

Box 1. Building the contractome database

This work is focused on actomyosin contractility, rather than on myosin II per se; therefore it does not include studies that did not suggest the involvement of contractile forces, such as structural or other non-canonical role(s) for non-muscle myosin II. To assemble the list of the contractome components, we searched the literature using PubMed for papers that mentioned both myosin II ('myosin II OR *Myh9* OR *Myh10* OR *Myh14*') and forces ('contractility OR tension OR force') in non-muscle cells. This search yielded about 600 papers, from which 100 unique components (supplementary material Table S2) and 49 unique cellular functions (Table 1) were derived.

Several contractome proteins in vertebrates have multiple isoforms (e.g. myosin, α -actinin and tropomyosin), which often have specialized functions (Quick and Skalli, 2010; Tojkander et al., 2011; Wang et al., 2011). There are differences in the biochemical and biophysical properties (e.g. ATPase activity, duty ratio) of the three non-muscle myosin II (NMII) isoforms, rendering them with unique as well as redundant functions. For example, NMIIA propels actin filaments the fastest whereas NMIIB can sustain tension for the longest period of time (Kovacs et al., 2003; Wang et al., 2003). The isoforms can have distinct cellular localizations (Kolega, 1998; Betapudi et al., 2006; Smutny et al., 2010; Wang et al., 2011), although co-assembly of NMII isoforms also occurs *in vivo* (Beach et al., 2014; Shutova et al., 2014). However, because part of the contractome literature involves cells that have only a single representative of these proteins (e.g. *Dictyostelium*, *Saccharomyces*, *Drosophila*) and also studies in vertebrates did not necessarily differentiate between different isoforms of these proteins, in our work we combined the different isoforms into single entries (e.g. MYH represents all myosin heavy chains).

Interactions between the contractome components were identified in the prePPI database (Zhang et al., 2012, 2013) and verified to be direct by accessing the primary literature. Phosphorylation events could result in activation or inhibition of the modified protein. For example, phosphorylation of LIMK by ROCK results in its activation and subsequent phosphorylation of cofilin (Maekawa et al., 1999), whereas phosphorylation of cofilin by LIMK inhibits its ability to depolymerize F-actin (Yang et al., 1998) and thus enhances contractility (Maekawa et al., 1999). In order to better represent their consequence for protein activity, each phosphorylation event in the contractome was annotated based on the primary literature as either activating or inhibiting (or undefined) with regard to the activity of the target protein (supplementary material Table S3).

Actomyosin contractility takes place when bipolar myosin II filaments interact with anti-parallel actin filaments (F-actin) and convert chemical energy (ATP) into mechanical energy [movement of myosin head towards F-actin barbed (+) end]. Essentially, actomyosin activity takes place in every cell in our body. In non-muscle cells, which are the focus of this Cell Science at a Glance article, up to three isoforms of myosin II heavy chains (*MYH9*, *MYH10* and *MYH14*, which encode myosin heavy chain a, b and c respectively) and two isoforms of actin (*ACTB*, *ACTG1*) can be detected (reviewed in Vicente-Manzanares et al., 2009). Despite differences between the isoforms we treat them as one in this article and poster (see Box 1).

Classic *in vitro* experiments have demonstrated that actomyosin activity can take place in simple systems that contain purified actin and myosin II (Kron and Spudich, 1986; Spudich et al., 1985). However, *in vivo*, many proteins have been shown to modulate actomyosin contractility, suggesting that actomyosin activity must be tightly regulated in space, time and magnitude. Control over actomyosin contractility within non-muscle cells can be achieved at the architectural level, which entails the assembly of the contractile machinery, and by regulation of myosin II motor activity, which involves input from multiple signaling cascades that ultimately

determine the phosphorylation state of myosin regulatory light chain and myosin conformation and motor activity. An additional modulator of contractility is mechanical force, which through changes to protein conformation and/or lifetime of interactions affects both the assembly, molecular composition and activity of actomyosin networks.

