Biochemistry

Volume 11, Number 18 August 29, 1972

Recommendations for the Nomenclature of Human Immunoglobulins

The following is a document prepared by a Subcommittee[1] for Human Immunoglobulins of the IUIS Nomenclature Committee, and reproduced by permission of its chairman.[2]

Preamble

The final draft was developed after receiving additional suggestions from colleagues who had assisted in reaching agreement on the earlier nomenclatures published in 1964 and 1969. The report of the Subcommittee has been reviewed and approved by the Nomenclature Committee of the IUIS.

Terminology for Immunoglobulin Molecules

Following a proposal made in 1964,[1] two symbols (Ig and γ) have been used interchangeably to designate human or animal immunoglobulins. Although it was pointed out that Ig is a logical symbol for immunoglobulins, the symbol γ was retained as an acceptable substitute, mainly in view of the tradition that had long associated it with the immunoglobulins.

In recent years there has been a trend among editors and authors to give increasing preference to the symbol Ig. A major reason for dissatisfaction with the existing dual terminology, Ig and γ, is that the symbol γ is also employed to designate the heavy polypeptide chains of a particular class of immunoglobulins.

It is therefore proposed to discontinue the use of the symbol γ for the term immunoglobulin and to apply γ to designate exclusively the heavy chains of immunoglobulin G (IgG). Symbols such γG1, γD, etc., should be replaced by IgG1, IgD, etc. The term γ-globulins should not be used as a synonym for immunoglobulins.

Use of the Symbols L and K

The symbol L is now being used in two senses, firstly as an abbreviation for light chains and secondly to designate that type of immunoglobulin molecules whose light chains are of the lambda variety. The intrinsic defect in this terminology becomes apparent in expressions such as "L chains of the L type" as opposed to "L chains of the K type."

It is therefore proposed to restrict the use of the symbol L to the designation of light chains as opposed to the symbol H for heavy chains and to discard the use of the symbol K. The terms kappa type and lambda type should be used to indicate the type of whole molecules or isolated light chains formerly described as belonging to the K type and L type, respectively.

This amendment to the terminology proposed in 1964 also makes it necessary to discontinue the use of symbols such as IgGK or IgML, etc., which should be discarded in favor of notations such as IgG(κ), IgM(λ), etc.

Use of the Terms Classes, Subclasses, Types, Subtypes, Groups, and Subgroups

The previous proposals[3,4] for the use of the terms classes, subclasses, types, and subtypes are retained. Specifically, these terms may be applied both to the entire molecule and to its chains.

The terms type and subtype designate variants of nonallotypic nature defined by characteristics of the constant (C_L) regions of light chains. The terms class and subclass designate variants of nonallotypic nature defined by characteristics of the constant (C_H) regions of heavy chains.

All variable regions associated with κ chains, λ chains, or H

[1] Composition of the Subcommittee: Dr. J. D. Capra (Mount Sinai School of Medicine, New York, N. Y. 10029, U. S. A.), Dr. M. O. Dayhoff (National Biomedical Research Foundation, Georgetown University Medical Center, Washington, D. C. 20007, U. S. A.), Dr. H. H. Fudenberg (University of California Medical Center, San Francisco, Calif. 94122, U. S. A.), Dr. J. F. Heremans (University of Louvain, B-1200 Brussels, Belgium), Dr. N. Hilschmann (Max-Planck-Institut, D-3400 Göttingen, Federal Republic of Germany), Dr. L. E. Hood (California Institute of Technology, Pasadena, Calif. 91109, U. S. A.), Dr. C. Milstein (University Postgraduate Medical School, Cambridge, CB2 2QH, England), Dr. E. Osserman (Columbia University, College of Physicians and Surgeons, New York, N. Y. 10032, U. S. A.), Dr. F. W. Putnam [chairman] (Indiana University, Bloomington, Ind. 47401, U. S. A.), Dr. D. S. Rowe (WHO International Reference Centre for Immunoglobulins, Institute of Biochemistry, CH-1005 Lausanne, Switzerland), Dr. A. Solomon (University of Tennessee Memorial Research Center and Hospital, Knoxville, Tenn. 37920, U. S. A.), Dr. W. D. Terry (National Institutes of Health, Bethesda, Md. 20014, U. S. A.), Dr. G. Torrigiani (Immunology Unit, World Health Organization, CH-1211 Geneva 27, Switzerland).

[2] Reprints may be obtained from Dr. Waldo E. Cohn, Office of Biochemical Nomenclature, Biology Division, Oak Ridge National Laboratory, Post Office Box Y, Oak Ridge, Tennessee 37830.

[3] *Bull. W. H. O. 30*, 447 (1964).

