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Filamin: A Structural and Functional Biomolecule with Important Roles in Cell Biology, Signaling and Mechanics

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Abstract: Focal adhesions are the immediate sites of the cell's adhesive interaction with the extracellular matrix and as such play a key role in mechanosensing and mechanotransduction at the edge of the cell interface with its surrounding microenvironment. A multitude of proteins orchestrate this mechanochemical communication process between the cell and its outside world. Filamin is a member of focal adhesion protein machinery that also plays a key role in regulating and bundling the acting filament network. A brief review is presented here on filamin and its important protein partners with the aim to shed light on the role of filamin's protein-protein interaction network in cell mechanobiology.

1 Introduction

The cytoskeleton plays an integral role in cell shape and structure. It is crucial for several biological functions of the cell, e.g. locomotion, division, protein sorting and transport [1-7]. The cytoskeleton is an organized network of various biological polymers. Of the three key components of the cytoskeleton, actin is the most actively studied, due in part to its highly dynamic nature and historical underpinnings [8-10]. The actin cytoskeleton is composed of globular actin (G-actin) monomers that form filamentous structures (F-actin), which in turn can create bundles and networks of varying geometry [5]. The F-actin network topology is not random. Rather, it is organized by specific actin binding proteins that serve to orient the filaments and can physically modulate the mechanical strength of the cytoskeletal network [11].

There are different actin cross-linking proteins that bind actin through a special binding site called the actin-binding domain (ABD) [10, 12-15]. Filamin plays

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a primary role in this context and was one of the first actin-binding proteins discovered [8-10]. The molecular structure of filamin has been investigated using different methods such as electron microscopy, x-ray crystallography, florescence resonance energy transfer, genetic mutations, and molecular dynamics [2, 9, 10, 16-19]. Filamin forms a high molecular weight dimer with an elongated flexible v-shaped structure consisting of 2647 amino acids per monomer [8-10]. In addition to its role in the organization of actin filaments, filamin interacts directly with more than hundred cellular proteins of great functional diversity [8-10, 12, 17, 20-22]. Mutations of filamin is therefore expected to disrupt important processes in the cell and have been linked to a variety of diseases in highly organized tissues such as the brain, bone, and muscle, corresponding likely to distinct filamin interactions [23-28].

Despite numerous reports on filamin's biochemical activities and the structural and mechanistic aspects underlying its functions [1, 2, 8-10, 12, 16], the regulation of filamin and its many partners as well as the downstream effects have remained elusive.

In this article, we will review important topics related to mechanobiology of filamin. First, general and structural features of filamin are introduced. Focusing on filamin A (FLNA), we will then discuss the role of this protein in focal adhesions and present a brief report on the interactions of filamin with other protein partners that bestow it with a set of diverse roles in the cell. Finally, we will present an outlook for better understanding the role of filamin in cell mechaobiology.

2 The structure and overall properties of filamin

Filamin is an actin binding protein (ABP) initially isolated in macrophages [29]. Monomeric filamin contains 2647 amino acids with a molecular weight of 250 – 270 kDa, and Stokes radius of 12 nm [8, 10, 12, 21, 22, 30]. The molecular structure of filamin is depicted in Figure 1. In addition, the structure of filamin while crosslinking actin filaments is shown in Figure 2. Each monomer chain is composed of three general sub regions: the head, backbone, and tail [8-10, 12, 17, 20, 21].

Filamin head or actin binding domain (ABD)

Filamin's actin binding domain contains 274 residues and its amino acid sequence is similar to α-actinin, β-spectrin, and dystrophin Dictyostelium abp-120ABDs. ABD is composed of two calponin homology domains called CHD1 and CHD2 [8-10, 12, 17, 20, 21].

Filamin backbone

The backbone of filamin comprises 24 repeats, each of which contains approxi-

mately 96 residues. The two sequences proximal to repeats 16 and 24 constitute two hinges, which confer more flexibility to filamin and divide it into two domains; rod domain 1 (repeats 1-15) and rod domain 2 (repeats 16-23) with 55nm and 15nm lengths, respectively (Figure 1) [8-10, 12, 17, 20, 21, 30]. The majority of filamin interacting proteins relate with repeats on rod domain 2. Some of the important proteins interacting with FLNA and their corresponding filamin repeats are listed in Table 1.

Table 1: Some interacting proteins with FLNA and their corresponding filamin repeats.

Protein Name	**Interacting Repeat**	**Reference**
GP-Ibα	17-19	[31]
L1A, L1D, L2, 3, 7 integrin	20-24	[32, 33]
Tissue factor	23-24	[34]
Dopamine D2, 3 receptor	16-19	[35]
(D)-Presenilin1, 2	21-24	[36]
Furin receptor	13-14	[37]
Calveolin 1	22-24	[38]
Kv4.2 potassium channel	C-term	[39]
RalA, RhoA, Rac1, Cdc42	24	[40]
SEK1 (MEKK, JNKK)	22-23	[41]
TRAF2	15-19	[42]
Trio	23-24	[43]
Androgen receptor	16-19	[44]
cvHSP	23-24	[45]
Granzyme B	20-24	[46]
Adapter Protein SH2B1 beta	17-23	[47]
Vimentin, protein kinase C-epsilon	1-8	[48]

Filamin tail or association/dimerization domain

The tail region, filamin repeat 24, consists of unpaired hydrophobic surfaces from two filamin subunits that provide a domain to self associate leading to dimerization of two filamin monomers. Hence this region is also called the dimerization unit [8-10, 12, 17, 20, 21].

All of the mentioned subdomains are schematized in Figures 1 and 2.

In addition to sequence homology investigations, the crystal and solution structures of some FLN subdomains have been studied. Solved structures for FLNA, one of FLN isoforms, available in PDB repository, are summarized in Table 2.

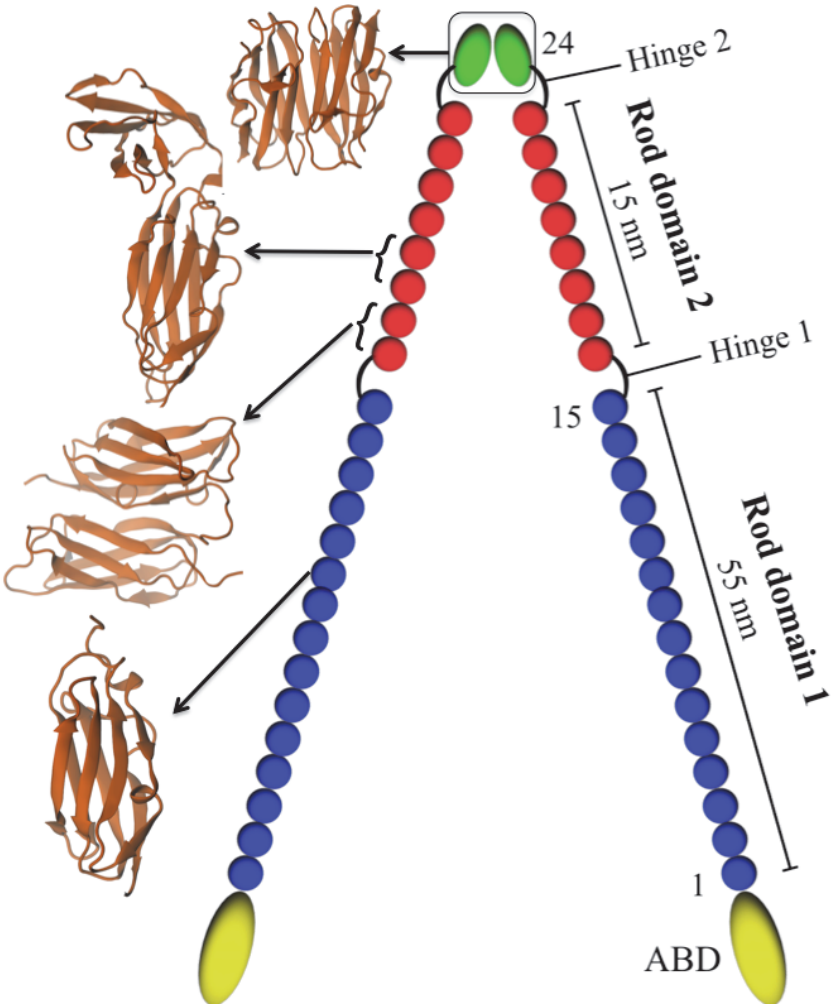

Figure 1: A schematic of the predicted dimeric structure of filamin. Each monomer contains an actin-binding domain, containing two CH, 55nm rod domain1, with 15 Ig like repeats, a hinge connecting rod domain 1 to rod domain 2, and 15nm rod domain 2, with 8 Ig like repeats. Hinge 2 connects rod domain 2 to domain 24, or dimerization domain, and dimerization domain connects two monomers together. The crystal structures of 6 repeats are also illustrated while their PDB IDs can be found in Table 2.