Here, we mine the literature and protein databases to create a comprehensive map of the network of proteins that generate and regulate actomyosin contractility in non-muscle cells, henceforth referred to as the 'contractome'. Our analysis reveals a high degree of complexity that presumably evolved to provide tight regulation of actomyosin activity in the cell, and it highlights major hubs and design principles of the network.

Cellular functions of the contractome

Actomyosin contractility plays a role in many biological processes. Here, we briefly describe the cellular functions of the contractome throughout the life of a cell (see also Table 1 and supplementary material Table S1). Our data excludes functions that have been described for specialized cells and contractile processes encompassing multiple cells. For descriptions of tissue level functions of actomyosin contractility, we refer the reader to other reviews (Gorfinkiel and Blanchard, 2011; Heisenberg and Bellaiche, 2013; Lecuit et al., 2011; Martin and Goldstein, 2014; Munjal and Lecuit, 2014).

The emergence of a new daughter cell starts as the mother cell enters mitosis. One of the hallmarks of this step is the assembly of the mitotic spindle. Contractility affects spindle architecture function and orientation and, therefore, can affect the fate of the daughter cell (Carreno et al., 2008; Chaigne et al., 2013; Kunda et al., 2008; They et al., 2005). The separation of the two cells takes place during cytokinesis; it relies on the cleavage furrow contractile zone, a structure in which actomyosin-derived forces play a major role (Mendes Pinto et al., 2013; Pollard, 2010). The mechanical properties and shape of the new daughter cell are determined by its ability to contract and maintain tension in its cortical cytoskeleton (Bischofs et al., 2008; Martens and Radmacher, 2008; Schafer and Radmacher, 2005). In addition, the dynamic properties of the actin cytoskeleton and its organization into a variety of actin-rich structures, such as lamellipodia and stress fibers, are also affected by contractility (Hirata et al., 2008; Hotulainen and Lappalainen, 2006; Medeiros et al., 2006; Svitkina et al., 1997; Wilson et al., 2010; Yang et al., 2012), which also affect the movement and bundling of microtubules (Burnette et al., 2008; Schaefer et al., 2008).

Actomyosin structures are intimately associated with cell adhesion to both the extracellular matrix (ECM) and its neighboring cells (Geiger et al., 2001; Priya and Yap, 2015; Wolfenson et al., 2013). The ability of a cell to achieve a complex, polarized architecture also relies on actomyosin contractility (Lee et al., 2012; Walters et al., 2006; Yu et al., 2008) as does its ability to migrate (Aguilar-Cuenca et al., 2014; Vicente-Manzanares et al., 2009). Moreover, actomyosin contractility regulates several aspects of endosome organization and trafficking (Chandrasekar et al., 2014; Lynch et al., 2013; Masedunskas et al., 2011; Nightingale et al., 2011; Olazabal et al., 2002; Zilberman et al., 2011).

Tension forces do not only affect the cell structure and function but also its environment. The assembly, remodeling and proteolytic degradation of the ECM are all affected by forces (Bloom et al., 2008; Kalson et al., 2013; Kirmse et al., 2011; Yoneda et al., 2007; Zhang et al., 1997; Zhong et al., 1998). In addition, the ability of the cell to sense the mechanical and topographical properties of its environment involves tension forces (Ghibaud et al., 2009);

