Protein evolution

Relationships of filaments

from Margaret Haugh and Brian Anderton

INTERMEDIATE or 10 nm filaments are new additions to the class of fibrous organelle that contains the microtubules and the microfilaments. The intermediate filament (IF) proteins are not highly conserved, unlike the microtubule protein, tubulin, and the microfilament protein, actin, and can be divided into five biochemically and immunologically distinct classes: cytokeratin, desmin, vimentin, glial filaments and neurofilaments[1,2]. X-ray diffraction studies first led to the suggestion that IF proteins are structurally similar to the keratin–myosin–epidermin–fibrinogen (KMEF) group of α-proteins — both are thought to have structures involving extended coiled-coil α-helices[3]. Now, Klaus Weber and Norbert Geisler[4] have found several remarkable similarities in structure between the IF proteins and wool keratin proteins despite their different functions.

The similarity appears to exist at two levels. First, in the gross organization of helical and non-helical domains, for which Weber and Giesler use the term 'motif'; and second, in a 70 per cent sequence homology detected in certain helical segments when they are aligned in the heptade manner. This is a manner of writing and comparing amino acid sequences of α-helices so that every seventh residue which falls on the same side of a cylindrical helix can be easily read and it makes it easy to depict the presence of hydrophobic residues in the appropriate sequential positions.

The motif for the IF proteins and the two wool keratins compared is simply that of a middle helical rod with non-helical head and tail pieces. The middle helical rod may be briefly disrupted by a non-helical segment, but if so the disruption is quite small, not as large as that suggested in an earlier model for IF proteins[5].

Amino acid sequence data are available for three IF proteins: desmin, vimentin and the neurofilament 68,000-molecular weight protein (NF68). Sequence homology is apparent in fragments from the helical-rod section. By using a single tryptophan residue as a reference point for aligning the heptade arrangement, a remarkable sequence homology emerges. A 68-residue fragment from one of the wool keratins has homology of around 60 per cent with similar fragments from chick desmin, NF68 and vimentin. A smaller fragment (17 residues) from the amino terminal of desmin, both wool keratins and glial filament protein shows a homology level close to 70 per cent. The sequence of cDNA for human epidermal keratin has also been elucidated recently and when compared with the partial sequences for other IF proteins a 20–30 per cent homology emerges, suggesting a distant relationship between the proteins[6].

Weber and Giesler also point out, by way of contrast with the above similarities between these α-proteins, that the polypeptides have diverged to a considerable degree. This is seen both in the range of molecular weights found and also in the comparisons of the overall known sequences. One interesting aspect of this divergence is clearly related to known physical properties and, presumably, to function. The head and tail pieces of the wool keratins contain many cysteine residues (the middle helical region contains only a few) whereas in the intracellular IF proteins the head pieces appear to be rich in arginine residues. These features account for the known high level of disulphide cross-links found in the keratin fibres and the weaker salt bridges and electrostatic links thought to stabilize the IFs. It seems plausible that the extracellular keratin would require the stronger covalent disulphide links for its stability whereas in the intracellular environment, which is reducing, disulphide bonding is rare.

It now seems legitimate to include the IF proteins in the α-protein group which could perhaps be collectively called KIFMEF proteins — any other offers from anagram enthusiasts to beat protein KEMIFFS?. □

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Geology

Short ice age 230,000 years ago?

from J.T. Andrews

RECENT evidence for a brief but severe period of glaciation about 230,000 years ago is important for two reasons. First, according to Ruddiman and McIntyre, who have reported it[1], both the glaciation and the deglaciation were surprisingly fast; and second, it provides strong support for the Milankovitch hypothesis according to which Northern Hemisphere glaciation should coincide with insolation minima — periods when the Sun is at its furthest from the Earth.

Published summer insolation curves show that one of the strongest minima of the last 1,000,000 yr occurred 231,000 yr ago when the summer insolation at 80°N was -40 langleys from the AD 1950 value. Insolation reached maximum values of about +30 langleys on either side of the minimum with astronomically calculated dates of about 218,000 and 250,000 yr BP. This extremely sharp minimum occurs, however, within marine isotope stage 7 (refs 2 and 3) which, by-and-large, has been considered a nonglacial period.

The evidence that Ruddiman and McIntyre present is entirely from deep-sea records and they make no attempt to link their proposed event into existing glacial chronologies or stratigraphies. At some point the proposal of intense glaciation about 230,000 yr ago has to be positively associated with glacial events on land. It is important to distinguish between events recorded in the deep sea, that are the product of a globally integrated response to a climatic change, and more localized events. The recognition of a major change in the ^{18}O record at 230,000 yr BP tells us nothing about where the glacial ice was stored.

This problem is both the beauty and the drawback of the deep-sea isotope record. It is essentially a black box that monitors and records several aspects of oceanographical change; it is not a simple measure of ice volume. If, for example, bottom-water cooling occurred in phase with the postulated interval of ice growth, then about 50 per cent of the isotopic signal that might be attributable to global glaciation could be explained by a 2°C cooling of the bottom water. Or, looking at it the other way, the actual amount of ice growth is largely unknown with ± 50 per cent.

Is there some independent index of ice volume that could falsify the suggestion of a rapid increase in global ice around 230,000 yr BP? The terrestrial glacial record is, unfortunately, a poor candidate for such a comparison. Dating methods that would give the required degree of accuracy and precision in this interval are largely lacking[4], nor does there seem to be any immediate prospect of accurately dating glacial and nonglacial sequences in the Hoxnian–Holsteinian interglacial interval.

Possible candidates for verification of the stage 7 glacial event are, however, offered by records of global sea-level fluctuations and high-latitude speleothem growth. Both depend on dating carbonates by the U-series method and involve precision errors of the order of 5–10 per cent. Harmon *et al.*[5] reported U-series dates on speleothems from the Mackenzie Mountains of north-west Arctic Canada that indicate that the major peak in dates occurs at 200,000 yr BP, although there is a single

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