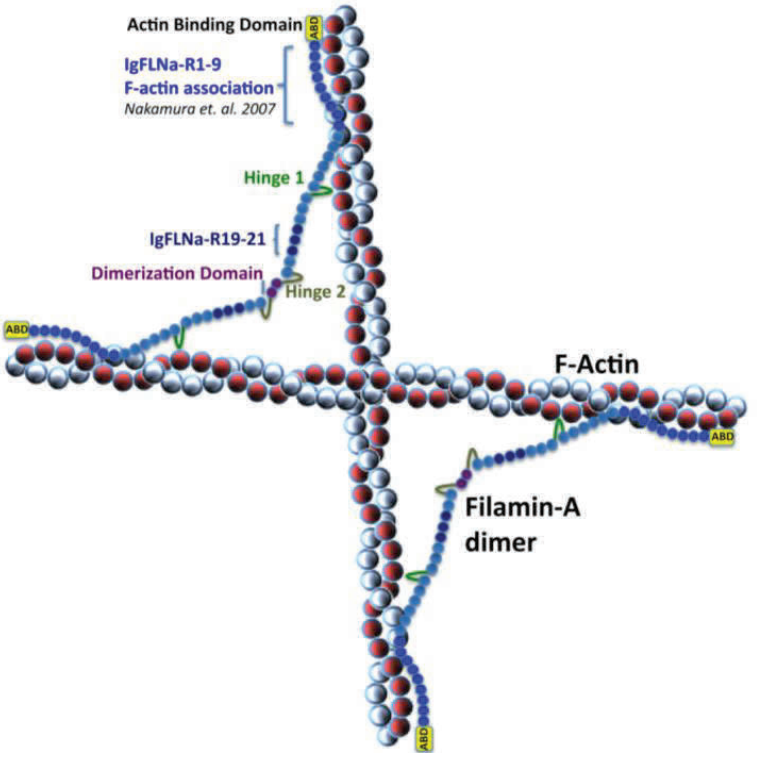

Figure 2: Illustration of the structure of a human FLNA. The figure also shows how filamins crosslinks actin filaments into orthogonal networks in cortical cytoplasm. At the N-terminus is the Actin Binding Domain (ABD), and is followed by the Ig-like repeats (IgFLNA-R1-IgFLNA-R24).

2.1 Filamin isoforms: FLNA, FLNB, and FLNC

Studies on filamin have revealed three main isogenes: FLNA, FLNB, and FLNC [15, 60-62]. In the filamin literature, different names have been used for filamin isoforms; filamin-A, actin binding protein 280 (ABP-280), and filamin-1, for FLNA [10, 17]; filamin-B, ABP-278/276, ß-filamin, and filamin-3 for FLNB [63, 64]; and filamin-C, γ-filamin, ABPL, and filamin-2 for FLNC [60-62, 65]. These three isoforms have functional and structural similarities and differences [15, 60-62]. Structurally, all of these isoforms contain 24 Ig-like repeats. Both FLNA and FLNB have two structural hinges (between repeats 15 and 16 and also between repeats 23 and 24), but there is only one hinge in skeletal muscle FLNC (between repeats 23 and 24). Additionally, there is a region with 82 amino acids between repeats 19

Table 2: FLNA solved structures.

System	PDB code	Reference
Repeat 10	3RGH	[49]
Repeat 16-17	2K7P	[50]
Repeat 18-19	2K7Q	[50]
Repeat 23	2K3T	[51]
Repeat 19 to 21	2J3S	[52]
Repeat 17	2AAV	[53]
Dimerization domain (repeat 24)	3CNK	[54]
ABD	2WFN	[55]
ABD	3HOP	[56]
ABD	3HOR	[56]
ABD (mutant E254K)	3HOC	[56]
Domain 17/GPIB alpha complex	2BP3	[53]
Repeat 21 bound to an N-terminal peptide of CFTR	3ISW	[57]
Repeat 21/MIGFILIN complex	2W0P	[58]
Repeat 21/INTEGRIN BETA2 complex	2JF1	[59]
Repeat 21/INTEGRIN BETA7 complex	2BRQ	[17]

and 20 in FLNC, which is not present in FLNA and FLNB [60, 61]. Unlike the ubiquitous expression of FLNA and FLNB, FLNC is muscle specific [62].

In the remainder of this review, we will focus on the FLNA isoform and illustrate its important role in cellular function.

3 FLNA: Mechanosensing behavior in the focal adhesions and cytoskeleton

Many cellular functions, ranging from migration and proliferation to apoptosis depend on cell adhesion to the extracellular matrix (ECM) and on mechanosensing and mechanotransduction at this interface [1, 6, 66-70]. Cell adhesion to ECM behavior is regulated by a complex of more than 150 different types of proteins, collectively called focal adhesions (FAs), which mechanically link ECM to cytoskeletal machinery [70-72]. Focal adhesion complexes are formed by ECM adhesion receptors, such as integrin, which sense applied forces from ECM and transmit the forces into the cell through the cell membrane, signaling molecules, such as FAK and Src, and adaptor proteins, such as paxillin [73]. Cell anchorage to ECM is mediated by these focal adhesion proteins through physical coupling of integrins (as the receptor of external forces applied to the cell) to the cytoskeletal proteins [70,

71].

Filamin is a member of the focal adhesion protein machinery, and therefore acts as a linker between the ECM and the actin cytoskeleton through integrins [1, 69-73]. Interacting with several partner proteins such as integrin, filamin regulates cell functions such as migration, proliferation, apoptosis, and mechanoprotection [1, 48, 66, 69, 74-79]. Actin and integrin are, therefore, the most studied interacting proteins with filamin, that participate in the mechanotransduction pathway across the focal adhesions.

3.1 Filamin and actin cytoskeleton

Several studies have addressed different aspects of filamin-actin complex including their interaction [20, 22, 30, 80, 81], mechanical and rheological properties [82-86], binding parameters [87, 88], and protein partners [14, 89-95]. Filamin is a soluble protein and binds actin through a specific binding site (ABD) followed by the gelation process [22, 30, 80]. It has been shown that the filamin ABD is homologous to α-actinin, dictyostelium 120-kDa actin gelation factor, P-spectrin, and dystrophin [20, 81].

The mechanical and rheological properties of filamin-actin complex and network have been studied extensively. Actin network stiffness and dynamic moduli have been observed to increase by the addition of filamin, even at small molar ratios of filamin:actin of less than 1:100 [82, 83]. The rheological behavior of filamin-actin networks strongly depends on filamin concentration [84]. Depending on the concentration of filamin, the network may take different architectures like crosslinked filamentous patterns or highly heterogeneous bundle clusters [85].