Table 1. Cellular functions of non-muscle myosin-II-mediated contractility

Process	Function
Cell birth	Spindle assembly, morphology, orientation and function Cleavage furrow contractile zone assembly and function
Cell architecture and cytoskeleton	Cell mechanical properties and shape Recruitment of BAR domain proteins Affect actin polymerization Promote actin network disassembly Regulate actin retrograde flow Assembly and function of stress fibers, arcs and circular bundles Lamellipodia formation Microtubule movement Microtubule bundling
Cell adhesion, polarity and migration	Focal adhesions – assembly, turnover, molecular composition, adhesion strength and signaling Podosomes – molecular composition, structural features, average life span, ECM degradation Adherens junctions – assembly and turnover, size, and adhesion strength and signaling Tight junctions – assembly and turnover Tunneling nanotubes (TNT) Apicobasal polarity Planar cell polarity Cell polarization under flow, substrate stretching, chemical gradients and electric fields Cell migration
Endoplasmic organization and trafficking	Endoplasmic spreading Phagocytic cup assembly, squeezing and closure Clathrin-mediated endocytosis Exocytosis ER stress Golgi architecture and dynamics
Cell fusion	Membrane fusion
Cell environment	Transport of ECM components ECM assembly ECM remodeling ECM proteolytic degradation Topography and stiffness sensing
Cell signaling	Exposing cryptic sites and changing the conformation of: ECM proteins, signaling proteins, enzymes, ion channels Receptor localization Receptor internalization
Nucleus and nuclear activity	Nucleus motility and positioning Nucleus morphology Histone acetylation Chromatin condensation DNA synthesis Gene expression Cell proliferation and differentiation
Cell Infection	Bacteria and viruses invasion Bacteria dissemination
Cell death or survival	Apoptotic cell compaction and detachment Release of nuclear RanGTP E4orf4-mediated cell death Entosis Survival of cultured human embryonic stem cells

References for all functions described in Table 1 appear in supplementary material Table S1.

Ozdemir et al., 2013). Contractility further affects signaling events by altering the configurations and activity of signaling proteins, enzymes and receptors (Vogel and Sheetz, 2006).

The nucleus, which is the target of many signaling events, is also sensitive to contractility forces that affect its architecture, stiffness, localization within the cell and its activity, for instance with regard to chromatin remodeling, DNA synthesis and gene expression (Chang et al., 2013; Goulding et al., 2007; Guilluy et al., 2014; Hossain et al., 2006; Kim et al., 2005; Kiss et al., 2014; Maeda et al., 2013; Sarasa-Renedo et al., 2006; Song et al., 2002; Szabo et al., 2011). With these key regulatory roles, it is not surprising that contractility has been shown to affect cell proliferation and differentiation in several experimental systems (Chowdhury et al., 2010; Ozdemir et al., 2013; Rottmar et al., 2014).

During its life, the cell might be infected by bacteria (Hanisch et al., 2011; Rajabian et al., 2009) and viruses (Lehmann et al., 2005; van Leeuwen et al., 2002), which also use contractility for their invasion into the cell, as well as for their dissemination. Finally, the death of a cell also involves contractility that affects several aspects of cell death at both the structural and molecular levels, such as release of nuclear RanGTP, compaction and entosis (Moss et al., 2009; Overholtzer et al., 2007; Smadja-Lamere et al., 2008; Solinet and Vitale, 2008).

Molecular composition of the contractome

Using defined criteria (see Box 1), we identified 100 contractome components, including 97 proteins and three cofactors (supplementary material Table S2). In addition to actin and myosin, the contractome

contains other bona fide structural proteins, such as actin cross-linking proteins, and bona fide regulatory proteins, such as serine/threonine protein kinases. However, many of the proteins that make up the contractome have both structural and regulatory functions. For example, tropomyosin binds along the actin filament and, although it has no enzymatic activity, it plays an important role in regulating myosin activity (Gunning et al., 2008).

