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Cytoskeletal crosstalk: A focus on intermediate filaments

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Abstract

The cytoskeleton, comprising actin microfilaments, microtubules, and intermediate filaments, is crucial for cell motility and tissue integrity. While prior studies largely focused on individual cytoskeletal networks, recent research underscores the interconnected nature of these systems in fundamental cellular functions like adhesion, migration, and division. Understanding the coordination of these distinct networks in both time and space is essential. This review synthesizes current findings on the intricate interplay between these networks, emphasizing the pivotal role of intermediate filaments. Notably, these filaments engage in extensive crosstalk with microfilaments and microtubules through direct molecular interactions, cytoskeletal linkers, and molecular motors that form molecular bridges, as well as via more complex regulation of intracellular signaling.

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Introduction

The cell cytoskeleton is involved in numerous aspects of cell biology from the maintenance of intracellular architecture and cell morphology to the realization of complex motile behaviors. To achieve these functions, the cytoskeleton is composed of different filamentous networks: actin microfilaments, microtubules, and intermediates filaments (IFs). IFs are homo- or heteropolymers of proteins encoded by more than 70 different genes and classified into 6 different classes based on sequence homology [1]. While five classes of IF proteins, including keratins and vimentin, form cytoplasmic networks whose composition is cell type-specific, the lamins, class V of IF proteins, form ubiquitous nuclear network. The versatile, cell-type specific filamentous networks perform both cytoplasmic and nuclear functions and their absence can result in significant disorders impacting various cellular processes such as cell proliferation, differentiation, or migration [2–6]. Mutations in IF genes cause diseases including laminopathies, keratinopathies, and desminopathies while alteration of IF composition is frequently associated with cancer progression [7–10].

Unlike microtubules and actin filaments, IFs self-assemble without any known cofactors or nucleoside triphosphates and do not present polarity. The self-assembly of IFs is promoted by the presence of the α-helical Rod domain, present in all IF proteins. Some IFs are homopolymers (e.g. vimentin IFs), others are obligate heteropolymers (e.g. keratin, neurofilaments IFs). Although the concomitant presence of keratins and vimentins is rare, this phenomenon can occur during the epithelial-mesenchymal transition (EMT). During EMT, these different types of IF proteins cannot assemble, resulting in the presence of distinct keratin and vimentin cytoplasmic IF network. Other IF proteins (e.g. nestin, synemin, Glial Fibrillary Acidic Protein (GFAP), neurofilaments, etc.) often hetero-polymerize with type III or type IV IF proteins and are more specific to certain cell types and/or functions. Concerning nuclear IF proteins, they can be divided into two groups: A-type lamins (lamins A and C) and B-types lamins (lamins B1 and B2) form two distinct nuclear networks.

The dynamics and the mechanical properties also distinguish IFs from actin microfilaments and microtubules. IFs are highly stretchable; those composed of desmin, vimentin, keratin, or lamins can be stretched from 240 % to 300 % of their original length before breaking [11]. These filaments not only possess exceptional elasticity but also exhibit a strain-stiffening response. A unique characteristic of IF proteins is their ability to undergo structural changes (coiled-coil α-helical domains stretching) in response to external forces [12,13]. Besides their primary function as structural scaffold, IFs also participate in intracellular signaling. The interplay between cytoplasmic IFs and various

cellular proteins initiates signaling cascades that govern critical cellular processes like cell proliferation, migration, and apoptosis, fundamental both during development and in the adult [14].

While actin, microtubules, and intermediate filaments (IFs) were initially studied as separate networks, first indications of cytoskeletal crosstalk emerged in the early 2000s. For instance, studies of actin filaments and microtubules at focal adhesions suggested potential cytoskeletal crosstalk during cell adhesion and migration [15]. More recently, IFs have been shown to also participate, together with the other elements of the cytoskeleton, in essential functions such as cell adhesion, division, and migration [6,16,17]. This raises the question of how diverse cytoskeletal networks cooperate to achieve intricate functions. Over the last decade, multiple direct and indirect connections between the different cytoskeletal networks including IFs, have been revealed both *in vitro* [18–20] and *in cellulo* [16,21,22]. In this review, we highlight recent evidences of direct and indirect interactions between cytoskeletal elements, as well as their involvement in diverse signaling pathways.

