layers such as dinosaurs can leave important clues about their reproductive behaviour, and there is undoubtedly much more to be learned from these recent finds. But the new data do have implications for previously known material. Two immediate examples spring to mind: abundant and well-preserved nests of the dinosaur *Protoceratops* were discovered[7,8] in the Gobi Desert by the American Asiatic expeditions between 1922 and 1925; and abundant dinosaur eggs attributed to the sauropod *Hypselosaurus* are known from Aix-en-Provence in France. Both these well-known localities could benefit substantially from more detailed studies. □

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Cell biology

Oncogenes and cell control

Matilda Katan and Peter J. Parker

NEW insights into cellular control mechanisms and oncogene function are provided this week by two papers on pages 269 and 272 of this issue[1,2] describing the predicted amino-acid sequences of two apparently unrelated proteins. One report, by Mayer *et al.*[2], examines the nature of the gene in an avian sarcoma virus that confers the ability of this defective retrovirus to transform cells. The companion paper, by Stahl *et al.*[1], describes the cloning of a complementary DNA encoding a phosphatidylinositol-specific phospholipase C. Surprisingly, the predicted sequences of these two polypeptides share regions of homology that are also present in tyrosine kinases, suggesting some conserved functional domains in these apparently diverse proteins.

Mayer *et al.*[2] report the amino-acid sequence of the avian saracoma virus CT10. The single long open reading frame encoded by this defective retrovirus produces a *gag*-fusion polypeptide p47$^{gag-crk}$ of relative molecular mass 47,000, of which

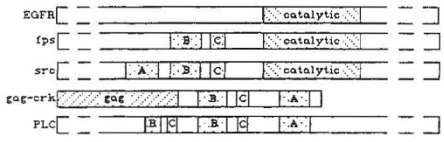

Fig. 1 Location of the A, B and C regions (see text) in: EGF receptor (EGFR); cytoplasmic tyrosine kinases (c-src and c-fps); the CT10-transforming protein p47$^{gag-crk}$ (gag–crk); and PLC-148 (PLC).

232 amino acids are non viral (non-*gag*) in origin. As observed with several other transforming retroviruses, CT10 induces an increase in phosphotyrosine content in infected target cells. In contrast to many of these previously described retroviruses, however, the transforming protein encoded by CT10 is similar to the non-catalytic domain of the cytoplasmic but not receptor members of the family (see ref. 3 for review). Three distinct stretches of amino acids in p47$^{gag-crk}$ seem to be similar to regions of the prototype cytoplasmic tyrosine kinase c-src (see Fig. 1). Similar regions are conserved in other cytoplasmic tyrosine kinases, though the 'A-domain' does not appear in all of these proteins (for example, c-fps; Fig. 1). Indeed, the transposition of A, B, C in c-src for B, C, A in p47$^{gag-crk}$ suggests that these domains could have independent functions (B+C and A). Previous work on tyrosine kinases has shown that one of the conserved non-catalytic domains, termed SH2, has a regulatory role perhaps in directing specific interaction with some cellular component(s)[4]; this SH2 domain encompasses B+C sequences. The intriguing question posed by the data of Mayer *et al.*[2] is how the expression of a regulatory-like domain confers transformation capability. Surprisingly, a clue to the answer comes from the companion paper[1] by Stahl *et al.*, on the sequence of a bovine phosphatidylinositol-specific phospholipase C (PLC-148).

There has been much interest in phospholipase C enzymes specific for inositol-containing phospholipids (PI–PLC) since it was realized that these enzymes mediated production of the second messengers inositol 1,4,5-trisphosphate and diacylglycerol (see ref. 5 for review). From studies of PI–PLC it has become apparent that there are several species of this enzyme, differing in molecular properties and immunologically unrelated[6,7]. Stahl *et al.*[1] describe the first sequence of a mammalian phosphatidylinositol-specific phospholipase C. The predicted amino-acid sequence for this polypeptide derived from complementary DNA cloning reveals that, like p47$^{gag-crk}$, it possesses regions homologous to the A, B and C regions of c-src. Interestingly, like p47$^{gag-crk}$, in PLC-148 these regions are transposed, and in the case of B and C duplicated (see Fig. 1).

It is not clear how these conserved domains fit into the overall structure of PLC-148 since there is as yet no definition of the regulatory and catalytic domains of this enzyme. Nevertheless, the homology itself tends to suggest that this central region of the PLC performs a regulatory function. The implication is that several tyrosine kinases and PLC-148 share some common regulatory mechanism and that expression of p47$^{gag-crk}$ is interfering with or mimicking one, or perhaps both, processes.

The regulation of PI–PLCs has yet to be rigorously defined, and the multiplicity of such activities could infer that, like the tyrosine kinases, there are different means of regulation. It is clear that PI–PLC activity is increased in cells following addition of various agonists, and there is circumstantial evidence that G-proteins are involved in receptor coupling (see ref. 8). Thus, it is tempting to speculate that G-proteins, or perhaps a new class of regulatory molecules, control both PI–PLC and tyrosine kinases (see Fig. 2). Although the simplicity of such a model is appealing, it would not account for the consequences of p47$^{gag-crk}$ expression. As Mayer *et al.* discuss, one interpretation of the effects of p47$^{gag-crk}$ would be that it functions to deplete negative regulatory factors, leading to increased tyrosine kinase activity. Thus a minimal

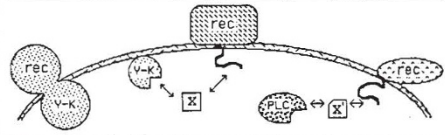

Fig. 2 Model for the regulation of cytoplasmic tyrosine kinase (Y–K) and phosphatidylinositol-specific phospholipase C (PLC). The common regulatory domain in the Y–K and phospholipase C interact with the same class of regulatory proteins (X,X′) linked to receptors (rec). This regulation is distinct from the Y–Ks that are part of the cytoplasmic tail of the receptors and that do not possess this conserved domain (left).

requirement would be to include both positive and negative interactions with these conserved regulatory domains to account for the transforming ability of CT10 (perhaps A and B+C define such separate recognition sites for positive and negative effectors). This would not be such a flight of fancy, as the prototype for G-protein action, receptor-adenylate cyclase coupling, involves both positive (G_s) and negative (G_i) protein effectors (see ref. 9). Whatever the intricacies of these systems, the homology between the tyrosine kinases, p47$^{gag-crk}$ and PI–PLC highlights the need to elucidate the factors or polypeptides that interact with these regulatory proteins. □

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