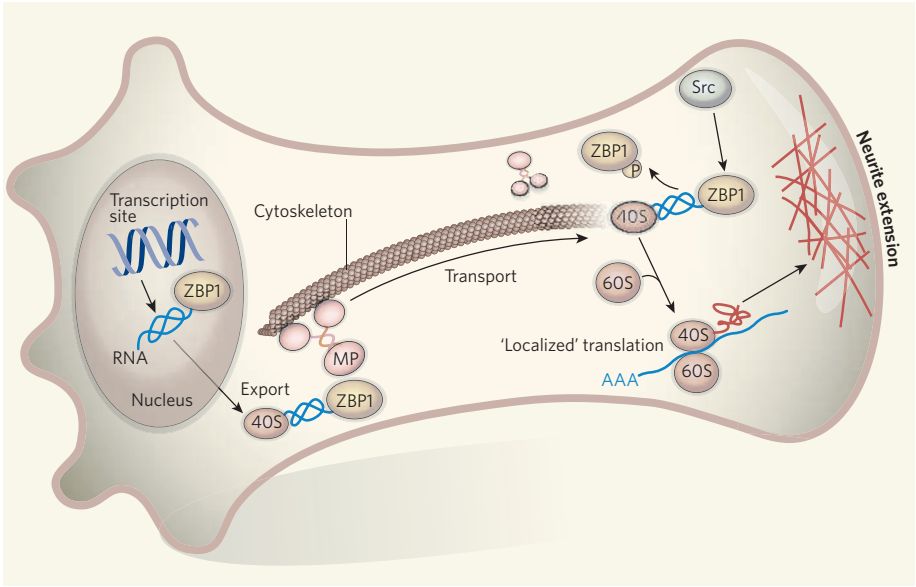


Figure 2 | Regulation of localized β-actin mRNA translation in a polarized neural cell. Hüttelmaier *et al.*[4] propose that the ZBP1 protein controls the transport of β-actin mRNA and its subsequent translation into β-actin protein. ZBP1 associates with the β-actin mRNA in the nucleus and is exported to the cytoplasm. Here, the ZBP1–β-actin RNA complex binds to a motor protein (MP) and is transported along the cytoskeleton, the cell's internal scaffolding, to the periphery. During transport, ZBP1 prevents the mRNA from being translated into protein. When the ZBP1–β-actin RNA complex reaches its destination near the plasma membrane, ZBP1 is phosphorylated (P) by the non-receptor tyrosine kinase Src. This releases the mRNA, allowing the 40S and 60S subunits of the ribosomes to assemble and synthesize β-actin protein (red). The monomeric β-actin protein then assembles into the 'subcortical actin cytoskeleton', which pushes the leading edge onwards.

activity of other RNA-binding proteins[6]. So to investigate whether phosphorylation of ZBP1 modulates its regulatory role in translation, the authors used cells lacking wild-type ZBP1 and introduced into them a mutant ZBP1 that cannot be phosphorylated. This mutant ZBP1 could no longer repress translation of the β-actin mRNA, suggesting that phosphorylation by Src is crucial for translational regulation by ZBP1.

Where does this regulatory step occur? Hüttelmaier *et al.* next used fluorescence imaging to watch ZBP1 and Src in neuroblastoma cells. The two proteins came together only at the base of filopodia and in growth cones — motile, actin-rich structures that lead the way for outgrowing neurites. To obtain evidence that this interaction is functionally significant, the authors examined neurite outgrowth in cells lacking ZBP1. These cells have much shorter projections than usual, but adding ZBP1 back into the cells allowed them to grow normal-looking neurites. Adding the mutant, phosphorylation-incompetent ZBP1 did not produce normal outgrowths, and markedly reduced the amount of newly synthesized actin at the cell's periphery.

This is the first evidence that tyrosine phosphorylation of ZBP1 induces *de novo* synthesis of β-actin in a cellular compartment. It implies that ZBP1 could control a range of cellular processes, including cell migration and the formation of cellular polarity, especially the establishment of neuronal connections. The findings suggest a multi-step model for the regulation of mRNA transport and translation (Fig. 2): in the nucleus, RNAs that will act at specific locations associate with corresponding RNA-binding proteins ('nuclear priming'). Once assembled, these 'transport-competent' RNA–protein complexes are exported into the cytoplasm[7], where they associate with the cytoskeleton (the cell's internal scaffolding) and are transported to the cell's periphery with the help of molecular motors[8]. During their journey, the transcripts are translationally repressed by their protein partners, but on arrival at their destination they under- go a spatially controlled de-repression to initiate translation in specific compartments of a cell.

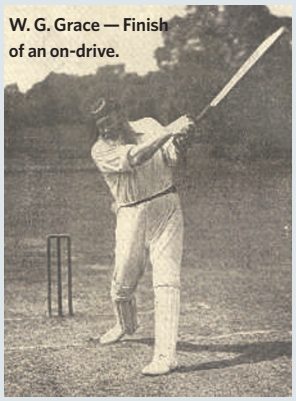
This study generates many interesting questions that now need to be addressed. First, the mechanism of how ZBP1 controls translation is unknown, although the authors present preliminary evidence that unphosphorylated ZBP1 may inhibit the joining of the 40S and 60S subunits of the ribosome (the protein synthesis machinery). Second, it remains to be shown that the phosphorylation of ZBP1 regulates its RNA-binding capacity in an intact cell — there might be additional mechanisms that control ZBP1 function. Third, we do not understand how β-actin mRNA translation is restricted to the leading edge of a fibroblast or to the growth cones of developing neurons, rather than occurring all round the cell's periphery. Is Src kinase localized in a more restrictive manner than generally assumed, or is it spatially regulated? Fourth, how does this

50 YEARS AGO

"Laboratory design" — It was decided to carry out a survey of the use actually made of space and services by scientists working in reasonably well-provided laboratories... Differences in the [bench] lengths used by scientific and experimental officers were small; it was found for these grades that about 12ft. of benching satisfied one man's requirements for 97 per cent of the time... A finding of some interest was that for 57 per cent of a scientist's time and 33 per cent of an assistant's time no bench was in use at all.
From *Nature* 26 November 1955.

100 YEARS AGO

Great Batsmen, their Methods at a Glance. By G. W. Beldam & C. B. Fry; Pp. xiv+716; illustrated by 600 Action photographs. Price 21s. net.



W. G. Grace — Finish of an on-drive.

Each of the many batsmen pictured has been photographed in one or more characteristic attitudes before, during or after the striking of the ball, and after a careful study of every picture, Mr Fry has set down his own interpretation for the guidance of the reader... W. G. Grace, for example, is shown in twenty-six different attitudes, and all have some lesson to tell. In the photograph reproduced we have the finish of an on-drive, in which the turn of the body has aided powerfully in giving full effect to the stroke. The eyes are still looking at the spot where the ball was when it was struck. The whole series of photographs prove that all great batsmen follow the ball with their eye right up to the moment of striking.
From *Nature* 23 November 1905.

50 & 100 YEARS AGO