

# This Week's Citation Classic®

Schleifer K H & Kandler O. Peptidoglycan types of bacterial cell walls and their taxonomic implications. *Bacteriol. Rev.* 36:407-77, 1972.

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The peptidoglycan (murein, mucopeptide) is a heteropolymer consisting of glycan strands cross-linked through short peptides. The occurrence of muramic acid and of amino acids with D configuration is a typical feature of the peptidoglycan. The peptide moiety reveals, in contrast to the uniform structure of the glycan, considerable variations. Differences in the amino acid composition and sequence are useful as a chemotaxonomic character, particularly within Gram-positive bacteria. [The *SCI*® indicates that this paper has been cited in over 775 publications.]

very little and that the peptide moiety is built from a limited number of amino acids, it was possible to use a combination of purely chemical methods to elucidate the primary structure of the peptide moiety of the many different types of peptidoglycan.

During my PhD thesis under the guidance of Otto Kandler of the Technical University of Munich, this chemical method was developed<sup>2</sup> and has been used extensively since then. The most important step of this method is the isolation and identification of oligopeptides after partial acid hydrolysis of purified cell walls. Two-dimensionally descending paper chromatography was used for the separation of amino sugars, amino acids, and oligopeptides. The characteristic "fingerprints" are sufficient to recognize a known peptidoglycan type. The chemical method may miss some minor details, but it is a rather rapid method and is very useful for screening a great number of bacteria.

I still remember our studies on the peptidoglycan structure of *Micrococcus luteus* (formerly called *M. lysodeikticus*). We were aware that J.M. Ghuysen and his group were also working on this structure. The chemical method had to undergo its crucial test. Fortunately, we were successful and could elucidate the structure<sup>3</sup> shortly before the investigators who were using the enzymatic method came to the same conclusion.<sup>4</sup>

To date, almost 100 different peptidoglycan types are known.<sup>5</sup> Most of them are found among Gram-positive bacteria. In order to establish the value of the peptidoglycan structure as a taxonomic criterion, it was necessary to demonstrate its phenotypic stability and to determine whether structural changes, dependent on the growth phase or environmental factors, could be observed. We could show that growing the bacteria in batch cultures under balanced conditions caused no phenotypic alterations of the peptidoglycan types.<sup>6</sup>

The different peptidoglycan types are a valuable chemotaxonomic characteristic for the classification of Gram-positive bacteria. Therefore, it is understandable that this review is highly cited, especially in studies dealing with those bacteria.

## Peptide Variations in Bacterial Membranes

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The first known amino-acid sequences of peptidoglycans were determined by the use of bacteriolytic enzymes. Bacterial cell walls were hydrolyzed with these enzymes, fragments were isolated, and their primary structures were determined.<sup>1</sup> However, this was a rather tedious and time-consuming way to determine the primary structure of peptidoglycan. Only the primary structure of the peptidoglycan of *Escherichia coli* and that of a few Gram-positive bacteria had been determined by this enzymatic method. When it was known that the glycan moiety varies

1. Ghuysen J M. Use of bacteriolytic enzymes in determination of wall structure and their role in cell metabolism. *Bacteriol. Rev.* 32:425-64, 1968. (Cited 430 times.)
2. Schleifer K H & Kandler O. Zur chemischen Zusammensetzung der Zellwand der Streptokokken. I. Die Aminosäuresequenz des Mureins von *Str. thermophilus* und *Str. faecalis* (On the chemical composition of the cell wall of streptococci. I. The amino acid sequence of murein of *Str. thermophilus* and *Str. faecalis*). *Arch. Mikrobiol.* 57:335-64, 1967. (Cited 155 times.)
3. ———. *Micrococcus lysodeikticus*: a new type of cross-linkage of the murein. *Biochem. Biophys. Res. Commun.* 28:965-71, 1967. (Cited 35 times.)
4. Ghuysen J M, Bricas E, Lache M & Leyh-Bouille M. Structure of the cell walls of *Micrococcus lysodeikticus*. 3. Isolation of a new peptide dimer, N-alpha-[L-alanyl-gamma-(alpha-D-glutamylglycine)]-L-lysyl-D-alanyl-N-alpha-[L-alanyl-gamma-(alpha-D-glutamylglycine)]-L-lysyl-D-alanine. *Biochemistry—USA* 7:1450-60, 1968. (Cited 90 times.)
5. Schleifer K H & Stäckerbrandt E. Molecular systematics of prokaryotes. *Annu. Rev. Microbiol.* 37:143-87, 1983. (Cited 55 times.)
6. Schleifer K H, Hammes W P & Kandler O. Effect of endogenous and exogenous factors on the primary structures of bacterial peptidoglycan. *Advan. Microb. Physiol.* 13:245-92, 1976. (Cited 30 times.)