Extreme Mechanics Letters 20 (2018) 99–103

Contents lists available at ScienceDirect

Extreme Mechanics Letters

journal homepage: www.elsevier.com/locate/eml

Mechanical LINCs of the nuclear envelope: Where SUN meets KASH

Zeinab Jahed, Mohammad R.K. Mofrad *

Molecular Cell Biomechanics Laboratory, Departments of Bioengineering and Mechanical Engineering, University of California, Berkeley, CA 94720, United States

ARTICLE INFO

Article history:
Received 1 November 2017
Received in revised form 12 January 2018
Accepted 22 January 2018
Available online 31 January 2018

Keywords:
Nuclear envelope
LINC complex
Nucleus
Cytoskeleton
Mechanics
Mechanotransduction

ABSTRACT

The transmission of mechanical signals across the nuclear envelope is primarily mediated by linkers of the nucleoskeleton and cytoskeleton (LINC complexes). These complexes bridge the inner and outer nuclear membrane and connect various elements of the cytoskeleton to the nucleoskeleton. Through their interaction with various cytoskeletal elements, LINC complexes repeatedly endure different types of mechanical loading. In this short review, we discuss the structural features of LINC complexes that allow them to withstand and transmit mechanical forces across the nuclear envelope, the types of mechanical forces on these complexes, and the consequences of these forces on the integrity of the nuclear envelope.

Contents

1. Introduction

The skeletal elements in the cytoplasm and nucleus, namely the cytoskeleton and nucleoskeleton, maintain the structural integrity of the cell in these regions. Comparably, the linkers of cytoskeleton and nucleoskeleton (LINC complexes) can be considered as the chief structural elements of the nuclear envelope (NE), elegantly connecting the nucleus to the cytoskeletal network and transmitting mechanical signals across the NE. The nuclear pore complexes that perforate the NE also conceivably contribute to the mechanics of the NE, however their primary function is to control the exchange of biochemical signals between the cytoplasm and nucleus. The LINC complexes are increasingly established as the rivets that transmit mechanical signals across the NE. Fittingly, LINC complexes are structured for load bearing and force transmission and perform central roles in several cellular processes.

Herein we review the roles of LINC complexes in maintaining or disrupting the structural integrity of the NE. We first examine the current crystallographic data on LINC complexes at the nuclear envelope. Next we discuss the various types of mechanical loading that is experienced by the nuclear envelope through LINC complexes during various cellular processes. Finally, we survey available knowledge of the role of LINC in the loss of structural integrity of the nuclear envelope during nuclear rupture.

The nuclear envelope of eukaryotes is double layered and composed of an inner and outer nuclear membrane (INM and ONM). The structural integrity of the NE is essential for the isolation and protection of genomic information from the cytoplasm. With an intact NE, the exchange of material between the nucleus and cytoplasm can be conducted in a controlled manner through macromolecular protein complexes known as nuclear pore complexes. Although NPCs may also contribute to the mechanical integrity of the nucleus as discussed in Jahed et al. [1], the only other protein complex known to span the NE and physically link the INM

* Correspondence to: Department of Bioengineering, University of California, Berkeley, 208A Stanley Hall #1762, Berkeley, CA 94720-1762, United States
E-mail address: mofrad@berkeley.edu (M.R.K. Mofrad).
URL: http://biomechanics.berkeley.edu (M.R.K. Mofrad).
Abbreviations: CC, Coiled-coil; KASH, *Klarsicht*, *ANC-1*, *SYNE* Homology; INM, Inner nuclear membrane; NE, Nuclear envelope; NPC, Nuclear pore complex; ONM, Outer nuclear membrane; PNS, Perinuclear space; SUN, *Sad-1* and UNC-84

https://doi.org/10.1016/j.eml.2018.01.010
2352-4316/

List of abbreviations

CC	Coiled-coil
KASH	*Klarsicht*, *ANC-1*, *SYNE* Homology
INM	Inner nuclear membrane
NE	Nuclear envelope
NPC	Nuclear pore complex
ONM	Outer nuclear membrane
PNS	Perinuclear space
SUN	*Sad-1* and UNC-84

and ONM are LINC complexes. LINC complexes are responsible for the transmission of forces across the nuclear envelope [2,3]. Force transmission across the nuclear envelope through LINC complexes is essential for several cellular processes reliant on nuclear movement and positioning, and nuclear mechanotransduction [4].