[4] *Bull. W. H. O. 41*, 975 (1969).

chains should be defined as forming a group. Three such groups, to be called the V_κ group, the V_λ group, and the V_H group, have so far been characterized. The variable regions from the V_κ group and the V_λ group appear to be associated exclusively with constant regions from, respectively, κ-type and λ-type light chains. In contrast, the variable regions from the V_H group seem to occur in association with the constant regions from any of the heavy chain classes.

Within a group of variable regions it is possible to distinguish a number of subgroups. It is now clear that the nomenclature earlier proposed for subgroups[4] needs revision. Criteria for the differentiation of subgroups are being developed and will form the basis for future recommendations. Current information can be obtained from Dr. F. Putnam, Chairman of the Subcommittee on Human Immunoglobulins of the International Union of Immunological Societies.

Similarly to the proposal for the terms class and subclass, type and subtype, the terms group and subgroup may also be used to characterize the variable region of the immunoglobulin molecule.

Conformational Change(s) Induced in Sheep Calcium-Dependent Antibody upon Interaction with Homologous Polypeptide Antigen. I. Hydrogen-Exchange Studies of Immunoglobulin G and $(Fab')_2$ Fragment†

Paul A. Liberti,* William A. Stylos, and Paul H. Maurer

ABSTRACT: Hydrogen-exchange studies have been done on highly purified calcium-dependent sheep anti-poly($Glu^{60}Ala^{30}$-Tyr^{10}) and its $(Fab')_2$ fragment accompanying reaction with homologous antigen. These studies were performed on antigen–antibody soluble complexes formed in antigen excess. Levels of antigen varied from 2.4 to 10.5 times that required for maximum precipitation. At antigen levels greater than 3.5, there are 52–54 hydrogens/molecule of both antibody and $(Fab')_2$ fragment which do not exchange when these molecules react. It is believed that these hydrogens are from antibody combining site residues (27/site), and are prevented from exchange by interaction with antigen. This value exhibits some concentration dependence. At lower levels of antigen excess, two changes occur for both molecules which are (1) the number of hydrogens blocked decreases to about 40 hydrogens/molecule and (2) hydrogens which normally exchange very slowly in unreacted antibody experience an accelerated exchange. At the lowest levels of antigen studied, about 27 antibody hydrogens are released. Based on the extent of tritiation of the samples it is likely that a greater number may be involved.

From the absence of the release phenomenon in studies with Fab (Liberti *et al.*, 1972), it is likely that these hydrogens (which exchange slowly in unreacted antibody) are involved in significant structural changes near or at the hinge region of IgG and $(Fab')_2$ fragment. Because the release depends on antigen:antibody ratios it is suggested that conformational changes are induced in both IgG and $(Fab')_2$ by virtue of stresses imposed on them *via* the formation of large complexes. The probable relationship of this phenomenon with the Y-shaped model of antibody and the opening of the combining site–hinge region–combining site angle upon complex formation is discussed.

The biological significance of this phenomenon is unclear at this time since in at least two species (rabbit and guinea pig) considerable complement fixing ability has recently been demonstrated for $(Fab')_2$ fragment compared with intact antibody. The possibility that these changes are related to alterations at the complement binding site is considered.

One of the fundamental unresolved problems of immunochemistry is an understanding of the physical relation between primary union of antibody with antigen and various *in vitro* and *in vivo* sequelae such as complement fixation and passive cutaneous anaphylaxis. Additionally, there is considerable new interest in the existence of such a relationship because of recent findings of "antibody-like" receptors on immunocompetent cells (Mitchison, 1969). Currently, it is thought that antigen binding by cell receptors may result in some physical change(s) in the receptor which then triggers the cell to undergo other activities involved in antibody synthesis (Siskind and Benacerraf, 1969; Ada, 1970).

Based on accumulated data it is generally held that the 7S immunoglobulin molecule is "Y" shaped, the arms and base corresponding to the two Fab and Fc segments, respectively (Noelken *et al.*, 1965; Feinstein and Rowe, 1965; Valantine and Green, 1967; Cathou and O'Konski, 1970). Further, there is evidence from electron microscopy studies (Feinstein and Rowe, 1965) that interaction of antibody with antigen results in an increase in the angle between the arms of the "Y," *i.e.*, combining site–hinge region–combining site angle (cs–hr–cs angle). It has been suggested that this change possibly exposes a critical disulfide bond or the complement binding site (Edelman, 1970). Attempts to demonstrate such changes in gross conformation of the antibody molecule in solution as measured by a variety of techniques have been unsuccessful

† From the Department of Biochemistry, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania 19107. *Received February 22, 1972.* This work was supported by National Institutes of Health Grant T1A1334 and A107825 and also in part by Public Health Service General Research Support Grant RR-5414.