Insulin is recognized as a life-saving drug for millions of people with diabetes. Nevertheless, complications of diabetes can lead to premature death due to the fact that insulin treatment remains less than ideal for glucose control. My lab is interested in using synthetic organic chemistry to incorporate novel properties into insulin to achieve superior glucose control for diabetes treatment. In this presentation, I will discuss our efforts in developing ultrafast-acting insulin (UFI) and glucose-responsive insulin (GRI). Our development of UFI came from a natural product identified from the venom of fish-hunting cone snails. A series of protein engineering efforts coupled with insights from structural biological work have enabled us to identify the smallest insulin discovered to date, which possesses promising fast-acting clinical benefits. Our development of GRI came from the concept of currently available long-lasting insulin analogues. By incorporating a glucose-sensing element, we have developed GRI with glucose-dependent potencies. Both types of next-generation insulin molecules have the potential to vastly improve the disease management in clinical settings.