

# NATURAL ANTITISSUE PRECIPITINS OF MOUSE SERUM AS POSSIBLE AUTOANTIBODIES OF A SPECIAL TYPE

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The serum of intact mice contains precipitins reacting with autologous, isologous, and homologous liver extracts. The reaction is immunologic in character, although in their electrophoretic properties the precipitins behave as albumins and  $\alpha$ -globulins.

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The object of this investigation was to continue the study of the autologous precipitation reaction of serum with mouse tissue extracts [5] in order to determine the nature of the phenomenon and its possible physiological role.

## EXPERIMENTAL METHOD

Experiments were carried out on adult mice of lines C<sub>3</sub>HA, C<sub>3</sub>H, and BALB/C and noninbred mice, of both sexes. Sera and liver extracts obtained from individual mice or from groups of 5-10 animals, and prepared as described in [5], were tested by a micromodification of Ouchterlony's precipitation reaction [2] and by immunoelectrophoresis [7]. Ten preparations of sera and liver extracts were tested from mice of each line and from noninbred mice. Some extracts were treated with trypsin [6].

## EXPERIMENTAL RESULTS

All the sera behaved indently in Ouchterlony's reaction with autologous, isologous, and homologous native liver extracts, forming one (or rarely two) precipitation lines after 24-48 h. Extracts with a protein concentration of 2.3% gave a positive reaction with serum in tests when one central well with antigen was surrounded by six wells with serum. If the ratio between these reagents was the opposite one (extract: serum=6:1), no reaction was observed. Extracts concentrated to 8% gave a positive reaction with an antigen: serum ratio of 6:1, but in a higher concentration and under the same experimental conditions they no longer reacted with the serum. A negative result was obtained in reactions between extracts in a concentration of 8% and sera concentrated 3 times. The precipitation reaction between liver extract and serum thus took place only when the reagents were present in a certain ratio; if an excess of one reagent was present the reaction was inhibited. Evidently two types of precipitinogens are present in liver extracts: the content of one type is relatively low, while that of the other is higher. Extracts to which a particular quantity of serum was added preliminarily formed a more intensive precipitation line than usually in Ouchterlony's reaction with serum. This phenomenon cannot be explained by simple exhaustion of an excess of precipitinogens in the extracts by the action of serum precipitins. It may be that under these circumstances the precipitating activity of the liver proteins is increased. An increase in antigenicity of proteins when they are bound with antibodies in a certain ratio has been described in the literature [8, 9].

Liver extracts treated with trypsin constantly formed two or three precipitation lines with serum in Ouchterlony's reaction, set up in a manner in which native extract usually did not react with the serum. Under the action of trypsin, new and hitherto latent antigenic determinants capable of reacting with the serum precipitins were evidently set free in the liver proteins.

In the immunoelectrophoresis test, native liver extracts formed one line, and trypsinized extracts two parallel precipitation lines, located in the zone of albumins and  $\alpha$ -globulins. The liver extracts thus reacted with serum proteins belonging to the anode fractions, of which they evidently formed only a part.

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During electrophoresis of native liver extracts, these reacted with serum to form one continuous precipitation line located mainly in the zone of anode protein fractions and partly in the zone of rapid cathode protein fractions. Participation of identically charged proteins in the precipitation reaction between sera and liver extracts indicates that this reaction is not due to electrostatic forces but is probably immunologic in nature. Heating the serum on a water bath at 65° for 30 min inactivates it, although at 56° it does not lose its precipitating power [5]. This rules out the participation of substances of complement type in the reaction.

Hence, the natural precipitins of mouse serum possess a number of properties of antibodies in general, although they are not immune globulins. These precipitins may perhaps be autoantibodies, the mechanism of formation of which differs from immunization [1, 3, 4]. The ability of natural antitissue precipitins of the serum to combine with tissue proteins and their breakdown products may play a role in protein metabolism and in the maintenance of "immunologic homeostasis" in the body.

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