

## EDITORIAL

# Professor Dr Hans Zähler: an appreciation

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When Hans Zähler passed away on 18 December 2008 at the age of 79 after a long illness, he left the world a rich scientific legacy. His work has resulted in the discovery of a great number of antibiotics and other natural products from microbial sources, representing most major compound classes. Through studies on their mode of action, particularly in the producing organism, he also contributed greatly to the understanding of physiology and biochemistry, especially of microorganisms. One of the compounds he discovered early on, desferri-ferrioxamine B, became a marketed drug (Desferal) for the treatment of iron-overload diseases. Beyond these discoveries, important both qualitatively and quantitatively, he has shaped his field by training several generations of students who continued his mission and left their mark both in academia and in industry.

In his early work at the ETH Zürich and in his 30 years at the University of Tübingen, he developed an integrated approach to the discovery of microbial natural products, based on novel methods of isolation of producer organisms and new strategies of screening, cultivation and fermentation scale-up. In this way, his students learned real-world skills that served them well in their future careers not only in academia, but particularly in industry. Early on and throughout his career, he also recognized the importance of interdisciplinary collaboration, particularly with natural-products chemists. He developed close collaborations with Professors Walter Keller-Schierlein and Vladimir Prelog at the ETH Zürich and with Professor Axel Zeeck at the University of Göttingen. These interactions were very intense, involving mutual visits at the student level and frequent joint meetings of the groups, endowing students with an interdisciplinary outlook and the ability to communicate and interact across disciplinary lines. In 1972, he tried to recruit me to the University of Tübingen to expand this interdisciplinary approach to include biosynthetic studies. Although in the end I turned down the offer to move to Tübingen, it did result in our studying the biosynthesis of many 'Zähler' antibiotics.

Zähler's thinking profoundly influenced his co-workers and his discipline. He developed a number of important concepts. Contemplating the reasons for the occurrence of so many natural product structures, he developed the concept of the 'evolutionary game room',<sup>1</sup> in which nature randomly alters and recombines genetic information to constantly create new chemical structures. For any newly invented structures to persist, Zähler postulated that they only should have no negative effects on the essential functions of the producing organism. More current thinking, based on insights from the molecular biology

of secondary metabolism, would postulate that for new structures to persist, their formation should represent a selectable advantage to the producer.<sup>2</sup> Zähler also argued that the antibiotic activity of many microbial natural products is an incidental property, unrelated to the reason for their formation. Therefore, he argued that it makes sense to use screening methods unrelated to the traditional antibiotic screens, in the extreme chemical screening, for example, by TLC, to discover new natural products that can then be evaluated in depth for their biological activities.<sup>3</sup> This approach, which he pursued extensively and successfully, may have seemed counterintuitive at the time, but has been amply validated by the more recent successes in discovering non-antibiotic biological activities by screening known natural products and natural product libraries.

Hans Zähler shaped the professional lives of many people, both students and colleagues, through the force of his personality. His impact derived not only from his creativity as a researcher, but also from his charisma, his inquisitiveness and his infectious enthusiasm for science and discovery. He had high expectations of his students and set rigorous standards. Other outstanding traits were his honesty and his strong convictions on many issues, such as the impact of applications of biotechnology on the environment. In his convictions, he was usually rather uncompromising and willing to fight for his beliefs. Although he spent the majority of his academic career in Germany, he was a Swiss at heart. He viewed his countrymen with affectionate wonderment—I remember him telling me with an amused smile that in his youth in many Swiss villages the farmers still braided their manure piles. When it was time to retire, he returned to his native country and spent the rest of his days in Bern.

In many ways, Hans Zähler was a man larger than life, and he is sorely missed.

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1 Zähler, H. What are secondary metabolites? *Folia Microbiol.* 24, 435–443 (1979).

2 Floss, H. G. Combinatorial biosynthesis—potential and problems. *J. Biotechnol.* 124, 242–257 (2006).

3 Zähler, H. Some aspects of antibiotics research. *Angew Chem. Int. Ed. Engl.* 16, 687–694 (1977).