Bearing in mind that multidomain proteins can fulfill more than one function, we nevertheless used the published information (The UniProt Consortium, 2015) to assign the proteins to functional categories (supplementary material Table S2). Based on this manual annotation, the largest functional group in the contractome is serine/threonine phosphorylation regulators, which consists of 26 serine/threonine kinases and a single serine/threonine phosphatase. The second largest group consists of 24 scaffolds or adaptors, which have multiple protein-binding domains that bring together structural proteins and enzymes with their substrates. Proteins controlling actin polymerization and depolymerization dynamics and bundling actin filaments make up the third largest group (12 proteins). It is important to note that the list of contractome components pools together proteins that have been identified in a variety of non-muscle cellular contractile systems. Many are core components common to most – if not all – contractile structures, whereas others might be specific for a particular cellular location or function. For example, the tyrosine kinase receptor PTK7 appears to be involved specifically in planar cell polarity (Lee et al., 2012), whereas the serine/threonine kinase NUA2 appears to be specific for stress fibers (Vallénius et al., 2011). Bearing in mind that our knowledge is fragmented, we provide a current view of the unique and shared components between focal adhesions, adherens junctions and the cytokinetic apparatus shown in the poster and supplementary material Table S2. A comprehensive proteomic analysis of isolated contractile apparatus from non-muscle cells is still lacking, but proteomic analysis of MYH9-interacting proteins in podocytes identified several hundred proteins (Hays et al., 2014), suggesting that the literature-based contractome presented here is still far from complete.

Interactions between contractome components

With the list of contractome components in hand, we used protein interaction databases and the literature to assemble a comprehensive list of over 230 experimentally validated direct interactions between contractome components (supplementary material Table S3). The most prevalent interaction in the contractome is phosphorylation, of which there are 84. In contrast, there is only one dephosphorylation event: that of myosin light chain by myosin light chain phosphatase. Obviously every phosphorylation event is reversible, but the identity of the phosphatase(s) in most cases is still unknown. In addition to 26 phosphorylation events that are ‘on’ switches, there are another 42 activating interactions in the contractome. These include enzymatic activation of GTPases by guanine-nucleotide-exchange factors (GEFs), and non-enzymatic activation by protein binding, such as activation of the Arp2/3 complex mediated by neuronal Wiskott–Aldrich syndrome protein (N-WASP, also known as WASL) (Egile et al., 1999) and calmodulin-mediated activation of myosin light chain kinase (MLCK or MYLK, of which there are several isoforms) (Means et al., 1991). On the flipside, 36 phosphorylation events are ‘off’ switches and there are another 33 inhibitory interactions, including induction of GTP hydrolysis on GTPases [modulated by GTPase-activating proteins (GAPs)] and non-enzymatic inhibition by protein binding, such as calmodulin-induced inhibition of caldesmon and inhibition of

myosin heavy chain by caldesmon (Lin et al., 2009). There are another 69 protein–protein interactions for which it is not known whether they are inhibitory or activating and they are thus defined as ‘binding’.

Examining the entire contractome network (see main poster panel) reveals a high degree of connectivity – primarily between the different functional groups – with an average of 4.8 interactions per protein. The proteins with the highest number of potential interactions in the contractome are F-actin, RhoA, myosin heavy chain (MYH), protein kinase C (PKC), myosin phosphatase (MYPT1), and Rho kinase (ROCK, for which there are two isoforms ROCK1 and ROCK2) with 25, 22, 21, 17, 15 and 13 interactions, respectively. In order to better comprehend the interconnectivity between functional groups, we merged all the proteins within each of the groups into a single node while retaining all of their interactions (see poster). By doing so, the following four main features of the network become visible: (1) serine/threonine kinases are activated by RhoGTPases, cyclic nucleotides and Ca^{2+} , and function primarily in the regulation of myosin phosphatase, actin regulators and themselves; (2) scaffolding proteins link F-actin with myosin, and they also bind serine/threonine kinases, RhoGTPases and their upstream regulators (RhoGEFs and RhoGAPs); (3) actin regulators are controlled by RhoGTPases and serine/threonine kinases; and (4) the myosin light chain is primarily regulated by serine/threonine phosphorylation, whereas the myosin heavy chain is primarily regulated by scaffolding proteins.

Contractome subnetworks

From the complete contractome, we carved out three subnetworks focusing on actomyosin structure, myosin regulation by Ca^{2+} and phosphorylation, and Rho GTPase regulatory pathways (see poster). This approach sacrifices much of the connectivity between functional groups in return for increased clarity in portraying a particular aspect of the contractome.

