

## Interprotein Corporation

Revolutionizing the discovery and development of small molecule protein-protein interaction inhibitors

[www.interprotein.com](http://www.interprotein.com)

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**November 2009:** Interprotein is focused on developing small molecule medicine as an alternative to monoclonal antibody drugs. The company leverages its sophisticated structure-based drug design technology for competitive advantage.



Venture Valuation (VV) interviewed Mr. Masato Hosoda, President and CEO.

**VV:** **Would you please describe your business?**

Hosoda:

Interprotein specializes in discovering and developing small molecule inhibitors of protein-protein interactions. Our objective is to provide small molecule medicine as an alternative to monoclonal antibody drugs. Monoclonal antibodies are difficult and expensive to manufacture. Also they lack oral bioavailability. Small molecules, to the contrary, are relatively easy and cheap to produce and, therefore, affordable to patients. Moreover, they can be orally administered, which is convenient to patients.

Developing small molecules that modulate protein-protein interactions is a challenging endeavor. A major issue is the lack of well-defined binding pockets. We are pioneering in this field by making the best use of a new structure-based drug design method, CPADD (Closest Packing Approach for de novo Drug Design).

Strategically, we are developing small molecule drug candidates for which therapeutic targets have been clinically well proven by monoclonal antibodies. They are Vascular Endothelial Growth Factor (VEGF), Notch1, Interleukin 6 (IL-6), and Immunoglobulin E (IgE) (See Table of Pipeline).

For the VEGF and Notch1 projects, we have discovered a number of hit molecules. Now they are in the stage of lead optimization. In the IL-6 project, we have been collaborating with Evotec (Hamburg, Germany) to develop novel orally active drugs for the treatment of inflammatory diseases.

### Interprotein's Research and Product Pipeline

Target	Domain	Early Stage Development			Middle Stage Development	
		Discovery to Hit Compound	Hit to Lead Compound	Lead Optimization	Non Clinical Study	Phase 1 Clinical Study
VEGF	Oncology	[Progress bar]				
Notch1	Hematology Oncology	[Progress bar]				
Interleukin 6	Inflammation	[Progress bar]				
Immuno-globulin E	Allergy	[Progress bar]				
Zinc	Allergy Inflammation	[Progress bar]				
Cold-stress response of CHO cells	Production of recombinant protein	Production yield improvement of recombinant protein Cold-inducible RNA-binding protein cDNA and investigation of its role in cold-stress response of mammalian cells. Mild hypothermia protects cells from a variety of stress by p53-dependent and p53-independent mechanisms.				

In addition to the four projects I just described, we have two programs in progress: development of novel zinc chelator compounds for allergic diseases and biologics production technology to improve recombinant protein production in mammalian cells.

**VV:**

Hosoda:

**What are your strengths?**

Our company is based on strong science with innovative technologies. One of them is CPADD invented by Dr. Takao Matsuzaki, our drug design advisor. He is a protein crystallographer and has demonstrated pioneering achievements in SBDD (Structure-Based Drug Design) field since 1980s. His drug design method, the closest packing, is a simple approach to create compound's 3D-structure complementary to a protein pocket by filling the binding site with putative atoms. Compound structure is extracted from networks of the packed atoms. CPADD generates almost all possible ligand structures fitting in a binding pocket of target protein.

CPADD applies a filtering method instead of the molecular dynamics energy calculation commonly used for conventional methods such as Docking and Ludi (See Table of Comparison). This dramatically ameliorates identification of compounds with strong activity.

Compared to the conventional methods that are limited to identifying a few active compounds among 100 proposed, CPADD is able to discover 60 with IC50<10 micro M among 136, and 72 with IC50<100 micro M among 194. CPADD demonstrates higher probability in the drug design process. Our business is to offer validated targets and qualified compounds to biotech and pharmaceutical companies. Consequently, the companies will be able to maximize successful drug development and minimize development time and costs.

### Comparison with existing methods

Item \ Method	CPADD	Docking	Ludi
Coverage of search space	Complete	Limited to DB compounds	Not considered ( Partial )
Examined compounds	ca.4x10 <sup>9</sup> All promising compounds created virtually	ca.10 <sup>6</sup> DB Compounds	ca. 10 <sup>6</sup> Combinations of DB Fragments
Major driving force in search	Closest packing structures	Calculated binding energy	Calculated binding energy
Scoring of compounds	Filtering by structure-based mechanism	Calculated binding energy	Calculated binding energy
Results			
Hit finding rate	10 – 90 % Mostly 40 %	0 – 10 % Mostly 3 %	0 – 10 % Mostly 3 %
on PPI targets	40 – 60 %	0	0
Complete failure	None for 12 projects	ca.30 % of projects	ca.30 % of projects

**VV: What are your objectives in the future?**

Hosoda: We have been approached by global pharmaceutical companies who are looking for next generation drug development technologies. Our immediate objective is to close a deal with one or more of them for collaboration, partnering, and/or out-licensing.

We rely on big pharmaceutical companies to conduct clinical studies, marketing, sales and distribution. Our role, as a small biotech venture, is to conduct in-depth research and development activities.

**VV: What opportunities are you exploring?**

Hosoda: Controlling protein-protein interactions provides a key element for the discovery of new drugs. We believe there is a huge opportunity to collaborate with the industry at the early stage so that we contribute to improve the drug discovery process.

**VV: How do you differentiate from your competitors and position your company?**

Hosoda: There are a few drug discovery companies in the U.S. developing drug targets for protein-protein interactions. However, none of them uses an advanced method similar to CPADD that enables drug design to bring near to high precision engineering process.

**VV Comments after the Interview:**

Interprotein 's challenge seems to be how and when to demonstrate and apply its sophisticated technologies in the global industry. Once the company establishes its technological credibility, it may receive a de facto standard in the drug development process.



Development of small molecule protein-protein interaction inhibitors is a field with tremendous potential. The interactions are involved in large biological processes in intracellular communication, programmed cell death and so on. In 2001 the target drugs related to protein-protein interactions accounted for only 0.5% of the total number of 250 therapeutic targets. They increased to 20% of about 600 targets in 2005<sup>1</sup>.

Small molecules benefit from the easy and low-cost production process compared to that of monoclonal antibodies. The global market of monoclonal antibody drug was estimated to US\$33 billion in 2007 and is predicted to double by 2013<sup>2</sup>. It will be interesting to watch how the development of small molecule protein-protein interaction inhibitors will influence the antibody drug market.

## Contact

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Venture Valuation specializes in independent assessment and valuation of technology-driven companies in growth industries, such as the Life Sciences (Biotech, Pharma, Medtech), ICT, high-tech, Nanotech, Cleantech and Renewable energy. In addition to valuation products, Venture Valuation offers high-quality, focused information services like the Global Life Sciences Database, Biotechgate.com and this "*Let's Interview Series*" with leading Life Sciences companies. We select and interview thriving companies and organizations all over the world.

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<sup>1</sup> Bartfai T, Lees GV, Drug Discovery, Page 95

<sup>2</sup> Yoshikawa Iyaku Keizai Report August 2008, Daiwa Institute of Research 26 January 2009