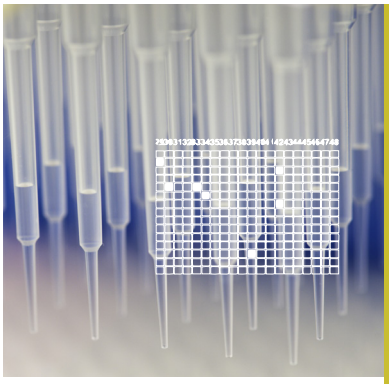
.01. Screening Sciences

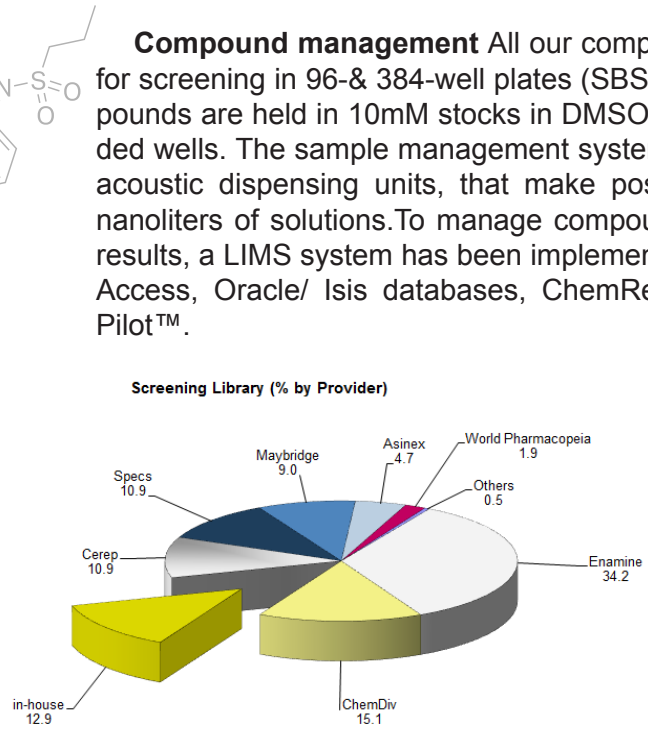


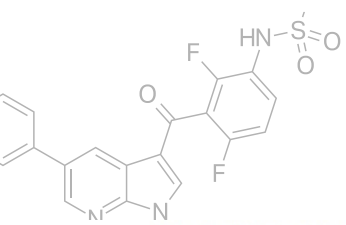
Screening Libraries

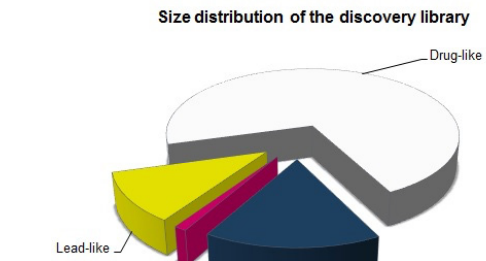
Chemical Libraries The laboratory has assembled a library of more than 90.000 compounds. They have been selected from commercial vendors or prepared by our chemists using state-of-the-art selection and design criteria, in terms of diversity and and “drug / lead-likeness” properties.

siRNA Libraries Using our synthetic siRNA libraries formated for acoustic nanovolume dispensing, we can screen the whole druggable genome in mouse and human models (18 126 genes).

Compound management All our compounds are formatted for screening in 96-& 384-well plates (SBS standards). All compounds are held in 10mM stocks in DMSO in Matrix 2D bar-coded wells. The sample management system includes two Echo acoustic dispensing units, that make possible to manipulate nanoliters of solutions.To manage compounds and associated results, a LIMS system has been implemented in the Unit using Access, Oracle/ Isis databases, ChemReg/BioReg &Pipeline Pilot™.







