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Combinatorial Chemistry at Lead Finding

EDITORIAL

One of the most challenging tasks in preclinical research is the identification of original lead compound structures for new molecular targets. Combinatorial Technology offers Medicinal Chemists a technical approach to meet this challenge. A frequently asked question is whether this approach has been able to fulfil the high expectations which it has generated: Are there convincing examples of Combinatorial Chemistry-initiated discoveries of unique lead molecules; or are the reported successes limited more to optimisation of known lead compound structures?

This issue of CHIMIA contains summaries of lectures presented by leading scientists from pharmaceutical companies at a mini-symposium on 'Applications of Combinatorial Libraries to Lead Finding' held on May 15, 1997, at the Institute of Organic Chemistry of the University of Basel, under the auspices of the Section of Medicinal Chemistry of the NSCS, the Chemical Society of Basel, and the pharmaceutical companies of Basel. *H. Mario Geysen*, *Eric M. Gordon*, *Michael Pavia*, and *Richard Storer* illustrated results from their work and discussed current developments in this field.

Increasingly it appears that the combinatorial approach is benefiting from past experience of Medicinal Chemists. Efforts to increase the success of lead discovery from combinatorial libraries has focussed on screening of medium-sized single compound arrays and improvement of the chemical quality of these compounds. This trend has been made possible as a consequence of recent technical progress in parallel synthesis, automated high throughput analysis and purification systems. The shift of interest from crude mixtures to purified single compounds is dictated, on one side, by the recurring requirement to carry out tedious deconvolution procedures when screening compound mixtures and, on the other side, by the opportunities to generate more reliable biological data and obtain valuable insights into structure-activity relationships.

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