic macromolecular crowding. *bioRxiv: Prepr Serv Biol.* 2025. doi: [10.1101/2025.09.22.677926](https://doi.org/10.1101/2025.09.22.677926)
- [142] Zhang Q, Ragnauth CD, Skepper JN, et al. Nesprin-2 is a multi-isomeric protein that binds lamin and emerin at the nuclear envelope and forms a subcellular network in skeletal muscle. *J Cell Sci.* 2005;118(Pt 4):673–687. doi: [10.1242/jcs.01642](https://doi.org/10.1242/jcs.01642)
- [143] Guo Y, Zheng Y. Lamins position the nuclear pores and centrosomes by modulating dynein. *Mol Biol Cell.* 2015;26(19):3379–3389. doi: [10.1091/mbc.E15-07-0482](https://doi.org/10.1091/mbc.E15-07-0482)
- [144] Goldberg MW. Nuclear pore complex tethers to the cytoskeleton. *Semin Cell Dev Biol.* 2017;68:52–58. doi: [10.1016/j.semcdb.2017.06.017](https://doi.org/10.1016/j.semcdb.2017.06.017)
- [145] Salpingidou G, Smertenko A, Hausmanowa-Petruciewicz I, et al. A novel role for the nuclear membrane protein emerin in association of the centrosome to the outer nuclear membrane. *J Cell Biol.* 2007;178(6):897–904. doi: [10.1083/jcb.200702026](https://doi.org/10.1083/jcb.200702026)
- [146] Holaska JM, Wilson KL. An emerin “proteome”: purification of distinct emerin-containing complexes from HeLa cells suggests molecular basis for diverse roles including gene regulation, mRNA splicing, signaling, mechanosensing, and nuclear architecture. *Biochemistry.* 2007;46(30):8897–8908. doi: [10.1021/bi602636m](https://doi.org/10.1021/bi602636m)
- [147] Ganguly A, Zmuda H, Abello J, et al. The Nemp1–Nesprin complex mediates cellular responses to matrix mechanics. *Proc Natl Acad Sci.* 2026;123(9):e2521253123. doi: [10.1073/pnas.2521253123](https://doi.org/10.1073/pnas.2521253123)
- [148] Irianto J, Pfeifer CR, Ivanovska IL, et al. Nuclear lamins in cancer. *Cell Mol Bioeng.* 2016;9(2):258–267. doi: [10.1007/s12195-016-0437-8](https://doi.org/10.1007/s12195-016-0437-8)
- [149] Zuela-Sopilniak N, Lammerding J. Can't handle the stress? Mechanobiology and disease. *Trends Mol Med.* 2022;28(9):710–725. doi: [10.1016/j.molmed.2022.05.010](https://doi.org/10.1016/j.molmed.2022.05.010)
- [150] Henretta S, Lammerding J. Nuclear envelope proteins, mechanotransduction, and their contribution to breast cancer progression. *NPJ Biol Phys Mech.* 2025;2(1):14. doi: [10.1038/s44341-025-00018-2](https://doi.org/10.1038/s44341-025-00018-2)
- [151] Greiner AM, Klein F, Gudzenko T, et al. Cell type-specific adaptation of cellular and nuclear volume in micro-engineered 3D environments. *Biomaterials.* 2015;69:121–132. doi: [10.1016/j.biomaterials.2015.08.016](https://doi.org/10.1016/j.biomaterials.2015.08.016)
- [152] Jain N, Vogel V. Spatial confinement downsizes the inflammatory response of macrophages. *Nat Mater.* 2018;17(12):1134–1144. doi: [10.1038/s41563-018-0190-6](https://doi.org/10.1038/s41563-018-0190-6)
- [153] Wilson RE, Denisin AK, Dunn AR, et al. 3D microwell platforms for control of single Cell 3D geometry and intracellular organization. *Cell Mol Bioeng.* 2021;14(1):1–14. doi: [10.1007/s12195-020-00646-9](https://doi.org/10.1007/s12195-020-00646-9)
- [154] Remuzzi A, Bonandrini B, Tironi M, et al. Effect of the 3D artificial Nichoid on the morphology and mechanobiological response of mesenchymal stem cells cultured in vitro. *Cells.* 2020;9(8):1873. doi: [10.3390/cells9081873](https://doi.org/10.3390/cells9081873)
- [155] Kalukula Y, Ciccone G, Mohammed D, et al. Unlocking the therapeutic potential of cellular mechanobiology. *Sci Adv.* 2025;11(44):eaea6817. doi: [10.1126/sciadv.aea6817](https://doi.org/10.1126/sciadv.aea6817)
- [156] Smith ER, Wang JQ, Yang DH, et al. Paclitaxel resistance related to nuclear envelope structural sturdiness. *Drug*