Intermediate filaments physically interact with actin and microtubule networks

Numerous *in vitro* studies have been carried out to reveal the direct physical interactions between the various cytoskeletal networks [23] (Figure 1). One of them uncovered that the stiffness of complex *in vitro* actin-vimentin networks is increased compared with pure vimentin or actin networks, suggesting an actin-vimentin interplay. This interaction was shown to depend on the vimentin carboxy-terminal tail domain, suggesting but not formally demonstrating a direct binding of the vimentin carboxy-terminal tail to actin filaments [24]. However, this result was not confirmed in more recent studies, suggesting that this interaction is weak or dependent on the buffer conditions. In an *in vitro* reconstituted actin-keratin 8/18 filament systems, keratin has also been recognized as an actin partner, involved in network responses to mechanical constraints. For small deformations, all actin-keratins composites with varying ratios displayed a linear viscoelastic behavior intermediate to one of pure actin or keratin networks. In contrast, when high strains were applied to actin-keratin composites, an increasing stiffening behavior was observed, correlating with increasing keratin content [25]. A direct interaction between desmin and actin was also observed in cell-sized artificial droplets of 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE). When both networks polymerized together in these droplets, they increased the propensity for deformation and protrusions, much more than what was observed with separate networks. Both desmin and actin were found in these protrusions [26].

IF interaction with microtubules was initially illustrated by the *in vitro* interaction of dephosphorylated neurofilaments with microtubules via the NF–H subunits [27]. More recently, an innovative combination of cutting-edge techniques (microfluidics and optical trapping) showed the direct interaction of vimentin IFs with microtubules and its role in microtubules stabilization [28]. The development of *in vitro* Interpenetrating Multicomponent Cytoskeletal Networks (IPNs), composed of actin, vimentin IF, and microtubules without crosslinker, has determined that the vimentin presence influences the overall structure and dynamic of the network and its rheological characteristics. Specifically, the presence of vimentin IFs extends the network's elastic regime to longer time scales, leading to a substantial enhancement in the relaxation time of the IPN network [29].

Results obtained with *in vitro* reconstituted systems may explain some observations made in cells. The unique mechanical properties of IFs are reflected by their crucial participation in cell mechanical properties [30]. The study of individual fibroblasts shows a cell active stiffening under compressive stress, which appears mainly dependent on vimentin IFs [31]. However, cytoskeletal perturbations, such as reduced dynamic instability of microtubules or partial depolymerization of actin filaments, influence the apparent persistence length and lateral mobility of IFs, suggesting that actin and microtubules may influence the mechanical functions of IFs [32]. Whether these interactions between the networks are involved in their tight association in cells [22,33] and in the role of vimentin in controlling microtubule elongation and stability, still remains to be determined [34,35]. At the cell cortex, vimentin IFs and F-actin were shown to form an IPN that enhances cell contractility, resilience, and structural integrity after transient stretch, emphasizing the synergistic role of actin and vimentin in shaping the cytoskeleton [36].

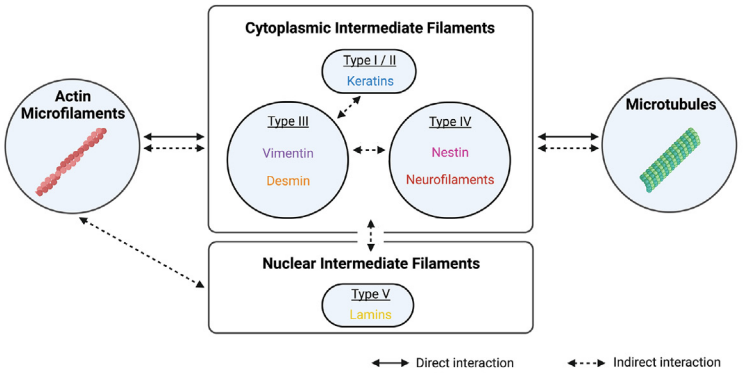
Accumulating evidence both *in vitro* and *in cellulo* suggests that direct physical interactions between cytoskeletal networks can contribute to cytoskeletal coordination and integrity, and to the overall mechanical properties of cells (Figure 1). Although some characteristics of this cytoskeletal crosstalk can be elucidated with *in vitro* reconstituted systems, only the comparison to experiments performed in cells will allow to decipher the whole complexity of cytoskeletal interplay. This intricacy of cytoskeletal crosstalk is certainly regulated at the subcellular levels by the relative concentration of the networks, of cytoskeletal linkers as well as by a number of post-translational modifications which may fine tune their interactions.