LINC complexes are formed by the interaction of conserved *Sad1/UNC-84* (SUN) — domain and *Klarsicht/ANC-1/SYNE* homology (KASH) — domain proteins in the perinuclear space (PNS) [2,5–7]. At least six KASH proteins (nesprin-1–4, lymphoid-restricted membrane protein, and KASH5) and five SUN proteins (SUN1–5) have been identified in mammals [8–12]. KASH proteins are anchored to the outer nuclear membrane (ONM) and contain large cytoplasmic domains, and a short ∼10–32 residue C-terminal KASH domain that protrudes in to the PNS (Fig. 1). SUN proteins are anchored to the inner nuclear membrane (INM) and their conserved C-terminal SUN domains reside in the PNS where they bind to KASH. The N-terminal nucleoplasmic domains of SUN interact with nucleoskeletal elements such as A-type lamins and chromatin, as well as other INM proteins such as Emerin [13,2,14,15] (Fig. 1). Lamins are type V nuclear intermediate filaments that form a filamentous meshwork at the nuclear periphery, and interact with chromatin, SUN proteins, and other INM proteins, to maintain the structural integrity of the nucleus [16,17].

The N-terminal cytoplasmic domains of KASH proteins associate with various elements of the cytoskeleton, including direct interactions with the actin cytoskeleton through their actin binding domains, and indirect bindings to microtubules and intermediate filaments through motor proteins such as kinesin, dynein and plectin (Fig. 1) [3,2,18,14,19,20,12,21].

2. LINC is structured for load bearing

Several studies have shown that SUN proteins must oligomerize to bind to KASH proteins and are inactive for KASH binding in a monomeric state [22,18,23,24]. Recent crystallographic data suggest that in a monomeric state, the main KASH binding domain of SUN2 (i.e. the KASH-lid) is inhibited by a three-helix bundle preceding the SUN domain (α1–α3) (Fig. 1(i)). Large coiled coil (CC) domains preceding the SUN domain force the SUN domain into a trimeric state, and activate it for KASH binding [22,18,23,24]. Upon trimerization, the minimal region required for KASH binding consists of an alpha helix (α3) that forms a trimeric CC, and a beta sandwich core from which the KASH-lid emanates (Fig. 1(ii)). In this conformation, the SUN trimer can bind to three KASH peptides simultaneously, and form an overall hexameric SUN–KASH complex (Fig. 1(iii)). Two coiled coil regions are predicted in most SUN domain proteins [2,6], and the recently solved crystal structure of one of the predicted CC regions of SUN2 revealed that it also forms a trimer (Fig. 1(iv)) [23].

Based on the abovementioned crystallographic data, four main attributes of LINC complexes contribute to their suitability as load bearing elements in the nuclear envelope:

(1) The SUN domain is functional in a trimeric state and the higher order oligomerization of these proteins allows for their high stability under force. Additionally, some studies have suggested that SUN proteins can further cluster into even higher order oligomers, which would allow the transmission of even higher forces [25,14,26].

(2) The interaction between the mammalian SUN2 trimer and the KASH domains of nesprin 1 and nesprin 2 is highly stable, with 24 hydrogen bonds between each KASH peptide and the SUN2 trimer, and 1520 Å^2 of the SUN2 trimer buried upon binding to one KASH peptide [18].

(3) The interaction between mammalian SUN2 and the KASH domains of nesprin 1 and nesprin 2 terminates with a covalent disulfide bond between two highly conserved cysteine residues on each protein. This intermolecular disulfide bond not only further stabilizes the SUN2–KASH2 interaction, but it also allows the transmission of forces to the coiled coil regions of SUN2 (Fig. 1(iii)) [27,18,22].

(4) Most Sun proteins are predicted to contain at least two long coiled coil domains. Coiled coils have been identified as elastic elements in proteins [28–31]. In some cases like myosin, the CC regions have been characterized and show truly elastic properties where they can reversibly extent more than two times their length [28]. Although the mechanical properties of the CC regions of SUN proteins have yet to be identified, it is likely that these CCs can also extend reversibly under mechanical forces, and hence contribute to the elasticity of the nuclear envelope.

