# Studies on Fibrinopeptides from Primates

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Studies on fibrinopeptides from different species have as pointed out in a following article [1] aimed at the elucidation of thrombin specificity and of phylogeny of the fibrinogen molecule. The amino acid sequences of fibrinopeptides A and B from different primates are shown in Figs. 1 and 2. The sequences were obtained by using the Edman degradation technique (Refs. 11—13, 3 in following article [1]). In *Cercopithecus aethiops* two types of B chains have been isolated from the clot supernatant of pooled fibrinogen, one being that shown in Fig. 2 and one being five amino acid residues longer and blocked at the N-terminal end. Amino acid analysis of an acid hydrolysate of the peptide indicates that these additional amino acid residues are $ASP_1$, $GLU_1$, $GLY_2$, $VAL_1$. The amino acid composition indicates that this peptide is at the N-terminal end similar but not identical to the human B-peptide. Furthermore it has the same chain length.

Conclusions: Striking similarities in structure with human fibrinopeptides [2-5] are found. Like in other species investigated [1] positions 1 and 9 in the A peptides of primates are occupied by arginine and phenylalanine, respectively. The C-terminal nonapeptide of the primate A peptide is very similar to the corresponding peptide of especially artiodactyls and some carnivors. The B chain has changed faster than the A chain during primate evolution. Investigations of the amino acid sequence of the fibrinopeptides in primates can well be used in taxonomic and phylogenetic studies. Too few species are at present available to allow any correct phylogenetic interpretation. The findings of different types of B peptides in the *Cercopithecus aethiops* is analogous to the findings in human fibrinopeptides.[2-4] The implications of this heterogeneity in fibrinopeptides have been discussed [3-4] and will be further evolved in forthcoming papers.

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FIBRINOPEPTIDE A

| 16 | 15 | 14 | 13 | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| H- | ALA- | ASP- | SER- | GLY- | GLU- | GLY- | ASP- | PHE- | LEU- | ALA- | GLU- | GLY- | GLY- | GLY- | VAL- | ARG-OH Man |
| H- | ALA- | ASP- | THR- | GLY- | GLU- | GLY- | ASP- | PHE- | LEU- | ALA- | GLU- | GLY- | GLY- | GLY- | VAL- | ARG-OH Green monkey (C.aeth.) |
| H- | ALA- | ASP- | THR- | GLY- | GLU- | GLY- | ASP- | PHE- | LEU- | ALA- | GLU- | GLY- | GLY- | GLY- | VAL- | ARG-OH Macaque (Rh.,Cyn.) |

*Fig. 1.* Human fibrinopeptide A, described earlier,[2,4] is partially recovered with a phosphorylated serine residue (AP-peptide) [2,4] and partially as a peptide being one amino acid residue shorter from the N-terminal end (Y-peptide).[3] Rh. = *Rhesus macaque.* Cyn. = *Cynomolgous macaque.*

FIBRINOPEPTIDE B

| 14 | 13 | 12 | 11 | 10 | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PGLU- | GLY- | VAL- | ASN- | ASP- | ASN- | GLU- | GLU- | GLY- | PHE- | PHE- | SER- | ALA- | ARG-OH Man | |
| | | | | | H- | ASN- | GLU- | GLU- | GLY- | LEU- | PHE- | GLY- | GLY- | ARG-OH Green monkey (C.aeth.) |
| | | | | | H- | ASN- | GLU- | GLU- | SER- | PRO- | PHE- | SER- | GLY- | ARG-OH Macaque (Rh.,Cyn.) |

*Fig. 2.* [GLU = pyroglutamyl residue. The sequence of human fibrinopeptide B has been reported earlier.[4,5]

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## Studies on Fibrinopeptides from Mammals

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As has been shown in previous reports amino acid sequence studies of fibrinopeptides, released from fibrinogen by the action of thrombin, can give information on the specificity of thrombin action and on the phylogeny of the fibrinogen molecule.[1-9] Until now 22 animal species belonging to different orders have been investigated. Isolation of fibrinopeptides was made as described previously.[10,3] Amino acid sequence analysis was done according to Edman.[11-13, *cf.* 3]

Two main types of fibrinopeptides, A and B, are usually found. However, analogs of both A and B peptides can be isolated in smaller amounts. These analogs will be described and discussed in forthcoming papers. In Figs. 1 and 2 the amino acid sequences of fibrinopeptides A and B are shown.

Conclusions: Taken together with the results obtained in primates [14] positions 1, 5, and 9 in the A-peptides have been stationary during mammalian evolution. This indicates that these amino acid residues might be of importance for directing thrombin action. Substantial support to this view comes from the recent finding that only one of the four trypsin susceptible arginyl bonds in the gastrointestinal hormone secretin could be split by thrombin.[15] At position 9 from this arginine residue, was also in secretin a phenylalanine residue located. Position 5 from the arginyl bond was occupied by leucine. It is believed that the narrow specificity of thrombin on fibrinogen is at least partially explained by the location of a phenylalanine residue in a certain space relationship to the thrombin susceptible arginyl bond.

In peptide B only the arginine residue in position 1 is common to all species. This peptide is, at least in all species investigated, cleaved off at a slower rate [16, 10, 17, *cf.* 9] and is probably a result of secondary splitting by thrombin.

It is evident from the results that the data can be used for taxonomy of species and for obtaining phylogenetic data. These points will be discussed in detail in a complete forthcoming paper.

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