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Characterization of κ-Casein and Keratin Domains in Fibrinogen

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Summary. Following the observation of a close sequence homology between the N-terminal moiety of the γ-chain of fibrinogen with large parts of κ-casein, the occurrence of a keratin domain in the middle section of the Aα-chain is suggested.

Key words: Keratin – κ-Casein – Domain – Fibrinogen

Suggestions have recently been made (1) to account for the presence of domains of apparently similar structure and function in different enzymes (11, 14). The evidence from protein structure is consistent with Gilbert's proposal (4) that new protein molecules can be constructed from parts of pre-existing ones and suggests the possibility that the parts, the transcripts of the exonic regions (4), are folded protein units. These hypotheses are especially of interest to those investigating larger proteins which might be made up of "pieces". We encountered such an example in the course of our recent studies devoted to the molecular comparison of the milk- and blood clotting processes (8, 9). Indeed we observed that the γ-chain of human fibrinogen presented a close sequence homology with large parts of cow or

Table 1. Internal homology occurring in the fibrinogen Aα-chain between residues 253 and 368 (3, 6, 7, 12, 13): homology with a cystine-free and glycine-rich segment of keratin (2), identical residues being boxed. The one-letter notation was used for amino acid abbreviations

SCMK-B2A sheep keratin fraction	81												93
	G	G	S	I	G	Y	G	Q	V	G	S	S	G
Aα-chain (internal repeats)	253												264
	G	G	S	T	S	Y	G	–	T	G	S	E	T
	265												277
	E	S	P	R	N	P	S	S	A	G	S	W	N
	278												290
	S	G	G	S	G	P	G	G	T	G	N	R	N
	291												303
	P	G	S	S	G	T	G	G	T	A	T	W	K
	304												316
	P	G	S	S	G	P	G	S	T	G	S	W	N
	317												329
	S	G	S	S	G	T	G	S	T	G	N	Q	N
	330												342
	P	G	S	P	R	P	G	S	T	G	T	W	N
	343												355
	P	G	S	S	E	R	G	S	A	G	H	W	T
	356												368
	S	E	S	S	V	S	G	S	T	G	Q	W	H

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sheep κ-caseins: 80 % of the κ-casein molecule contained in three large segments (one of them being 79 amino acid residues long) is homologous to six large γ-chain segments, in that 31 - 42 % of the positions are occupied by identical amino acid residues (10). Among the κ-casein fragments is included the section which contains the chymosin-sensitive bond and for which a counterpart was characterized in the γ-chain. All homologies between κ-caseins and the γ-chain of fibrinogen are limited to the N-terminal part of the γ-chain: it can thus be considered as a fibrinogen domain homologous to κ-casein. The C-terminal part of the γ-chain (beyond residue 225) contains no more sequences homologous to those of κ-caseins. Furthermore as the γ and Bβ-chains of fibrinogen are very similar (5), it was of interest to note that a limited sequence similarity was also found on comparing the Bβ-chain with κ-casein (8, 10).

In the present note we extended our studies to the human fibrinogen Aα-chain, as its amino acid sequence became available (3, 6, 7, 12, 13) and we suggest the occurrence of a keratin domain in this chain.

The Aα-chain is the largest of the three chains (610 residues) and contains 149 and 199 more amino acids than the Bβ and γ-chains, respectively. Its middle section is particularly rich in glycine residues and Doolittle et al. noted a series of homology repeats (3).

We considered more particularly the section composed of residues 253 - 368: 26% of the 115 residues in this section are glycine. It presents an internal sequence homology: a 13 amino acid long segment is repeated at least nine times (Table 1). This segment is homologous to the unique cystine-free and glycine-rich segment of sheep keratin, high-sulfur fractions SCMK-B2A (residues 81 - 93), SCMK-B2B (residues 71 - 83) and SCMK-B2C (residues 61 - 73) (2): *G G* S I *G* Y *G* Q V *G* S S *G* as indicated in Table 1.

The nine Aα-chain repeats share an average of 33 % identical amino acid residues with the keratin fragment. Out of the 39 Aα-chain residues which are matched by keratin residues, 38 are glycines or serines. In fact, 28 of the 31 glycine residues in the Aα-chain segment occur in those positions where the keratin segment has a glycine residue. We suggest that the middle section of the Aα-chain represents a keratin domain: it might be considered as an insertion between the N- and C-terminal parts of the Aα-chain and explain that this chain is larger than the Bβ and γ-chains.

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