Crosslinkers and molecular motors mechanically connect intermediate filaments to actin and microtubules

While direct physical interactions between cytoskeletal networks can influence their properties, cytoskeletal-

Figure 1

A.



B.1

Direct interactions :

Type	IF protein	Interactor	Function	Refs:
I/II	Keratin	Actin microfilaments	- Strain-stiffening behavior of actin/keratin networks	[25]
III	Vimentin	Actin microfilaments	- Stiffness of complex in vitro actin-vimentin networks - Rheological properties of IPN - Compressive stress induced cell stiffening - IFs persistence length and lateral mobility - Cell contractility and structural integrity after stretching	[24, 29, 31, 32, 36]
		Microtubules	- Microtubules stabilization - Rheological properties of IPN - IFs persistence length and lateral mobility	[28, 29, 32]
	Desmin	Actin microfilaments	- Deformation and protrusions of cell-sized lipidic droplets	[26]
IV	Neuro-filament	Microtubules	- Transport regulation in neuronal axon	[27]

B.2

Indirect interactions :

Type	IF protein	Interactor	Linker Protein	Function	Refs:
I/II	Keratin	Vimentin	ND	- Desmosomes disruption - EMT - Vimentin-mediated PTMs of keratins	[74, 75]
		Lamin	LINC complex ?	- Keratinocytes mechano-transduction - Stiffness-dependent chromatin remodeling	[72]
		Actin microfilaments	Plectin	- Actin network organization - Stress fiber formation - Acto-myosin contractility - Desmosomes and inter-cellular forces - Microridge protusions morphogenesis - Keratinocytes mechano-sensitivity	[48, 49, 50, 72]
III	Vimentin	Nestin	ND	- Airway smooth muscle contraction	[73]
		Lamin	LINC complex ?	- Cell-squeezing induced amoeboid migration	[79, 80]
		Actin microfilaments	Plectin, FLNA, CARMIL2, FAK	- Vascular integrity - Lobopodial cell migration - Mitosis - Cell protusions formation - Focal adhesion assembly - Directional cell migration - Stress fiber assembly - Actin polymerization and muscle contraction	[38, 39, 47, 51, 52, 53, 67, 68, 69, 70, 73]
		Microtubules	ND	- Cell polarization - Microtubules network stability - Cell persistent migration - Microtubule organization	[37, 63]
	Desmin	Actin microfilaments	Nebulette	- Desmin - Actin organization - Mouse hearts contractility	[40]
IV	Nestin	Actin microfilaments	Fhos2	- Stress fiber assembly	[71]
V	Lamin	Actin microfilaments	LINC complex ?	- Mechano-sensitivity - Mechano-transduction - Stress fiber formation	[72, 77]

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Direct and indirect interactions in tripartite cytoskeletal crosstalk. a. Cytoplasmic and nuclear intermediate filaments interact with each other and with actin networks and microtubules, both directly (via physical interaction between the protein structures) and indirectly (via cytoskeletal linkers or molecular motors). **b.** Table detailing direct **(b.1)** and indirect **(b.2)** pairwise interactions between cytoskeleton components (ND: Non-determined). Created with the help of BioRender.com.

associated proteins also participate in cytoskeletal crosstalk. Numerous cytoskeletal crosslinkers facilitate IF interplay with other cytoskeletal components, playing pivotal roles in the maintenance of the intercellular junctions to the realization of complex cellular processes such as cell division. Examples include the Adenomatous Polyposis Coli tumor suppressor (APC) [37], Capping protein - Arp2/3 - Myosin I Linker 2 (CARMIL2) [38], Filamin A [39], Nebulette [40], as well as cytolinkers from the Plakin family like Envoplakin, Periplakin, and Plectin (Figure 1). A recent *in vitro* reconstitution shows that a mini plectin or mini-APC including the vimentin and actin-binding sites can trigger the formation of actin-vimentin filament bundles and stiffen the vimentin-actin mix [41].

