

BIOLOGICAL CHEMISTRY

*Founded in 1877 by Felix Hoppe-Seyler as
Zeitschrift für Physiologische Chemie*

Felix Hoppe-Seyler (1825–1895) was a pioneer of biochemistry, remembered not only for his discovery of hemoglobin and his contributions to the chemical characterization of many other biological compounds and processes but also for having been the mentor of Friedrich Miescher and Albrecht Kossel. In his preface to the first issue of *Zeitschrift für Physiologische Chemie*, Felix Hoppe-Seyler coined the term *Biochemistry* ('Biochemie') for the then newly emerging discipline.



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COVER ILLUSTRATION

The cover illustration shows the position of aspartate 496 from the subsite S2 of human dipeptidyl peptidase III (DPP III), a member of metallopeptidase family M49, in a complex with the pentapeptide tynorphin (Val-Val-Tyr-Pro-Trp) (PDB: 3T6B). In their article on pp. 359–366 in this issue, Abramić and colleagues present the results of investigations on the structural basis of human DPP III preference for diarginyl arylamide substrates by altering its S2 subsite (by site-directed mutagenesis) to mimic the situation in the yeast enzyme, which is known to be non-selective. Asp496 was identified as a critical residue for the known specificity of human DPP III (and many other mammalian orthologs) towards Arg-Arg-arylamine, and plays an important role in determining this enzyme's preferential binding of peptides with an N-terminal arginine, but also of tynorphin. Since Asp496 is one of 13 residues forming the S2 subsite of human DPP III, these results demonstrate the significant influence that one single amino acid residue from the substrate binding site can have on enzyme specificity. This phenomenon has been reported also for the papain family of cysteine peptidases, and for representatives of the M1, M3 and M4 family of metallopeptidases.

Image courtesy of Marija Abramić, Zagreb, Croatia. The structure was generated using PyMOL (© 2006 DeLano Scientific LLC) and GIMP 2.8.



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