ABSTRACT

Human MYO1C gene encodes three myosin 1c (Myo1c) isoforms which differ only at their N-ends. Interestingly, all three isoforms localize to the nucleus and also to the cytoplasm, where they are anchored to the plasma membrane by the interaction with phosphatidyl inositol-4,5-bisphosphate (PIP2). However, studies reporting functional involvement of these isoforms are inconsistent. While the shortest isoform C (Myo1c-isoC) has been implicated exclusively in the cytoplasmic processes, the longer isoform B (termed the nuclear myosin 1, NM1) has been employed in the nuclear and processes, such as DNA transcription and rRNA maturation. Similarly, the longest isoform A (Myo1c-isoA) exerts its functions in the nucleus solely.

To complete the information on the cellular functions of Myo1c isoforms, we searched for the cytoplasmic functions of NM1 and nuclear functions of Myo1c-isoC. In mouse, only two isoforms (NM1 and Myo1c-isoC) are expressed. We prepared the knock-out mouse (KO) which lacks specifically NM1 while retaining Myo1c-isoC unchanged. Surprisingly, this manifested in no phenotype observed. Since we demonstrated that even Myo1c-isoC acts in the transcription in the similar manner as NM1, it suggests that Myo1c-isoC functionally overlap with NM1 in the nuclear functions.

Besides its localization to the plasma membrane, PIP2 is also present in the nucleus where it modulates transcription and splicing. We found that nuclear PIP2 anchors NM1 and Myo1c into nuclear lipo-protein microdomains. Moreover, only the NM1/Myo1c-isoC-PIP2 complex is transcriptionally active in comparison to NM1/Myo1c-isoC alone.

Our results reveal that both NM1 and Myo1c-isoC are enriched at the plasma membrane. Skin fibroblasts derived from NM1 KO mouse show higher tolerance to hypotonic conditions and increased elasticity of plasma membrane. This observation highlights that NM1 serves as a link between the plasma membrane and cytoskeleton, similarly as Myo1c-isoC.

Myosins require actin filaments as a track along which they slide. However, the form that actin bears in the nucleus remains elusive. After the ectopic expression of β-actin fused to nuclear localization signal, we observed formation of actin bundles in the nucleus. When we check their localization with respect to NM1, we found no overlap. We concluded that actin is able to form filaments in the nucleus; however their generation affects cellular processes such as transcription and mitosis.