Plectin connects IFs to various cytoplasmic organelles and associated processes, as well as other cytoskeleton and associated components. In some, but not all cases, the specific plectin isoform involved has been identified (i.e. plectin P1b and P1d in mitochondria organization and shape dynamic [42,43], plectin isoform 1 in nuclear mechanotransduction [44], and plectin P1f at focal adhesions [45,46]). Plectin-mediated crosstalk between the actin and vimentin networks is essential for vascular integrity [47]. In epithelial sheets the absence of plectin triggers a disorganization of the keratin-desmosome network, impacting the actin network organization and inducing acto-myosin hyper-contractility. This leads to a reduction in intercellular cohesion, associated with a general destabilization of the epithelial sheets under mechanical stress [48,49]. Other plakin family cytolinkers, such as envoplakin and periplakin, connect keratins and actin and play a pivotal role in the microridge protusions morphogenesis and shaping of mucosal epithelial cells [50]. Plectin has also been involved in mediating IF functions in cell adhesion and adhesion-dependent migration [4]. In lobopodial cell migration, IFs contribute with the acto-myosin network in the formation of a high-pressure compartment in front of the nucleus, required for directional forward movement. Plectin polarizes the distribution of myosin II at the front of the nucleus and promotes the formation of a perinuclear vimentin cage. In response to myosin activity, plectin interacts with vimentin in a mechanosensitive manner and facilitates the nuclear piston mechanism [51].

As cells divide, vimentin undergoes a crucial redistribution towards the cell cortex to form a complex network intertwined with actin, resulting in a change in morphology and cell rounding. Absence of the vimentin tail region alters vimentin redistribution and leads to mitotic defects. Furthermore, disruption of actin filaments induces vimentin IF bundling near chromosomes [52]. The direct interaction of the carboxy-terminal region of vimentin with actin may be involved. However, a comparative interactomic analysis of F-actin in interphase cells compared to mitotic cells identified plectin as a potential regulator of cortical architecture. Vimentin is recruited to the mitotic cortex in a plectin-dependent manner to coordinate the structure and mechanics of the actin network for successful mitosis in a confined environment [53]. While plectin appears an unmistakable IF partner, only the characterization of the interactomes of all IF proteins will reveal the potentially extensive list of cytoskeletal linkers bridging IFs to the cytoskeletal components.