Filamin partners play a major role in regulating the behavior of filamin-actin complex, e.g. gelation rate, strength, and organization. CaM kinase phosphorylating FLNA regulates its binding to actin filaments [90], tyrosine kinase p56lck increases the actin crosslinking by phosphorylation of FLNA [91], and combination of α-actinin and FLNA, rather than using FLNA alone results in enhancement of actin network formation [14, 89, 94]. On the other hand, cyclin B1 and cyclin dependent kinase 1 (cyclin B1/Cdk1) could reduce FLNA gelation activity on actin [92], and Ca^{2+}-calmodulin binds to the ABD of FLNA and triggers the dissolution of FLNA-actin gels [96]. Key aspects of filamin-actin interaction are illustrated in Figures 2-4.

3.2 Filamin and integrin

Integrin works as an adhesion receptor and plays major roles in cell-matrix mechano-chemical communication, linking the ECM with cytoskeletal network [17, 97, 98].

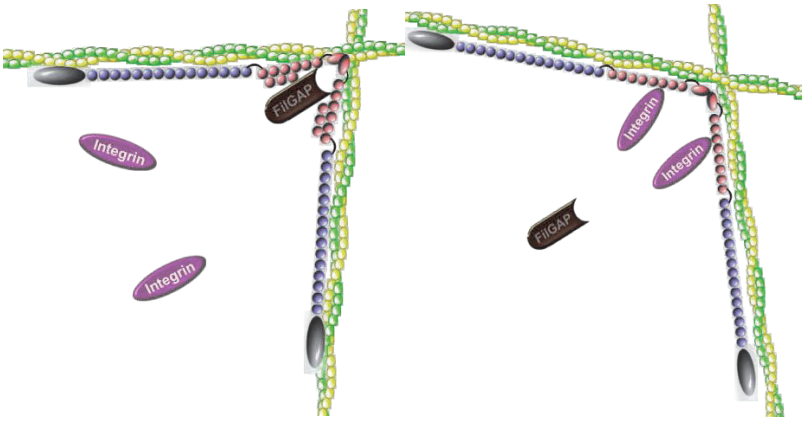

Figure 3: Filamin-actin interaction. Binding of FilGAP to repeats 23 spatially prevents β7-integrin from binding to repeat 21 (left panel). Deformation of FLNA by mechanical stress makes the integrin binding site on repeat 21 exposed to bind β7-integrin and spatially separating repeats 23 prevents FilGAP from binding two repeat 23 on two FLNA monomers (right panel) (figure adapted with permission from [108]).

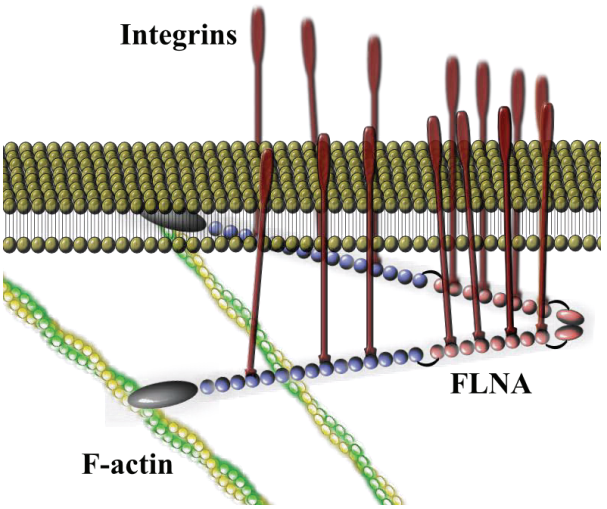

Figure 4: A proposed model for integrin clustering by FLNA. Seven repeats on each FLNA monomer mediate integrin clustering (figure adapted with permission from [100]).

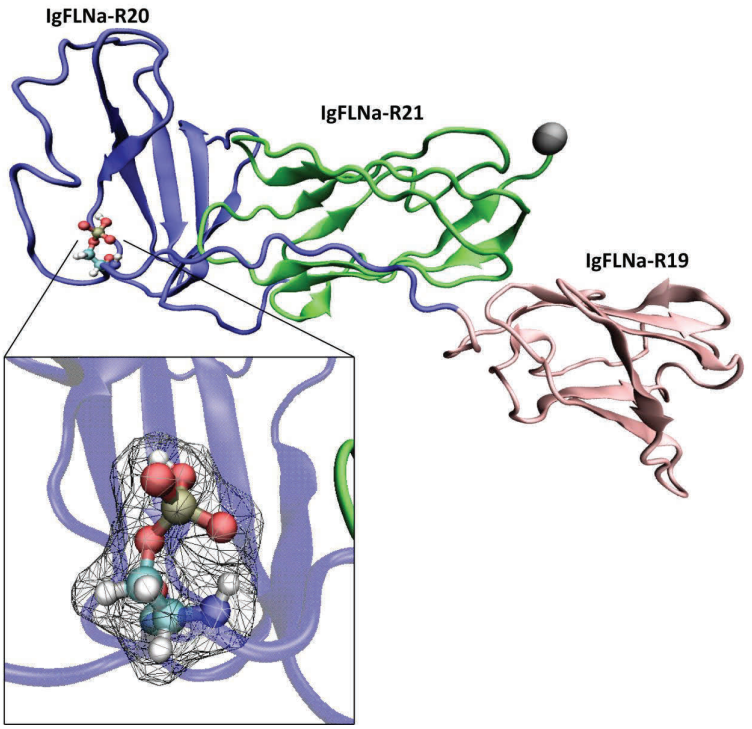

Figure 5: The structure of IgFLNa-R19 to 21 with ser-2152 phosphorylation illustrated in yellow. Each repeat is assigned a unique color. IgFLNa-R19 is pink; IgFLNa-R20 is blue; IgFLNa-R21 is green. The phosphoser-2152 residue is shown in orange, and the phosphate group is illustrated in yellow. See [19] for further details.

Focal adhesion proteins such as filamin, talin, tensin, plectin and α-actinin are important molecules that bridge between integrin and actin cytoskeleton [99].

Among filamin's 24 repeats, seven repeats, namely repeats R4, R9, R12, R17, R19, R21, and R23, have conserved the integrin-binding site (Figure 4) [100, 101]. Among these binding repeats, repeat R21 is known as a general integrin-binding site [17]. Competing with talin, FLNA interacts with integrin directly through integrin's β tail [17, 33, 102, 103] and integrin's Thr758 phosphorylation has inhibitory effect on this interaction [59]. Effective regulation of the cytoskeleton requires a cooperative balance between FLNAs and integrins. It has been proposed that a sufficient number of integrin-FLNA binding leads to stabilization of cell-matrix adhesion, whereas excessive binding results in inefficient actin remodeling and cell

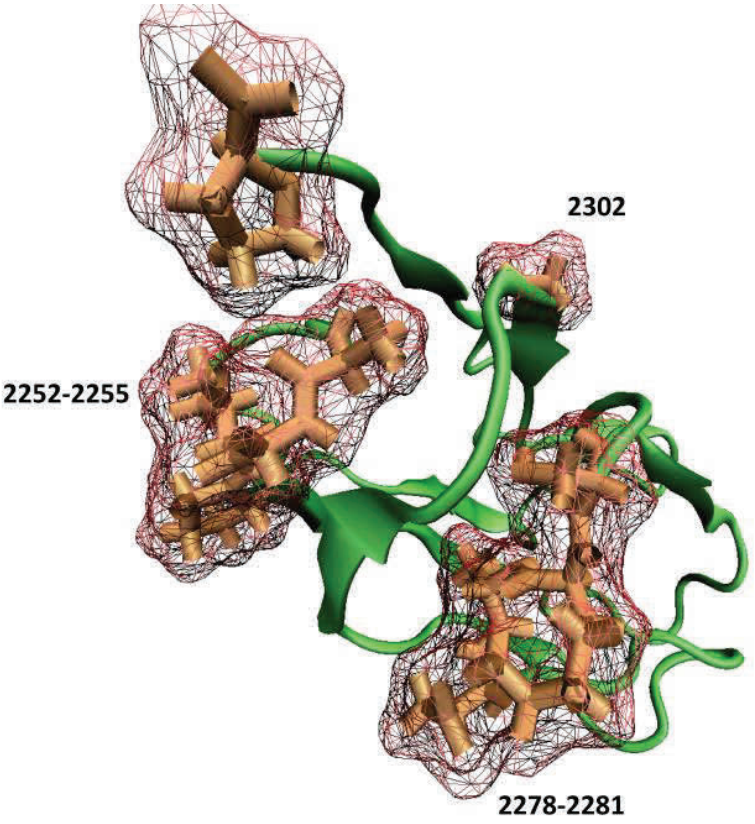

Figure 6: An illustration of the positions of the multiple stabilizing constraints on repeat 21. Of all these 10 amino acids, 4 of them (2328, 2302, 2255, and 2278) are proline. By stabilizing these C-terminal loops of Repeat 21, the structure was increasingly stable during tension. See [19] for further details.

mobility [104]. Moreover, tight filamin-integrin binding has been linked to cell polarization and transient membrane [105].

