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**Customer Case Study** 

#### Institut Pasteur's PF-CCB Platform Relies on CDD Vault as Central Hub for Compound Inventory and Screening Data

Headquartered in France and established in 1887, Institut Pasteur is today a leading global nonprofit biomedical research centre with 32 member institutions around the world. Focused on collaborative research and education in areas as diverse as infectious diseases, cancer, and neurodegenerative disorders, Institut Pasteur's 12 research departments gathering 142 research units - including 7 World Health Organization Collaborating Centres - work with 32 technology platforms and core facilities.

The 12 Institut Pasteur research departments:

- Cell biology and infection
- Developmental and stem cell biology
- Structural biology and chemistry
- Genomes and genetics
- Immunology
- Global health

- Microbiology
- Mycology
- Neuroscience
- Parasites and insect vectors
- Virology
- Computational biology



Credit: Musée Pasteur - © Olivier Panier des Touches

### Scientific priorities and ongoing research

In January 2024, Institut Pasteur welcomed renowned immunologist, Yasmine Belkaid, as its new director. Aware of the need to keep evolving in today's complex and challenging world, Institut Pasteur's scientific strategy is guided by several key public health challenges. The strategic axes for the next 5 years are currently being finalized, and will focus on: - Antimicrobial resistance

- Emerging infections associated with climate and environmental changes, including vector borne diseases
- Inflammatory disorders
- Cancer and age-related diseases

# Dedicated small molecule screening core facility

Central to Institute Pasteur's disease and drug discovery programs is the Chemogenomic and Biological Screening platform (PF-CCB), one of the core facilities, which houses the organization's expanding compound library and automated robotic platform for high throughput experimental assays for compound screening. A dedicated team of scientists curates the library and manages the platform for small molecule screening programs undertaken by the organization's internal research teams, and for external collaborators.

Since the platform was established in 2015 under the direction of Dr Fabrice Agou, PF-CCB has relied on CDD Vault as the single repository for its small molecule compound library inventory, and since 2019 the PF-CCB has used CDD Vault for more in depth management and analysis of screening assay data generated by projects in many different areas of disease and biology. The PF-CCB platform comprises a full suite of state-of-the-art instrumentation and automation, including acoustic liquid handling technology to support both high-content (phenotypic) screening and high-throughput, target-based screening. Currently offering expertise in biochemical, cellular and fluorescence microscopy screening, the platform plans to expand its capabilities to embrace emerging technologies.

The PF-CCB compound libraries currently contain more than 70,000 compounds, and the Institute also has paid access to the 80,000 compounds of The French National chemical library (Chimiothèque Nationale) explained Jeanne Chiaravalli, PF-CCB research engineer. Separately, the PF-CCB is working towards quality certification that will allow its entry to the ChembioFrance's French network of screening facilities. Chiaravalli works with research teams for the development of screening assays, alongside Agnès Zettor, who is the compound manager. Zettor also oversees Vault access, assay data management and uploads.

CDD Vault was selected as the unit's inventory management platform following a visit by PF-CCB head Fabrice Agou to the Rockefeller Institute in 2017, where Chiaravalli - who had previously been a research engineer at the Institut Pasteur - was working with the Vault as part of her role as research engineer at the Rockefeller's High Throughput Screening and Spectroscopy Resource Center (HTSRC). Agou saw the Vault in action, and brought that experience back with him to France. "Agou wanted to set up a similar facility here at Institut Pasteur to offer these same kinds of screening assays," Zettor continued. "So, when the PF-CCB was established, CDD Vault was deployed as the inventory platform for our first compound libraries."

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Agnès Zettor, Compound Manager, Institut Pasteur

Implementing CDD Vault into the new facility's setup was a fairly easy process, she suggested. "We had a few training sessions with CDD first. But actually, the software is quite intuitive, so for the inventory parts it was quite easy to process the data and learn just by using it." On rejoining the Institut as a research engineer with the PF-CCB in 2019, Chiaravalli then brought with her considerable Vault experience, and helped to train the PF-CCB team to use the Vault to manage assay data and use its breadth of features for carrying out data analysis. "The CDD team has always been very fast to respond to any technical queries or support that we've needed," Zettor added, "so we always feel well supported."

#### Partnering on small molecule assay development

The PF-CCB collaborates with multiple teams across the 12 Institut Pasteur research departments and external institutions. "We assist the research teams with the development and the application of their drug discovery programs," Chiaravalli explained. "Researchers approach the platform with an idea, such as a target of interest, and once projects have been approved, we help them set up the initial screening assay, carry out the primary screen and select active compounds."