Resist Updat. 2022;65:100881. doi: 10.1016/j.drug.2022.100881

- [157] Hale T, Hale VL, Kolata P, et al. Paclitaxel compromises nuclear integrity in interphase through SUN2-mediated cytoskeletal coupling. *J Cell Sci.* 2026;139(12):jcs264494. doi: 10.1242/jcs.264494

Jan Lammerding
Weill Institute for Cell and Molecular Biology &
Meinig School of Biomedical Engineering, Cornell
University, Ithaca, NY, USA
✉ jan.lammerding@cornell.edu
 <http://orcid.org/0000-0003-4335-8611>

Jorine Eeftens
Radboud Institute for Molecular Life Sciences,
Radboud University, Nijmegen, The Netherlands
 <http://orcid.org/0000-0001-6784-9955>

Gregg G. Gundersen
Department of Pathology and Cell Biology,
Columbia University, New York, NY, USA
 <http://orcid.org/0000-0003-3903-7380>

Megan C. King
Department of Cell Biology, Yale School of
Medicine, New Haven, CT, USA
 <http://orcid.org/0000-0002-1688-2226>

Tanmay P. Lele
Department of Biomedical Engineering, Texas
A&M University, College Station, TX, USA
 <http://orcid.org/0000-0001-8574-1251>

Song Li
Department of Bioengineering, University of
California Los Angeles, Los Angeles, CA, USA
 <http://orcid.org/0000-0002-4760-8828>

Gant Luxton, G. W.
Department of Molecular and Cellular Biology,
University of California Davis; Davis, CA, USA
 <http://orcid.org/0000-0002-6180-8906>

Ohad Medalia
Department of Biochemistry, University of Zurich,
Zurich, Switzerland
 <http://orcid.org/0000-0003-0994-2937>

Matthieu Piel
Cell Biology and Cancer, Paris, France

Pere Roca-Cusachs
Institute for Bioengineering of Catalonia (IBEC),
The Barcelona Institute of Science and Technology
(BIST), Barcelona, Spain
Department of Biomedical Sciences, University of
Barcelona, Barcelona, Spain
 <http://orcid.org/0000-0001-6947-961X>

Jörg Renkawitz
Biomedical Center, Walter Brendel Center of
Experimental Medicine, Institute of Cardiovascular
Physiology and Pathophysiology, Klinikum der
Universität, Ludwig Maximilians Universität
München, Munich, Germany
 <http://orcid.org/0000-0003-2856-3369>

Kyle Roux
Center for Genetics and Rare Diseases Research,
Sanford Research Institute, Sioux Falls, SD, USA
 <http://orcid.org/0000-0001-7530-5528>

Daniel A. Starr
Department of Molecular and Cellular Biology,
University of California Davis; Davis, CA, USA
 <http://orcid.org/0000-0001-7339-6606>

Amy R. Strom
Department of Discovery Oncology, Genentech,
South San Francisco, CA, USA
 <http://orcid.org/0000-0002-1674-3242>

Hawa Racine Thiam
Department of Bioengineering and Department of
Microbiology and Immunology, Sarafan ChEM-H
Institute, Stanford University, Palo Alto, CA, USA
Biohub, San Francisco, CA, USA
 <http://orcid.org/0000-0002-2381-1442>

Sara A. Wickström
Department of Cell and Tissue Dynamics, Max
Planck Institute for Molecular Biomedicine,
Münster, Germany
 <http://orcid.org/0000-0001-6383-6292>

Howard J. Worman
Department of Pathology and Cell Biology,
Columbia University, New York, NY, USA
Department of Medicine, Columbia University,
New York, NY, USA
 <http://orcid.org/0000-0002-7063-7889>