Actomyosin structure

F-actin is polymerized from G-actin and three nucleation- or elongation-promoting proteins, namely Arp2/3, formin and VASP, are implicated in polymerizing F-actin used for contractility (reviewed in Campellone and Welch, 2010; Chesarone and Goode, 2009). The basic architecture of the actin filaments, that is linear (formin-mediated) or branched (Arp2/3-mediated), may affect its ability to interact with Myosin II and generate tension. For example, the branched actin network that is generated by Arp2/3 in the protruding lamellipodium is devoid of myosin II, but upon retraction the network is compressed into parallel actin arcs that quickly recruit myosin II and become contractile (Burnette et al., 2011). The absence of myosin from the lamellipodium could also be due to differential signaling and not an inherent inability to bind branched actin.

Effective contractility depends on cross-linking of actin filaments into bundles (Inoue et al., 2011). Filamin-A, α -actinin and plastrin (also known as fimbrin) are three cross-linkers that differ in their mode of crosslinking and yet have all been implicated in this role (Kasza et al., 2009; Reichl et al., 2008; Shao et al., 2010). The molecular details of how F-actin and mini-filaments of myosin co-assemble into actomyosin structures are still far from complete (Ren et al., 2014; Shutova et al., 2012). Several scaffolding proteins that can bind to both F-actin and MYH proteins are likely candidates to have a role in this process. Such scaffold proteins include anillin (Piekny and Glotzer, 2008), supravillin (Smith et al., 2013) and

septins (Mavrakakis et al., 2014). Several F-actin-binding proteins, most notably tropomyosin, inhibit binding of myosin to the actin filament through steric hindrance, such that even the assembled actomyosin structure is not capable of generating contractility unless tropomyosin shifts its position along the filament (von der Ecken et al., 2014). A number of tropomyosin isoforms have a positive role in recruiting myosin to stress fibers (Tojkander et al., 2011). The F-actin-severing protein cofilin 1 has also been shown to compete with myosin for binding sites on F-actin (Wiggin et al., 2012). Actomyosin activity is also negatively regulated by proteins that directly bind to MYH proteins and either inhibit the assembly of myosin into filaments (e.g. MYBPH and S100A4) or inhibit its ATPase activity (e.g. calponin and caldesmon). Some of these inhibitions can be effectively released by Ca^{2+} -calmodulin and/or by phosphorylation by various kinases, as detailed in the next section.

An important factor, affecting several key contractome proteins, that acts to promote the assembly of actomyosin structures is mechanical force, either intrinsic or extrinsic. The mechanosensitivity of the contractome establishes a positive-feedback loop for increased local contractility, which is used in various cell processes, such as cytokinesis, cell adhesion, intercalation and membrane fusion (Luo et al., 2013; Schiller and Fassler, 2013; West-Foyle and Robinson, 2012; Fernandez-Gonzalez et al., 2009; Kim et al., 2015). Actin polymerization is enhanced under mechanical tension in a mechanism involving zyxin (Hirata et al., 2008) or by directly augmenting formin activity (Courtemanche et al., 2013; Jegou et al., 2013), and actin severing by cofilin is inhibited by tension in the actin filament (Hayakawa et al., 2011). Strikingly, the affinity of myosin II motor domain towards actin is enhanced when the actin filament is under tension, suggesting that this is the basis for cooperative assembly of actomyosin structures.

