Table 1 Amino acid sequence comparisons

Scotophobin[5]	(NH_2)	YGGQQASKGQQNNDS
Substance P precursor[11]	(88)	YGHGQLSHKRHKTDS
Enkephalins[9]	(NH_2)	YGGF$^{M}_{L}$
β-Lipotropin[12]	(61)	YGGFMTSEKSQTPLV
MSEL-neurophysin[13]	(63)	SGGRCAAFGVCCNDE

Numbers in parentheses give number of residues along polypeptide chain from amino terminal end. "NH_2" indicates amino terminal end. Underlined amino acids indicate sequence similarity to scotophobin.

confusion over the biochemical identity of the transfer factors . . . which most damaged the credibility of the transfer paradigm, but simply the unreliability of the phenomenon"[8].

It is interesting to consider what these experiments might have, and might still contribute to the field of neuroscience. Ungar *et al.*[4,5] appear to have presented early evidence of a peptidergic influence on behaviour, several years before the enkephalins were described[9], but scotophobin is not mentioned in reviews of neuropeptides and is often omitted from descriptions of the history of development of this young field (for examples, see refs 1, 10). It does not appear that the identification and characterization of scotophobin contributed to the surge of interest in neuropeptides. Instead, one might suggest that the failure of the scientific community to accept the paradigm of molecular transfer of memory resulted in the scotophobin molecule being largely ignored.

With the now widely accepted view that certain neuropeptides play important roles as neurotransmitters and as modulators of brain function and behaviour[1,3], it might be worthwhile to consider scotophobin's possible role as a neuropeptide, more generally influencing behaviour as a neurotransmitter or neuromodulator. To that end, it is interesting to compare the amino acid sequence of scotophobin[5] with that of other brain peptides and proteins (Table 1). The pentadecapeptide scotophobin has an amino-terminal peptide triplet that is identical to the enkephalins. Scotophobin also has sequence similarities to the precursor molecule for substance P. There appears to be an evolutionary relationship between substance P precursor and scotophobin, as judged by the stability of the sequence similarity under simulated evolutionary change (Protein Identification Resource program, $P<0.01$).

Thus, scotophobin appears to be related structurally to neuropeptides and their precursors, including polypeptides that play a role in the processing of information concerning pain in the nervous system. In that regard it is interesting to note that the animals in which scotophobin was said to have been induced underwent an extended and stressful training, including footshock. Induction of pain- or stress-related factors might be expected with such treatment.

Despite the uncertainty about the accuracy of scotophobin's structure, it might be worth reconsidering whether scotophobin or a related neuropeptide plays, or can play, a role in the modulation of behaviour in animals.

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Origin of anti-parallelism in β-keratin

SIR—Steinert and Steven[1], in a recent article on intermediate filaments, accepted as likely that the neighbouring pairs of two-chain coiled-coil molecules in the intermediate filaments of α-keratins are anti-parallel, and hence the filaments are non-polar structures. The primary evidence for an anti-parallel organization existing for the α-helices comes from the knowledge that the highly ordered β-crystalline state is derived from α-keratin. The β-chains have been shown to be primarily anti-parallel[2] and hence the α-helices, from which the β-chains were derived, presumably by extension, are also anti-parallel. It should, however, be noted that Menefee[3] obtained in experiments on dipole disordering in fibrous keratins, a very definite net dipole vector for porcupine quill specimens which, on the basis of some elementary assumptions, he concluded gave a value of 38% by volume for unidirectional oriented α-helical protein. In work on β-keratin derived by heating under pressure α-keratin fibres[4,5] in water at 120–130°C, it has been shown that the α-keratin is converted to the β-state with little overall change to length of the keratin fibre.

The conclusion from these data[4,6] was that the β-keratin structure resulted from the conversion of each α-helix into a β-chain folded into a single hairpin. Under these circumstances, the length change from the α-helix to the β-hairpin is about 10% compared with over 120% for the conversion of an α-helix to an extended β-chain. In the hairpin structure, the molecular chains on both sides of the hairpin are automatically anti-parallel.

In the case of β-keratin formation by the extension of an α-keratin fibre, there is little doubt that the β-keratin is formed in the extended state, for fibres extended in water at room temperature. However, to obtain their highly crystalline β-keratin specimens, Fraser *et al.*[7] not only extended their α-keratin structure but also steamed the structure. This treatment, at elevated temperatures, conveys considerable mobility to the molecules. This mobility results not only from temperature activation, but also by the removal of the restriction on the molecular chains of the covalent interchain bonding of the cystine group via the process of sulphydryl disulphide interchange[8]. This increase of mobility produced in steaming of the keratin structure could result in the folding of the elongated β-chains into β-hairpins.

The folding would be favoured by the lower energy state of the anti-parallel β-keratin as against the parallel β-structure[2]. Similar folding has been observed in many long chain polymeric structures at a temperature just below the melting point of the polymer[9]. The possibility of anti-parallel β-chains being formed from parallel α-helices, certainly exists, with considerable physical evidence in its favour. Rather than suggesting[1] for α-keratin fibres that the 'intermediate filaments don't know whether they are coming or going', it may be more appropriate to suggest that we are all in this rather parlous state.

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