3.3 Filamin is a mechanosensor

Given the role of filamin in the focal adhesions, it is important to understand how filamin responds to mechanical force and how its interaction with integrin and the rest of focal adhesion machinery is regulated. It has been reported that wildtype and FLNA-deficient cells show different responses to applied mechanical forces [106]. These observations could be related to the specific interactions of filamin with its

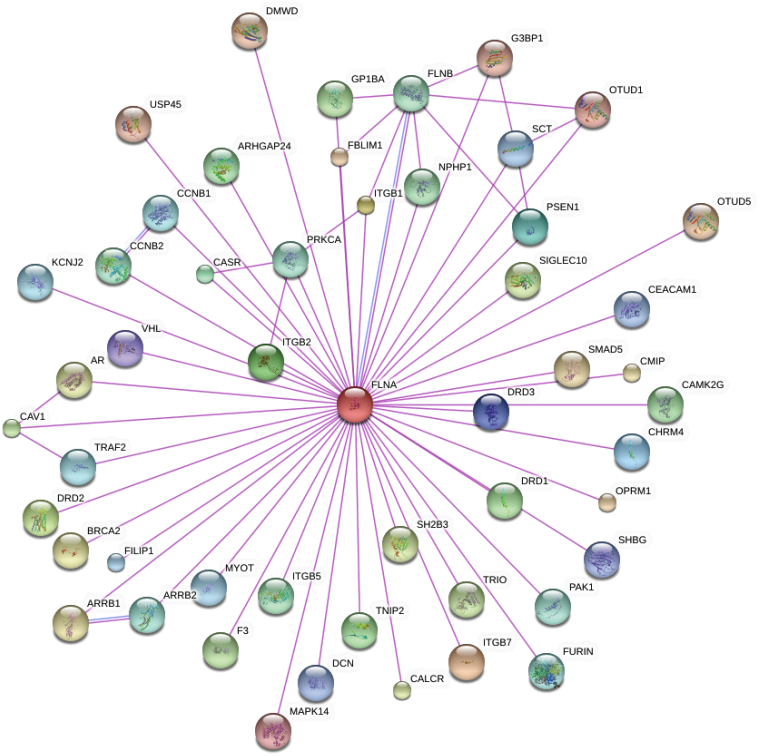

Figure 7: FLNA-Protein interaction network extracted using the STRING database [147].

binding partners like integrin [106].

Mechanical force application to cells has been observed to yield phosphorylation of serine residues on filamin [66], FLNA upregulation [67] and exposure of integrin binding sites [18, 19, 107] (Figures 5 and 6). Furthermore, mechanical strain on FLNA-actin complex leads to unbinding of FilGAP, from repeat 23 of FLNA which in turn results in β-integrin binding to FLNA [108] (Figure 3). After binding to filamin, integrin mechanically stretches it by multisite binding mechanism [101] (Figure 4). This complex can then sense the matrix tension and respond to it by regulation of cell contractility [109].

In addition to its role under normal range of physiological forces, filamin plays a crucial role in protecting the cell against intense forces that may harm the cell. FLNA takes a 'mechanoprotection' role via reinforcing the membrane cortex by actin accumulation and arrangement and destabilizing calcium-permeable channels

[66]. It has been shown that when strong forces are applied through integrins, FLNA prevents the membrane depolarization resulting in cell mechanoprotection [1].

3.4 Interaction of FLNA with other protein partners

To regulate important cellular functions such as cell migration, further protein partners besides actin and integrin are associated with FLNA. For example it is reported that in addition to FLNA and integrin $\beta 1$, androgen receptor (AR) in the complex of FLNA-AR- integrin $\beta 1$ plays a role in cell migration by controlling the activity of focal adhesion kinase (FAK), paxillin, and Rac [110]. Some of FLNA protein partners and the functional role of their interaction with FLNA are listed in Table 3 and the protein-protein interaction network of FLNA interacting partners is shown in Figure 7.

In addition to direct interactions with its protein partners, other biological roles have been reported for FLNA, e.g. in regulation, modification and expression of a number of proteins [44, 142-144] and DNA repair [122, 145].

Table 3: Important FLNA binding partners and the role of the interaction.

Protein name	**Function of interaction**	**Reference**
Glycoprotein (GP) Ib alpha	Membrane skeleton architecture regulation and maintenance of plasma membrane mechanical stability under high shear condition.	[111-115]
GST-PTP-PEST	Control of cytokinesis in mammalian cells	[116]
Mig-2, migfilin	Actin assembly and cell shape modulation	[74]
SEK-1	SAPK regulation	[41]
PKC	Cell signaling	[117]
Pak1	Pak1-induced cytoskeletal reorganization	[43]
TRAF2	Inhibited TRAF2-induced activation of JNK/SAPK and NF-κB by FLNA	[42]
NF-kappa B	Inducing kinase (NIK)	[118]
Adapter Protein SH2B1 beta	Regulation of prolactin-dependent cytoskeletal reorganization and cell motility	[47]
R-Ras	Endothelial barrier function maintenance and integrin-dependent migration regulation	[75, 76]
Vimentin and protein kinase	Activation of beta 1 and cell spreading on collagen.	[48, 119, 120]
Cyclin D1/Cyclin-Dependent Kinase 4	Cell migration	[77]

Protein name	**Function of interaction**	**Reference**
BRCA1, 2	DNA repair	[121, 122]
Stress signalling kinases MKK7 and MKK4	Regulation of JNK activation	[123]
CCR2B	Controlling CCR2B internalization and spatial localization	[124]
Mu Opioid Receptor	Activation of MAP kinase p38	[125]
Pro- prion	Facilitating FLNA Interaction with integrin beta 1, and Contributes to Melanomagenesis	[126-128]
Kv4.2	Colocalization of Kv4.2 with FLNAat filopodial roots	[39]
Smad proteins	Regulation of transforming growth factor-beta signaling	[129]
Calcium-sensing receptor	Organizing cell signaling	[130, 131]
Glycoprotein Ib-α	Regulating adhesion and signalling mechanisms in platelets	[113, 114, 132]
Pacemaker channel HCN1	Contribution to localizing HCN1 channels to specific neuronal areas	[133]
Dopamine D2 and D3 receptors	Linking Dopamine D2 and D3 receptors to the actin cytoskeleton	[134]
Metabotropic glutamate receptor type 7	Physically linking the metabotropic glutamate receptors to the actin cytoskeleton	[135]
Calcitonin receptor (CTR)	Recycling of the internalized CTR	[136]
Inwardly rectifying potassium channel, Kir2.1	Regulation of Kir2.1 surface expression	[137]
FAP52	Actin organization regulation	[78]
PEBPβ	PEBPβ regulatio	[138]
SHIP-2	Regulation of cortical and submembraneous actin	[139]
E3 ubiquitin ligase specificity subunit ASB2 al	Degradation of filamins	[140]
Beta-Arrestins (betaarr)	Regulation of ERK activation and actin cytoskeleton reorganization	[141]
IKAP	Regulation of actin cytoskeleton organization	[93]
GAPA	Remodeling the actin filaments	[95]

4 Conclusion

Filamin is one of the key focal adhesion and cytoskeletal proteins with important structural and functional roles in cyto mechanics and cell-ECM adhesive interactions. Filamin is a non-covalently associated dimer with three isoforms: FLNA, FLNB, and FLNC. It consists of an actin-binding domain, a backbone of 23 repeats, and a tail, repeat R24, at which the dimerization occurs. Filamin engages in important interactions with cytoskeletal proteins, like F-actin, and focal adhesion proteins, such as integrin, and as such plays an effective role in the overall mechanobiological function of the cell.

