

## **Interactive 3D visualisations of biological molecules to aid in drug design**

A new way for scientists to interact with and understand the structure of important biological molecules critical to human health is now available. Called iSee, it's now possible to interactively fly over, zoom into and dive through 3D visualisations of these molecules in atomic detail.

iSee has been developed in a collaboration between the SGC and MolSoft LLC and forms a key part of the SGC's 'open access' science philosophy to make its data freely available to all and to provide it in a manner which maximises the accessibility and understanding for researchers in all fields.

The iSee platform is now also a core part of a collection of peer-reviewed publications detailing research highlights from the SGC. This collection, published in the online journal PLoS ONE on October 20<sup>th</sup> 2009 and entitled "Structural Biology and Human Health: Medically Relevant Proteins from the SGC", includes a protein involved in the survival and proliferation of cancer cells, a protein associated with hereditary paraplegia, and a protein involved in degrading foreign compounds and pollutants in the body.

The SGC is a public-private partnership based at the University of Oxford, the University of Toronto, Canada and the Karolinska Institutet, Sweden and is dedicated to finding the structures of human proteins of medical relevance which could be targets for new drugs

The PLoS ONE iSee collection represents a breakthrough in publishing, moving away from a static and flat 2D set of images towards an intuitive and interactive 3D experience. This is made possible through a freely-available plug-in for web browsers from MolSoft which allow readers to click on hyperlinks within the text of the articles causing the visualisation of the structures to change to reflect the context of the text. The SGC has over 500 datapacks already available over the web and plan to publish a significant number of academic papers incorporating these datapacks over the next four years with *PLoS ONE*.

'If a picture is worth a thousand words, an interactive 3D image is worth considerably more' says Dr Wen Hwa Lee, Senior Scientist in Research Informatics at the SGC. 'iSee provides a quantum leap forward over the 500-year-old technology of static images in printed journals.'

Being able to understand the three-dimensional shape of a protein is a key part of gaining knowledge about the effects of a genetic mutation, or to design drugs to inhibit the action of a protein involved in disease. In the past scientists have had to use complicated software to view the structures in detail. Furthermore, this software does not integrate with other data or text. This makes it hard for scientists who do not work in this area such as geneticists, pharmaceutical chemists and clinicians to gain access and benefit from this data.

'iSee provides a unique way for us to make our data available and accessible to those who will really benefit from it,' says Dr Brian Marsden of the SGC at the University of Oxford. 'It's very intuitive and it should help drug developers in designing new targeted treatments.'

The iSee technology has already proven useful in understanding new discoveries. For example, a small molecule drug originally developed at Oxford University has been the main treatment for osteoporosis for decades. However, it was not understood how the drug worked. When the drug company, Proctor & Gamble, looked at the protein using iSee, it was obvious how their drug Actonel (also known as risedronate) worked within the protein. The drug molecule fitted perfectly in a pocket in the protein revealed in the 3D structure.

The ground-breaking technology underpinning iSee, developed by Ruben Abagyan and his team at MolSoft and known as activeICM, allows anyone with a PC or Mac to run and interact with the iSee viewer in web browsers such as Internet Explorer and Firefox (upon installing a plug-in) or to download a standalone viewer to run the datapacks independently of a browser.

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**Notes for Editors:**

**\* Details of the iSee plug-in**

The web plug-in technology used by iSee, known as activeICM (<http://www.molsoft.com/activeicm.html>) has been developed by Molsoft LLC to allow molecular documents to be embedded within a web page. Patent pending.

**\* SGC**

The SGC is a public-private partnership that was formed to place three dimensional structures of proteins of medical relevance into the public domain, without restriction on use. Its overarching aim is to provide tools and reagents to enable biomedical research and drug discovery. The SGC currently operates out of three laboratories at the Universities of Oxford and Toronto, and at Karolinska Institutet, Stockholm. The research programs derive from a funder-created Target List of ~2,000 proteins, vetted by leading academic and industrial scientists. Targets include human proteins associated with diseases such as cancer, diabetes, inflammation, and genetic disease, as well as proteins from human parasites such as those that cause malaria.

To support its activities from 2007-2011, the SGC received a total of ~USD\$120M from GlaxoSmithKline, Novartis and Merck) and public funders in the U.K. (Wellcome Trust), Canada (The Canada Foundation for Innovation (CFI), The Canadian Institutes of Health Research (CIHR), Genome Canada, The Ontario Genomics Institute (OGI), The Ontario Ministry of Research and Innovation (MRI)) and Sweden (The Knut and Alice Wallenberg Foundation, The Swedish Foundation for Strategic Research, VINNOVA and the Karolinska Institutet).

\* The SGC has already created **over 500 iSee datapacks** which are freely available via the SGC website: <http://www.thesgc.org/iSee>

\* **Oxford University's Medical Sciences Division** is one of the largest biomedical research centres in Europe. It represents almost one-third of Oxford University's income and expenditure, and two-thirds of its external research income. Oxford's world-renowned global health programme is a leader in the fight against infectious diseases (such as malaria, HIV/AIDS, tuberculosis and avian flu) and other prevalent diseases (such as cancer, stroke, heart disease and diabetes). Key to its success is a long-standing network of dedicated Wellcome Trust-funded research units in Asia (Thailand, Laos and Vietnam) and Kenya, and work at the MRC Unit in The Gambia. Long-term studies of patients around the world are supported by basic science at Oxford and have led to many exciting developments, including potential vaccines for tuberculosis, malaria and HIV, which are in clinical trials.

\* **MolSoft LLC**

Molsoft is a San Diego, California-based company that is a primary source of new breakthrough technologies in molecular graphics, visualization, molecular modeling, docking, virtual screening and cheminformatics. Molsoft offers complete solutions customized for a biotechnology or pharmaceutical company in the areas of computational biology and chemistry.

Laboratories in pharmaceutical and academic laboratories use MolSoft's main software platform called ICM-Pro to solve challenging problems in biology, chemistry and physics. The software is widely used for the discovery of new lead compounds for drug discovery. ICM-Pro recently delivered a star performance in a challenging competition to predict the interaction of a ligand to a G-Protein Coupled Receptor (GPCR) a key family of drug targets. Recent success stories have included identification of new lead compounds for GPCRs, nuclear receptors, kinases, proteases, and transferases, all of which are involved in a variety of diseases such as cancer, heart disease and obesity.

ActiveICM was developed to enable scientists to communicate their discoveries to their colleagues in a clear and user-friendly way and has now progressed to a complete tool for scientific publications.