



peakexplorer™ Libraries of Drug Discovery

Peakexplorer™ libraries are being developed by Peakdale to address gaps in commercially available compound collections and provide greater diversity. The initial focus of the libraries has been to push the boundaries of GPCR (G-Protein Coupled Receptor) related drug discovery, with over 6,000 well-characterised, highly diverse and novel drug-like compounds. Peakdale is currently developing kinase focused libraries to complement its collection of GPCR libraries.

In creating these targeted libraries, Peakdale's chemists combine proprietary chemistry capabilities with in silico pharmacophore modelling, design and virtual screening algorithms.

Computational chemistry

Peakdale applied the structure-based design expertise of De Novo Pharmaceuticals through a strategic partnership in the development of the GPCR libraries. This novel process includes pharmacophore modelling to provide a binding site model that defines both the volume and key site points, which is vital in the de novo design of novel ligands.

This information was then applied to fragment-based structure design, where molecular fragments are pieced together within the confines of the binding site model. In the initial GPCR range, these fragments were derived from known GPCR ligands and proprietary Peakdale chemistries to introduce novelty and increase diversity. The resulting chemical designs were then optimised by Peakdale's medicinal chemists, to define chemotypes suitable for the generation of focused combinatorial libraries.

Building on this approach, Peakdale has entered into a collaboration with BioLeap, a leader in fragment-based drug discovery, to design and synthesise highly focused kinase libraries for drug discovery, initially targeting the c-Abl tyrosine kinase.

We have also established our own in-house computational chemistry expertise, which means that we can build on our existing reputation for delivering novel compounds and key intermediates as well as offering further services to our customers.

GPCR libraries

Using both known and proprietary chemistries and methodologies, Peakdale chemists have created a library of chemotypes with lead-like properties to broaden the exploration of GPCR-relevant chemical space.

Peakdale provides five individual libraries designed, synthesised and characterised for screening against GPCR targets. The full peakexplorer™ GPCR library now exploits over 27 major chemotypes and offers more than 6,000 purified and characterised, drug-like compounds that are ready for screening.



The libraries, G1-G5, are based on the assessment of specific chemotypes balanced with recognisable GPCR privileged substructures and novel Peakdale chemistry. For example, the G4 library includes a proprietary Peakdale chemotype specifically designed to take advantage of the Company's aminergic GPCR pharmacophore know-how.

The peakexplorer™ sets have been shown to correlate well with data from customers' virtual screening programmes, providing a rich source with which to fill gaps in their own collections of compounds.

peakexplorer™ kinase libraries

The new libraries will focus on tyrosine kinase targets and will expand the current collections. Protein kinases play a crucial role in signal transduction and also in cellular proliferation, differentiation and various regulatory mechanisms. The inhibition of growth-related kinases, especially tyrosine kinases such as c-Abl tyrosine kinase, has the potential to provide new therapies for diseases such as cancer.

Of particular interest to Peakdale's chemists is BioLeap's proprietary technology, which rapidly calculates the free energies of interaction between small molecular fragments and biomolecular structures, and subsequently displays the distribution and orientation of these fragments. One immediate benefit of this technology is the prediction of sites where tightly bound waters can be identified that cannot otherwise be seen in crystallography due to their high entropy.

This information, which cannot be achieved from the static crystal structure alone or from methods that can only measure the enthalpic properties of binding, provides a unique insight into how small molecules bind into key protein binding sites. In addition to lead discovery, the quantitative free-energy based analysis of protein–ligand interactions adds significant value to the lead optimisation process. This information will allow Peakdale's chemists to design novel compounds with better drug-like properties than existing compounds.

Supply

All compounds are purified to >85% and are characterised for purity by HPLC and for structure by LC-MS and/or NMR before being formatted into standard or customer-supplied vials and plates as powders or solutions.

Peakdale operates a fully flexible despatch process, allowing customers to request compounds in their preferred format, for example, 20mg in barcoded vials or 10mM DMSO solutions in 384-well plates.

Further Information

To receive further information on the peakexplorer™ libraries please contact us;

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Applying its innovative chemistry expertise and flexible resources, Peakdale Molecular supports its customers' drug discovery activities through the following products and services;

- Medicinal Chemistry
- Custom Synthesis
- Analytical Services
- Contract Research
- CADD Services
- Intermediates Catalogue
- Peakexplorer Focused Libraries
- Lead-like Compounds for Screening
- *In Vitro* ADMET Services
- Microwave Synthesis Services

Founded in 1992, Peakdale Molecular is based in Chapel-en-le-Frith in the UK, where its purpose built facilities house organic research labs, parallel synthesis labs and a kilo scale-up lab, all of which are supported by a fully equipped analytical department.

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