Despite extensive progress in our understanding of filamin family, many aspects of this important protein have remained unknown. Further research is necessary to better establish the role of filamin in cell biology and mechanics.

Mutations in filamin have been linked to important human diseases [146]; hence a deeper understanding of this protein family is needed. Ultimately, finding the mechanisms in which these mutations lead to such diseases may lead to design of therapeutic interventions. Computational methods like bioinformatics, normal mode analysis, molecular dynamics simulation, and multi-scale modeling approaches may be instrumental to achieving this goal. A first step toward this objective is to understand the role of each structural repeat (see Figure 1) and to find out what molecules may interact with filamin at each of these specific sites. This calls for a well-planned set of experimental and theoretical investigations to carefully explore each of filamin's interaction sites. New computational tools and techniques must be devised and implemented to enable the prediction of binding sites based on structure and/or sequence. If more than one molecule interacts with the same site on filamin, it would be necessary to find the competitive or cooperative conditions and behavior among partner molecules. Finding a comprehensive list of filamin interacting partners, their role in cell, and their relationship to other filamin interacting proteins will make it possible to create a relationship (or 'interactome') network between filamin and its partners. This calls for the development of coarse-grained models of wildtype and mutated filamin and its interaction partners. These models will enable simulations of large-scale systems containing filamin interacting with other partners in detail for longer time scales in comparison to those currently available with molecular dynamics. Such 'systems biomechanics' models are necessary for understanding the bidirectional mechanochemical pathways that link the extracellular microenvironment to the nucleus [148].

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References

1. Kainulainen, T. et al. (2002) Cell death and mechanoprotection by filamin a in connective tissues after challenge by applied tensile forces. J Biol Chem, 277(24), 21998-2009.

2. Nakamura, F. et al. (2002) Comparison of filamin A-induced cross-linking and Arp2/3 complex-mediated branching on the mechanics of actin filaments. J Biol Chem, 277(11), 9148-54.

3. Mandadapu, K. K., Govindjee, S. & Mofrad, M. R. (2008) On the cytoskeleton and soft glassy rheology. J Biomech, 41(7), 1467-78.

4. Mack, P. J., et al. (2004) *Force-induced focal adhesion translocation: effects of force amplitude and frequency.* Am J Physiol Cell Physiol, 287(4), C954-62.

5. Mofrad, M. R. K. (2009) Rheology of the Cytoskeleton. Annual Review of Fluid Mechanics, 41, 433-453.

6. Mofrad, M. R. K. & Kamm, R. D. (2006) Cytoskeletal mechanics : models and measurements, New York: Cambridge University Press. x, 244 p.

7. Stossel, T. P. et al. (2001) Filamins as integrators of cell mechanics and signalling. Nature Reviews Molecular Cell Biology, 2(2), 138-145.

8. Feng, Y. Y. & Walsh, C. A. (2004) The many faces of filamin: A versatile molecular scaffold for cell motility and signalling. Nature Cell Biology, 6(11), 1034-1038.

9. Nakamura, F. et al. (2007) Structural basis of filamin A functions. Journal of Cell Biology, 179(5), 1011-1025.

10. Gorlin, J.B. et al. (1990) Human Endothelial Actin-Binding Protein (Abp-280, Nonmuscle Filamin) - a Molecular Leaf Spring. Journal of Cell Biology, 111(3), 1089-1105.

11. Gardel, M. L. et al. (2006) Prestressed F-actin networks cross-linked by hinged filamins replicate mechanical properties of cells. Proceedings of the National Academy of Sciences of the United States of America, 103(6), 1762-1767.

12. Koteliansky, V. E. et al. (1982) A Structural Study of Filamin, a Hight-Molecular-Weight Actin-Binding Protein from Chicken Gizzard. European Journal of Biochemistry, 121(3), 553-559.

13. Niederman, R., Amrein, P. C. & Hartwig, J. (1983) Three-dimensional structure of actin filaments and of an actin gel made with actin-binding protein. Journal of Cell Biology, 96(5), 1400-13.

14. Lebart, M. C. et al. (1994) Characterization of the Actin-Binding Site on Smooth-Muscle Filamin. Journal of Biological Chemistry, 269(6), 4279-4284.

15. van der Flier, A. et al. (2002) Different splice variants of filamin-B affect myogenesis, subcellular distribution, and determine binding to integrin beta subunits. Journal of Cell Biology, 156(2), 361-376.

16. Feng, Y. Y. et al. (2006) Filamin A (FLNA) is required for cell-cell contact in vascular development and cardiac morphogenesis. Proceedings of the National Academy of Sciences of the United States of America, 103(52),19836-19841.

17. Kiema, T. et al. (2006) The molecular basis of filamin binding to integrins and competition with talin. Mol Cell, 21(3), 337-347.

18. Kolahi, K. S.& Mofrad, M. R. (2008) Molecular mechanics of filamin's rod domain. Biophys J, 94(3), 1075-83.

19. Chen, H. S., Kolahi, K. S. & Mofrad, M. R. (2009) Phosphorylation facilitates the integrin binding of filamin under force. Biophys J, 97(12), 3095-104.

20. Hock, R. S., Davis, G. & Speicher, D. W. (1990) Purification of human smooth muscle filamin and characterization of structural domains and functional sites. Biochemistry, 29(40), 9441-51.

21. Wang, K., Ash, J. F. & Singer, S. J. (1975) Filamin, a New High-Molecular-Weight Protein Found in Smooth-Muscle and Non-Muscle Cells. Proceedings of the National Academy of Sciences of the United States of America, 72(11), 4483-4486.

22. Shizuta, Y. et al. (1976) Purification and Properties of Filamin, an Actin Binding-Protein from Chicken Gizzard. Journal of Biological Chemistry, 251(21), 6562-6567.

23. Bicknell, L. S. et al. (2005) Mutations in FLNB cause boomerang dysplasia. Journal of Medical Genetics, 42(7).

24. Vorgerd, M. et al. (2005) A mutation in the dimerization domain of filamin C causes a novel type of autosomal dominant myofibrillar myopathy. American Journal of Human Genetics, 2005. **77**(2): p. 297-304.

25. Sheen, V. L. et al. (2005) Filamin A mutations cause periventricular heterotopia with Ehlers-Danlos syndrome. Neurology, 64(2), 254-262.

26. Kyndt, F. et al. (2007) Mutations in the gene encoding filamin A as a cause for familial cardiac valvular dystrophy. Circulation, 115(1), 40-49.

27. Bicknell, L. S. et al. (2007) A molecular and clinical study of Larsen syndrome caused by mutations in FLNB. Journal of Medical Genetics, 44(2), 89-98.

28. Zhang, D. et al. (2006) Mutations responsible for Larsen syndrome cluster in the FLNB protein. Journal of Medical Genetics, 43(5).

29. Hartwig, J. H.& Stossel, T. P. (1975) Isolation and properties of actin, myosin, and a new actinbinding protein in rabbit alveolar macrophages. J Biol Chem, 250(14), 5696-705.