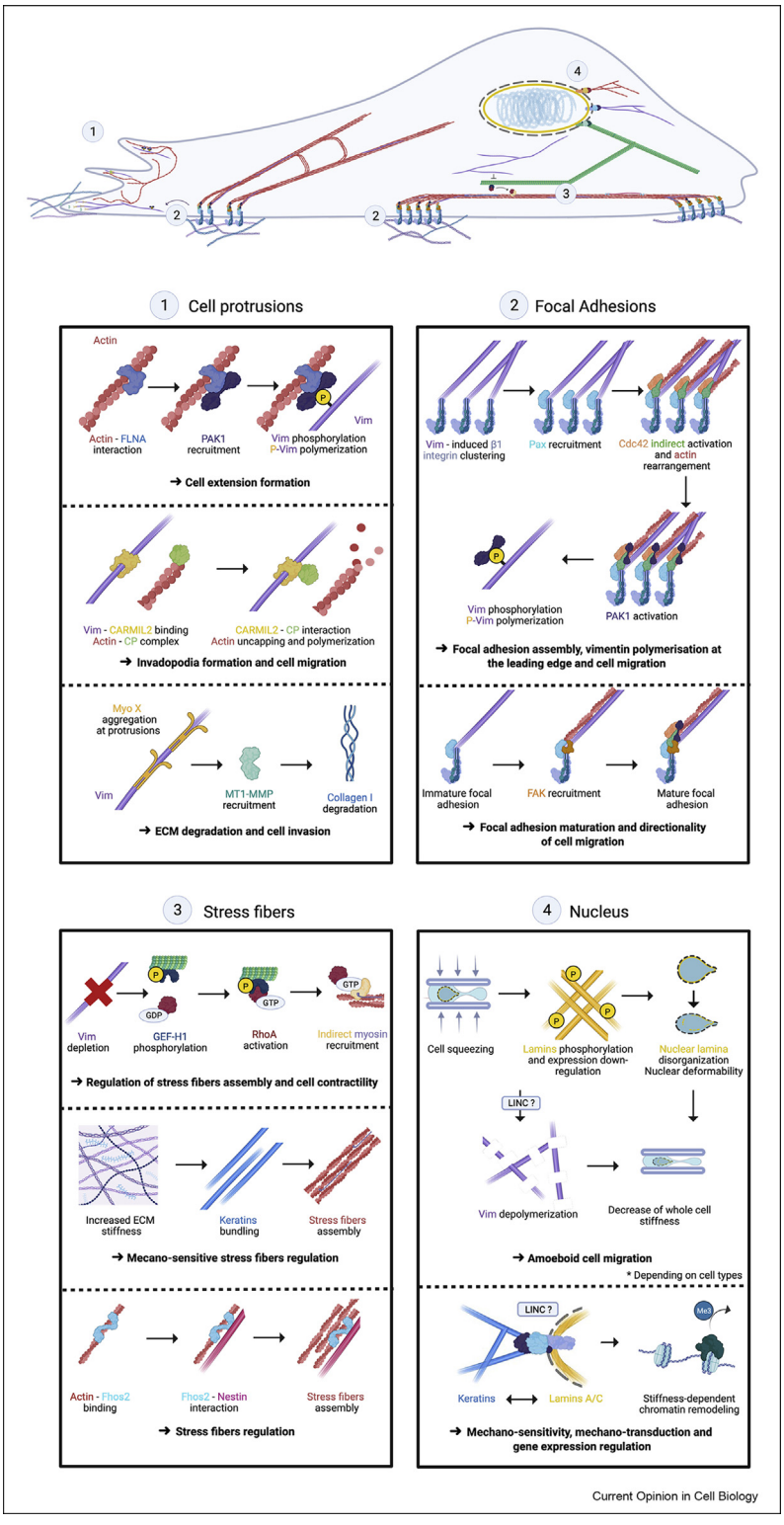
Another class of essential connectors between cytoskeletal elements are molecular motors such as dynein, kinesin, and myosin. They have been involved in IFs transport along microtubules and actin microfilaments [34,54,55]. They control the turnover of IFs in immobile cells and the polarized rearrangement of the IF network along the polarity axis in migrating cells. Transport of IFs along microtubules by both minus-end directed dynein and plus-end directed motors such as kinesin-1 has raised the question of the coordination of motors allowing the directional movement along elastic filaments. Both analytic and stochastic modeling of IF transport revealed the importance of dynein and kinesin-binding properties as essential parameters allowing a directional transport. Moreover, the filament elasticity plays a key role in promoting motor coordination [56,57]. Comparison between the analytic and stochastic models revealed that stochastic fluctuations effectively promote the collective movement of IFs and increase regulatory efficiency through the biochemical properties of cargo—motor interactions [58]. To investigate actin-based retrograde transport, cells were treated with nocodazole to disrupt the microtubule network. In these conditions, IFs move towards the center of the cell where they accumulate. Mathematical modeling suggests that a spatially dependent IF trapping or a spatially dependent speed of actin-dependent transport can explain the establishment of this steady-state situation [59]. Further analysis of IF transport is still required to understand how the coordination of microtubule-based and actin-based transport can orchestrate the organization of the IF network, which in turn influences actin and microtubule organization and functions.

Intermediate filaments participate in intracellular signaling which coordinates the different cytoskeletal networks

While physical direct or indirect interaction between cytoskeletal networks is clearly essential to cell architecture and mechanics and to tissue homeostasis, the cytoskeletal crosstalk also involves regulatory proteins and signaling cascades (Figure 2).

Intermediate filaments have been shown to influence microtubule organization and function by modifying tubulin acetylation. Microtubules acetylation and

Figure 2



IFs-mediated cytoskeletal crosstalk and intracellular signaling pathways. Legend: Filamin **A** (FLNA), p21-activated kinase 1 (PAK1), Vimentin (Vim), phosphorylated-Vimentin (p-Vim), Capping protein Arp2/3 Myosin-I Linker 2 (CARMIL2), Actin Capping protein (CP), Myosin X (MyoX), Membrane-type I matrix metalloproteinase (MT1-MMP), Paxillin (Pax), Cell division control protein 42 homolog (Cdc-42), Focal Adhesion Kinase (FAK), Guanine nucleotide exchange factor H1 (GEF-H1), Ras homolog family member A (RhoA), Linker of Nucleoskeleton and Cytoskeleton Complex (LINC). Created with the help of BioRender.com.

