CAMBRIDGE HEALTHTECH INSTITUTE'S
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Harnessing Venomics for Ion Channel Drug Discovery

Hongkai Zhang, Ph.D., Senior Scientist, Lerner Laboratory, The Scripps Research Institute

Cambridge Healthtech Institute recently spoke with Hongkai Zhang of the Richard Lerner Lab at The Scripps Research Institute about his upcoming presentation "**Harnessing Venomics for Ion Channel Drug Discovery**" at the **Antibodies Against Membrane Protein Targets - Part 2** conference to be held September 21-22, 2016, as part of the **14th Annual Discovery on Target event in Boston**.

SPEAKER Q&A

Q: Why is it better to screen venom peptide with autocrine based system rather than the conventional method?

The discovery of functional venom peptides traditionally relied upon bioactivity-guided fractionation that is time consuming and requires large volumes of crude venom. Many of these problems can be circumvented by the the autocrine based system. Firstly, venom peptide genes can be synthesized in a high throughput manner based on database and transcriptomics information, avoiding the need for capture of venomous organisms and the process of venom fractionation. Secondly, venom peptide libraries of large diversity can be efficiently sorted while the traditional patch clamp assay precludes the possibility of screening for a large number of venom peptides.

Q: What is the maximum size of a venom library that can be screened with this method?

Since flow cytometry sorting speed is generally around ten million cells per hour, it is reasonable to start with a library of one million members. It is demonstrated by our initial proof-of-concept, screening a combinatorial library of one million members.

Q: Is this method useful for screening peptide libraries generally against other targets, not just ion channels?

Our data showed that the selection system can be used for GPCRs as well. A key feature of the selection system is that the target is in its natural milieu of the plasma membrane.

Q: Is this method useful for screening antibody?

The method is general and only requires proximity of membrane protein and ligand displayed on cell surface. Since mammalian cell surface display of antibody libraries is screened for binding and more recently for activity, we believe the method can be easily adapted for screening antibodies.

Speaker Biography: **Hongkai Zhang, Ph.D.,** *Senior Scientist, Lerner Laboratory, The Scripps Research Institute*

Hongkai Zhang is a Senior Scientist in the Richard Lerner Laboratory at The Scripps Research Institute. He had supported many antibody discovery and development projects using phage display, yeast display and deep sequencing. He and his colleagues invented an autocrine based antibody and protein engineering method, by which the first GLP1R G-protein biased agonist and EpoR full agonist bispecific antibody were developed. He will introduce "activity based antibody & protein engineering" and his latest results on selection of natural and combinatorial venom peptide library for ion channel targets.