

**PARTNER PLATFORM**  
**High Throughput Screening / Hit to lead**

**CMBA (Criblage pour des Molécules BioActives)**

General information

Administrative information	
Structure	CMBA
Address	17 rue des Martyrs, 38000 Grenoble
Website	<a href="http://www.cea.fr/drf/IRIG/Pages/Infrastructures/CMBA.aspx">http://www.cea.fr/drf/IRIG/Pages/Infrastructures/CMBA.aspx</a>
Manager	Marie-Odile FAUVARQUE
Contact	<a href="mailto:marie-odile.fauvarque@cea.fr">marie-odile.fauvarque@cea.fr</a>
Date of implementation	2001

Labels / quality approach	
IBiSA	Yes / 2008
ISO 9001 certification	No
National networks	Yes / 2018 (ChemBioFrance)
International networks	No
Other	Cancéropôle CLARA

Team	
Number of researchers	1
Number of engineers	3 dont 2 PhD
Number of technicians	1
Number of administrative staff	1
Other	Specify

Main achievements	
Number of screenings performed since creation	120 (approx..)
Number of screenings performed per year	6 (approx..)
Fields of expertise / therapeutic areas	cancerology, immunology, infectiology, hematology, rare diseases, neurodegenerative disorders

Scientific Information

Chemical Library
Description of the collection (number of chemical molecules, natural, royalty-free products, known synthesis methods, etc)
About 75,000 chemical compounds, coming from several academic or commercial collections are available for screening at the CMBA platform. It includes in particular : <ul style="list-style-type: none"> <li>• 2,240 FDA-approved compounds from both the Prestwick Chemical library and the TargetMol's Custom Compound Library, for drug repositioning,</li> <li>• An InFarmatik's collection of 728 structurally-diverse compounds,</li> <li>• The Life Chemicals' PPI collection of 800 compounds, selected to target protein-protein interactions,</li> <li>• The academic, CNRS' National Collection (CN) of about 65,000 compounds, and its "essential" version of 1,140 structurally representative compounds.</li> </ul>

- the academic “FrPPIChem” collection of 10,314 commercially-available compounds, selected *in silico* by machine-learning methods to specifically target protein-protein interactions (DOI: 10.1021/acschembio.0c00179).

Commercial collections contain royalty-free compounds, whereas academic libraries are available after Material Transfer Agreement.

Compounds of a given collection from a commercial source can be supplied by the collection supplier and potentially by other compound suppliers. Any CN’s compound is the property of the chemistry laboratory which synthesized it. This laboratory has a right of first review on its compound, but can collaborate with the project investigator by providing additional quantities and various analogues, information on the synthesis method, and finally let him continue working on the compound on his own.

Beyond these various collections available at the CMBA, the purchase of any other collection that would be relevant for a given screening project can be considered.

Conditioning	Most of the compounds collections available at the CMBA are formatted in batches of daughter plates, ready-to-used for one-shot screening campaigns. The CMBA also stores a backup copy of the CN, but rather orders daughter plates from the CN’s official distributor, Evotec, for each screening campaign of this library
Database (structure, accessibility conditions)	SDF files of the compound collections can be provided upon request.
Member of the National Chemical Library	The CMBA platform is indeed a member of the ChemBioFrance national infrastructure that includes 3 pillars <ul style="list-style-type: none"> <li>- the laboratories contributing to the National Chemical Library,</li> <li>- Screening and ADME-tox platforms network to which the CMBA belongs</li> <li>- Chemo-informatics laboratories</li> </ul>

Targets
Targets for the screening service (e.g. protein targets, cell targets, etc.)
Any protein or cell target /model can be considered, up to and including Biosafety Level 2.
Activities (e.g. cloning, protein expression, obtaining cell lines, management and storage of lines, cell culture, etc.)
The CMBA’s activities include: <ol style="list-style-type: none"> <li>1. Obtaining commercial cell lines, managing and storing cell lines,</li> <li>2. Developing biological assays using protein, cell lines or any reagents provided by the project investigator and/or supplied from commercial sources,</li> <li>3. Helping the project investigator to set up a relevant and robust biological screening assay,</li> <li>4. Optimizing in-house the assay protocol provided by the project investigator to meet the constraints of compound screening,</li> <li>5. Automating the optimized assay protocol up to its statistical validation,</li> <li>6. Performing compound screening of the selected chemical collection(s),</li> <li>7. Analyzing data to list the most relevant, bioactive compounds identified by screening ;</li> <li>8. Suggesting further studies to characterize the most interesting compounds.</li> </ol>