3. Forces exerted on the nuclear envelope through the LINC complex: Tension, compression and shear

The direct binding of nesprin proteins to the actin cytoskeleton through their actin binding domains exposes the SUN–KASH linkage to actomyosin dependent mechanical forces. In 2D cultures, LINC complexes connect the apical surface of the nucleus to a highly ordered and dynamic filamentous actin structure known as the perinuclear actin cap (Fig. 2(A)) [32–36]. The perinuclear actin cap is terminated by focal adhesion molecules that transmit mechanical forces across the cell membrane. The coupling between LINC complexes and focal adhesions through actin filaments induces compressive stresses on the nuclear envelope at the top surface of the nucleus and shear and tensile force at the two ends (Fig. 2(A)). The magnitude and direction of local forces on SUN and KASH proteins is not well known. There are some evidences of tensile forces on elements of the LINC complex. For example, increased separations were observed between the INM and ONM in some regions of SUN1 and SUN2 depleted HeLa cells [2], as well as at the two ends of force-bearing *C. elegans* muscle nuclei with disrupted LINC complexes [37]. These observations suggest that the LINC complex withstands tension at the nuclear envelope, and plays a role in maintaining the even distance between the INM and ONM, at least in load bearing regions [38,1,22,14,37]. Furthermore, in mammalian cells, a fluorescence resonance energy transfer (FRET)-based tension biosensor for nesprin 2 showed that nesprin is subject to tension in adherent fibroblast [39]. Higher levels of tensile forces were observed on the apical and equatorial planes of the nucleus. This study suggested that even in compressive regions of the actin cap, nesprins are under tension and orient towards the long axis of the cell [39]. Since nesprins are anchored to the ONM, when oriented parallel to the NE, tensile forces on these proteins translates to shear on the ONM (Fig. 2(A)).

The indirect interaction of nesprin proteins with microtubules through motor proteins dynein and kinesin also exposes LINC complexes to constant velocity pulling as these motor proteins move along microtubules during several cellular processes reliant on this interaction (Fig. 2(B)) [40,41,7]. Nesprins are likely under

