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Interprotein Corporation (2nd interview)

Attracting major pharmaceutical companies with its in silico screening technology targeting small molecule protein-protein interaction (PPI) inhibitors

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February 2012: Since our first interview with Interprotein in November 2009 (see our article No.2009.13), the company's customized drug design technology has begun to attract major pharmaceutical companies for research on small molecule PPI inhibitors. Its technology is able to select active compounds by analyzing binding structures in detail, which is poorly executed by current binding energy based drug design programs and scoring functions. Venture Valuation (VV) again interviewed Mr. Masato Hosoda, President and CEO.

VV: **You have recently announced two partnership contracts in Japan.**

Hosoda: We are delighted that since last November we have been collaborating with Ajinomoto Pharmaceuticals on research and development on small molecular PPI inhibitors against a specific endogenous ligand in the field of gastrointestinal and metabolic disorders. We are working closely together from target selection, 3D molecular design, hit compound identification through to lead compound generation and optimization.

Ajinomoto Pharmaceuticals has been involved for many years in research on cytokines and its receptors. This is why it has shown a strong interest in our SBSG (Structure Based Scaffold Generation) method.

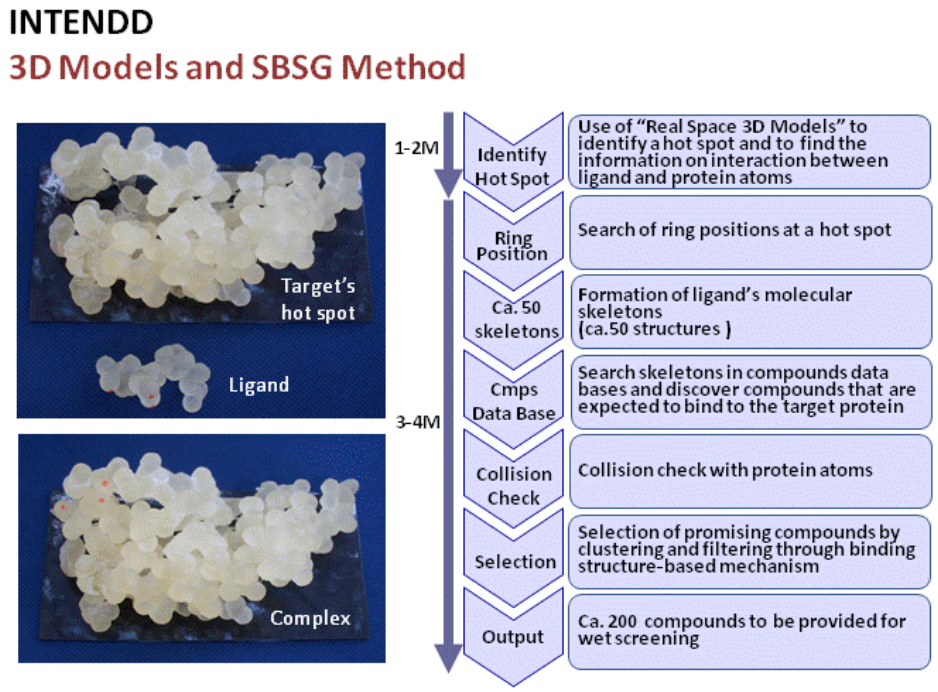
The second partnership started last December with Takeda Pharmaceutical in the field of cancer. We are pleased that Takeda is convinced that our unprecedented method is well worth a trial to improve the probability of success in drug development.

We are hoping that more pharmaceutical and biotech companies will take advantage of our SBSG method that provides a higher finding rate of promising hit compounds than the current
in silico drug design method.

VV: **What is the SBSG method?**

Hosoda: A distinctive feature of the SBSG (Structure Based Scaffold Generation) method, the core of our platform technology named INTEDD (Interprotein's Engine for New Drug Design), is to depend on "binding mechanism" at a final filtering process but not binding energy, unlike the current drug design methods.

The method is characterized by identifying the ligand binding site by use of precise 3D models, searching for ring positions at the binding site, forming about 50 ligand skeletons, searching in a compound database for skeletons possibly binding to target protein, checking collision with protein atoms, selecting all promising scaffolds by clustering and filtering by anticipated binding mechanism, and providing about 200 compounds. (see illustration below)



Based on our past records, the SBSG is able to discover active compounds with IC50 values of single-digit micro mol/L or sub micro mol/L for PPI targets and other disease related target proteins. We have successfully identified small molecular PPI inhibitors against VEGF (oncology), IL-6 (inflammation/autoimmune and oncology), IgE (allergy), Notch (oncology and hematology), and tubulin polymerization (oncology and hematology).

As an example, let me explain VEGF's case: a small molecule compound (MW=490) which is orally administered to mice demonstrates in vivo activity equivalent of bevacizumab (trade name Avastin, Roche /Genentech), an anti-VEGF antibody. Surface Plasmon Resonance measurement proves that the compound interacts with the target protein and inhibits binding of VEGF to its receptor.

Furthermore, as our proposal selected by the Japan Aerospace Exploration Agency (JAXA) last year, we are privileged to develop protein crystals in a microgravity environment. High-quality protein crystallization helps us measure precise interaction of small molecule with target protein by use of x-ray crystallography. This project will add technological value to our drug discovery activity.

VV: **Your growth strategy seems to be the establishment of further strategic partnerships?**

Hosoda: Yes, we are interested in demonstrating globally our technological advantages to biotech and pharmaceutical companies. Scientists in drug discovery are eagerly looking for high-quality hit compounds with various molecular structures.

Depending on each partner's need, we define our role from target selection, 3D molecular design, hit compound identification, lead compound generation and optimization. Our business focus is in principle to support drug discovery for fee for service.

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