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Editorial

Recent advances in medicinal chemistry

The special Symposium-in-Print entitled “Recent Advances in Medicinal Chemistry” coincides with the 20th anniversary launch of *Bioorganic and Medicinal Chemistry Letters*. Its launch in 1990 coincided with the increasing interest in the role of Chemistry at the Chemistry–Biology interface of which the field of Medicinal Chemistry has always embraced and has been instrumental in driving forward. At the time, there were few avenues available for the disclosure and publication of Medicinal Chemistry efforts and much of the seminal science in the field simply went undisclosed. As its founding editor, I witnessed the embrace of *Bioorganic and Medicinal Chemistry Letters* by the Medicinal Chemistry community and the remarkable annual rise in both the quality and quantity of the articles that the journal publishes, which continues today. Initially published monthly with 10–20 articles per issue, the journal is now published twice a month with more than 1500 articles per year – a growth of more than 10-fold over 20 years. It is an International journal with articles coming from all continents, with editorial offices in the US, Europe, and Asia, with a fabulous distribution of articles coming from both academic and pharmaceutical labs, with an increasing level of detail disclosed for communications often including routine PK optimizations and in vivo pharmacological activity, and often with *Bioorganic and Medicinal Chemistry Letters* being among the first to introduce or adopt innovations now standard for the publication industry (e.g., Symposium-in-Print, free color figures, graphical abstracts, BMCL Digests, online submissions and reviews). In addition to providing a publication outlet for academic labs to disclose their science, I believe the journal has changed the publication habits and opportunities for the Pharmaceutical Industry. Today, much more science on important and contemporary problems of interest to our readers is published than ever before. We anticipate that this role of *Bioorganic and Medicinal Chemistry Letters* will continue for years to come and we welcome suggestions from our authors and readers for mechanisms that can better serve you.

This special Symposium-in-Print entitled “Recent Advances in Medicinal Chemistry” was organized by three Guest Editors, Brian S. J. Blagg (University of Kansas), Douglas S. Johnson (Pfizer), and Robert M. Garbaccio (Merck), in recognition of the important role that Medicinal Chemistry has played in the science at the Chemistry–Biology interface and with the intention of highlighting advances in the field of Medicinal Chemistry that have transpired over the 20 years that *Bioorganic and Medicinal Chemistry Letters* has been publishing your science.

Dale L. Boger
Editor-in-Chief

The elucidation of the human genome was one of the most significant scientific discoveries during the past 20 years. As a consequence of this seminal accomplishment, many new genes were discovered and pathways central to disease progression unveiled. As biologists have continued to unravel the role different proteins play in cellular processes, target validation has also evolved and grown dependent upon genetic studies relying upon gene knockouts and RNA interference strategies for phenotypic screening. With the development of these pioneering technologies, assays designed to interrogate these new therapeutic targets were modified and optimized for use in high-throughput screening. Enhancements in screening throughput and miniaturization complemented the development of molecular libraries designed to represent vast chemical space in new ways: through dense combinatorially prepared libraries, diversity-oriented approaches and the smaller fragment space. As bandwidth for lead identification increased, many advances have been made in the lead-to-drug candidate space. A major focus has been placed on the improvement of physicochemical properties to reduce the risk of compound-related drug attrition. Companies have made significant investments in the screening and optimization of ADME (Absorption, Distribution, Metabolism, Excretion) parameters, which has reduced compound attrition that results from drug metabolism and poor pharmacokinetics. Compound-related attrition is now more often due to toxicity and an existing challenge to develop predictive toxicity screens that can be used earlier in drug discovery remains (similar to the role ADME screening has played over the past 10–15 years). It must not be forgotten that modern organic synthesis is a critical part of all medicinal chemistry efforts and this is nicely reflected in many of the papers within this issue. Eventually, the culmination of these achievements led to a platform upon which modern day drug discovery is based.

Yet, despite these advances, the medical benefits from mapping the human genome have not yet been fully realized, in part because of the difficulty associated with validating newly identified targets (translational medicine) and the tractability of some of these targets. As evidenced in this issue, medicinal chemists are playing a key role towards identifying innovative solutions for both of these problems (e.g., multitargeted drug discovery, allosteric/noncompetitive inhibition, protein–protein inhibition, tissue selective drug distribution, chemical probes to interrogate target biology). These, and continued innovations will put a powerful array of tools into the hands of today's bioorganic and medicinal chemist as they work towards greater realization of the modern drug discovery platform's potential.

As one peruses through this anniversary issue of *Bioorganic and Medicinal Chemistry Letters*, the role that both Biology and Chemistry has played in the development of science and drug discovery becomes increasingly obvious. Although other journals have since been inaugurated to represent further niches under this umbrella, *Bioorganic and Medicinal Chemistry Letters* has continued to play a preeminent role in providing both academic and industrial chemists a format for the rapid dissemination of results ranging from target identification to the first disclosure of a clinical candidate. Looking forward 20 years and to the next *Advances in Medicinal Chemistry* issue, we expect to see continual advances in the Medicinal Chemistry discipline that will provide novel methods to further expand the druggable genome.

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