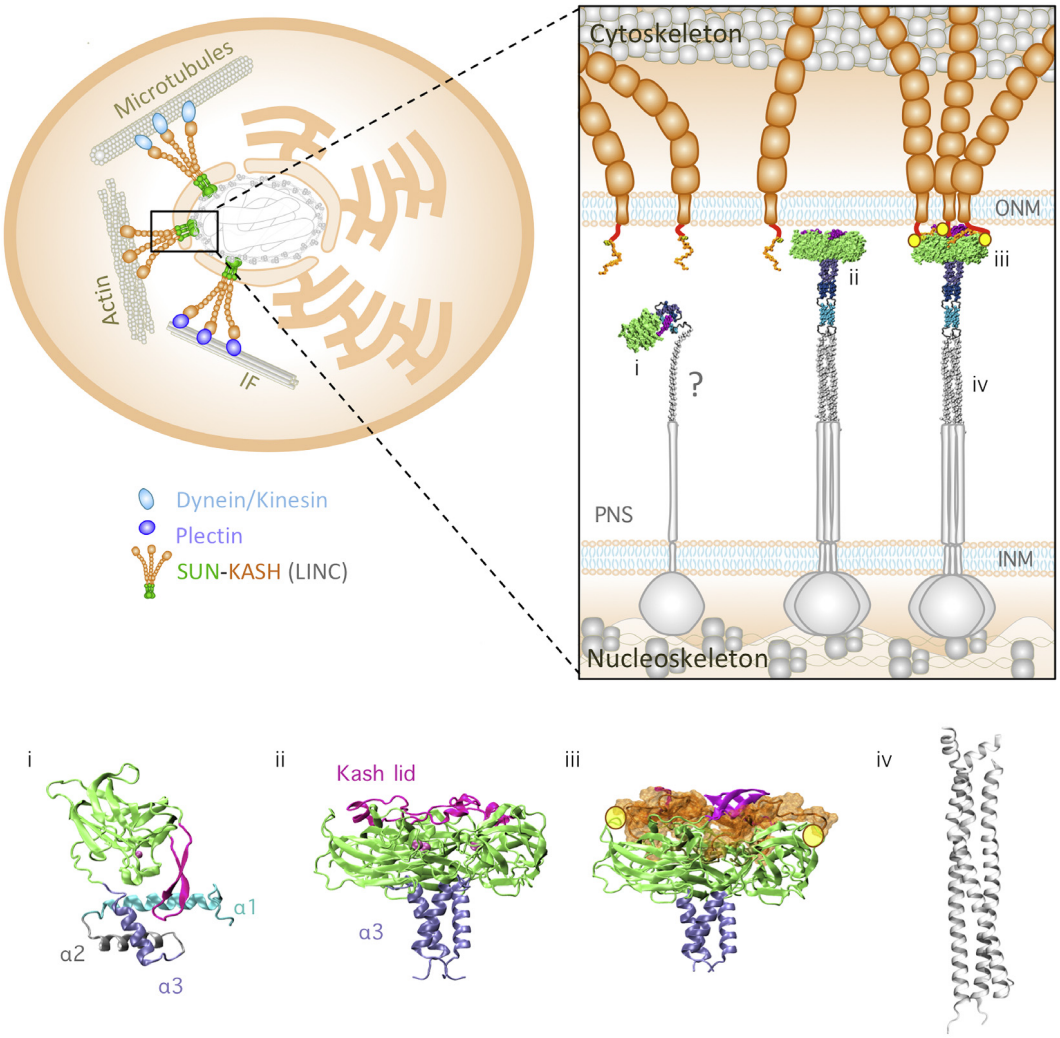

Fig. 1. Crystal structure of the LINC complex. Schematic representation of LINC complexes spanning the nuclear envelope and connecting various cytoskeletal elements to the nucleoskeleton (Top). Crystal structures of various fragments of LINC complex proteins SUN2 and KASH2 (bottom): (i) Structure of mouse SUN2 monomer (PDB ID: 5ed8), magenta: KASH-lid (ii) Human SUN2 trimer (PDB ID: 4DXT) (iii) Human SUN2 trimer (green/purple) in complex with KASH2 (orange) forming an overall hexamer, (iv) Coiled coil region of mouse SUN2. Yellow circles: covalent disulfide bonds between SUN and KASH. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

tension in these cellular processes and orient towards the direction of dynein movement, exerting shear and tensile forces on the ONM.

How are these cytoskeletal forces on KASH transmitted to SUN proteins? It has been shown that each SUN protein can interact with three KASH peptides simultaneously *in vitro*. If this is the case *in vivo* and three nesprin proteins can simultaneously bind a SUN trimer, the NE may be subjected to forces in various directions (Fig. 2(C)). However, since the LINC complex is anchored at the INM and ONM, when transmitted across the ONM, these forces likely translate to tensile forces in a direction perpendicular to the INM and ONM on SUN proteins (Fig. 2(C)). One can envision the design of new FRET-based tension sensors inserted into various regions of SUN proteins to better determine the stress state of SUN proteins in the nuclear envelope and further elucidate the molecular mechanisms of force transmission across the nuclear envelope. Similar approaches can be used to determine stress states of the nucleoplasmic domains of SUN proteins to understand how forces are ultimately transmitted through SUN proteins to their interacting partners in the nucleus. No crystallographic data is currently available on the nucleoplasmic domains of SUN proteins and their dynamics inside the nucleus remains widely unexplored.

4. Consequences of forces on the NE through LINC (Role of mechanical forces on LINC in NE rupture)

The mechanical forces exerted on the NE through LINC complexes are essential for several cellular processes reliant on nuclear movement and positioning, and nuclear mechanotransduction [4]. These forces are transmitted across the LINC complex to the filamentous lamin meshwork underlying the INM, resulting in nuclear stiffening through the recruitment of more A-type lamin, and hence, a change in the mechanical properties of the nucleus [42,4]. Additionally, these forces can lead to changes in genome organization and gene expression as discussed in a recent review by Uhler and Shivashankar [43].

On the other hand, recent studies have shown that mechanical stresses exerted on the nuclear envelope can also lead to nuclear rupture both *in vivo* and *in vitro*, compromising the integrity of DNA [44]. These stresses can be induced on the nucleus by an external environment as cells migrate through confined spaces, or by intracellular structures such as the perinuclear actin cap [45,46]. In the former case, external pressure is applied on the nucleus as the cells "squeeze" through confined spaces and nuclear rupture occurs in a LINC-independent manner. On the other hand, when the actin cap is responsible for nuclear confinement in cultured

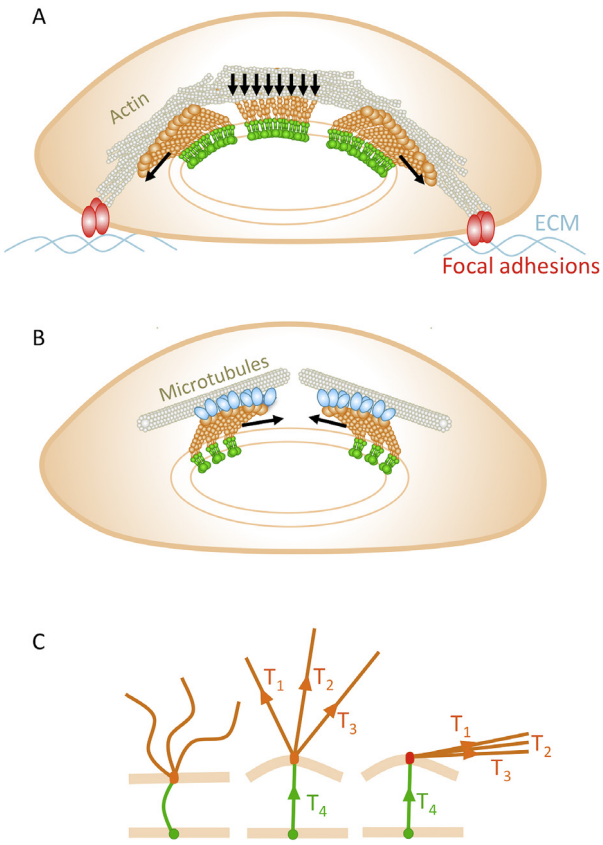

Fig. 2. Mechanical forces on the NE through LINC complexes. (A) The perinuclear actin cap exerts compressive forces on the apical surface of the nucleus and shear and tension at the two ends. These forces are transmitted to the nuclear envelope through LINC complexes. (B) KASH proteins bound to motor proteins moving along microtubules exert mechanical forces on the NE. (C) Tensile cytoskeletal forces on KASH proteins (orange) are translated to tension on SUN proteins (green). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