Myosin regulation by Ca^{2+} and phosphorylation

Both the heavy and regulatory light chains of myosin are tightly regulated. As explained above, the binding of proteins that inhibit MYH from assembling mini-filaments can be inhibited by phosphorylation. For example, phosphorylation of MYH proteins by casein kinase II blocks the binding site for S100A4 (Dulyaninova et al., 2005). PKC-dependent phosphorylation of MYH on S1916, downstream of Rac1 and integrin activation, promotes the capture and assembly of myosin IIA minifilaments in focal adhesions (Pasapera et al., 2015). Perhaps the most important phosphorylation switch in the contractome is the phosphorylation of T18 and/or S19 of the regulatory MLC, which activates myosin motor activity by increasing its ATPase activity and by inducing the conformational change from a compact folded structure to the extended conformation that can form mini-filaments (Smith et al., 1983). Mono-phosphorylation is sufficient for MLC activation, but di-phosphorylation, which appears to be the prevalent form of phosphorylation in cells, has an even stronger effect (Hirata et al., 2009; Ikebe et al., 1986; Umemoto et al., 1989). Importantly, myosin activation by phosphorylation is not sufficient to induce mini-filament assembly, especially given that myosin assembly is slower than myosin diffusion. As discussed above, additional proteins, as well as force, are required for actomyosin assembly, suggesting that localized kinase activity is essential but not sufficient to provide spatial control over contractility.

Seven kinases, including ROCK and MLCK, are known to phosphorylate MLC on the activating T18 and/or S19 (reviewed in Vicente-Manzanares et al., 2009) (Note: references for all interactions shown in the poster and mentioned here are provided

in supplementary material Table S3). A second group of residues located at the N-terminus of MLC (S1, S2 and T9) are phosphorylated by PKC and have been shown to have an inhibitory effect on myosin activity *in vitro*, but their importance for *in vivo* regulation is questionable (Beach et al., 2011). The phosphates on T18 and/or S19 are quickly removed by myosin phosphatase (a multi-protein complex including the catalytic subunit PP1c and a myosin-binding subunit encoded by *PPP1R12A* and henceforth referred to as MYPT1) (Grassie et al., 2011). The myosin-targeting ability of MYPT1 can be inhibited by phosphorylation and thus it is a major hub of regulation in the contractome with 11 different kinases known to phosphorylate it. Of note, many of the kinases employ a two-pronged approach; they phosphorylate MLC (thereby activating it) and phosphorylate MYPT1 (thereby inhibiting it) to maximize myosin activity. Other kinases can carry out both activating and inhibitory phosphorylation modifications, with respect to myosin activity, which might occur in different contexts or in parallel to yield an incoherent feed-forward regulatory loop. For example, p21-activated kinase (PAK, for which there are several isoforms) phosphorylates and inhibits MLCK (thereby reducing myosin activity), and it also inhibits MYPT1 by phosphorylating it and activating its inhibitor CPI17 (thereby increasing myosin activity).

In addition to posttranslational modification, MYPT1 can also be regulated by protein binding; it is activated by binding to Par4 and MRIP and inhibited by binding to 14-3-3 proteins. Ca^{2+} plays a fundamental role in regulating contractility in muscle (Stull et al., 1988). Although its role in non-muscle cells is less studied, Ca^{2+} appears poised to have a role in regulating contractility also in non-muscle cells, primarily through the activation of calmodulin, which activates MLCK and inhibits caldesmon. Ca^{2+} also activates PKC, which in turn can phosphorylate numerous components of the contractome.

Rho GTPase regulatory pathways

Rho GTPases are signaling proteins often activated downstream of growth factors that regulate actomyosin contractility through the activation of serine/threonine kinases and actin polymerization factors (Hall and Nobes, 2000). The Rho GTPase that is most commonly associated with actomyosin contractility is RhoA, but RhoC, Cdc42 and Rac1 can also be positive regulators of contractility and RhoE plays an inhibitory role. Several of the kinases that regulate myosin activity through phosphorylation are activated by the binding of active Rho GTPases. RhoA is known to activate ROCK and citron kinase, whereas the GTPase Cdc42 activates PAK and MRCK, and Rac1 has been shown to activate PAK, citron kinase and dystrophin myotonia protein kinase (DMPK). With respect to activation of actin polymerization factors, RhoA directly activates diaphanous-related formins by interfering with an autoinhibitory interaction within the protein. Rac1 and Cdc42 activate WASP-family verprolin-homologous protein-2 (WAVE2, also known as WASF2) and N-WASP, respectively, which in turn activate Arp2/3. A key step in the regulation of actomyosin by Rho GTPases is the activation of the Rho GTPases themselves. Rho GTPases are activated by RhoGEFs, which facilitate the exchange of GDP for GTP, and are switched off by hydrolysis of GTP to GDP, a process greatly enhanced by RhoGAPs. Guanine nucleotide dissociation inhibitors (GDIs) function to bind and maintain the inactive pool of GTPases in the cytosol, whereas active Rho GTPases localize to the plasma membrane (Garcia-Mata et al., 2011). Thus, the spatiotemporal regulation of RhoA depends on the spatiotemporal

