

## **Synthetic and Medicinal Chemistry for Biologics**

Modern bioactive molecules are often perceived as being split into two tribes – small molecules and biologics. This distinction extends not only the size of the molecules – with biologics being large therapeutic proteins, antibodies, vaccines, and nucleic acids – but to their mode of production. Small molecules benefit from the power of organic synthesis to manipulate and tailor every atom in their structure, while biologics are largely limited to natural building blocks with few opportunities for modification and manipulation by organic reactions. Advances in synthetic method for de novo construction of biologics, including therapeutic proteins, and innovative new approaches for site-specific modification of recombinant biologicals increasingly blur this line. Advances in new chemical and enzymatic reactions will make possible a new generation of biologicals that can be precisely tailored with systematic changes to their structure, making it possible to perform precise “medicinal chemistry” on biologics including cytokines, growth factors, and antibodies. With these advances, precisely turned proteins with new receptor signalling, conditional activation, and novel targeting strategy can be produced and evaluated. The same strategies can be extended to the construction of atomically tailored proteins for discovering and interrogating biological pathways.