

# On the Pentapeptide as the Measurement Unit in Immunology

Darja Kanduc<sup>1</sup> 

<sup>1</sup>Department of Biosciences, Biotechnologies, and Biopharmaceutics, University of Bari, Bari, Italy

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**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

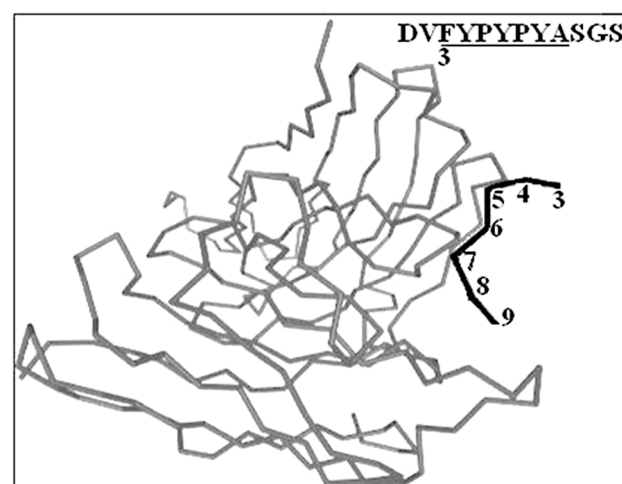
The contact surface between the membrane-bound B cell receptor and an antigenic epitope is made up of five amino acid (aa) residues. It is a pentapeptide.

This notion was defined with mathematical precision in 1939, when Landsteiner and van der Scheer<sup>1</sup> 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.”<sup>2</sup>

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.<sup>3–7</sup>

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](http://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

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pentapeptide-based vaccines can elicit specific antibodies capable of reacting with the full-length antigen without the risk of cross-reactivity and adverse events.<sup>8,9</sup>

#### Conflict of Interest

None declared.

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