

Expert Perspective



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Why is the “undruggable” industry so exciting right now?

Accessing the “undruggable” target space presents an opportunity to address unmet medical needs across many disease types with the potential to substantially improve patient care. Now is a particularly exciting time in this industry because we are at the verge of understanding whether several newer technologies will demonstrate clinical benefit in this space. Some of these newer approaches include RNA, allosteric modulators, chromatin modulators, proteolysis targeting chimeras, and the FogPharma™ modality, Helicon™ peptides.

What is the major limiting factor when utilizing Helicon™ peptides and how are you working to overcome this?

Like with small molecule drug discovery, one of the challenges is finding a molecular design that allows for aqueous solubility, ability to cross a lipid membrane, and stability in plasma. Small

molecule chemists have had decades to figure out the rules for designing optimal chemical matter. FogPharma is working to rapidly determine the rules for Helicon™ peptides. One advantage of peptides is that they are modular and easily synthesized in a routine manner. Thus, in addition to focused medicinal chemistry, we are utilizing multiplex, high-throughput approaches to rapidly interrogate large amounts of chemical space coupled with informatics approaches to decipher key patterns.

Outside of your areas of focus, what other areas of “undruggability” are you most excited about?

Targeted protein degradation via proteolysis targeting chimeras is a powerful way to access targets in a new way. Due to the catalytic degradation mechanism, lower affinity compounds may become actionable. Furthermore, the proteolytic activity is highly dependent on the geometry of association between target and E3 ubiquitin ligase, potentially enhancing target selectivity. These features may enable access to some currently “undruggable” targets. One of the reasons I follow this area so closely is that there is a potential to take this approach with Helicon™ peptides.

What is your vision for the “undruggable” industry?

The “undruggable” industry has

the potential to be bigger than the current “druggable” industry. As such, scalability will be an important determinant for realizing the full potential of this undertaking. I am thrilled to see so many different approaches in this space. Each target has unique challenges, and I believe the diversity in technology will enable modulation of a greater variety of targets and ultimately better outcomes for patients.

What conversations need to happen to advance the field?

Although there are a variety of technological approaches to “undruggable” targets, there are common challenges. Scalability is one challenge we all need to grapple with if we want to rapidly realize the potential of this vast target space. There are also some common technical challenges such as intracellular delivery and formulation for optimal bioavailability and tissue distribution that surely would benefit from cross-platform discussion.

What are you most looking forward to at the Virtual Undruggable Leaders Forum?

I look forward to hearing the latest advances in the many different approaches to “undruggable” targets. I also value the opportunity to put our heads together and discuss common challenges and ways to collectively drive the field to its fullest potential.