C4X Discovery & Southampton University collaborating on new cyclic peptides

C4XD technology to drive rational design of new drug candidates for HIV

Manchester, UK, September 23 2013 – C4X Discovery (C4XD), a leader in conformational drug discovery and design, is to collaborate with the University of Southampton on rational design of novel drug candidates derived from cyclic peptides. Led by Dr Ali Tavassoli, a world expert in this area[1,2], researchers at the University have discovered new blockers[3] of a protein-protein interaction in viral budding, a key step in the process by which HIV spreads in the body. The partners will use C4XD's 4D NMR technology to analyse the active confirmation of the inhibitors, with this enhanced understanding of activity leading to optimised second-generation compounds with more drug-like properties.

Cyclic peptides and macrocycles are rapidly emerging as an important class of molecule for interrupting otherwise intractable protein-protein interactions and providing the starting point for rational small molecule drug design. Dr Tavassoli is a world expert in the development of new methods for screening cyclic peptides and has published extensively on novel cyclic peptides for a range of therapeutically important targets, including HIV, Hif-1, Hif-2, methyltransferase and AICAR. C4XD's technology allows for the rapid determination of the 3D conformations of ligand molecules in solution, including small-molecule drugs, cyclic peptides and macrocycles. In the collaboration, Dr Tavassoli's group and C4XD will identify the active conformations of the HIV inhibitors and their key pharmacophores (groups of atoms responsible for activity) to enhance the design of second-generation inhibitors.

Knowledge of the bioactive conformation is crucial in driving rational drug design and, until now, X-ray co-crystallography has been the only method that can routinely measure it. C4XD has applied its technology to a wide range of ligands including peptides, carbohydrates, co-factors and small molecule drugs, and in every case, its dynamic 4D structures capture the bioactive conformation. This has powerful implications for drug discovery, significantly accelerating the design of improved molecules during hit discovery, hit-to-lead and lead optimisation processes.

Dr Sam Williams, CEO of C4X Discovery, said, 'We are delighted to be collaborating on this world-leading research with Dr Tavassoli and his team at the University of Southampton. C4X Discovery expects the project to further exemplify the versatility of our technology across a range of molecules and its ability to drive drug design in a rational way. Drugs derived from macrocycles and constrained peptides are expected to be a major therapeutic class in the future[4] and this work complements our proprietary research in this area.'

Dr Ali Tavassoli said, 'We are very excited to be working with C4X Discovery to further evolve our cyclic peptide inhibitor of HIV budding to a drug-like molecule. Budding inhibitors are an untapped class of HIV therapeutics, and the compound resulting from this collaboration could potentially lead to an important new class.' --ENDS—

[1] Miranda, Elena, Nordgren, Ida, Male, Abigail, Lawrence, Charlotte, Hoakwie, Franciane, Cuda, F., Court, William, Fox, Keith R., Townsend, Paul, Packham, Graham K., Eccles, Suzanne A. and Tavassoli, Ali (2013). Journal of the American Chemical Society, 135, (28), 10418-10425

[2] Birts, Charles N., Nijjar, Sharandip K., Mardle, Charlotte A., Hoakwie, Franciane, Duriez, Patrick J., Blaydes, Jeremy P. and Tavassoli, Ali (2013). Chemical Science, 4, (8), 3046-3057

[3] Tavassoli, A.; Lu, Q.; Gam, J.; Pan, H.; Benkovic, S. J.; Cohen, S. N. *ACS Chem Biol* **2008**, *3*, 757.

[4] SciBx collections April 2013, Macrocycles and constrained peptides

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About C4X Discovery Ltd
C4X Discovery is a Manchester-based company focused on optimising drug discovery and design. It was founded in 2008 as a spin-out from the University of Manchester. The company uses its NMR-based technology to solve the dynamic 3D structures of a broad range of biomolecules, including peptides, cofactors, oligonucleotides and carbohydrates. Since C4X Discovery's NMR technology shows what shapes molecules adopt when active, it provides high-quality templates for drug discovery and design, and valuable information for drug candidate optimisation. In addition, the data is generated faster and more reliably than standard techniques such as X-ray crystallography. C4X Discovery has solved structures for large pharmaceutical companies, is developing proprietary drug programmes and has signed a collaboration with AstraZeneca in 2012. It has been funded since inception by life science investor Aquarius Equity Partners. www.c4xdiscovery.com.

About C4X Discovery's technology
C4X Discovery's NMR technology determines accurate 3D structures of drug molecules in solution without the need for structural information for the protein target. These structures are predictive of the bioactive conformation and thereby provide researchers with valuable information on how to improve development-stage compounds. This new information should improve the efficiency and quality of the lead identification, lead optimisation and candidate selection stages of drug discovery programmes.

About the University of Southampton
The University of Southampton is a leading UK teaching and research institution with a global reputation for leading-edge research and scholarship across a wide range of subjects in engineering, science, social sciences, health and humanities. With over 23,000 students, around 5000 staff, and an annual turnover well in excess of £435 million, the University of Southampton is acknowledged as one of the country's top institutions for engineering, computer science and medicine. We combine academic excellence with an innovative and entrepreneurial approach to research, supporting a culture that engages and challenges students and staff in their pursuit of learning.