BIOCHEMICAL JOURNAL LETTERS

Antigenic sites of the nicotinic acetylcholine receptor

The antigenic structure of the nicotinic acetylcholine receptor (nAChR) is of major importance as the receptor represents the target autoantigen in the human neuromuscular disease, myasthenia gravis (reviewed by Vincent, 1980). On immunization of experimental animals with the purified nAChR, the majority of antibodies in polyclonal antisera and of monoclonal antibodies are directed against a relatively small site, the major immunogenic region (Tzartos & Lindstrom, 1980; Tzartos *et al.*, 1981), carried on the α chain of the receptor. A similar response to the major immunogenic region is seen in myasthenic patients (Tzartos *et al.*, 1982). Following the determination of the sequence of the α chain from cDNA data, Noda *et al.* (1982, 1983a,b) suggested that, based on the hydrophilicity profile, residues 161–166 might represent an antigenic site, if not the major immunogenic region.

McCormick *et al.* (1985) have recently reported that the peptide 159–169, although not the major immunogenic region, is recognized by antibodies to native nAChR and thus does represent an antigenic site which is readily accessible on soluble native nAChR. This conclusion is based on data showing that antibodies raised against nAChR which has not been deliberately denatured bind, to a certain extent, to the immobilized peptide. As pointed out by the authors, this would appear to conflict with our own experimental results using peptide 151–169 (Juillerat *et al.*, 1984) in which no binding to the peptide of antibodies to native nAChR was observed. Moreover, it is in direct contradiction to the later results of Lindstrom *et al.* (1984) who found no binding of the identical peptide 159–169 to antibodies to native nAChR. McCormick *et al.* (1985) suggest that the apparent discrepancy with our own results might be explained by steric effects using the longer peptide and do not mention the results of Lindstrom's group, which were published 6 weeks before the note was added in proof to McCormick *et al.* (1985).

We wish to point out that their results simply show that antibodies in the sera of animals immunized with 'native' nAChR bind to the peptide. This does not discount the possibility of a certain amount of denaturation of the receptor either during purification or immunization. As shown in our original paper, antibodies to denatured nAChR do bind to peptide 151–169. Conversely, antibodies to this peptide bind only to a form of the nAChR which can no longer bind the specific ligand, α -toxin, and is therefore presumably denatured. While not being able to exclude completely the possibility that peptide 159–169 might be exposed on the native receptor,

we would suggest that it is premature to come to this conclusion without a clear demonstration that either the anti-'native nAChR' antibodies which bind to the peptide, or antibodies raised against the peptide, can recognise truly native nAChR, either as a receptor-toxin complex or in the membrane.

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Received 19 March 1985

Antigenicity of synthetic peptides 159–169 and 151–169 of *Torpedo* acetylcholine receptor α chain

We demonstrated that a synthetic peptide corresponding to residues 159–169 (Ser-Pro-Glu-Ser-Asp-Arg-Pro-Asp-Leu-Ser-Thr) of the α -chain of *Torpedo* acetylcholine receptor (AChR) contained an antigenic site that in solubilized native AChR was readily accessible to antibodies (McCormick *et al.*, 1985a,b). This was demonstrated in a sensitive solid-phase radiobinding