Tryptophans in *myb* proteins

SIR—Biedenkapp *et al*[1] suggest that the amino terminus of *myb* proteins represents a novel DNA-binding domain structure as it bears no sequence resemblance to known DNA-binding motifs. We would like to speculate on a specific role for the periodic tryptophans in this domain.

The v-*myb* oncogene of avian myeloblastosis virus is a truncated and mutated version of its c-*myb* proto-oncogene homologue[2], and genes homologous to c-*myb* are found in vertebrates and in the fruitfly *Drosophila melanogaster*[3]. Two regions of the amino-acid sequence of *myb* proteins are highly conserved between vertebrates and *Drosophila* but only the more amino-terminal of the two is present in v-*myb*. This amino-terminal region has DNA-binding activity[2,3] and in c-*myb* proteins consists of three imperfect repeats[4]. The cellular role of the *myb* proteins is unknown but they may be involved in transcriptional regulation.

On examining the conserved 160-amino-acid DNA-binding region of the chicken and *Drosophila* proteins[3], we noticed that all nine tryptophans are conserved, and within each of the three repeats there are 18 or 19 amino acids between the first and second tryptophans and 18 amino acids between the second and third.

Because of truncation, the v-*myb* protein lacks the first and second tryptophans of the first repeat. Deletion analysis of the v-*myb* DNA-binding region suggests that a protein with only the last half of the second repeat plus the third repeat can still bind DNA, but that a protein with only the third repeat loses this property[2]. Perhaps the true functional repeat is out of phase with the sequence repeat.

Further support for the significance of the conserved tryptophans comes from the finding that the regulatory *c1* locus of *Zea mays* (maize) encodes a protein with clear homology to *myb* proteins[5]. The first 114 amino acids of the c1 protein has two repeats similar to the second and third repeats of c-*myb* proteins. Five of the six relevant tryptophans of the c-*myb* proteins are conserved in the c1 repeats with isoleucine replacing the first tryptophan of the third c-*myb* repeat. It may be significant that there is a tryptophan 17 residues after the last tryptophan of the second repeat of c1.

The evolutionary conservation of these abundant, periodic tryptophans strongly suggests that they play an important role in the structure and function of *myb* (and c1) proteins. We speculate that these residues may be involved in either stacking interactions and/or charge transfer interactions.

Thus, *myb* may be the prototype for a new class of DNA-binding proteins. The chicken c-*ets*-1 and c-*ets*-2 genes encode nuclear proteins. In a region highly conserved between the products of these genes and those of the related human *erg* genes there is a conserved triplet of tryptophans in which 17 amino acids separate the first and second tryptophans and 18 amino acids separate the second and third[6]. The degree of divergence in this region is not sufficient for the significance of this triplet to be clear. But the E26 transforming avian retrovirus contains both the v-*myb* and v-*ets* oncogenes.

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Fear of flying

SIR—I would like to draw attention to the possible hazard of the substantial quantity of uranium — more than 1,000 pounds in some cases — carried by many US-built civilian aircraft as counterweights.

Uranium counterweights are used in control surfaces of the aircraft[1], including the rudder and elevators, where space is very limited and very dense material, traditionally tungsten, must be used. The uranium used is 'depleted uranium', which contains only 0.2% of the fission isotope ^{235}U, compared with 0.7% in natural uranium and about 3% in uranium enriched for reactors; ^{238}U, which is not a fission isotope, constitutes the remainder.

Depleted uranium, a by-product of enriching natural uranium for use in reactors, was being sold by the US government, having 300,000 tons of it on hand, for only $2.50 a pound in 1980. Its low price and high density led to its use not only in counterweights but also as ballast, in X-ray shielding and, particularly, as ammunition that will penetrate armour. The civilian use of depleted uranium, however, is not without its hazards. Uranium (depleted or not) is chemically toxic, slightly radioactive and, in certain forms, is classified as a fire hazard[2], because it spontaneously combusts on exposure to air (which is considered as a benefit for its use as ammunition). Environmental problems have arisen from the use of depleted uranium ammunition on military firing ranges[3].

In aircraft, depleted uranium is only a hazard in the event of high-temperature fires that can arise after a crash. Extensive tests by the US Navy and NASA show that temperatures in jet aircraft fuel-pool fires can reach 1,200°C, and that values of 800–1,100°C are common[4]. Such temperatures are high enough to cause very rapid oxidation of depleted uranium[5,6]. Indeed, they are sufficient to produce ignition and complete[7] self-sustained oxidative combustion of 8.5-mm cubes of uranium. For larger pieces, complete combustion is not inevitable; oxidation of 3-kg armour penetrators in burning tests[8] varies from 6 to 47%.

It is the release of airborne and respirable oxide particles from such fires that presents a hazard. The extent of the release depends greatly on such factors as temperature, access to oxygen and wind speed. Largely from the penetrator burning tests, it is known that respirable (3.3-μm diameter or less) oxide particles are released in very variable amounts, with the maximum estimated at 4% of the total oxide[8]. The calculation of inhalation hazard proceeds from the maximum permissible concentration of oxide in the kidney (3 μg per gram), the weight of an adult kidney (300 g) and the fraction of inhaled uranium deposited in the kidney (2.8%). From this I calculate that about 250,000 people, at worst, could be put at risk, from the 1,000 pounds of depleted uranium in a Boeing 747.

Lower basic metal costs and the somewhat easier fabrication of large pieces seem to have been the reason for substituting depleted uranium for tungsten in US aircraft counterweights. But there is some evidence that cost was not a controlling factor. A joint National Research Council/industry report[9], published in 1971 soon after the first 747s entered service, discussed the huge and growing stockpile of depleted uranium, and suggested that its use in aircraft would not constitute much of a safety problem. One wonders whether the decision to use depleted uranium, which was neither controversial nor visible when made nearly 20 years ago, would be made today. While the metal clearly has useful properties, any substantial commercial use would seem to require, at a minimum, that any health hazards be clearly spelled out.

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