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Reviewing research at the interface where chemistry meets biology

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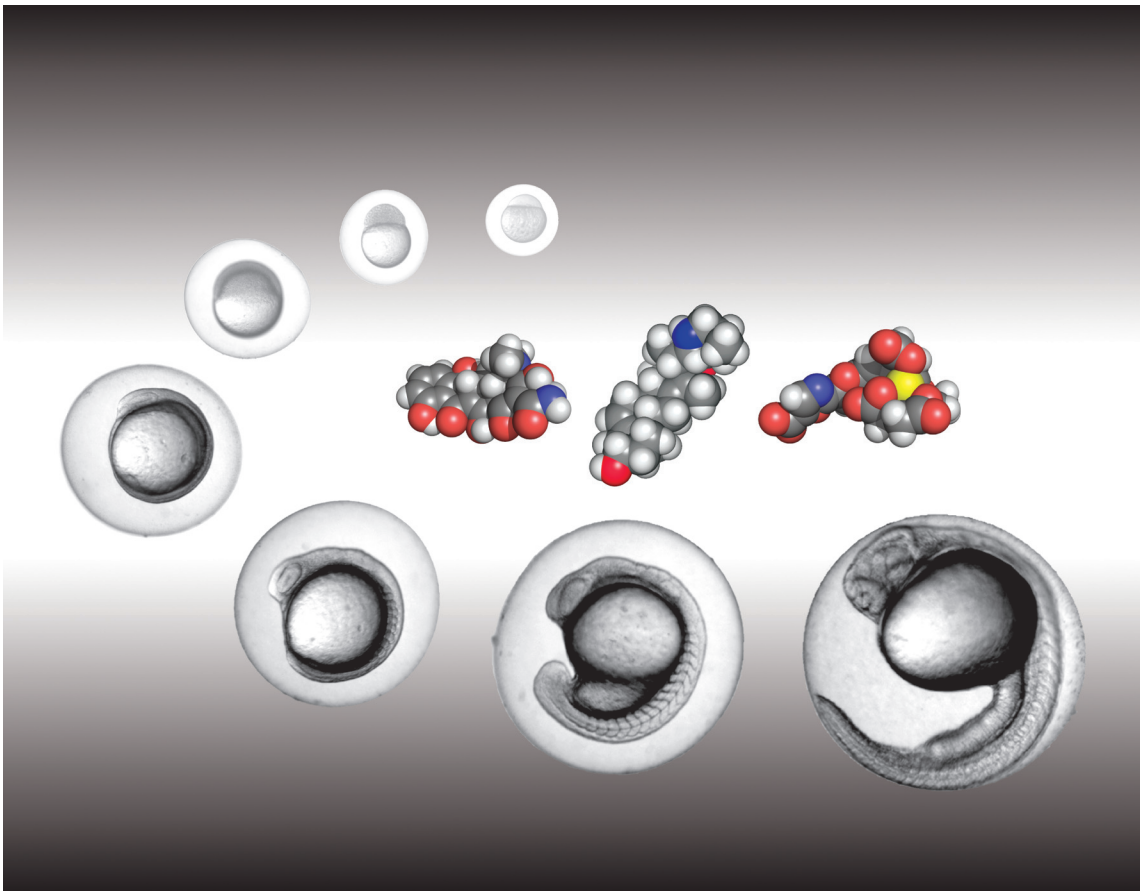

Editorial: the chemistry–biology interface

David Spring

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The interface with biology is a fertile scientific pursuit for chemists. A chemical training gives insight into reactivity and bonding interactions in molecular detail. This understanding can be exploited with small molecules to dissect biology directly. This issue will focus on a number of important recent topics that illustrate the breadth of the field.

The discovery of the molecular target of a bioactive small molecule remains a significant challenge. The tutorial review by Leslie and Hergenrother summarizes strategies for small molecule derivatization in order to make affinity probes, and provides a useful guide for newcomers. The review by Carrico delivers an overview of methodology for the selective modification of biopolymers. For example, chemoselective methodology to tag specific proteins within a physiological context is possible, but there is huge potential for new chemistry to be exploited.

A selective and cell-permeable small molecule modulator is the ultimate tool to study a biological process; however, there is a problem of how to identify such a small molecule. Hübel, Leßmann and Waldmann describe the concept and application of natural product inspired compound collections as a solution to this problem.

Cisar and Tan describe recent discoveries of microbial natural product biosynthesis inhibitors and analyse the approach as a way to identify new antibiotics.

Small molecules have been effectively used to study developmental biology. Shestopalov and Chen provide an overview of the chemical tools involved, and outline the limitations of current approaches and future challenges.

When animal cells experience a decrease in oxygen availability, then a response to counter this is mediated by the protein 'hypoxia inducible transcription factor', abbreviated HIF. The HIF system is a potential target for anaemia and cancer. Chowdhury, Hardy and Schofield review the HIF field to date and outline opportunities for therapeutic intervention.

Histone deacetylase (HDAC) proteins are a relatively new anticancer target, with the drug 'Zolinza' being the first of many HDAC inhibitors that will no doubt come into clinical use. Bieliauskas and Pflum describe the move towards discovering inhibitors that are selective for one of the eleven isoforms of HDAC proteins, and their potential use in understanding their biological roles.

Microarrays have molecular entities attached to a surface in an ordered and miniaturized way. Small molecule microarrays are introduced by Vegas, Fuller and Koehler, illustrating their use as tools to discover small molecule binding partners for any protein. The authors discuss manufacturing methods, attachment strategies of small molecules on to the microarray surface, and give a case study involving the discovery of novel ligands for HDAC proteins. In their review, Horlacher and Seeberger highlight the importance of carbohydrate microarrays in the high throughput investigation of sugar binding events.

Bacterial cell–cell communication is a process known as quorum sensing. In the review by Geske, O'Neill and Blackwell, the modulation of quorum sensing in Gram-negative bacteria is discussed. The topic is taken further by Lowery, Dickerson and Janda, who describe the capacity of bacterial quorum sensing to undergo interspecies and interkingdom interactions.

The use of oligonucleotides to encode heredity is well appreciated; however, their use beyond this is much less so. Chemical biology applications in programmed self-assembly of nucleic acids is introduced by Pianowski and Winssinger. In the review by Huppert, the guanine rich quadruplex structure of DNA is depicted. Due to its proposed biological functions, G-quadruplexes have become a target for small molecule modulators.

Protein aggregation is a common problem in recombinant protein production, as well as the cause for many neurological and systemic diseases. Using a computational chemical approach, such as the Zyggregator method, predictions of the propensity of a polypeptide chain to form a protofibrillar assembly can now be made. This topic is introduced by Tartaglia and Vendruscolo.

The chemistry–biology interface, as led by scientists with a chemical background, is an exciting place for research. It is hoped that this issue will be a useful introduction to the area and provide inspiration and encouragement for further reading and involvement.

Finally, I would like to share my appreciation for the authors, for their expert contributions and cooperation with this project. Also, I wish to acknowledge my fellow editorial board members for support, and especially the editor Dr Robert Eagling for his help and guidance with the production of this issue.

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