deacetylation mainly rely on two different enzymes: α-tubulin acetyltransferase 1 (α-TAT1) and histone deacetylase 6 (HDAC6). Oncogene expression in fibroblasts leads to an up-regulation of HDAC6, which decreases microtubule acetylation and induces cell stiffening. The decreased acetylation of microtubules results in the structural collapse of the vimentin filament network [60], possibly because microtubules acetylation modulates vimentin transport along microtubules [34]. Conversely, PLK4-induced-centrosome amplification in human retinal epithelial cells leads to an increase in microtubule acetylation and induces vimentin IFs repositioning towards the cell periphery. The repositioning of centrosomes and vimentin can be rescued by inhibiting tubulin acetylation through αTAT1 depletion [61]. Overexpression of HDAC6 may also influence vimentin filament functions by modifying the vimentin interactome (cytoskeletal and cell-extracellular matrix adhesion components), as recently shown in oncogene-expressing fibroblasts [62]. Whether this is due to a change in the vimentin filament structure or in the organization of the vimentin network is not clear. The interplay between vimentin and microtubule acetylation appears bi-directional. Vimentin increases the level of stable acetylated microtubules in mouse embryonic fibroblasts, although the role of HDAC6 or α-TAT1 in this regulation remains to be investigated. Vimentin impact on microtubule stability participates in cell polarity by mediating centrosome repositioning during wound healing-induced cell migration [63]. During human parainfluenza virus type 3 infection, vimentin promotes α-TAT1 degradation and inhibits microtubule acetylation and viral replication [64], illustrating another function of vimentin-microtubule crosstalk.

Besides, vimentin IFs also control the dynamics of focal adhesions [5]. This regulation encompasses their association with focal adhesion components as well as their role in microtubule or actin organization or their influence on Rho family of GTPases, which act as master regulators of the cytoskeleton. Vimentin acts as an adaptor protein, which activates and clusters of β1 integrins in fibroblasts plated on collagen matrices. It also contributes to the recruitment of Paxillin to activate the small G protein Cdc42, a major actin cytoskeleton organizer, directly influencing focal adhesion-mediated signaling to promote the maturation of focal adhesion, cell protrusion, and efficient cell migration [65]. Interestingly, Cdc42's direct effector, PAK1 phosphorylates vimentin to facilitate cell adhesion and cell migration rate in transformed human fibroblasts [66]. Moreover, PAK1 interacts with Filamin A (FLNA), an actin and vimentin crosslinker to promote the formation of fibroblast protrusions on fibronectin matrix [39], further confirming the tight connection between vimentin IFs and focal adhesions. Another recent study nicely illustrates the influence of vimentin in maturation, stability, dynamics, arrangement, and more importantly in the orientation of focal adhesions, to maintain the directionality of cell migration in fibroblasts [67]. This regulation may rely on a dynamic interaction between vimentin and FAK, a crucial focal adhesion component [67,68]. The effect of vimentin IFs on focal adhesion orientation could involve the control of acto-myosin contractility and the transmission of traction forces through focal adhesions. Vimentin may also influence cell polarization by controlling centrosome positioning to promote microtubule orientation and stability and directed vesicular traffic required for cell persistent migration [37,63].

The crosstalk between IFs and acto-myosin contractility has been the subject of in-depth studies in recent years. The presence of entangled vimentin filaments in the stress fibers was observed by electron microscopy, but the relevance of this entanglement was unclear [22,36]. Generally, vimentin IFs tend to minimize traction forces [4]. Vimentin depletion was shown to activate RhoA-mediated contractility via the RhoGEF GEF-H1, although the exact mechanism remains unclear [69]. Consistently, in case of cell stimulation by electrophiles, disruption of vimentin and in particular of its cysteine 328 residue, allows induction of stress fibers [70]. Other IF proteins such as nestin or keratin also appear to promote stress fiber assembly. Fhos2, a mammalian protein of the formin family, associates with nestin to promote the formation of stress fibers and potentially to bridge nestin IFs with microfilaments [71]. In keratinocytes, keratin IFs form a rigid, interconnected network of bundles associated with stress fibers to increase the overall cell rigidity in response to an increased matrix stiffness. Overexpression of the dominant R416P mutation in keratin 14 disrupts keratin stability, leading to a loss of stress fibers and decrease in cell stiffness [72]. These recent examples illustrate the versatile role of IFs in the control of the actin network and cell contractility, suggesting that changes in the composition and possibly in the organization of the IF network may have important consequences on all actin-driven cellular functions. As each IF protein appears to exert its function through the regulation of distinct signaling pathways, the presence of several IF proteins in one cell may lead to subtle adaptations of mechanosensitive cell responses. Such complex regulation has been illustrated in airway smooth muscles. There, a tripartite interaction involving nestin, vimentin, and actin controls cytoskeleton signaling. Contractile stimulation induces autophosphorylation of Polo-Like Kinase 1 (PLK1) and PLK1-dependent phosphorylation of nestin on threonine 315. This phosphorylation promotes the formation of a PLK1-Nestin complex, enabling phosphorylation of vimentin on serine 65. Phosphorylated Vimentin recruits cortactin and Profilin-1 to induce actin polymerization and muscle contraction [73]. While vimentin and nestin can co-polymerize, in other cases, different independent cytoplasmic IF networks co-exist. During EMT, the vimentin and keratin networks influence each other, creating a

