INTERNATIONAL SOLVAY INSTITUTES BRUSSELS

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.

Development and Characterization of Precision Genome Editing Tools

Abstract: Prior to the development of base editing in 2016, genome editing technologies functioned by introducing double stranded DNA breaks (DSBs) at a target genomic locus as the first step of genome editing. This is typically accomplished using Cas9 (a programmable endonuclease) and a piece of RNA called a guide RNA (gRNA) that encodes for the genomic location at which Cas9 will bind and cleave using simple Watson-Crick-Franklin base pairing rules. The cellular processing of DSBs results in a mixture of genome editing products, including both precision editing outcomes and insertion and deletion (indel) byproducts. The high frequency of indels versus precision products has been a long-standing challenge in the genome editing field since its inception in the 1990's. Here I will describe here my lab's efforts to develop new genome editing methodologies with improved efficiency and precision. These include the development of new base editor (BE) tools, as well as new methods to improve the precision of DSB-reliant methods.

Tuesday 5 November 2024 at 4.00 pm.

COFFEE AND TEA WILL BE SERVED AT 3:45 P.M IN FRONT OF THE SOLVAY ROOM

UNIVERSITÉ LIBRE DE BRUXELLES - CAMPUS PLAINE
BOULEVARD DE LA PLAINE - ACCESS 2 - 1050 BRUSSELS
Quartier Jaune - Building N.O. - 5th Floor - Solvay Room

Prof. Komor will deliver two other lectures on:
Wednesday 6 November at University of Ghent (time and venue TBC)
Thursday 7 November at de Duve Institute (time and venue TBC)
Please see overleaf to see the abstracts.

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Engineering and Evolving Nucleic Acid Modifying Enzymes

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.

Wednesday 6 November 2024 - University of Ghent (time and venue TBC)

Understanding Human Genetic Variation with Precision Genome Editing Tools

Technological advances are making the routine sequencing of human genomes increasingly ubiquitous, including in clinical settings. However, our inability to interpret the disease-relevance of genetic variants discovered by sequencing remains a critical obstacle to the progress of precision medicine: there are currently over 685 million human single nucleotide variants (SNVs) identified from sequencing data, and less than 0.5% have a defined clinical characterization. New laboratory-based methods capable of interpreting SNVs and predicting the clinical relevance of previously unobserved mutations would not only enhance the efficacy of current therapies by better informing patient selection strategies, but also accelerate the development of new approaches to combat diseases with a genetic component. Here I will describe my lab's work to develop new methods and strategies to characterize the impact of SNVs in cellular contexts.

Thursday 7 November 2024 - de Duve Institute UCLouvain (time and venue TBC)

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