



PEPTALK

The Protein Science Week

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Cambridge Healthtech Institute's Kent Simmons recently spoke with Fortunato Ferrara of the University of New Mexico about his upcoming presentation "A Pipeline to Select Human Antibodies *in vivo* Against Defined Cancer Targets" at the *Emerging Technologies for Antibody Discovery and Engineering* conference taking place January 21-22, 2016, as part of the 15th Annual PepTalk in San Diego, CA.

Q: Could you please give an overview of your antibody selection strategy?

The use of monoclonal antibody based therapies to treat human disease, including cancer, shows promise, with a growing number of immunoglobulins either in clinical trial or already in the market as effective treatments. However the standard approaches to generate antibodies against targets of interest with therapeutic properties are time-consuming and not always successful. For this reason we developed a modular approach that relies on a combination of *in vitro* and *in vivo* selection methods, combined with deep sequencing to generate and characterize tumor-targeting antibodies for therapeutic purposes.

Q: Why have you chosen this specific "modular approach" to isolate potential therapeutic antibodies?

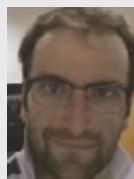
We are confident that our novel platform will accelerate the development of antibody-based drugs for cancer diagnosis and treatment. Our strategy consist in a hierarchical selection strategy: during the first phase a large recombinant antibody library is enriched for potential target-binders by phage display, followed by a refined identification of high affinity, high specific binders thanks to the subcloning of the enriched population in a yeast display system and its flow cytometry-based sorting. Finally the enriched population is challenged directly *in vivo* in preclinical models of the tumors under investigation to screen for antibodies with particular biological properties, suitable either for the delivery of therapeutic or diagnostic payloads or for the use as biologically active naked antibodies.

Q: What are the advantages of this strategy?

Unlike other antibody-selection strategy where potential binders are usually selected either against recombinant proteins or using tumor cell lines where the target of interest is overexpressed, we added an extra critical step where antibodies are finally selected *in vivo*. In this way only antibodies capable of binding to physiologically accessible drug targets displayed in their native conformation are pursued. Moreover the use of two different screening platforms (filamentous phage and yeast) with different physicochemical and biological properties, combined with deep sequencing to assess the similarity and diversity of antibodies, ensures that selected antibodies are platform-independent and, therefore, more suitable for development as therapeutic leads.

Q: Personalized medicine is now becoming a topic of great interest. Do you think your selection strategy can fit into this research field?

We are exploring the advantages of using a patient specific antibody library, generated directly from the tumor microenvironment. We plan to select such library directly on the same patient's tumor to hopefully isolate anti-tumor antibodies. A precise characterization of the humoral response in cancer patient will help to identify antibodies produced directly at the tumor site. Such antibodies are expected to recognize surface receptors on tumor cells, and may have a greater therapeutic and diagnostic potential.



Fortunato Ferrara, Ph.D., Research Assistant Professor, Experimental Therapeutics, University of New Mexico

After completing his undergraduate and Ph.D. studies at the University of Trieste in Italy, he got the opportunity to work in collaboration with Dr. Andrew Bradbury, a recognized leader in the field of antibody engineering, at the Los Alamos National Laboratory. With Dr. Bradbury, Dr. Ferrara has established new strategies to effectively select binders from recombinant antibody libraries. Since January 2015 he has been working at the University of New Mexico Cancer Center, with the goal to improve selection strategies for recombinant antibodies against cancer biomarkers.

To learn more about Dr. Ferrara's presentation and *Emerging Technologies for Antibody Discovery* conference, visit CHI-PepTalk.com/antibody-discovery