

On the Pentapeptide as the Measurement Unit in Immunology

Darja Kanduc¹ 

¹Department of Biosciences, Biotechnologies, and Biopharmaceutics, University of Bari, Bari, Italy

Glob Med Genet 2024;11:34–35.

Address for correspondence Darja Kanduc, PhD, Department of Biosciences, Biotechnologies, and Biopharmaceutics, University of Bari, Bari 70126, Italy (e-mail: dkanduc@gmail.com).

Abstract

Keywords

- epitope dimensions
- pentapeptides
- vaccines

This communication concerns a crucial query in immunology, that is, the dimension of an epitope. The issue has essential implications in vaccine formulations.

Introduction

The contact surface between the membrane-bound B cell receptor and an antigenic epitope is made up of five amino acid (aa) residues. It is a pentapeptide.

This notion was defined with mathematical precision in 1939, when Landsteiner and van der Scheer¹ demonstrated by inhibition reactions that pentapeptides serve as specific immune determinants in the generation of specific antibodies. Those studies are a fundamental step in immunology. Indeed, as Landsteiner stated: “one cannot safely offer an opinion concerning the specific groups of proteins (‘determinants’) as long as it is not known what the size of such a determinant can be.”²

Then, analysis of the binding energy in antigen–antibody complexes, site-directed mutagenesis, and epitope mapping experiments definitively validated the pentapeptide as a minimal antigenic determinant.^{3–7}

Moreover, in the early 2000s, Salunke’s lab “photographed” the interaction of 2D10 single-chain variable fragment with the dodecapeptide DVFYPPYASGS (► **Fig. 1**, <https://doi.org/10.2210/pdb4H0H/pdb>). It can be seen that the interaction involves the five residues numbered 4 to 8 along the black line and corresponding to the sequence YPPY (see inset in ► **Fig. 1**).

However, in spite of such incontrovertible data, current immunology reports aa sequences of whatsoever length as epitopes. One example is the sequence AAGKATTEEQKLIEDINVGFKAAVAAAASVPAA, 33 aa long, which is cataloged as

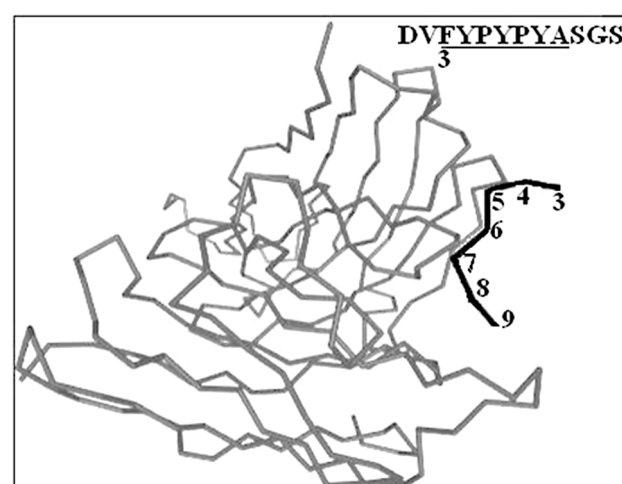


Fig. 1 Crystal structure of mimicry-recognizing 2D10 scFv (gray line) with peptide DVFYPPYASGS (black line). (Source: www.rcsb.org/3d-view/4H0H/1; authors: Tapryal S, Gaur V, Kaur KJ, Salunke DM. DOI: 10.2210/pdb4H0H/pdb.)

an epitope in the Immune Epitope Database (<https://www.iedb.org/>) with the IEDB ID 160.

Conclusion

This communication is of relevant importance for defining safe and effective vaccine formulations. Indeed, only

DOI <https://doi.org/10.1055/s-0044-1779041>.
ISSN 2699-9404.

© 2024. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution License, permitting unrestricted use, distribution, and reproduction so long as the original work is properly cited. (<https://creativecommons.org/licenses/by/4.0/>)

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

pentapeptide-based vaccines can elicit specific antibodies capable of reacting with the full-length antigen without the risk of cross-reactivity and adverse events.^{8,9}

Conflict of Interest

None declared.

References

- 1 Landsteiner K, van der Scheer J. On the serological specificity of peptides. III. *J Exp Med* 1939;69(05):705–719
- 2 Landsteiner K. *The Specificity of Serological Reactions*. New York: Dover Publications, Inc.; 1962:58
- 3 Heymer B, Bernstein D, Schleifer KH, Krause RM. A radioactive hapten-binding assay for measuring antibodies to the pentapeptide determinant of peptidoglycan. *J Immunol* 1975;114(04):1191–1196
- 4 Van Oss CJ. Nature of specific ligand-receptor bonds, in particular the antigen-antibody bond. In: van Oss CJ, van Regenmortel MHV, eds. *Immunochemistry*. New York: Marcel Dekker; 1994:581–614
- 5 van Oss CJ. Antigen-antibody reactions. In: van Regenmortel MHV, ed. *Structure of Antigens*. Boca Raton: CRC Press; 1992:99–126
- 6 Kanduc D. Immunogenicity in peptide-immunotherapy: from self/nonself to similar/dissimilar sequences. *Adv Exp Med Biol* 2008;640:198–207
- 7 Kanduc D. Homology, similarity, and identity in peptide epitope immunodefinition. *J Pept Sci* 2012;18(08):487–494
- 8 Kanduc D. Hydrophobicity and the physico-chemical basis of immunotolerance. *Pathobiology* 2020;87(04):268–276
- 9 Kanduc D. The role of proteomics in defining autoimmunity. *Expert Rev Proteomics* 2021;18(03):177–184