Bioconjugate Chemistry

Editorial

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It has been an exciting year for us at *Bioconjugate Chemistry*. Over the past 12 months we have worked hard to broaden the scope and impact of the journal while maintaining the rigor that *BC* was known for. One area we have focused on is enhancing the manuscript review process. Through meaningful feedback to authors and excellent help from the reviewer community, we have lowered the submission to online publication to less than 40 days. We have also created a social media presence—check us out at https://www.facebook.com/bioconjugatechemistry. Editors and EAB members have provided a presence for *BC* at conferences worldwide, with help from the folks at ACS.

Coming into Year 2, I thought it would be helpful for you to meet the Editors at *BC*. This way you can get an idea of what our visions are for the future, and pragmatically whom you'll suggest as Editor for your next submission.

JAN VAN HEST

The discipline of science dedicated to the construction of hybrid polymers, in which the properties of molecules from synthetic and biological origin are combined to attain materials with emergent properties, has experienced rapid development over the past decade. One of the important drivers for the advancement of this field is the availability of novel conjugation methods. Techniques predominantly developed for chemical biology applications, with important features such as high reaction rate and bio-orthogonality, have found their way into materials science to construct structures with a high level of control over the number and site of conjugation. These advances have furthermore been facilitated by the emergence of protein engineering methods that allow the ribosomal incorporation of noncanonical amino acids with unnatural functional moieties. These developments are of crucial importance to achieve the synthesis of well-defined pegylated proteins, hybrid hydrogels, and polymeric nanocarriers functionalized with complex biological targeting motifs.

Although the bioconjugate chemistry toolbox has been extended tremendously over the past years, there are still many challenges ahead. First of all, in most cases, only conceptual studies have been executed, and the exploration of hybrid systems in real applications has been limited. It is up to you to show the actual benefits of well-defined bioconjugates to gain more insight in biological processes and/or to achieve more efficient therapeutic materials. Besides the translation of existing methods from concept to application, there is also ample room for the design of novel conjugation methodologies. A highly important development in the soft matter field is the introduction of stimulus-responsiveness and adaptability in molecules and materials, to allow them to change their properties based on the environment they are in. Bioconjugation methods that are responsive and reversible, and which can be executed with spatiotemporal control, will be highly valuable for the development of this class of bioconjugates, in particular, if this chemistry could be extended to living systems.

As a polymer chemist by training, I have always been interested in approaches that allow the synthesis of highly defined materials with unique properties, such as controlled polymerization, dendrimer synthesis, and protein engineering. During a short stay in industry, with the chemical company DSM, I realized that combining properties of biomolecules with synthetic polymers could lead to a new class of hybrid materials with unprecedented properties. This has also become the mission of my bio-organic chemistry group at Radboud University Nijmegen, where we use a range of synthetic methodologies to construct protein and peptide-based hybrid materials. Bioconjugation naturally plays a crucial role in this endeavor. One of the focal points of our research is the construction of well-defined polymer capsules that are used to store and protect (bio)catalysts; these nanoreactors are applied as cell and organelle mimics. Polymer capsules are furthermore also used for targeted drug delivery, for example, to cross the blood-brain barrier.

ERIN LAVIK

There are a host of technologies being developed with potential therapeutic value in the bioconjugate universe. It is a tremendously exciting time. The challenge faced with this field, though, is that small variations in chemistry can have unexpected impacts on a range of biological outcomes. We, as a field, however, often design experiments focused on looking for

Published: January 15, 2015

DOI: 10.1021/acs.bioconjchem.5b00002
Bioconjugate Chem. 2015, 26, 163−165

expected outcomes and not the unexpected ones. We need to look at both the anticipated outcomes of a therapy such as targeting a tumor or promoting tissue repair, as well as the off target effects such as inflammatory responses or unexpected thrombosis. It is often very challenging to design experiments and approach the findings with a perspective that allows for the unexpected, but the best science is doing just this and opening new possibilities for therapies that are thrilling.

I started out as a chemist by mixing together everything in the chemistry kit my mom found at a yard sale to see what would happen. It was incredibly disappointing. I next moved to ceramics, but my career was redirected when my mom sat next to Martha Gray on an airplane and Prof. Gray suggested I look into biomaterials. I took that advice, and now my lab works on developing materials to leverage biological processes for applications in trauma, neural repair, and ocular disease. We are interested in approaches that use well-characterized materials for biological applications to facilitate translation of successful approaches toward therapies. I am constantly humbled and surprised by how a simple system with RGD moieties can have a major biological impact. We focus much of our work on developing and applying these systems for hemostasis and drug delivery. Through this work, we have found that small changes at the molecular level in these systems can have dramatic impacts on biological processes over a range of length scales. We complement this work with research focusing on new scaffolds for regenerative medicine. The overall approach is to develop materials that leverage biology to augment the response to injury and promote repair.