30. Wang, K.& Singer, S. J. Interaction of Filamin with F-Actin in Solution. Proceedings of the National Academy of Sciences of the United States of America, 74(5), 2021-2025.

31. Zenker, M. et al. (2004) A dual phenotype of periventricular nodular heterotopia and frontometaphyseal dysplasia in one patient caused by a single FLNA mutation leading to two functionally different aberrant transcripts. American Journal of Human Genetics, 74(4), 731-7.

32. Loo, D. T., Kanner, S. B. & Aruffo, A. (1998) Filamin binds to the cytoplasmic domain of the beta1-integrin. Identification of amino acids responsible for this interaction. J Biol Chem, 273(36), 23304-12.

33. Sharma, C. P., Ezzell, R. M. & Arnaout, M. A. (1995) Direct interaction of filamin (ABP-280) with the beta 2-integrin subunit CD18. J Immunol, 154(7), 3461-70.

34. Ott, I. et al. (1998) A role for tissue factor in cell adhesion and migration mediated by interaction with actin-binding protein 280. Journal of Cell Biology, 140(5), 1241-53.

35. Li, M. et al. (2000) Modulation of dopamine D-2 receptor signaling by actin-binding protein (ABP-280). Molecular Pharmacology, 57(3), 446-452.

36. Zhang, W. J. et al. (1998) Interaction of presenilins with the filamin family of actin-binding proteins. Journal of Neuroscience, 18(3), 914-922.

37. Liu, G. P. et al. (1997) Cytoskeletal protein ABP-280 directs the intracellular trafficking of furin and modulates proprotein processing in the endocytic pathway. Journal of Cell Biology, 139(7), 1719-1733.

38. Stahlhut, M. & van Deurs, B. (2000) Identification of filamin as a novel ligand for caveolin-1: Evidence for the organization of caveolin-1-associated membrane domains by the actin cytoskeleton. Molecular Biology of the Cell, 11(1), 325-337.

39. Petrecca, K., Miller, D.M. & Shrier, A. (2000) Localization and enhanced current density of the Kv4.2 potassium channel by interaction with the actin-binding protein filamin. Journal of Neuroscience, 20(23), 8736-8744.

40. Ohta, Y. et al. (1999) The small GTPase RalA targets filamin to induce filopodia. Proceedings of the National Academy of Sciences of the United States of America, 96(5), 2122-2128.

41. Marti, A. et al. (1997) Actin-binding protein-280 binds the stress-activated protein kinase (SAPK) activator SEK-1 and is required for tumor necrosis factor-alpha activation of SAPK in melanoma cells. Journal of Biological Chemistry, 272(5), 2620-2628.

42. Leonardi, A. et al. (2000) Physical and functional interaction of filamin (actin-binding protein-280) and tumor necrosis factor receptor-associated factor 2. Journal of Biological Chemistry, 275(1), 271-278.

43. Bellanger, J. M. et al. (2000) The Rac1-and RhoG-specific GEF domain of Trio targets filamin to remodel cytoskeletal actin. Nature Cell Biology, 2(12), 888-892.

44. Ozanne, D. M. et al. (2000) Androgen receptor nuclear translocation is facilitated by the f-actin cross-linking protein filamin. Molecular Endocrinology, 14(10), 1618-1626.

45. Krief, S. et al. (1999) Identification and characterization of cvHsp - A novel human small stress protein selectively expressed in cardiovascular and insulin-sensitive tissues. Journal of Biological Chemistry, 274(51), 36592-36600.

46. Browne, K. A. et al. (2000) Filamin (280-kDa actin-binding protein) is a caspase substrate and is also cleaved directly by the cytotoxic T lymphocyte protease granzyme B during apoptosis. Journal of Biological Chemistry, 275(50), 39262-39266.

47. Rider, L. & Diakonova, M. (2011) Adapter Protein SH2B1 beta Binds Filamin A to Regulate Prolactin-Dependent Cytoskeletal Reorganization and Cell Motility. Molecular Endocrinology, 25(7), 1231-1243.

48. Kim, H. et al. (2010) Regulation of cell adhesion to collagen via beta 1 integrins is dependent on interactions of filamin A with vimentin and protein kinase C epsilon. Experimental Cell Research, 316(11), 1829-1844.

49. Page, R. C., Clark, J. G. & Misra, S. (2011) Structure of filamin A immunoglobulin-like repeat 10 from Homo sapiens. Acta Crystallographica Section F-Structural Biology and Crystallization Communications, 67, 871-876.

50. Heikkinen, O. K. et al. (2009) Atomic Structures of Two Novel Immunoglobulin-like Domain Pairs in the Actin Cross-linking Protein Filamin. Journal of Biological Chemistry, 284(37), 25450-25458.

51. Nakamura, F. et al. (2009) Molecular Basis of Filamin A-FilGAP Interaction and Its Impairment in Congenital Disorders Associated with Filamin A Mutations. Plos One, 4(3).

52. Lad, Y. et al. (2007) Structure of three tandem filamin domains reveals auto-inhibition of ligand binding. Embo Journal, 26(17), 3993-4004.

53. Nakamura, F. et al. (2006) The structure of the GPIb-filamin A complex. Blood, 107(5), 1925-1932.

54. Seo, M. D. et al. (2009) Crystal structure of the dimerization domain of human filamin A. Proteins-Structure Function and Bioinformatics, 75(1), 258-263.

55. Ruskamo, S. & Ylanne, J. (2007) Structure of the human filamin A actin-binding domain. Acta Crystallographica Section D-Biological Crystallography, 65, 1217-1221.

56. Clark, A. R. et al. (2009) Skeletal dysplasias due to filamin A mutations result from a gain-of-function mechanism distinct from allelic neurological disorders dagger. Human Molecular Genetics, 18(24), 4791-4800.

57. Smith, L. et al. (2010) Biochemical Basis of the Interaction between Cystic Fibrosis Transmembrane Conductance Regulator and Immunoglobulin-like Repeats of Filamin. Journal of Biological Chemistry, 285(22), 17166-17176.

58. Lad, Y. et al. (2008) Structural Basis of the Migfilin-Filamin Interaction and Competition with Integrin beta Tails. Journal of Biological Chemistry, 283(50), 35154-35163.

59. Takala, H. et al. (2008) Beta2 integrin phosphorylation on Thr758 acts as a molecular switch to regulate 14-3-3 and filamin binding. Blood, 112(5), 1853-62.

60. Thompson, T. G. et al. (2000) Filamin 2 (FLN2): A muscle-specific sarcoglycan interacting protein. Journal of Cell Biology, 148(1), 115-26.

61. Xie, Z. et al. (1998) Molecular cloning of human ABPL, an actin-binding protein homologue. Biochem Biophys Res Commun, 251(3), 914-9.

62. Pudas, R. et al. (2005) Structural basis for vertebrate filamin dimerization. Structure, 13(1), 111-9.

63. Xu, W. et al. (1998) A novel human actin-binding protein homologue that binds to platelet glycoprotein Ibalpha. Blood, 92(4), 1268-76.

64. Takafuta, T. et al. (1998) Human beta-filamin is a new protein that interacts with the cytoplasmic tail of glycoprotein Ibalpha. J Biol Chem, 273(28), 17531-8.

65. van der Ven, P. F. et al. (2000) Indications for a novel muscular dystrophy pathway. gamma-filamin, the muscle-specific filamin isoform, interacts with myotilin. Journal of Cell Biology, 151(2), 235-48.

66. Glogauer, M. et al. (1998) The role of actin-binding protein 280 in integrin-dependent mechanoprotection. J Biol Chem, 273(3), 1689-98.

67. D'Addario, M. et al. (2001) Cytoprotection against mechanical forces delivered through beta 1 integrins requires induction of filamin A. J Biol Chem, 276(34), 31969-77.

68. D'Addario, M. et al. (2002) Interaction of p38 and Sp1 in a mechanical force-induced, beta 1 integrin-mediated transcriptional circuit that regulates the actin-binding protein filamin-A. J Biol Chem, 277(49), 47541-50.