new layer of cytoskeletal crosstalk [74]. Expression of vimentin in MCF7 epithelial cells induces a hybrid epithelial-mesenchymal state associated with a decrease of intercellular forces and an increased expression of genes linked to EMT. These events are paralleled by the reorganization of the keratin network, possibly due to vimentin-induced post-translational modification of keratins, as suggested by a shift of apparent molecular weight [75]. The effect of vimentin IF in cancer invasion appears more and more diverse as vimentin was also recently involved in ECM degradation, via aggregation of another cytoskeletal component, the unconventional Myosin 10 which promotes the recruitment of membrane-type 1 matrix metalloproteinase (MT1-MMP) at the plasma membrane, weakening the extracellular matrix to enhance cancer cell invasion [76].

Crosstalk between the cytoplasmic and nuclear IF networks is also emerging as a pivotal regulator of nuclear mechano-transduction. In keratinocytes, the stability of keratin IFs and lamin expression are necessary for regulation of stiffness-dependent chromatin remodeling. The dominant R416P mutation in keratin 14 impairs mechano-transduction to the nuclear lamina by decreasing both the formation of F-actin stress fibers and the expression of lamins A and C, which is normally involved in stiffness-dependent chromatin remodeling [72]. This crosstalk is likely to be mediated by the Linker of Nucleoskeleton and Cytoskeleton (LINC) complex linking the cytoplasmic cytoskeletal elements with the lamin IF networks [77]. In mouse embryonic fibroblasts (MEFs) lamins (A-type or B-type lamins) participate in the regulation of cortical and cytoplasmic stiffness and cell contractility by controlling the dynamics of LINC complex [78]. The role of lamins in influencing whole-cell mechanics is particularly evident during the amoeboid migration [79]. Confinement of HeLa cells in a microscale cell squeezing system decreases lamin A and C expression and increases its phosphorylation on serine 390, promoting nuclear deformability. In parallel, vimentin depolymerization is observed leading to a reduction of cell stiffness. Together these changes promote myosin IIA-dependent amoeboid migration [79] and suggest the existence of an interplay between A-type lamins and vimentin. However, the nature of the connection between lamin A or lamin C and vimentin remains elusive. It would also be important to investigate the role of vimentin-lamin crosstalk in other cell types such as dendritic cells in which the presence of vimentin enhances ameboid migration [80].

Moreover, interactions between IFs and other cytoskeletal elements such as septins SEPT9 and SEPT12 have emerged, unveiling intriguing functional implications during spermiogenesis [81,82]. This raises the possibility of additional cytoskeletal crosstalk, whose role in cell shape, adhesion, and dynamic behavior remains to be studied.

Conclusion

To conclude, IFs play a pivotal role in cytoskeletal crosstalk, serving as critical partners and regulators between actin microfilaments and microtubules. Understanding the intricate crosstalk between IFs and other cytoskeletal components is crucial for deciphering the mechanisms underlying cell functions and tissue homeostasis. Dysregulation of this crosstalk, affecting the cytoskeleton, has been implicated in various human diseases, including cancer, neurodegenerative disorders, and genetic diseases. However, further investigations are required to fully decipher the precise nature of cytoskeletal interactions. While *in vitro* reconstitution assays offer insights into the impact of direct interactions between networks, they fall short in capturing the full complexity of the molecular mechanisms within living cells. Analyzing the interactomes of IF proteins holds promise in providing a more exhaustive catalogue of cytolinkers and signaling molecules involved in these processes and may shed light on the specificity inherent in the diverse IF proteins. The collaborative synergy among various cytoskeletal networks prompts us to perceive the cytoskeleton as a global, adaptable network, regulated locally and instrumental in an array of cellular functions. Unraveling the functional consequences of this crosstalk promises to deepen our comprehension of cellular physiology and, potentially, reveal novel therapeutic targets for a multitude of cytoskeleton-related diseases.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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- • of special interest
- •• of outstanding interest

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