cells, nuclear rupture is dependent on LINC complexes [45,46]. The *in vivo* relevance of LINC complex-dependent nuclear envelope rupture requires further studies.

5. Outlook

Although our understanding of the role of LINC complexes in the mechanical integrity of the nuclear envelope has significantly increased in the past decade, several questions remain unanswered. It is unknown whether KASH proteins are able to oligomerize similar to SUN proteins, and if so, how their oligomerization would influence the magnitude and direction of forces on the NE. Currently, no crystallographic data is available on the structure of cytoplasmic domains of nesprins or other KASH proteins. Such information would greatly enhance our understanding of the structural features of these proteins and their response to mechanical forces. Additionally, no crystallographic data is available on the nucleoplasmic domains of SUN protein where they interact with A-type lamins and chromatin. Unraveling atomic level details of the nucleoplasmic domains of SUN proteins, and the nature of their interaction with the nucleoskeleton, will help better understand how forces may be transmitted to nuclear contents, specially chromatin, and how this may ultimately modulate gene expression [43,4].

Moreover, the structural data on SUN proteins is limited to the most widely expressed mammalian SUN protein, SUN2. The crystal structures of other mammalian SUN proteins such as SUN1 and SUN3–5 are yet to be solved. Particularly interesting are SUN3–5 which contain much shorter CC regions than SUN1–2 proteins and it is unclear how these shorter proteins are able to overcome the NE spacing and reach across the NE to bind to KASH and withstand cytoskeletal forces [22,38,1]. Also, how do mechanical boundary conditions on SUN and KASH, i.e. anchorage to the INM and ONM, affect their structures, mobility, interactions with other proteins, and force transmission to the nucleus? It is important to note that the small-scale mechanics of the lipid bilayers at the INM and ONM, and their ability to rupture, largely influences the forces experienced by and transmitted across the transmembrane domains of SUN and KASH proteins. Limited studies have addressed this topic; however, recent advances in experimental and computational biophysical approaches to study cell membranes [47] will allow researchers to better characterize local membrane responses to mechanical force.

Finally, most of the current information on the structure and higher order assembly mechanism of SUN proteins are based on *in vitro* data. Recent developments of *In vivo* techniques allowing the imaging and quantification of protein–protein interactions inside the nuclear envelope of living cells promise new developments on the LINC complex assembly at the nuclear envelope [48,49].

