Terminology/Terminologie

Nomenclature for synthetic peptides representative of immunoglobulin chain sequences*

WHO–IUIS Nomenclature Sub-Committee[1]

The source (species of origin), type, and subgroup (where applicable) of the immunoglobulin chain are indicated prior to the numbers of the first and last amino acid residues comprising the synthesized sequence (stated in parentheses), e g., human γ_1 (289–298) or rat ε (143–147).

Square brackets indicate that the peptide is an analogue; substituted amino acids are identified by the three-letter code; superscripted numbers indicating the residue at which the substitution, removal or addition occurs Further substitutions are specified within round brackets For example, human γ_1 (289–298) [D-Thr^{298}] and human γ_1 (289–298) [Asn (CHO)^{297}].

Background

Current interest in immunologically active peptides is by no means confined to analogues of thymic hormones or complement components; nor to those short-chain peptides which have been shown to possess granulocyte chemotactic activity. In recent years, there has been growing interest in the application of protein synthesis as an alternative strategy to proteolytic and chemical fragmentation in the location and characterization of immunoglobulins (as discussed, for instance, by Stanworth (*16*)). Furthermore, this is leading, in many cases, to the development of potentially therapeutic peptides with important immunomodulatory properties The forerunner of these developments was the synthesis of tuftsin (Thr-Lys-Pro-Arg), representative of a tetrapeptide sequence within the C_H2 domains of human IgG (*13*), which was shown to possess phagocytosis-stimulating activity.

Since then, short-chain linear peptides with sequences representative of other putative immunoglobulin Fc effector sites have been synthesized and studied; for instance, peptides capable of inhibiting the binding by IgG of C1q (*1,10*), the binding of IgG to Fc receptors on monocytes and macrophages (*3, 14*), and the action of IgG antibody in ADCC (antibody-dependent cellular cytotoxicity) (*5*) and NK (natural killer cell) activity (*6*).

The synthetic peptide approach has also been exploited extensively in attempts to identify both mast cell Fc receptor-binding sites (*7,17*) and trigger sites (*16, 17*). More recently, antibodies raised against peptides have been used as IgE structural probes (e.g., Burt et al. (*2*)); and immunoglobulin peptides produced by DNA recombinant technology have been employed in similar types of investigation (e.g., Helm et al. (*8*), Duncan & Winter (*4*)). Furthermore, synthetic peptides representative of both C_H2 and C_H3 domain sequences within human IgG have been shown to provide a direct activating signal to resting human B lymphocytes and to enhance antibody production *in vitro* and *in vivo* (*15*), as well as to induce immunoglobulin synthesis by murine B cells (*9, 12*).

It is against this background that it is considered timely to establish a nomenclature for synthetic peptides representative of imunoglobulin heavy and light chain sequences that is acceptable to investigators working in this field and which will facilitate communication and discussion. In the preparation of the following peptide nomenclature proposals, it was considered most important (in view of the tendency

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of different laboratories to use a different immunoglobulin amino acid numbering system) to refer to a standard source for information about the detailed primary structures of immunoglobulin polypeptide chains; it is suggested that this source should be *Sequences of proteins of immunological interest* edited by Elvin A. Kabat and colleagues. The 4th edition was published by the U.S. Elvin A. Kabat and colleagues. The 4th edition was published by the U.S. Department of Health and Human Services in 1987.

Nomenclature for synthetic peptides

Human immunoglobulin heavy or light chain sequences

Where a peptide has been assigned a name, e.g., tuftsin (comprising residues 289–301 of the human γ_1 chain) or rigin (comprising residues 345–349 of the same chain), it would be expected that it would be referred to in this way in the rest of an article. Otherwise, it is suggested that a nomenclature be adopted which is consistent with that applied to other types of peptide, e.g., hormones. Thus, the source, type and subgroup (where applicable) of the immunoglobulin chain will be indicated prior to the numbers of the first and last amino acid residues comprising the synthesized sequence (stated in parentheses), e.g., human γ_1 (289–298), rat ε (143–147), and human $K_{\parallel}$[pGlú-6].

It will be important to indicate the species of origin and the subclass of heavy chain; but it should not be necessary to specify the domain, provided that the complete numbered sequence of the chain in question has been reported in the literature (to which reference would presumably be made in any publication in which the peptide is referred to). If this is not the case, it will be necessary to specify the full primary sequence of the synthesized peptide, preferably using the three letter code (unless lack of space dictates otherwise). Indeed, at an appropriate position in any publication (e.g., as a table or footnote), it would be expected to provide the full peptide sequences alongside the nomenclatures which have been assigned to them.

It is customary now to specify the numbers of the amino acids comprising the synthesized sequence on the line and in parentheses; rather than below, as a subscript (as was the practice in referring to peptide hormones, etc. in the past).

Analogues

It is important to specify when synthetic peptides are *derivatives* of sequences contained within the native immunoglobulin polypeptide chain structure. Thus the use of [ ] indicates that the peptide referred to is an *analogue*; and the substitutions or modifications in the analogue are indicated as to type (the amino acid identified by three-letter code). The use of ( ) within the square brackets specifies further substitution; whilst superscripted number(s) indicate the residue at which the substitution, removal or addition occurs. Obviously, where there have been several substitutions (or derivatizations) of particular residues in the parent peptide it will not be feasible to give anything but the full modified sequence. But, where such changes have been minimal, an abbreviated nomenclature would be useful. Examples of these are:

human γ_1 (289–298) [D-Thr^{298}]
human γ_1 (289–298) [Asn^{297}]
human γ_1 (289–298) [Gly $(NH_2)^{298}$]
human γ_1 (289–298) [Glu^{293}, Lys^{297}]
human γ_1 (289–298) [Asn(CHO)^{297}].

As indicated in the third example above, and in one of the examples given in the previous section, it is necessary to indicate whether the COOH-terminal carboxyl or the NH_2-terminal α-amino group has been derivatized.

Allotypic differences can be identified in the same manner as substitutions, provided that the reference sequence is understood or there is agreement as to the original form. For example:

human γ_3 (289–298) [Thr^{296}]—referring to the G3m(g) allotype
human γ_1 (289–298) [Phe^{296}]—referring to the nG3m(g) allotype.

Proteolytic and chemical cleavage fragments

It is assumed that the currently accepted nomenclature referring to cleavage fragments of immunoglobulins (for example, Fc, Fab, Fc', F(ab')$_2$, Facb, pFc', tFc', TLmFc, etc.) will continue to be used, in which case it is suggested that such products are referred to as *fragments* rather than as peptides, as has sometimes been the practice (e.g., Morgan et al. (*11*)).

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