First peer-reviewed report of potential of C4XD's technology in drug design

Dynamic solution structure of streptomycin in Bioorganic & Medicinal Chemistry

Manchester, UK, July 17 2013 – C4X Discovery (C4XD), a leader in conformational drug discovery and design, announces the publication of a seminal paper describing the use of its novel NMR-based technology to determine the dynamic 3D structures of ligand molecules in solution. The publication in Bioorganic & Medicinal Chemistry[1] is the first peer-reviewed description of the technology and demonstrates its potential value in drug discovery and development.

In the study, C4XD's technology was used to quantify the range of 3D conformations that the antibiotic streptomycin occupies in solution, which reveals that its preferred conformation is the same as its shape when bound to its target (*i.e.,* its 'bioactive' conformation). 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. The results demonstrate that C4XD's technology reveals the bioactive conformation via a much-needed alternative route which, in contrast to X-ray co-crystallography, takes only a few weeks and works for all target classes.

C4XD has applied its technology to a wide range of ligands including peptides, carbohydrates, co-factors and small molecule drugs. In every case, its dynamic 3D structures capture the bioactive conformation. This has powerful implications for drug discovery, significantly accelerating the design of improved molecules during the hit discovery, hit-to-lead and lead optimisation processes.

In its in-house programmes, C4X Discovery has used the technology to identify hits and leads against high-value targets that are intractable to co-crystallography, including GPCRs and ion channels. Moreover, for targets that are amenable to co-crystallography, C4XD's technology provides surprising insights into how to optimise 'druggable' metrics such as affinity, selectivity and ADMET properties.

Dr Sam Williams, CEO of C4X Discovery, said, 'The publication of this study brings an important validation of our innovative NMR technology and its utility in drug development. We believe our technology is an important complement to the discovery tools already used by the pharmaceutical and biotechnology industries, with the potential to be integrated across multiple R&D programmes.'

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[1]**Quantification of free ligand conformational preferences by NMR and their relationship to the bioactive conformation,** Blundell CD, Packer MJ and Almond A, **Bioorganic & Medicinal Chemistry** *In Press, Accepted Manuscript*. Available online July 3 2013. http://dx.doi.org/10.1016/j.bmc.2013.06.056

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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.