Prostate α-Protein

COMPLETE AMINO ACID SEQUENCE OF THE COMPONENT THAT INHIBITS NUCLEAR RETENTION OF THE ANDROGEN-RECEPTOR COMPLEX

(Received for publication, April 16, 1981)

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The amino acid sequence of Component I of α-protein, a glutamic acid-rich protein, is presented. Component I is a single chain polypeptide which consists of 88 amino acid residues with a molecular weight of 10,191. Component I has the amino acid composition Lys5, His, Arg2, Cys3, Asp5, Asn2, Thr5, Ser8, Glu13, Gln3, Pro9, Gly2, Ala6, Val9, Met4, Ile5, Leu4, Tyr1, Phe3, Trp, with serine and asparagine as NH2- and COOH-terminal amino acids, respectively.

Automated sequence analysis of the whole protein, as well as characterization of the peptides obtained from trypsin, chymotrypsin, and staphylococcal protease digestion and cyanogen bromide treatment, led to the elucidation of the complete primary structure of this protein.

Amino acid sequence

NH2-Ser-Gln-Ile-Cys-Glu-Leu-Val-Ala-His-Glu-Thr-Ile-Ser-Phe-Leu-Met-Lys-Ser-Glu-Glu-Leu-

Lys-Lys-Glu-Leu-Glu-Met-Tyr-Asn-Ala-Pro-Pro-Ala-Val-Glu-Glu-Leu-Glu-Met-Arg-

Cys-Val-Asp-Gln-Met-Ser-Asp-Gly-Asp-Arg-Leu-Val-Ala-Glu-Thr-Leu-Val-Tyr-Ile-Phe-Leu-

Glu-Cys-Gly-Val-Lys-Gln-Trp-Val-Glu-Thr-Tyr-Asp-Pro-Glu-Asp-Phe-Tyr-Tyr-Asp-Met-Asn-OH

Amino acid composition: Molecular weight:

Glu13, Gln3, Asp5, Asn2, Lys5, Arg2, His1, Val9, Leu4, Ala6, Ser4, Ile5, Thr3, Gly2, Tyr1, Phe3, Pro9, Trp1, Met4, Cys3

10,191

FIG. 9. Complete amino acid sequence of Component I of α-protein.

α-Protein was first identified as a nonreceptor steroid-binding protein in the rat ventral prostate which could, in vitro, inhibit the association of an androgen-receptor complex with nuclear chromatin (1). The inhibitory effect is not related to the steroid-binding capability of α-protein (2). In the accompanying paper (3), we showed that α-protein has two subunits (A and B), each of which consists of two polypeptide components. Component I in subunit A was identified as the active polypeptide that can interfere with the retention of the androgen-receptor complex by prostate cell nuclei. For a better understanding of the mechanism involved in this inhibition, we have determined the complete amino acid sequence of Component I.

EXPERIMENTAL PROCEDURES AND RESULTS

1 Portions of this paper (including "Experimental Procedures," "Results," Figs. 1-8, and Tables I-VIII) are presented in miniprint at the end of this paper. Miniprint is easily read with the aid of a standard magnifying glass. Full size photocopies are available from the Journal of Biological Chemistry, 9650 Rockville Pike, Bethesda, MD 20814. Request Document No. 81M-899, cite authors, and include a check or money order for $9.20 per set of photocopies. Full size photocopies are also included in the microfilm edition of the Journal that is available from Waverly Press.

2 The abbreviations used in the miniprint are: PTH, phenylthiohydantoin; dansyl, 5-dimethylaminonaphthalene-1-sulfonyl; TLC, thin layer chromatography on polyamide sheet; BC, back conversion of PTH-derivatives with 5.7 N HCl containing 0.1% SnCl2; α-ABA, α-aminobutyrilic acid. The designations of peptides used in the mini-
Amino Acid Sequence of Component I of α-Protein

α-Protein and its Component I were isolated from the ventral prostate of Sprague-Dawley rats by the procedure described in the accompanying paper (3).

The complete amino acid sequence of Component I of α-protein is shown in Fig. 9.

DISCUSSION

In the accompanying paper (3), we presented evidence that the inhibition of chromatin retention of the prostatic androgen-receptor complex by α-protein is due to Component I. Although this component is a glutamic acid-rich polypeptide, the inhibitory activity may not be dependent on the high acidic amino acid content alone, since Component III and subunit B of α-protein, which have acidic amino acid contents similar to that of Component I, are not active.

Most of the glutamic acid and lysine residues in Component I are localized in the N-terminal half, whereas all aspartic acid residues and nearly all of the aromatic acids are in the COOH-terminal half of the protein. Whether these features are important in the inhibition of the chromatin retention of the receptor complex is not clear. It is possible that the inhibitory activity is due to a small oligopeptide stretch in Component I and that it does not require a complex structure.

Although the biological importance of α-protein in the rat ventral prostate is not clear, it is known that this secretory protein can interact with several cellular components, such as cholesterol, androgens, and polyamines, which can play major roles in prostate growth. A thorough knowledge of the molecular assembly of α-protein may provide a better understanding of these protein-ligand interactions and of the mechanism by which this complex protein is synthesized and secreted.

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Amino Acid Sequence of Component I of α-Protein

Table 8

| Cycle | H | T | V |
|-------|---|---|---|
| 1     | 150 | 18 | 84 |
| 2     | 108 | 17 | 83 |
| 3     | 72  | 16 | 82 |
| 4     | 48  | 13 | 80 |
| 5     | 20  | 12 | 79 |
| 6     | 12  | 11 | 78 |
| 7     | 8   | 10 | 77 |
| 8     | 6   | 9  | 76 |
| 9     | 5   | 8  | 75 |
| 10    | 4   | 7  | 74 |

*Data are taken from a previous publication.*
Amino Acid Sequence of Component I of a Protein
Prostate alpha-protein. Complete amino acid sequence of the component that inhibits nuclear retention of the androgen-receptor complex.
S Liao, C Chen and I Y Huang

J. Biol. Chem. 1982, 257:122-125.

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