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Molecular cross-fertilization

The ability of chemists to synthesize molecules has been invaluable to biological research. As a result, the development and application of chemical tools for gaining molecular-level insights into biological systems has emerged as an important facet of chemical biology research. We consistently hear chemists express hopes that their compounds and chemical approaches will be widely adopted by biologists. Most biologists seek easy-to-use chemical probes and methods to enhance their molecular understanding of biological systems within cells and organisms. In a Commentary in this issue of *Nature Chemical Biology*, Soderholm *et al.* provide firsthand insight into the challenges that biologists encounter as they search for new chemical probes. However, chemists and biologists alike express frustration with the difficulties of adapting published chemical compounds, libraries and methodologies for use in their own laboratories.

Biological researchers have benefited from a culture in which research materials such as cell lines, genetic constructs and structural data have been made freely available upon publication. A leading study, entitled *Sharing Publication-Related Data and Materials: Responsibilities of Authorship in the Life Sciences*, was published in 2003 by the United States National Academy of Sciences. This document established standards for the sharing of research data and materials for the life science community, which included the timely sharing of published software, data and research materials, and the deposition of biological information (such as sequence, structural and microarray data) into publicly accessible databases. These standards, which have been widely adopted by researchers, funding agencies and life science publishers as criteria required of authors, have greatly enhanced the progress of biological research and aided chemists working at its interface with biology.

Although the sharing of biological reagents and information is well established, the same is not true for published chemical compounds. While collaboration among chemists is common, making noncommercial synthetic compounds available to other researchers has not been a community standard for chemists in the same way that materials sharing has been for biologists. Given the specialized nature of chemical synthesis, making even relatively simple molecules remains a costly and time-consuming technical challenge. In most cases, the preparation of interesting small molecules requires effort from a skilled synthetic chemist and produces relatively small amounts of the compound (as compared to biomolecular materials, most of which can be easily made and amplified by molecular cloning), which limits the availability of most newly discovered compounds. Although some chemists make their materials freely available, this can be a significant expense, with some labs employing full-time staff for this task. Instead, many chemists explore biological applications in collaboration with a small group of biologists or clinicians. Other chemists offer their compounds through commercial vendors. However, the market for specialized research reagents can be relatively small, which may limit the interest of companies to invest in such products. Thus, despite a strong desire by chemists to have their compounds widely used by biologists, significant historical and technical barriers impede progress toward this goal.

The chemical and biological communities also take different approaches in regard to how information from the published literature is archived and accessed. In biological sciences, most information (including genetic sequences, macromolecular structural data and so on) has been deposited in public databases. In contrast, chemical information traditionally has been consolidated in private-sector repositories, which offer comprehensive coverage of the chemical literature and sophisticated retrieval functionality, but require institutional subscriptions for access.

Given these cultural and technical differences, how can access to bioactive chemical compounds, libraries and tools be enhanced for chemists and biologists? Numerous universities and research institutes have taken the lead in this effort by developing small-molecule screening facilities on their campuses, some of which offer services to other regional institutions. A model for scientists in the United States is provided by the Molecular Libraries Screening Centers Network (MLSCN), which is part of the Molecular Libraries Initiative of the National Institutes of Health Roadmap for Medical Research (http://www.nihroadmap.nih.gov). Nearly $90 million is being invested over three years in nine extramural high-throughput screening centers. These geographically dispersed centers offer small-molecule screening across hundreds of assay types and are developing the Small Molecule Repository (SMR) to a projected size of 200,000 compounds by the end of 2006. All data produced by the MLSCN will appear in PubChem, the public repository of chemical structure and biological assay data. The MLSCN initiative shares the goals of most chemical biologists—to discover small molecules useful for probing biological systems and to identify potential molecular targets for therapeutic intervention—and, as such, may provide an excellent model for other organizations seeking to broaden access to chemical compounds and bioactivity data.

There is a great need for community standards for sharing data, materials and information between chemists and biologists, which will require chemical biologists to consider numerous questions. How do we create a system that will be widely adopted by researchers worldwide? How do we avoid overspecialization, where chemists are reagent suppliers and biologists make the major discoveries? How will organizations manage the increasing costs and regulatory issues necessary for distribution of materials? What roles will the private, public and government sectors play in these decisions? We are interested to hear your views on community standards, which might make chemical compounds and tools more accessible and useful to everyone. We welcome your correspondence at our website: http://www.nature.com/naturechemicalbiology. ■