# New Horizons Solvay Lectures in Chemistry

## Prof. Alexis Komor

### University of California, San Diego, USA

Profile: Alexis Komor received her B. S. degree in chemistry from the University of California, Berkeley in December of 2008. She then joined the lab of Jacqueline K. Barton at the California Institute of Technology for her doctoral studies. While at Caltech, she worked as an NSF Graduate Research Fellow on the design, synthesis, and study of DNA mismatch-binding metal complexes and received her Ph.D. in 2014. She pursued postdoctoral work as a Ruth L. Kirschstein NIH Postdoctoral Fellow in the laboratory of David R. Liu, where she developed base editing, a new approach to genome editing that enables the direct, irreversible chemical conversion of one target DNA base into another in a programmable manner, without requiring double-stranded DNA backbone cleavage. Alexis joined the Department of Chemistry and Biochemistry at the University of California at San Diego in 2017, where her lab develops and applies new precision genome editing techniques to the functional genomics field. Alexis's contributions in teaching, mentoring, and research have been recognized through many awards, including the Cottrell Scholar Award, the "Talented 12" recognition by C&EN News, an NSF Faculty Early Career Development (CAREER) award, an NIH early stage investigator Maximizing Investigators' Research Award (MIRA), and a "40 under 40" recognition in healthcare by Fortune Magazine.

## Engineering and Evolving Nucleic Acid Modifying Enzymes

Abstract: Base editors (BEs) are comprised of a catalytically inactivated Cas9 (dCas9 or Cas9n) tethered to a single-stranded DNA (ssDNA) modifying enzyme, which directly chemically modifies target nucleobases within a "base editing window". Two classes of base editors exist, which use cytosine and adenine deamination chemistries to catalyze the conversion of C•G base pairs to T•A (CBEs), and A•T base pairs to G•C (ABEs), respectively. These transition mutations (purine-purine or pyrimidine-pyrimidine) are mediated by uracil (cytosine deamination) or inosine (adenine deamination) intermediates, and occur with high efficiencies (up to 90% conversion) with little to no competing indel formation. Expansion of the BE toolbox to include transversion editors will require engineering of new nucleic acid editing enzymes. As ABEs were developed by engineering and evolving a tRNA adenosine deaminase enzyme, TadA, into a ssDNA adenosine deaminase enzyme, TadA7.10, the development of future BEs may be accomplished by converting additional tRNA modifying enzymes into ssDNA editing enzymes. In this talk I will describe my lab's efforts to mechanistically understand how current BE enzymes function. The enhanced understanding of how known DNA editing enzymes function, and in particular how wtTadA was converted into TadA7.10, can inform the development of future DNA editing enzymes.

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Jozef Schell seminar room, Technologiepark-Zwijnaarde 71 - 9052 Ghent

Hosted by Prof. Thomas Jacobs, VIB-UGent Center for Plant Systems Biology