High throughput screening	
Number of measurements/days (approx.)	From a hundred to several thousands (depending on the complexity and duration of each assay protocol).
Biological tests proposed (e.g. in vitro enzymatic tests, cell tests (binding tests, cell survival, image analysis, etc))	
<ul style="list-style-type: none"> <li>- Protein-protein interaction assays,</li> <li>- <i>in vitro</i> enzymatic assays,</li> <li>- cell-based assays (binding, biomarker quantification/subcellular localization, cell survival/ differentiation/ signalling/ migration/ apoptosis, ROS production, spheroids growth, etc.)</li> <li>- Custom assay development</li> <li>- using whole microplate's well measurements of absorbance/fluorescence/luminescence signal (High-Throughput Screening or HTS approach),</li> <li>- using fluorescence-based image acquisition and analysis (High-Content Screening or HCS approach).</li> <li>-</li> </ul>	
Technologies / Equipment (robots, automates, etc.)	
<p>The HTS facility benefits from a fully-integrated robotic platform, including</p> <ol style="list-style-type: none"> <li>1. a Tecan MCA 96-channel pipetting head allowing to work in a 96- or 384-well plate format,</li> <li>2. a LiCONiC STX44-ICBT automated cell incubator,</li> <li>3. a Tecan HydroSpeed™ 96-/384-channel microplate washer,</li> <li>4. a Tecan Infinite M1000 multimode microplate reader, for quantifying signals of absorbance, luminescence and fluorescence (including time-resolved fluorescence and fluorescence anisotropy)</li> <li>5. a LiCONiC LPT 220 carousel for storing microplates and tips boxes,</li> <li>6. a Tecan RoMA robotic arm to move the microplates from one instrument to another.</li> </ol> <p>This robotized instrumentation allows to fully automating a large variety of biological, and is installed in a BSL2 safety cabinet to screen under sterile conditions when required.</p> <p>The HCS facility is based on two complementary, automated microscopes:</p> <ol style="list-style-type: none"> <li>1. a CellInsight CX7, which is a powerful confocal imaging system in terms of image resolution and high-content image analysis. It is equipped with a 7-color LED illumination, and acquires images at multiple magnifications (4x to 60x) of 2D cultured cells or 3D structures (acquisitions on different Z-planes, with the confocal mode if necessary). An integrated incubation chamber regulated in temperature and CO2 allows performing tests on living cells.</li> <li>1. an IncuCyte Zoom live-cell microscope to investigate, during hours to days, phenotypic modifications of live cells grown on microplates as 2D monolayers or 3D structures. It allows automated imaging and quantification of compounds effect at each time of the kinetic, in label-free and non-invasive experiments, with cell event quantification thanks to AI algorithms, for studying essential biological processes.</li> </ol> <p>Both CMBA's facilities benefits from a fully equipped cell culture room, and dedicated instruments including a cell incubator, and an automated dispenser for quick and homogenous cell seeding on numerous microplates in parallel.</p>	

Access	
Site teams	Under conditions <ul style="list-style-type: none"> <li>- operated by staff for HTS</li> <li>- operated by staff, or after training and charter acceptance for HCS</li> </ul>
External academic teams	Under conditions <ul style="list-style-type: none"> <li>- operated by staff for HTS</li> <li>- operated by staff, or after training and charter acceptance for HCS</li> </ul>
Private Outdoor Teams	Under conditions <ul style="list-style-type: none"> <li>- operated by staff for HTS</li> <li>- operated by staff, or after training and charter acceptance for HCS</li> </ul>

Training courses offered
<p>The automated microscopes of the HCS facilities of the platform are accessible to the scientific community (academia, private companies) either with the help of CMBA staff or free access after a training period with the person in charge of the HCS activity.</p>