69. Chen, C. S. (2008) Mechanotransduction - a field pulling together? J Cell Sci, 121(Pt 20), 3285-92.

70. Pathak, A. et al. (2008) The simulation of stress fibre and focal adhesion development in cells on patterned substrates. J R Soc Interface, 5(22), 507-24.

71. Shemesh, T. et al. (2005) Focal adhesions as mechanosensors: A physical mechanism. Proceedings of the National Academy of Sciences of the United States of America, 102(35), 12383-12388.

72. Zamir, E. & Geiger, B. (2001) Molecular complexity and dynamics of cell-matrix adhesions. J Cell Sci, 114(20), 3583-3590.

73. Campbell, I. D. (2008) Studies of focal adhesion assembly. Biochemical Society Transactions, 36, 263-266.

74. Tu, Y. et al. (2003) Migfilin and Mig-2 link focal adhesions to filamin and the actin cytoskeleton and function in cell shape modulation. Cell, 113(1), 37-47.

75. Griffiths, G. S. et al. (2011) R-Ras interacts with filamin a to maintain endothelial barrier function. J Cell Physiol, 226(9), 2287-96.

76. Gawecka, J. E. et al. (2010) R-Ras Regulates Migration through an Interaction with Filamin A in Melanoma Cells. Plos One, 5(6).

77. Zhong, Z. J. et al. (2010) Cyclin D1/Cyclin-Dependent Kinase 4 Interacts with Filamin A and Affects the Migration and Invasion Potential of Breast Cancer Cells. Cancer Research, 70(5), 2105-2114.

78. Nikki, M., Merilainen, J. & Lehto, V. P. (2002) FAP52 regulates actin organization via binding to filamin. Journal of Biological Chemistry, 277(13), 11432-11440.

79. Zhou, A. X. et al. (2011) Filamin A mediates HGF/c-MET signaling in tumor cell migration. International Journal of Cancer, 128(4), 839-846.

80. Davies, P. J. et al. (1978) Filamin-actin interaction. Dissociation of binding from gelation by Ca2+-activated proteolysis. J Biol Chem, 253(11), 4036-42.

81. Mejean, C. et al. (1992) Localization and Identification of Actin Structures Involved in the Filamin Actin Interaction. European Journal of Biochemistry, 209(2), 555-562.

82. Goldmann, W. H. et al. (1997) Viscoelasticity of actin-gelsolin networks in the presence of filamin. European Journal of Biochemistry, 246(2), 373-9.

83. Zaner, K. S. (1986) The Effect of the 540-Kilodalton Actin Cross-Linking Protein, Actin-Binding Protein, on the Mechanical-Properties of F-Actin. Journal of Biological Chemistry, 261(17), 7615-7620.

84. Tseng, Y. et al. (2004) The bimodal role of filamin in controlling the architecture and mechanics of F-actin networks. Journal of Biological Chemistry, 279(3), 1819-1826.

85. Schmoller, K. M., Lieleg, O. & Bausch, A. R. (2009) Structural and Viscoelastic Properties of Actin/Filamin Networks: Cross-Linked versus Bundled Networks. Biophys J, 97(1), 83-89.

86. Furuike, S., Ito, T. & Yamazaki, M. (2001) Mechanical unfolding of single filamin A (ABP-280) molecules detected by atomic force microscopy. Febs Letters, 498(1), 72-75.

87. Goldmann, W. H., Senger, R. & Isenberg, G. (1994) Analysis of filamin-actin binding and cross-linking/bundling by kinetic method. Biochem Biophys Res Commun, 203(1), 338-43.

88. Goldmann, W. H. & Isenberg, G. (1993) Analysis of filamin and alpha-actinin binding to actin by the stopped flow method. Febs Letters, 336(3), 408-10.

89. Lebart, M. C. et al. (1993) Further Characterization of the Alpha-Actinin-Actin Interface and Comparison with Filamin-Binding Sites on Actin. Journal of Biological Chemistry, 268(8), 5642-5648.

90. Yasutaka, O. & Hartwig, J. H. (1995) Actin Filament Cross-Linking by Chicken Gizzard Filamin Is Regulated by Phosphorylation in-Vitro. Biochemistry, 34(20), 6745-6754.

91. Pal Sharma, C. & Goldmann, W. H. (2004) Phosphorylation of actin-binding protein (ABP-280; filamin) by tyrosine kinase p56lck modulates actin filament cross-linking. Cell Biol Int, 28(12),935-41.

92. Cukier, I. H., Li, Y. & Lee, J. M. (2007) Cyclin B1/Cdk1 binds and phosphorylates Filamin A and regulates its ability to cross-link actin. Febs Letters, 581(8), 1661-72.

93. Johansen, L. D. et al. (2008) IKAP localizes to membrane ruffles with filamin A and regulates actin cytoskeleton organization and cell migration. J Cell Sci, 121(Pt 6), 854-64.

94. Esue, O., Tseng, Y. & Wirtz, D. (2009) Alpha-actinin and filamin cooperatively enhance the stiffness of actin filament networks. Plos One, 4(2), e4411.

95. Mondal, S. et al. (2010) Regulation of the actin cytoskeleton by an interaction of IQGAP related protein GAPA with filamin and cortexillin I. Plos One, 5(11), e15440.

96. Nakamura, F. et al. (2005) Ca2+ and calmodulin regulate the binding of filamin A to actin filaments. Journal of Biological Chemistry, 280(37), 32426-32433.

97. Hynes, R. O. (1987) Integrins - a Family of Cell-Surface Receptors. Cell, 48(4), 549-554.

98. Hynes, R. O. (2002) Integrins: Bidirectional, allosteric signaling machines. Cell, 110(6), 673-687.

99. Zaidel-Bar, R. et al. (2007) Functional atlas of the integrin adhesome. Nature Cell Biology, 9(8), 858-868.

100. Ithychanda, S. S. et al. (2009) Identification and Characterization of Multiple Similar Ligand-binding Repeats in Filamin IMPLICATION ON FILAMIN-MEDIATED RECEPTOR CLUSTERING AND CROSS-TALK. Journal of Biological Chemistry, 284(50), 35113-35121.

101. Ithychanda, S. S. & Qin, J. (2011) Evidence for Multisite Ligand Binding and Stretching of Filamin by Integrin and Migfilin. Biochemistry, 50(20), 4229-4231.

102. Travis, M. A. et al. (2004) Interaction of filamin A with the integrin beta 7 cytoplasmic domain: role of alternative splicing and phosphorylation. Febs Letters, 569(1-3), 185-90.

103. Pentikainen, U. & Ylanne, J. (2009) The Regulation Mechanism for the Auto-Inhibition of Binding of Human Filamin A to Integrin. J Mol Biol, 393(3), 644-657.

104. Kim, H. et al. (2008) Filamin A regulates cell spreading and survival via beta 1 integrins. Experimental Cell Research, 314(4), 834-846.

105. Calderwood, D. A. et al. (2001) Increased filamin binding to beta-integrin cytoplasmic domains inhibits cell migration. Nature Cell Biology, 3(12), 1060-1068.

106. Shifrin, Y. et al. (2009) The Role of FilGAP-Filamin A Interactions in Mechanoprotection. Molecular Biology of the Cell, 20(5), 1269-1279.

107. Kesner, B. A. et al. (2010) N-terminal strands of filamin Ig domains act as a conformational switch under biological forces. Proteins-Structure Function and Bioinformatics, 78(1), 12-24.

108. Ehrlicher, A. J. et al. (2011) Mechanical strain in actin networks regulates FilGAP and integrin binding to filamin A. Nature, 478(7368), 260-U154.

109. Gehler, S. et al. (2009) Filamin A-beta 1 Integrin Complex Tunes Epithelial Cell Response to Matrix Tension. Molecular Biology of the Cell, 20(14), 3224-3238.