localization of the RhoGAPs and RhoGEFs. For example, prior to the assembly of a cytokinetic ring, the RhoGEF Ect2 along with the RhoGAP MgcRacGAP (also known as RACGAP1) concentrate at the future furrow, and together they are responsible for an increase in RhoA at the membrane and the subsequent assembly of a contractile ring.

Physiological significance of the contractome

In the mouse, the loss of *Myh9* (encoding myosin IIa) (Conti et al., 2004) or *Myh10* (encoding myosin IIb) (Tullio et al., 1997, 2001) result in death during embryonic development. To evaluate the physiological importance of contractome components in the context of the whole organism, we accessed the mouse genome informatics database (Blake et al., 2014; Bult et al., 2013) and extracted information on phenotypes that have been observed in mice with mutations in contractome genes (supplementary material Fig. S1). Many of the contractome genes function in other processes in addition to the contractome. Importantly, our phenotypic analysis does not differentiate between phenotypes that are caused by misregulation of contractility and phenotypes that result from other functions of contractome genes. Nevertheless, this analysis provides a glimpse into the physiological processes in which contractome genes play a role. In line with the aforementioned phenotypes of myosin genes, mortality and aging is the most common group of phenotypes of contractome genes (9.6% of the genes). The second largest group is the cardiovascular system (7.4%); this group includes genes that are associated with defects in cardiac muscle contractility. Moreover, muscle phenotypes are also represented (4.5%), likely because some of the non-muscle contractome genes are also part of the muscle cell contractome. These data highlight the profound importance of genes of the contractome in a physiologically relevant mammalian system.

Perspectives

In the last decade, the expanding research of non-muscle myosin II and mechanobiology in general have highlighted the fact that actomyosin contractility plays a key role in many structural, mechanical and regulatory processes (Eyckmans et al., 2011; Mammoto et al., 2013; Sun and Fu, 2013; Swartz and Lund, 2012). Summarizing the current knowledge in the field brings to light the molecular and functional complexity of actomyosin contractility. It is tempting to speculate that this complexity emerged during the evolution of eukaryotes as a growing number of biological processes became interwoven with mechanical cues. Nevertheless, our analysis succeeded in identifying key pathways and principles in the regulation of actomyosin contractility.

Assembly of the contractome also points out important gaps in our knowledge. Although studies in cultured cells and model organisms demonstrate differential expression, distribution and functions for different MYH proteins, it is still poorly understood whether these MYH proteins utilize different contractome networks to exert their role. Moreover, direct measurements of contractile forces in a variety of contractome mutants and during different contractility-based biological processes are still highly limited. The ability to integrate the insights from these systems into the contractome will enhance our understanding of this complex machinery and thus likely provide novel insights into numerous fundamental biological processes.

Competing interests

The authors declare no competing or financial interests.

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Cell science at a glance

A high-resolution version of the poster is available for downloading in the online version of this article at jcs.biologists.org. Individual poster panels are available as JPEG files at <http://jcs.biologists.org/lookup/suppl/doi:10.1242/jcs.170068/-/DC2>.

Supplementary material

Supplementary material available online at <http://jcs.biologists.org/lookup/suppl/doi:10.1242/jcs.170068/-/DC1>

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