FIGURE 3 | Molecular connectivity from the ECM to the nucleus.

FROM THE FOLLOWING ARTICLE:

Mechanotransduction at a distance: mechanically coupling the extracellular matrix with the nucleus

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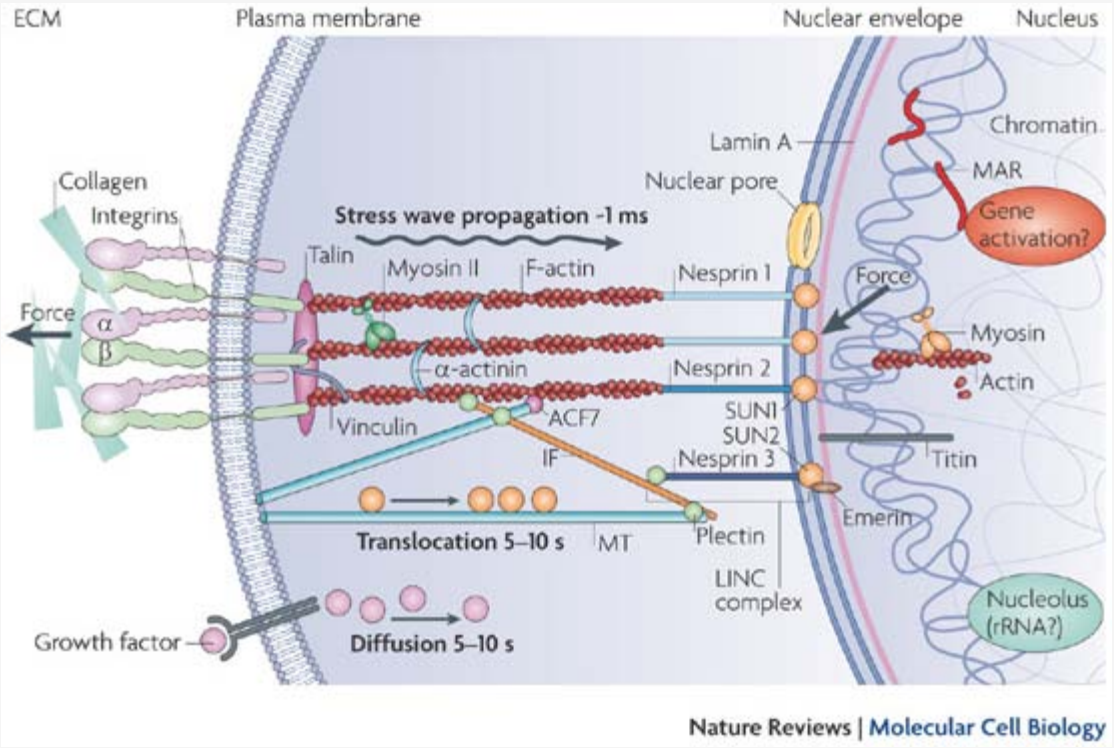

A local force applied to integrins through the extracellular matrix (ECM) is concentrated at focal adhesions and channelled to filamentous (F)-actin, which is bundled by α-actinin and made tense by myosin II, which generates prestress. F-actins are connected to microtubules (MTs) through actin-crosslinking factor 7 (ACF7), and to intermediate filaments (IFs) through plectin 1. Plectin 1 also connects IFs with MTs and IFs with nesprin 3 on the outer nuclear membrane. Nesprin 1 and nesprin 2 connect F-actin to the inner nuclear membrane protein SUN1; nesprin 3 connects plectin 1 to SUN1 and SUN2. Owing to cytoplasmic viscoelasticity, force propagation from the ECM to the nucleus might take up to ~1 ms. The sun proteins connect to the lamins that form the lamina and nuclear scaffold, which attaches to chromatin and DNA (for example, through matrix attachment regions (MARs)). Nuclear actin and myosin[102] (and nuclear titin) might help to form the nuclear scaffold, control gene positioning and regulate nuclear prestress. The force channelled into the nuclear scaffold might directly affect gene activation within milliseconds of surface deformation. By contrast, it takes seconds for growth factors to alter nuclear functions by eliciting

chemical cascades of signalling, which are mediated by motor-based translocation or chemical diffusion. LINC, linker of nucleoskeleton and cytoskeleton; rRNA, ribosomal RNA.

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