References

[1] Zeinab Jahed, Mohammad Soheilypour, Mohaddeseh Peyro, Mohammad R.K. Mofrad, The LINC and NPC relationship — it's complicated!, J. Cell Sci. 184184 (2016). http://dx.doi.org/10.1242/jcs.184184.
[2] Melissa Crisp, Qian Liu, Kyle Roux, J.B. Rattner, Catherine Shanahan, Brian Burke, Phillip D. Stahl, Didier Hodzic, Coupling of the nucleus and cytoplasm: Role of the LINC complex, J. Cell Biol. 172 (1) (2006) 41–53. http://jcb.rupress.org/content/172/1/41.abstract.
[3] Maria L. Lombardi, Diana E. Jaalouk, Catherine M. Shanahan, Brian Burke, Kyle J. Roux, Jan Lammerding, The interaction between nesprins and sun proteins at the nuclear envelope is critical for force transmission between the nucleus and cytoskeleton, J. Biol. Chem. 286 (30) (2011) 26743–26753. http://dx.doi.org/10.1074/jbc.M111.233700.
[4] Philipp Isermann, Jan Lammerding, Nuclear mechanics and mechanotransduction in health and disease, Curr. Biol. 23 (24) (2013) R1113–R1121. http://dx.doi.org/10.1016/j.cub.2013.11.009.
[5] Daniel A. Starr, Min Han, Role of ANC-1 in tethering nuclei to the actin cytoskeleton, 298 (October) (2002) 2000–2003.
[6] V.C. Padmakumar, Thorsten Libotte, Wenshu Lu, Hafida Zaim, Sabu Abraham, Angelika a. Noegel, Josef Gotzmann, Roland Foisner, Iakowos Karakesisoglou, The inner nuclear membrane protein Sun1 mediates the anchorage of Nesprin-2 to the nuclear envelope, J. Cell Sci. 118 (15) (2005) 3419–3430. http://dx.doi.org/10.1242/jcs.02471.
[7] Matthew D. McGee, Regina Rillo, Amy S. Anderson, Daniel A. Starr, UNC-83 is a KASH protein required for nuclear migration and is recruited to the outer nuclear membrane by a physical interaction with the SUN Protein UNC-84, Mol. Biol. Cell 17 (2006) 1790–1801. http://dx.doi.org/10.1091/mbc.E05.
[8] Yu Nishioka, Hiromasa Imaizumi, Junko Imada, Jun Katahira, Nariaki Matsuura, Miki Hieda, SUN1 splice variants, SUN1_888, SUN1_785, and predominant SUN1_916, variably function in directional cell migration, Nucleus 7 (6) (2016). http://dx.doi.org/10.1080/19491034.2016.1260802.
[9] Dipen Rajgor, Catherine M. Shanahan, Nesprins: From the nuclear envelope and beyond, Expert Rev. Mol. Med. 15 (July) (2013) e5. http://dx.doi.org/10.1017/erm.2013.6.
[10] Peter Meinke, Eric C. Schirmer, LINC'ing form and function at the nuclear envelope, 589 (2015) 2514–2521. doi:10.1016/j.febslet.2015.06.011.
[11] Nguyen Thuy Duong, Glenn E. Morris, Le Thanh Lam, Qiuping Zhang, Caroline A. Sewry, Catherine M. Shanahan, Ian Holt, Nesprins: Tissue-specific expression of epsilon and other short isoforms, 9 (4) (2014). doi:10.1371/journal.pone.0094380.
[12] Akihiro Morimoto, Hiroki Shibuya, Xiaoqiang Zhu, Jihye Kim, Kei Ichiro Ishiguro, Min Han, Yoshinori Watanabe, A conserved KASH domain protein associates with telomeres, SUN1, and dynactin during mammalian meiosis, J. Cell Biol. 198 (2) (2012) 165–172. http://dx.doi.org/10.1083/jcb.201204085.
[13] Wakam Chang, Howard J. Worman, Gregg G. Gundersen, Accessorizing and anchoring the LINC complex for multifunctionality, J. Cell Biol. 208 (1) (2015) 11–22. http://dx.doi.org/10.1083/jcb.201409047.
[14] Q. Liu, N. Pante, T. Misteli, M. Elsagga, M. Crisp, D. Hodzic, B. Burke, K.J. Roux, Functional association of Sun1 with nuclear pore complexes, J. Cell Biol. 178 (5) (2007) 785–798. http://dx.doi.org/10.1083/jcb.200704108.

