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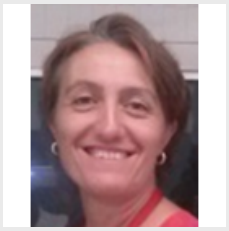

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Activity

The Institute Curie/CNRS Chemical Library was created from the chemical molecules synthesized by the chemists of the Institute Curie of Paris (UMR3666 / U1143) and Orsay (UMR9187 / U1196). This academic chemical library, one of the most important of France, contains almost 10000 substances. Such a set of chemicals is constituted not only of the final products, but also of synthetic intermediates obtained during the programs of optimization against various therapeutic targets.
Since its creation, 65 years ago, the main motivation of the chemistry laboratory of the Institute

Curie has been the discovery of molecules for cancer treatment. A direct consequence of this activity is the existence (often in significant quantities) of samples of several thousands of synthesized compounds. Moreover, advances in proteomics and genomics have led to the discovery of an increasing number of new protein targets with therapeutic potential.

By screening small molecules, either individually or, preferably, as collections called libraries of small molecules (chemical libraries), many opportunities are offered to discover or identify biologically active molecules, which are tools in “Chemical Biology” or “drugs of tomorrow”. In parallel the approach of rational conception, the serendipity is at the origin of the identification of many active ingredients. So, in coupling chemical libraries and platforms of screening, it is possible “to accelerate the fate”. In this context, the chemical libraries of diverse institutes and French universities federated to form the National Chemical library (CN), this federation is supported by the CNRS (GIS-Chimiothèque nationale). This movement begun in 2001 was at the origin of the creation of the Chemical library of the institute Curie.

The compounds of the chemical library are available on 96 or 384 wells microplates directly usable for diverse tests. The Chemical library continues to grow by addition of the new molecules synthesized by the chemists.

Aims

As platform, the biologists in particular those of the Institute Curie and the customers of the National Chemical library can access to these molecules for selected assays by contract as part of a discovery partnership. The miniaturization and the automation of the biological tests allow screening the set or the part of the Chemical library to discover “Hits”. The screenings can serve to select compounds which can interfere with biological phenomena. The results of these tests then give rise to scientific productions (publication and\or patent).

An expertise in chemical optimization of “Hit” (synthesis of structural analogues to establish for example a relation Structure / activity) is also proposed to the partner biologists by the platform Chemical library to understand better the involved biological phenomena or to improve the activity in a therapeutic purpose. The development of molecular tools to identify the biological targets of “hit” can be also envisaged at the end of the assays of chemical optimization. The screening of the chemical library thus leads to scientific collaborations between biologists and chemists.

Network

- Chimiothèque Nationale CN “French Chemical Library”
- GDR ChemBioScreen
- GDR Chemoinformatique

Collaborations

Screening platforms

Biophenics "Plateforme de criblage cellulaire à haut débit" – ***Institut Curie*** – Paris – Elaine DEL NERY SANTOS –
PCBIS « Plate-forme de Chimie Biologique Intégrative de Strasbourg » – Pascal VILLA –
CMBA « Plate-forme de Criblage pour des molécules BioActives » – CEA Grenoble – Caroline BARETTE –
PICT « Plateforme Intégrée de Criblage de Toulouse » – Frédéric AUSSEIL –
CBC « Criblage Biologique et Chimiothèque » – Institut Pasteur – Paris – Hélène LEHMANN-MUNIER –

Drug Technologies platform

TechMedIll – Strasbourg- Patrick GIZZY-
http://www.pcbis.fr/fr/TechMed-IntroductionPresentation

Collaboration inside Curie

Johannes Ludger – Chemical Biology of membranes and therapeutic delivery, UMR3666/U1143, http://chemicalbiology.curie.fr/fr

Mounira Amor-Guéret – UMR 3348 – Stress génotoxiques et cancer – http://umr3348.curie.fr/fr

Yves Pommier – Developmental Therapeutics Branch, Center for Cancer Research, National Cancer Institute, Bethesda, USA – https://ccr.cancer.gov/Developmental-Therapeutics-Branch

