Abstract

Nuclear myosin 1 (NM1) was the first myosin described in the cell nucleus. From its discovery, it has been found to function in processes of Pol I and Pol II transcription, chromatin remodeling, and chromosomal movements. However, direct mechanisms of how NM1 works in the cell nucleus were still missing. We therefore decided to prepare NM1 knock-out mice to answer questions about phyiological functioning of this protein. Myo1c is an isoform of NM1 protein, previously described in the cytoplasm. The only difference between these isoforms is 16 amino-acids at the N-terminus of NM1, which were thought to be the nuclear localization signal. However, we discovered that the nuclear localization signal is located in the neck domain of myosin, and therefore it is able to direct both isoforms to the nucleus. Moreover, we found that the ratio between both proteins is nearly the same in the nucleus and deletion of NM1 does not cause compensatory overexpression of Myo1c.

NM1 KO mice are fully viable with minor changes in bone mineral density and red blood cells size. We found that the function of NM1 in processes such as Pol I transcription can be fully covered by Myo1c protein, suggesting redundancy and interchangeability of these two isoforms in the cell nucleus.

We also found that PIP_2, a phosphoinositol lipid known to bind to Myo1c in cytoplasm, works in the nucleus where it contributes to crosslinking early and late steps of Pol I transcription via its interaction with UBF, fibrillarin and NM1. Finally, we found that NM1 is predominantly localized to cytoplasm and plasma membrane, and the localization pattern highly overlaps with Myo1c. Moreover, microarray analysis from NMI KO mice revealed several genes with changed expression most of which were cytoplasmic. This suggests similar roles for nuclear myosin 1 in the cytoplasm as was described for Myosin 1c.

In conclusion, we found that two myosin isoforms are translocated to the nucleus by the same mechanism and can contribute to the same functions. We found that NM1, previously described as nuclear protein, is highly localized to the cytoplasm and plasma membrane where it contributes to similar processes as Myo1c. Finally, we showed that PIP_2, phosphoinositol lipid binding to Myo1c in the cytoplasm is able to bind both isoforms also in the nucleus and contribute to rRNA biogenesis via interaction with UBF and fibrillarin proteins.