[15] Huajiang Xiong, Francisco Rivero, Ursula Euteneuer, Subhanjan Mondal, Sebastian Mana-Capelli, Denis Larochelle, Annette Vogel, Berthold Gassen, Angelika a. Noegel, Dictyostelium Sun-1 connects the centrosome to chromatin and ensures genome stability, Traffic 9 (5) (2008) 708–724. http://dx.doi.org/10.1111/j.1600-0854.2008.00721.x.
[16] Chin Yee Ho, Jan Lammerding, Lamins at a glance, J. Cell Sci. 125 (Pt 9) (2012) 2087–2093. http://jcs.biologists.org/content/125/9/2087.short.
[17] Yagmur Turgay, Matthias Eibauer, Anne E. Goldman, Takeshi Shimi, Maayan Khayat, Kfir Ben-harush, Anna Dubrovsky-gaupp, K. Tanuj Sapra, Robert D. Goldman, Ohad Medalia, The Molecular Architecture of Lamins in Somatic Cells, Nature Publishing Group, 2017. http://dx.doi.org/10.1038/nature21382.
[18] Brian a. Sosa, Andrea Rothballer, Ulrike Kutay, Thomas U. Schwartz, LINC complexes form by binding of three KASH peptides to domain interfaces of trimeric SUN proteins, Cell 149 (5) (2012) 1035–1047. http://dx.doi.org/10.1016/j.cell.2012.03.046.
[19] Henning F. Horn, Zippora Brownstein, Danielle R. Lenz, Shaked Shivatzki, Amiel A. Dror, Orit Dagan-rosenfeld, Lilach M. Friedman, et al., The LINC complex is essential for hearing, 123 (2) (2013). doi:10.1172/JCI66911.740.
[20] Jun Fan, Kenneth a. Beck, A role for the spectrin superfamily member Syne-1 and Kinesin II in cytokinesis, J. Cell Sci. 117 (Pt 4) (2004) 619–629. http://dx.doi.org/10.1242/jcs.00892.
[21] K. Wilhelmsen, Nesprin-3, a novel outer nuclear membrane protein, associates with the cytoskeletal linker protein plectin, J. Cell Biol. 171 (5) (2005) 799–810. http://dx.doi.org/10.1083/jcb.200506083.
[22] Brian a. Sosa, Ulrike Kutay, Thomas U. Schwartz, Structural insights into LINC complexes, Curr. Opin. Struct. Biol. 23 (2) (2013) 285–291. http://dx.doi.org/10.1016/j.sbi.2013.03.005.
[23] Si Nie, Huimin Ke, Feng Gao, Jinqi Ren, Mingzhu Wang, Lin Huo, Weimin Gong, Wei Feng, Coiled-coil domains of SUN proteins as intrinsic dynamic regulators, Structure 24 (1) (2016) 80–91. http://dx.doi.org/10.1016/j.str.2015.10.024.
[24] Zhaocai Zhou, Xiulian Du, Zheng Cai, Xiaomin Song, Hongtao Zhang, Takako Mizuno, Emi Suzuki, et al., Structure of Sad1-UNC84 homology (SUN) domain defines features of molecular bridge in nuclear envelope, J. Biol. Chem. 287 (8) (2012) 5317–5326. http://dx.doi.org/10.1074/jbc.M111.304543.
[25] Wenshu Lu, Josef Gotzmann, Lucia Sironi, Verena-Maren Jaeger, Maria Schneider, Yvonne Lüke, Mathias Uhlén, et al., Sun1 forms immobile macromolecular assemblies at the nuclear envelope, Biochim. Biophys. Acta 1783 (12) (2008) 2415–2426. http://dx.doi.org/10.1016/j.bbamcr.2008.09.001.
[26] Zeinab Jahed, Darya Fadavi, Uyen T. Vu, Ehsannedin Asgari, G.W. GantLuxton, Mohammad R.K. Mofrad, Molecular insights into the mechanisms of SUN1 oligomerization in the nuclear envelope, Biophys. J. 114 (2018).
[27] Zeinab Jahed, Hengameh Shams, Mohammad R.K. Mofrad, A disulfide bond is required for the transmission of forces through SUN-KASH complexes, Biophys. J. 109 (August) (2015) 1–9. http://dx.doi.org/10.1016/j.bpj.2015.06.057.
[28] Ingo Schwaiger, Clara Sattler, Daniel R. Hostetter, Matthias Rief, The myosin coiled-coil is a truly elastic protein structure, Nature Mater. 1 (4) (2002) 232–235. http://dx.doi.org/10.1038/nmat776.
[29] Steven M. Kreuzer, Ron Elber, Coiled-coil response to mechanical force: Global stability and local cracking, Biophys. J. 105 (4) (2013) 951–961. http://dx.doi.org/10.1016/j.bpj.2013.05.064.
[30] Sara Sadeghi, Eldon Emberly, Length-dependent force characteristics of coiled coils, Phys. Rev. E 80 (6) (2009) 61909. http://dx.doi.org/10.1103/PhysRevE.80.061909.
[31] Charles Wolgemuth, Sean Sun, Elasticity of α-helical coiled coils, Phys. Rev. Lett. 97 (24) (2006) 248101. http://dx.doi.org/10.1103/PhysRevLett.97.248101.
[32] Dong-Hwee Kim, Shyam B. Khatau, Yunfeng Feng, Sam Walcott, Sean X. Sun, Gregory D. Longmore, Denis Wirtz, Actin cap associated focal adhesions and their distinct role in cellular mechanosensing, Sci. Rep. 2 (January) (2012) 555. http://dx.doi.org/10.1038/srep00555.
