Transformation by the p21 protein

Sir - Ralph has questioned the validity of certain speculative comments of mine concerning the mechanisms by which p21 proteins transform mammalian cells. He has obviously misunderstood the point of my remarks.

In my article, I drew an analogy between nuclear findings showing loss of GTPase activity in the transforming protein and the fixation of adenylyl cyclase G protein in the GTP state after cholera toxin binding. In case it was not made clear in the article, perhaps I should state that there is no evidence of a functional link between the adenylyl cyclase system and p21 protein, and therefore for a direct role of cyclic AMP regulation in ras-mediated transformation. Examples of some of the known effects of cholera toxin on cell physiology and proliferation were mentioned solely to illustrate the profound consequences which result from fixation of the adenylyl cyclase G-protein in the GTP form. As stated in my article, which (if any) specific effector systems involve p21 protein in signal transduction remains to be established.

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The gyroscope test of relativity

Sir - Your account of the “relativity gyroscope experiment”1 does not go beyond that of Schiff2, who proposed that two effects, the geodetic (de Sitter or spin-orbit) and motional (Lense-Thirring or spin-spin) precessions, could be measured separately by having two gyroscopes free in space. An accuracy of 0.3 milliarcseconds per year is the desired goal. However, there are many other contributions which are well above 0.3 milliarcseconds per year (for a review see ref. 3).

The goal of the experimentalists is to make a sphere of fused quartz accurate to one part in 108, but even a perfect sphere is distorted when set spinning, acquiring a quadrupole moment, which for an altitude of 500 miles, will contribute more than 0.3 milliarcseconds per year to the gyro drift rate if the spin axis is more than 20 minutes of arc away from the orbit plane or the perpendicular to the orbit plane4.

Second, the Earth's quadrupole moment will contribute an amount of 4 milliarcseconds per year, more than ten times the desired accuracy, and, more subtly, distorts the satellite orbit so that, in averaging over a polar orbit, one obtains an additional “indirect contribution” of 1.33 milliarcseconds per year.

Third, the contribution due to the Sun will give rise to a geodetic precession of the gyro (due to interaction of the spin of the gyro with its orbital angular momentum about the Sun), with the relatively large value of 19.2 milliarcseconds per year, while the deflection of light from the reference star (Rigel in Orion) can cause an apparent drift of the gyroscope of up to 1.4 milliarcseconds per year.

The relativity gyro experiment test of general relativity is thus more complex than originally envisaged. Hence, there is a need for other tests of the geodetic and motional precessions, particularly the latter. A promising suggestion in this direction is the proposal of Scully and co-workers5 to use a ring laser interferometer to test both the geodetic and the motional precessions, which has the attraction that it can be carried out on Earth, while another proposal is to use a Foucault pendulum at the South Pole6. Also, the binary pulsar PSR 1913+16 may provide a test of the spin-orbit precession and our calculations predict a precession rate for the pulsar spin axis of 1.23 milliarcseconds per year, based on the data of Taylor and Weiss7.

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Mouse Igk sequence elements in Drosophila

Sir — Two sequence elements may be needed for correct transcription of the mouse immunoglobulin κ gene. They are: (a) the TATGTTTATG motif, an inverted and complementary sequence ATGGAAATN (cd), upstream of the H-chain gene and TGCAATTCCTGTGNNCCAG (pd), the same sequences (8 out of 10 base pairs) ATGGTCAT ATGGCAAT have been found by Paskiewicz et al. independently. Sequences related to the above elements were found upstream of all human and mouse κ and λ variable region genes and within the mouse heavy-chain enhancer. One of which we have called homology of 50-100%. The same elements are present in high homology in chicken ovovitellin gene, sea urchin histone gene cluster and in other genes. This report here that the elements of κ and λ are present upstream of the homocopic gene f2 of Drosophila. The element ATGGCAATAC is found upstream the coding region of f2 (first

nucleotide position -794)3. This has 78% homology with the cd element ATGGAAATN. The sequence ATGGTTTATG is also found upstream of the coding region of fj (first nucleotide -853)4 and shares 78% homology with the cd element ATGGAAATN. Other sequence elements can also be found upstream or within the fj gene with less homology with the cd, cd or pd 59-67%, but this does not seem to be significant since cd, cd or pd can be found in many genes when homology less than 70% is considered (F. G. Falkner and H. G. Zachau, personal communication).

The cd and cd elements are highly conserved among many genes. Their location within the immunoglobulin genes suggests functional relation. The homoeoic gene fj is associated with Drosophila development and contains a highly conserved region, the homoeo box, which has been found in other homoeotic genes - Antp and Ubx of Drosophila as well as in a wide spectrum of animals. The relationship of conserved sequences needed for transcription to upstream sequences needed for segmentation during development is unknown. It is, of course, possible that the homologies might be chance events, and more information is needed before evolutionary or functional relationships are considered.

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FALKNER AND ZACHAU REPLY — We agree that the occurrence of d-related elements upstream of genes deserves attention. We quote some examples for that in our previous paper7 and others in a forthcoming one (F. G. F., E. Neumann and H. G. Z., manuscript in preparation). At this point we would like to mention that a sequence homologous to cd was found upstream of all or most histone H2B genes5, a point which we had missed previously. In general, we searched sequence libraries for cd at the 39% homology level since at lower levels too many sequences are picked up. But also cd (and pd) related sequences with lower homology may be interesting if they can be correlated with putative regulatory elements. One of which we recently encountered is the finding of the cd and cd related sequences in the regulatory regions upstream of catabolite-sensitive genes of Escherichia coli1,4.