inhibited only by liposomes containing both glycophorin and PtdIns(4,5)P_2 (Fig. 3*a*–*c*). Furthermore, quantitation of the competition of ^{32}P-protein 4.1 binding to IOVs demonstrated that liposomes must contain both glycophorin and PtdIns(4,5)P_2 before they can compete for protein 4.1 binding with IOVs (Fig. 3*b*, *c*). Liposomes containing glycophorin as well as other phospholipids did not compete with IOVs for protein 4.1 binding. The fact that liposomes containing up to 19 mol% phosphatidylserine (PS) did not compete with IOVs for protein 4.1 binding demonstrates that the association between protein 4.1 and membranes containing PS[28] is of lower affinity than that of the protein 4.1-glycophorin association. Interestingly, liposomes containing glycophorin and both PtdIns(4,5)P_2 and PtdIns(4)P are more effective competitors of protein 4.1 binding to IOVs than liposomes containing glycophorin and PtdIns(4,5)P_2 (Fig. 3*c*). This result suggests that while PtdIns(4)P by itself does not promote glycophorin-protein 4.1 interactions in the membrane, it may have a synergistic effect on the association of protein 4.1 with glycophorin-PtdIns(4,5)P_2.

Thus, the association between protein 4.1 and the glycophorins appears to be regulated by the polyphosphoinositides. While neither glycophorin nor the polyphosphoinositides bind protein 4.1 in the absence of the other, the association of PtdIns(4,5)P_2 with the cytoplasmic domain of glycophorin forms a high-affinity membrane binding site for protein 4.1. The concentration of the polyphosphoinositides in the membrane is maintained by kinases and phosphatases which are specific for each of the *myo*-inositol phosphate monoesters[7,29–31]. The red cell also has a membrane-bound Ca^{2+}-activated phospholipase C which is highly specific for the polyphosphoinositides[32–34]. The concentrations of PtdIns(4,5)P_2 in the red cell membrane decreases when the cellular ATP concentration falls, or when the Ca^{2+} concentration increases; in both conditions the cell membrane undergoes striking physical changes[12,15,32,33]. Many hypotheses have been proposed to account for this correlation[12,15,34,35]; the data presented here provide yet another possible mechanism.

A reduction in the concentration of PtdIns(4,5)P_2 available for binding to the cytoplasmic domain of glycophorin could lead to the release of protein 4.1 from its glycophorin binding site, and hence to its relocation within the cell, possibly binding to band 3 (ref. 11). Indeed, a decrease in the concentration of the polyphosphoinositides as a consequence of metabolic depletion or increased cytoplasmic Ca^{2+}concentration resulted in a dramatic decrease in the ability of stripped IOVs to bind protein 4.1 (our unpublished results).

An exciting implication of this finding is an expansion of the role that the polyphosphoinositides may have in cellular regulation. In most cells the polyphosphoinositides are cleaved by phospholipase C in response to stimulation by extracellular ligands that bind to transmembrane receptors. Cleavage of the polyphosphoinositides results in the release of inositol 1,4,5-trisphosphate and 1,2-diacylglycerol, both of which may act as second messengers[29–31,36–38]. However, an alteration of the membrane levels of the polyphosphoinositides may also affect the interaction of membrane proteins with other proteins or enzymes, possibly modifying their intracellular biological activities. In this manner, the polyphosphoinositides may play a more versatile part as membrane-bound phosphorylated cofactors. So far, the only example of this potential regulatory role is the interaction of protein 4.1 with glycophroin. However, analogues of protein 4.1 are found in most cells[39–46]. In the brain, the protein 4.1 analogue appears to be synapsin I[45], a protein which is associated with synaptic vesicles and may play a part in the release of neural transmitters[47,48]. If synapsin I retains functional as well as structural similarity to protein 4.1, the polyphosphoinositides may also have a key role in the interaction of synapsin I with the synaptic vesicles.

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Erratum

Flow law for ice in polar sheets

W. S. B. Paterson; Reply by C. S. M. Doake & E. W. Wolff

Nature **318**, 82–83 (1985)

AN error in *Nature*'s editorial office led to the use of an uncorrected proof for W. S. B. Paterson's contribution to this Matters Arising item. In line 5, the word 'constant' should read 'parameter'. The first sentence in paragraph 3 should read '(2) At Camp Century, the strain rate measured for $\tau_{xz} = 10$ kPa, where x and z define a regular coordinate system, is less than the observational error[4].' In the address, the postcode should read 'Canada VOP 1HO'.