[33] Shyam B. Khatau, Christopher M. Hale, P.J. Stewart-Hutchinson, Meet S. Patel, Colin L. Stewart, Peter C. Searson, Didier Hodzic, Denis Wirtz, A perinuclear actin cap regulates nuclear shape, Proc. Natl. Acad. Sci. USA 106 (45) (2009) 19017–19022. http://dx.doi.org/10.1073/pnas.0908686106.
[34] Peter Meinke, Elisabetta Mattioli, Farhana Haque, Susumu Antoku, Marta Columbaro, Kees R. Straatman, Howard J. Worman, et al., Muscular dystrophy-associated SUN1 and SUN2 variants disrupt nuclear-cytoskeletal connections and myonuclear organization, PLoS Genet. 10 (9) (2014) e1004605. http://dx.doi.org/10.1371/journal.pgen.1004605.
[35] Edgar R. Gomes, Shantanu Jani, Gregg G. Gundersen, Nuclear movement regulated by Cdc42, MRCK, Myosin, and actin flow establishes MTOC polarization in migrating cells, Cell 121 (3) (2005) 451–463. http://dx.doi.org/10.1016/j.cell.2005.02.022.
[36] G.W. Gant Luxton, Edgar R. Gomes, Eric S. Folker, Erin Vintinner, Gregg G. Gundersen, Linear arrays of nuclear envelope proteins harness retrograde actin flow for nuclear movement, Science 329 (5994) (2010) 956–959. http://dx.doi.org/10.1126/science.1189072.
[37] Natalie E. Cain, Erin C. Tapley, Kent L. McDonald, Benjamin M. Cain, Daniel a. Starr, The SUN protein UNC-84 is required only in force-bearing cells to maintain nuclear envelope architecture, J. Cell Biol. 206 (2) (2014) 163–172. http://dx.doi.org/10.1083/jcb.201405081.
[38] Natalie E. Cain, Daniel A. Starr, SUN proteins and nuclear envelope spacing, Nucleus 6 (1) (2015) 2–7. http://dx.doi.org/10.4161/19491034.2014.990857.
[39] Paul T. Arsenovic, Iswarya Ramachandran, Kranthidhar Bathula, Ruijun Zhu, Jiten D. Narang, Natalie A. Noll, Christopher A. Lemmon, Gregg G. Gundersen, Daniel E. Conway, Nesprin-2G, a component of the nuclear LINC complex, is subject to myosin-dependent tension, Biophys. J. 110 (1) (2016) 34–43. http://dx.doi.org/10.1016/j.bpj.2015.11.014.
[40] Xu Ding, Rene Xu, Juehua Yu, Tian Xu, Yuan Zhuang, Min Han, SUN1 is required for telomere attachment to nuclear envelope and gametogenesis in mice, no. June, 2007, pp. 863–872. doi:10.1016/j.devcel.2007.03.018.
[41] Henning F. Horn, Dae In Kim, Graham D. Wright, Esther Sook Miin Wong, Colin L. Stewart, Brian Burke, Kyle J. Roux, A mammalian KASH domain protein coupling meiotic chromosomes to the cytoskeleton, J. Cell Biol. 202 (7) (2013) 1023–1039. http://dx.doi.org/10.1083/jcb.201304004.
[42] Christophe Guilluy, Lukas D. Osborne, Laurianne Van Landeghem, Lisa Sharek, Richard Superfine, Rafael Garcia-Mata, Keith Burridge, Isolated nuclei adapt to force and reveal a mechanotransduction pathway in the nucleus, Nature Cell Biol. August 2013 (March) (2014). http://dx.doi.org/10.1038/ncb2927.
[43] Caroline Uhler, G.V. Shivashankar, Regulation of genome organization and gene expression by nuclear mechanotransduction, Nature Rev. Mol. Cell Biol. 18 (12) (2017) 717–727. http://dx.doi.org/10.1038/nrm.2017.101.
[44] C.M. Denais, Celine M. Denais, Rachel M. Gilbert, Philipp Isermann, Alexandra L. Mcgregor, Mariska Lindert, Bettina Weigelin, et al., Nuclear envelope rupture and repair during cancer cell migration, 7297 (March) (2016) 1–9.
[45] Emily M. Hatch, Martin W. Hetzer, Nuclear envelope rupture is induced by actin-based nucleus confinement, J. Cell Biol. 1 (2016). http://dx.doi.org/10.1083/jcb.201603053.
[46] Jan Lammerding, Katarina Wolf, Nuclear envelope rupture: Actin fibers are putting the squeeze on the nucleus, (2016) 1–4. doi:10.1083/jcb.201609102.
[47] Morgan Chabanon, Jeanne C. Stachowiak, Padmini Rangamani, Systems biology of cellular membranes: A convergence with biophysics, Wiley Interdiscip. Rev. Syst. Biol. Med. 9 (5) (2017) 20–22. http://dx.doi.org/10.1002/wsbm.1386.
[48] J. Hennen, K.H. Hur, C.A. Saunders, G.W.G. Luxton, J.D. Mueller, Quantitative brightness analysis of protein oligomerization in the nuclear envelope, Mol. Biol. Cell (2017).
[49] Danielle M. Jorgens, Jamie L. Inman, Michal Wojcik, Claire Robertson, Hildur Palsdottir, Wen-Ting Tsai, Haina Huang, et al., Deep nuclear invaginations linked to cytoskeletal filaments: Integrated bioimaging of epithelial cells in 3D culture danielle, J. Cell Sci. 94720 (August) (2016).