2016

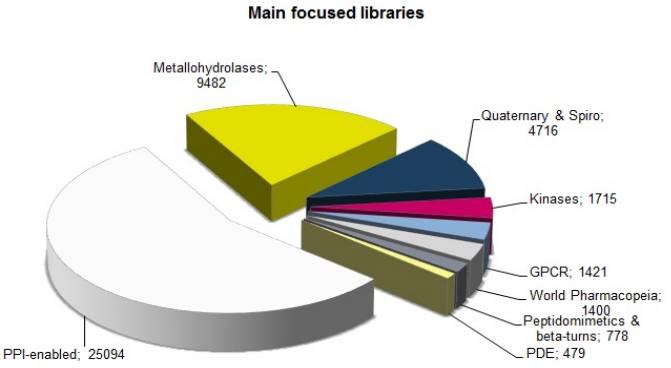
Compound Collections

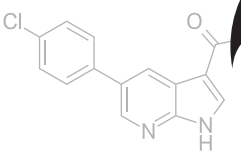
Small Molecule Sets
- Diversity set: 90,000 (includes a 15,000 core subset)
- Spiro & quaternary: 4,716
- Peptidomimetics, β-turns : 778
- Acidic set : 9,400
- World Pharmacopeia: 1,400
- PPI set: 25,000*
- Kinases set : 1,715
- GPCRs set : 1,421

Fragment sets
- 1,040 in house selected and/ or synthesized

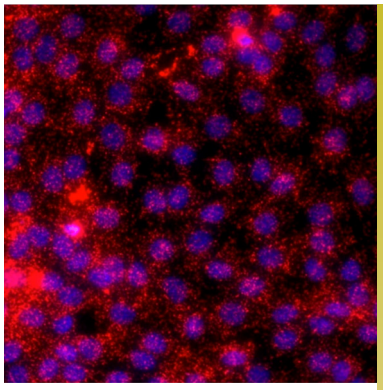
siRNA
-mouse & human
-72505 (4/well)

** As defined by in-silico screen Reynes, C.; et al Designing Focused Chemical Libraries Enriched in Protein-Protein Interaction Inhibitors using Machine-Learning Methods. Plos Computational Biology 2010, 6, e1000695.*





Drugs & Molecules for Living Systems



2016

Screening Techniques

- AlphaLISA
- Biacore
- BRET
- ELISA
- ELISA/membrane
- FACS
- Fluorescence Intensity
- Fluorescence Polarisation
- FRET
- HCS
- HTRF
- LCMS (TOF)
- Luminescence
- Magpix
- nanoLC
- Radioligand
- Transcription assay/FI
- Transcription assay/ luminescence
- TR-FRET
- TSA
- Western-Blot

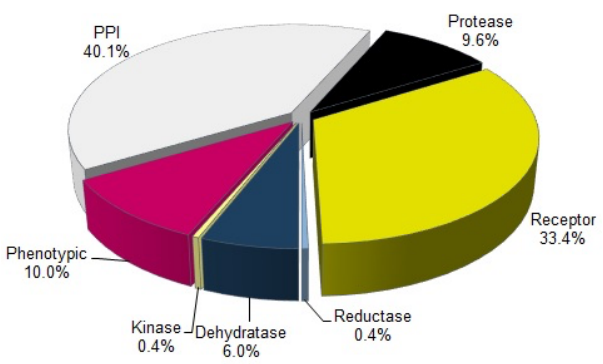
Screening Platforms

High-throughput Screening platform. U1177 includes a screening facility set up at the Institut Pasteur de Lille and operated by six biologists. Its mission spans the whole medicinal chemistry support process: compound library management, assay development, screening to hit generation and the hit-to-lead process. Key workstations are liquid handling systems (CyBITM-Well, Biomek NX), automated multi-mode fluorescence/ lumines- cence readers (Mithras LB940 Research III, VictorT-M3V), a lightcycler 480 and a cell culture unit. Since 2008, this facility was recognized as an IBiSA platform.

High-Content Screening plaform. U1177 is part of the HCS Equipex ImagInEx BioMed. http://www.bicel.org/. On our fully automated HCS platform from Agilent, we screen siRNA and compounds libraries at high throughput in complex systems using confocal microscopy and image analysis.

Assay Development and Compound Screening. The laboratory has a recognized expertise in the development of miniaturized, fast and robust assays for medium to high-throughput screening. All critical screening parameters are optimized in terms of reagent cost, required manpower and time, as well as its discriminating power, as measured by the Z' and eventually the Z factor. We develop homogenous assays, highly convenient to perform high throughput screening, as well as ELISA assays or cell-based assays (reporter gene, BRET...) to study enzymatic reactions, protein-protein interactions, DNA-protein interaction, GPCR....Thermal shift assays are also used to measure protein-ligand interactions. Assay development and screening campaigns are performed using good laboratory practices to ensure the traceability and the quality of the data. We work in collaboration with national and international biological research teams with whom we develop quantitative assays on targets of interest.

Screening datapoints



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