IRE1? governs cytoskeleton remodelling and cell migration through a direct interaction with filamin A

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© 2018, The Author(s). Maintenance of endoplasmic reticulum (ER) proteostasis is controlled by a signalling network known as the unfolded protein response (UPR). Here, we identified filamin A as a major binding partner of the ER stress transducer IRE1?. Filamin A is an actin crosslinking factor involved in cytoskeleton remodelling. We show that IRE1? controls actin cytoskeleton dynamics and affects cell migration upstream of filamin A. The regulation of cytoskeleton dynamics by IRE1? is independent of its canonical role as a UPR mediator, serving instead as a scaffold that recruits and regulates filamin A. Targeting IRE1? expression in mice affected normal brain development, generating a phenotype resembling periventricular heterotopia, a disease linked to the loss of function of filamin A. IRE1? also modulated cell movement and cytoskeleton dynamics in fly and zebrafish models. This study unveils an unanticipated biological function of IRE1? in cell migration,
whereby filamin A operat