# A-to-I RNA editing of Filamin A (FLNA) regulates cellular adhesion, migration and mechanical properties

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A-to-I RNA-editing by ADARs is an abundant epitranscriptomic RNA-modification in metazoa [1]. Flna pre-mRNA in mammals harbors a single conserved A-to-I RNA editing site that introduces a Q-R amino acid change in Ig-repeat 22 of Rod2 domain of the encoded protein [2-4]. Previously, we showed that FLNA editing regulates smooth muscle contraction in the cardiovascular system and cardiac health [5]. The present study investigates how ADAR2-mediated A-to-I RNA editing of Flna affects actin crosslinking, cell mechanics, cellular adhesion and cell migration. Cellular assays and AFM measurements demonstrate that the edited version of FLNA increases cellular stiffness and adhesion but impairs cell migration in both mouse fibroblasts and human tumor cells. In vitro, edited FLNA leads to increased actin crosslinking forming actin gels of higher stress resistance. Our study shows that Flna RNA editing is a novel regulator of cytoskeletal organization, mechanical propertiesy of cells and mechanotransduction.

[1] Nishikura, K. (2010). Functions and regulation of RNA editing by ADAR deaminases. Annu Rev Biochem 79, 321-349.

[2] Nishikura, K. (2016). A-to-I editing of coding and non-coding RNAs by ADARs. Nat Rev Mol Cell Biol 17, 83-96.

[3] Pullirsch, D., and Jantsch, M.F. (2010). Proteome diversification by adenosine to inosine RNA editing. RNA Biol 7, 205-212.

[4] Jain, M., Jantsch, M.F., and Licht, K. (2019). The Editor's I on Disease Development. Trends in Genetics 35, 903-913.

[5] Jain, M., Mann, T.D., Stulic, M., Rao, S.P., Kirsch, A., Pullirsch, D., Strobl, X., Rath, C., Reissig, L., Moreth, K., et al. (2018). RNA editing of Filamin A pre-mRNA regulates vascular contraction and diastolic blood pressure. EMBO J 37.