

***UNIVERSITY OF RHODE ISLAND***  
***Department of Chemistry***  
***SEMINAR***

***3:00 P.M., Monday, April 20, 2026***  
***Room 105 – Beaupre Center***

***Prof. Juan Del Valle***

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***University of Notre Dame***

***Supernatural Peptides***

***HOST***

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## Supernatural Peptides

**Abstract:** As peptide-based modalities gain prominence in drug discovery, a central challenge is the ability to predictably encode structure, stability, reactivity, and function into host sequences. Peptide natural products provide a rich but underexploited source of such design principles, particularly through noncanonical modifications that impose strong conformational bias. Our laboratory develops programmable peptide architectures using backbone N-heteroatom substitution and intramolecular cross-linking strategies inspired by NRPs and RiPPs. Here, we demonstrate that backbone N-amination promotes  $\beta$ -strand conformations while enhancing proteolytic stability and preserving native side chain functionality. N-Hydroxylation of the peptide backbone introduces new reactivity, enabling chemoselective ligation and providing a sequence-agnostic approach to peptide and protein synthesis. In parallel, we show that nature-inspired side chain tethering, including  $i \rightarrow i+2$  di-cysteine staples, can be used to stabilize  $\beta$ -sheet folds and drive self-assembly, yielding amyloids capable of templating protein aggregation. Together, these studies illustrate how design principles borrowed from nature can enable precise control of peptide structure, function, and reactivity.

**Bio:** Juan Del Valle earned a B.S. in chemistry from Carleton College in 1999 and a Ph.D. from UC San Diego in 2004. After postdoctoral studies at the University of Montreal, he began his independent career at New Mexico State University and moved to the Moffitt Cancer Center at the University of South Florida in 2009. In 2019, Juan joined the University of Notre Dame, where he is currently the Warren Family Professor of Chemistry & Biochemistry. Juan's research program lies at the interface of organic synthesis and chemical biology, with particular interests in protein mimicry, peptide natural products, and modulators of proteostasis.