110. Castoria, G. et al. (2011) Androgen-Induced Cell Migration: Role of Androgen Receptor/Filamin A Association. Plos One, 6(2).

111. Cranmer, S. L. et al. (2011) High shear-dependent loss of membrane integrity and defective platelet adhesion following disruption of the GPIb alpha-filamin interaction. Blood, 117(9), 2718-2727.

112. Berny-Lang, M. A. & McCarty, O. J. T. (2011) Breakup feared after filamin leaves GPIb. Blood, 117(9), 2564-2565.

113. Feng, S. J., Lu, X. & Kroll, M. H. (2004) Filamin a binding stabilizes nascent glycoprotein Ib alpha trafficking and thereby enhances its surface expression. Blood, 104(11), 994A-995A.

114. Feng, S. J. et al. (2003) Filamin A binding to the cytoplasmic tail of glycoprotein Ib alpha regulates von Willebrand factor-induced platelet activation. Blood, 102(6), 2122-2129.

115. Williamson, D. et al. (2002) Interaction between platelet glycoprotein Ib alpha and filamin-1 is essential for glycoprotein Ib/IX receptor anchorage at high shear. Journal of Biological Chemistry, 277(3), 2151-2159.

116. Playford, M. P. et al. (2006) Identification of a filamin docking site on PTP-PEST. Journal of Biological Chemistry, 281(45), 34104-34112.

117. Tigges, U. et al. (2003) The F-actin cross-linking and focal adhesion protein filamin A is a ligand and in vivo substrate for protein kinase C alpha. Journal of Biological Chemistry, 278(26), 23561-23569.

118. Muscolini, M. et al. (2011) A novel association between filamin A and NF-kappa B inducing kinase couples CD28 to inhibitor of NF-kappa B kinase alpha and NF-kappa B activation. Immunology Letters, 136(2), 203-212.

119. Kim, H. et al. (2010) Filamin A is required for vimentin-mediated cell adhesion and spreading. American Journal of Physiology-Cell Physiology, 298(2), C221-C236.

120. Hayashi, K. & Altman, A. (2006) Filamin A is required for T cell activation mediated by protein kinase C-theta. Journal of Immunology, 177(3), 1721-1728.

121. Velkova, A. et al. (2010) Identification of filamin A as a BRCA1-interacting protein required for efficient DNA repair. Cell Cycle, 9(7), 1421-1433.

122. Yuan, Y. & Shen, Z. Y. (2001) Interaction with BRCA2 suggests a role for filamin-1 (hsFLNa) in DNA damage response. Journal of Biological Chemistry, 276(51), 48318-48324.

123. Nakagawa, K. et al. (2010) Filamin associates with stress signalling kinases MKK7 and MKK4 and regulates JNK activation. Biochemical Journal, 427, 237-245.

124. Minsaas, L. et al. (2010) Filamin A Binds to CCR2B and Regulates Its Internalization. Plos One, 5(8).

125. Simon, E. J. & Onoprishvili, I. (2010) The Interaction Between the Mu Opioid Receptor and Filamin A. Neurochemical Research, 35(12), 1859-1866.

126. Li, C. Y. et al. (2010) Pro-prion Binds Filamin A, Facilitating Its Interaction with Integrin beta 1, and Contributes to Melanomagenesis. Journal of Biological Chemistry, 285(39), 30328-30339.

127. Li, C., Xin, W. & Sy, M. S. (2010) Binding of pro-prion to filamin A: by design or an unfortunate blunder. Oncogene, 29(39), 5329-5345.

128. Sy, M. S. et al. (2010) The fatal attraction between pro-prion and filamin A: prion as a marker in human cancers. Biomarkers in Medicine, 4(3), 453-464.

129. Sasaki, A. et al. (2001) Filamin associates with Smads and regulates transforming growth factor-beta signaling. Journal of Biological Chemistry, 276(21), 17871-17877.

130. Awata, H. et al. (2001) Interaction of the calcium-sensing receptor and filamin, a potential scaffolding protein. Journal of Biological Chemistry, 276(37), 34871-34879.

131. Tu, C. L., Chang, W. & Bikle, D. D. (2011) The calcium-sensing receptor-dependent regulation of cell-cell adhesion and keratinocyte differentiation requires Rho and filamin A. J Invest Dermatol, 131(5), 1119-28.

132. Cranmer, S. L. et al. (2005) Identification of a unique filamin A binding region within the cytoplasmic domain of glycoprotein Ib alpha. Biochemical Journal, 387, 849-858.

133. Gravante, B. et al. (2004) Interaction of the pacemaker channel HCN1 with filamin A. Journal of Biological Chemistry, 279(42), 43847-43853.

134. Lin, R.W. et al. (2001) Dopamine D2 and D3 receptors are linked to the actin cytoskeleton via interaction with filamin A. Proceedings of the National Academy of Sciences of the United States of America, 98(9), 5258-5263.

135. Enz, R. (2002) The actin-binding protein Filamin-A interacts with the metabotropic glutamate receptor type 7. Febs Letters, 514(2-3), 184-188.

136. Seck, T., Baron, R. & Horne, W. C. (2003) Binding of filamin to the C-terminal tail of the calcitonin receptor controls recycling. Journal of Biological Chemistry, 278(12), 10408-10416.

137. Sampson, L. J., Leyland, M. L. & Dart, C. (2003) Direct interaction between the actin-binding protein filamin-A and the inwardly rectifying potassium channel, Kir2.1. Journal of Biological Chemistry, 278(43), 41988-41997.

138. Yoshida, N. et al. (2005) Filamin A-bound PEBP2 beta/CBF beta is retained in the cytoplasm and prevented from functioning as a partner of the Runx1 transcription factor. Molecular and Cellular Biology, 25(3), 1003-1012.

139. Dyson, J. M. et al. (2003) SHIP-2 forms a tetrameric complex with filamin, actin, and GPIb-IX-V: localization of SHIP-2 to the activated platelet actin cytoskeleton. Blood, 102(3), 940-948.

140. Razinia, Z. et al. (2011) The E3 ubiquitin ligase specificity subunit ASB2 alpha targets filamins for proteasomal degradation by interacting with the filamin actin-binding domain. J Cell Sci, 124(15), 2631-2641.

141. Scott, M. G. H. et al. (2006) Cooperative regulation of extracellular signal-regulated kinase activation and cell shape change by filamin A and beta-arrestins. Molecular and Cellular Biology, 26(9), 3432-3445.

142. Beekman, J. M. et al. (2008) Filamin A stabilizes Fc gamma RI surface expression and prevents its lysosomal routing. Journal of Immunology, 180(6), 3938-3945.

143. Kim, E. J., Park, J. S.& Um, S.J. (2007) Filamin A negatively regulates the transcriptional activity of p73 alpha in the cytoplasm. Biochem Biophys Res Commun, 362(4), 1101-1106.

144. Fiori, J. L. et al. (2009) Filamin A Modulates Kinase Activation and Intracellular Trafficking of Epidermal Growth Factor Receptors in Human Melanoma Cells. Endocrinology, 150(6), 2551-2560.

145. Yue, J. Y. et al. (2009) The Cytoskeleton Protein Filamin-A Is Required for an Efficient Recombinational DNA Double Strand Break Repair. Cancer Research, 69(20), 7978-7985.

146. Fox, J. W. et al. (1998) Mutations in filamin 1 prevent migration of cerebral cortical neurons in human periventricular heterotopia. Neuron, 21(6), 1315-1325.

147. Szklarczyk, D. et al. (2011) The STRING database in 2011: functional interaction networks of proteins, globally integrated and scored. Nucleic Acids Research, 39, D561-D568.

148. Jahed, Z. et al. (2014) Mechanotransduction pathways linking the extracellular matrix to the nucleus. International Review of Cell and Molecular Biology, 310, 171-220.