Services

- The collection can be supplied in its entirety or partially by contract as part of a discovery partnership. Samples are available under various formats: powder or in solution in the DMSO (in plate 96 wells or 384 wells, 10 mM).
- A help to the selection of samples is also proposed by molecular modeling and virtual screening: research by similarity, sub-structure, fragments, classification by family… Other sharper methods (docking, QSAR, pharmacophore) can be also proposed.
- An expertise in chemistry "hit-to-lead" is also possible. Resynthesis of active products or hits, synthesis of structural analogues can be realized by the chemists of units or by the platform chemical library. To assure this service, the platform is equipped by a robot of synthesis, an automated microwave, and automatic purifiers.
- Tools of molecular chemistry to identify the biological target can be developed on request by the platform.

- Collaborations with platforms of academic screening or drug discovery can be proposed

Equipment

- Nouveau robot en cours d'achat
- Microwave CEM
- Synthesis robot Chemspeed
- LC-MS Waters
- Combi Flash Companion/ Puriflash Interchim

Key publications

Year of publication 2017

Morgan Pellerano, Sergey Tcherniuk, Corine Perals, Thi Nhu Ngoc Van, Elsa Garcin, Florence Mahuteau-Betzer, Marie-Paule Teulade-Fichou, May C Morris (2017 Apr 22)
Targeting Conformational Activation of CDK2 Kinase.
Biotechnology journal : 12 : 1600531 : DOI : 10.1002/biot.201600531

Guillaume Kellermann, Florent Dingli, Vanessa Masson, Daniel Dauzonne, Evelyne Ségal-Bendirdjian, Marie-Paule Teulade-Fichou, Damarys Loew, Sophie Bombard (2017 Mar 1)
Exploring the mechanism of inhibition of human telomerase by cysteine-reactive compounds.
FEBS letters : 591 : 863-874 : DOI : 10.1002/1873-3468.12589

Year of publication 2016

Laetitia Saint-Paul, Chi-Hung Nguyen, Anne Buffière, Jean-Paul Pais de Barros, Arlette Hammann, Corinne Landras-Guetta, Rodolphe Filomenko, Marie-Lorraine Chrétien, Pauline Johnson, Jean-Noël Bastie, Laurent Delva, Ronan Quéré (2016 Sep 1)
CD45 phosphatase is crucial for human and murine acute myeloid leukemia maintenance through its localization in lipid rafts.
Oncotarget : 7 : 64785-64797 : DOI : 10.18632/oncotarget.11622

Year of publication 2015

Florence Mahuteau-Betzer (2015 May 12)
The French National Compound Library: advances and future prospects.
Médecine sciences : M/S : 31 : 417-22 : DOI : 10.1051/medsci/20153104016

Guillaume Kellermann, Markus Kaiser, Florent Dingli, Olivier Lahuna, Delphine Naud-Martin, Florence Mahuteau-Betzer, Damarys Loew, Evelyne Ségal-Bendirdjian, Marie-Paule Teulade-Fichou, Sophie Bombard (2015 May 9)
Identification of human telomerase assembly inhibitors enabled by a novel method to produce hTERT.
Nucleic acids research : 43 : e99 : DOI : 10.1093/nar/gkv425

Year of publication 2013

Marianne Lucas-Hourani, Daniel Dauzonne, Pierre Jorda, Gaëlle Cousin, Alexandru Lupan, Olivier Helynck, Grégory Caignard, Geneviève Janvier, Gwénaëlle André-Leroux, Samira Khiar, Nicolas Escriou, Philippe Desprès, Yves Jacob, Hélène Munier-Lehmann, Frédéric Tangy, Pierre-Olivier Vidalain (2013 Oct 8)
Inhibition of pyrimidine biosynthesis pathway suppresses viral growth through innate immunity.
PLoS pathogens : e1003678 : DOI : 10.1371/journal.ppat.1003678