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A novel isoform of Tensin1 promotes actin filament assembly for efficient erythroblast enucleation

Abstract: Mammalian red blood cells are generated via a terminal erythroid differentiation pathway culminating in cell polarization and enucleation. Actin filament polymerization is critical for enucleation, but the molecular regulatory mechanisms remain poorly understood. We utilized publicly available RNA-seq and proteomics datasets to mine for actin-binding proteins and actin-nucleation factors differentially expressed during human erythroid differentiation and discovered that a focal adhesion protein—Tensin-1—dramatically increases in expression late in differentiation. Remarkably, we found that differentiating human CD34⁺ cells express a novel truncated form of Tensin-1 (eTNS1; M_r ~125 kDa) missing the N-terminal half of the protein, due to an internal mRNA translation start site resulting in a unique exon 1. eTNS1 localized to the cytoplasm during terminal erythroid differentiation, with no apparent membrane association or focal adhesion formation. Knocking out eTNS1 had no effect on assembly of the spectrin membrane skeleton but led to impaired enucleation and absent or mis-localized actin filament foci in enucleating erythroblasts. We conclude that eTNS1 is a novel regulator of actin filament assembly during human erythroid terminal differentiation required for efficient enucleation.

Keywords: Actin Polymerization / Enucleation / Enucleosome / Erythroid Differentiation / Tensin1

Biography: Velia M. Fowler received a B.A. from Oberlin College (1974), Ph.D. from Harvard University (1980), and a Jane Coffin Childs Postdoctoral Fellowship at the NIH and Johns Hopkins University School of Medicine (1980-82). Her research investigates how actin dynamics and myosin contractility provide stability and exert forces to shape membrane curvature, cell & tissue morphology, biomechanics and physiology in red blood cells, eye lens, and striated muscle. She has published >140 articles, chapters and reviews, and mentored >30 graduate students and postdoctoral fellows. She served as Associate Editor for Journal of Biological Chemistry and Program Chair for many international conferences.