BRAD SMITH

There is little doubt that the development of click chemistry over the past decade has produced many notable and remarkable advances. There has been widespread exploitation of this chemistry for bioconjugation of polymers, surfaces, and nanoparticles, leading to new imaging and therapeutic agents. I foresee continued advances in synthetic methodology to create new types of covalent bonds and new classes of bioconjugation methods. The chemistry will permit orthogonal attachment of multiple building blocks, producing new classes of multifunctional molecular and nanoparticle constructs. These constructs will have synergistic targeting, reporting, and therapeutic capabilities, and increasingly they will be shown to operate effectively in complex biomedical media, including living subjects. While there will still be a place in *BC* for bioconjugates made by traditional methods, it reasonable to expect that the performance properties of these traditional constructs will be exceptional. For example, future studies of oligonuceotide transfection, cell permeation, and molecular imaging will increasingly demonstrate unique targeting features such as tissue specific in vivo delivery. In all cases, the expectation of analytically well-characterized bioconjugates and robust synthetic methods will remain a hallmark of *BC*.

I was raised in rural Australia but I have spent most of my professional life in the US. I joined the Department of Chemistry and Biochemistry at the University of Notre Dame in 1991. I serve as Director of the Notre Dame Integrated Imaging Facility, a research resource that provides an integrated suite of sophisticated microscopes and imaging stations for the campus. My research interests are quite broad and are perhaps best labeled as supramolecular chemistry applied to biological systems. My group develops small organic molecules that selectively target cell surfaces and we use these molecules for imaging and therapeutic applications. We have created molecular imaging probes for detecting cancer, cell death, and microbial infections in living animals. Many of these molecular probes are now commercially available for preclinical research applications.

GANG ZHENG

Bioconjugate chemistry is essential for achieving targeted imaging and therapy. It is also the critical enabler to permit new methods to be discovered that result in better imaging probes and therapeutic agents. New approaches are developed to create novel molecular constructs for biological applications, and new design principles are introduced for molecular assembly and nanomedicine. Bioconjugate chemistry forms the very foundation that many medical discoveries and advancements have been built upon. As *BC* stands at the interface of biology and chemistry, contributions that underscore the synergy and report the convergence of these two fields are highly desired. The broad chemistry community has been constantly introducing exciting new technologies and is at the same time highly enthusiastic to translate their discoveries into practical utilities. However, one common hurdle is the lack of resources and biological understanding to validate these utilities in vivo. I believe *BC* can bridge this gap by encouraging the creative use of these new chemistry methods for novel biological applications in both in vitro and in vivo research.

An organic chemist by training, I have been associated with major research hospitals for all my academic life. This experience helped to shape both my research interests and my personal view of how bioconjugate chemistry can impact medical research. My lab focuses on developing novel molecular constructs to combat diseases. As the era of nanomedicine dawns, targeted and activatable diagnostics and

DOI: 10.1021/acs.bioconjchem.5b00002
Bioconjugate Chem. 2015, 26, 163−165

therapeutics hold the potential to become an important part of medicine. We are taking new approaches to engineer experimental and intelligent molecules that are designed to translate into clinical benefits in the future. One such example is the porphysome: porphyrin nanoparticles self-assembled from single porphyrin−lipid conjugates, enabling multimodal imaging and therapeutic functions (photoacoustic, fluorescence, positron emission tomography, magnetic resonance imaging, photothermal, photodynamic and radiation therapy).

VINCE ROTELLO

I'd like to echo the enthusiasm and sense of adventure described by the rest of the team. I strongly feel that the interface between synthesis and biology is where many of the greatest discoveries will be made, materials and insights that will improve human health, and enable new technologies across the scientific community. As also discussed above, this excitement needs to be coupled with scientific rigor in all aspects of the research, from characterization of new materials through analysis of data. When we do this combination effectively we have the potential to change science, and by doing so improve the human condition.

Like Erin, I started out disappointed by a chemistry set—nothing interesting or pyrotechnic happened when I mixed things together. I stayed interested in chemistry, however, and I started out my professional career in natural products synthesis, moving next to supramolecular chemistry. After a while I found that small molecule work was a bit too predictable, and that I wanted to do research where we could see some real surprises. These surprises (some good!) started happening when we moved to polymers and nanomaterials, and increased exponentially as we moved into biology. In our current research we integrate synthetic and supramolecular methodologies with nanomaterials, polymers, and surfaces to create new tools for biomedicine. We have programs in sensors, where we are developing new strategies for diagnostics, high-content screening, and low-cost test trip platforms for the developing world. We are concurrently pursuing a range of delivery strategies for proteins and nucleic acids, focusing on systems that circumvent endosomal pathways. Finally, we are taking all of the above tools and integrating them with materials technologies to create responsive materials for tissue engineering and wound healing applications.

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Notes

Views expressed in this editorial are those of the author and not necessarily the views of the ACS.

DOI: 10.1021/acs.bioconjchem.5b00002
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