Requests for screening projects are made through an application and review process

overseen by a steering committee. "Initial contact is usually made via email, Chiaravalli further noted. "The platform director and myself have an initial discussion with the researchers and the principal investigator about aims and feasibility before presenting the project to the steering committee." Once approved, the PF-CCB and researchers work together to outline the structure and scope of the screening work.

"We support teams from initial assay development and optimization through hit-tolead and lead optimization," Chiaravalli added. "We assist them with primary hit identification and initial validation, and then with development of orthogonal assays to further validate the molecules. We can also cherry pick hits for retesting in dose-response studies, which are key to help define those active compounds that are most likely to progress to preclinical development." The platform's expertise extends to initial toxicity studies, mechanism of action studies, and aggregation/solubility testing. The collaboration can sometimes progress as far as initial testing in animal models. "For CoVID, for example, we developed a pipeline from initial compound screening through to in vivo proof of concept in a hamster model."

### Using CDD Vault to track and compare

Importantly, using the Vault to monitor and evaluate assay data can also help to highlight potential issues. "The Vault makes it possible to directly compare compound and assay data from different projects," Chiaravalli stated. Keeping track of hits, their associated data and related compound collections is really important, she pointed out. Tracking compound collections at each screening stage within a project, but also between projects can highlight any potential anomalies, for example "When we are looking to buy a new library, we can carry out a 'fake' upload into CDD to quickly check how many compounds may already be in the database, and this is a really valuable feature of the Vault."

Agnès Zettor, Compound Manager, Institut Pasteur

identifying frequent hitters, which may be compounds that can non-specifically interact with a broad range of targets. "We like to compare the assay results and data between projects, especially hit lists. I always check if hits are already in other collections as active compounds because such frequent hitters can represent a real red flag."

Institut Pasteur is continually growing its compound collections and aims to build a new library every year, if possible, Zettor explained. CDD Vault allows the PF-CCB scientists to see how many compounds in a potential new library may already be in the PF-CCB's inventory. "When we are looking to buy a new library, we can carry out a 'fake' upload into CDD to quickly check how many compounds may already be in the database, and this is a really valuable feature of the Vault."

Another major plus point for the PF-CCB's perspective is that CDD Vault makes it relatively easy to customize reports and has the flexibility to let users create files that contain the most important information and relevant information for each different project. "We commonly work with bioinformaticians on campus who may need access to our library to compare structures, or do virtual screenings, for example," Zettor noted. "We can easily upload the information they need directly from the Vault."

One particularly valued Vault feature is the ability to visualize assay data as heat maps that can indicate if and where there may be a problem with hardware, such as dispensing robots, Chiaravalli continued. "The dispensing robots deliver the compounds to the plate wells, but, for example, if there is one or more clogged tips in a dispensing instrument the same well or wells in each plate will be affected, and this can be visualized quickly with the heat map. If you are dispensing with a multichannel pipette and there is a line that always has a lower or higher value, then you can go back to QC, load the data into CDD again, and quickly get a heat map to show where the problem is."

# A focus on teaching and training

The PF-CCB is not responsible for handling all the activities for every project, however. "There are not enough of us here at the PF-CCB to run all the assays ourselves. We store the library, and we provide the screening plates, but generally someone from the requesting lab needs to be here to fill the plates and generate the data," Chiaravalli added. "They then send us the data, which we upload into the Vault, and then analyze for them." It's more of a collaboration than a service, she suggested. Giving the researchers this hands-on experience is also a useful form of education and training. "Education is an important part of what we do here at Institut Pasteur, and using this model we can train students, PhDs, post-docs, technicians and professors how to carry out a screening project."

#### **Security and licensing**

Vault security is a key consideration for any screening project, whether for external partners or in-house research teams. External researchers are not provided with Vault access, and Institut Pasteur researchers have only "Read and Download" access relating to their own projects. All assay results are passed to PF-CCB scientists, who upload the data into the Vault. "We have floating read and download licenses that can be assigned to researchers involved in an active project so they can access their own research, view and download relevant data on their compounds and assays. When the project is complete, that license is then passed to another researcher," Chiaravalli noted. Only a handful of individuals have permanent and complete administrative-level access to the platform and all its data, and fewer individuals are authorized to import new library data into the compound inventory part of the Vault.

Researchers use the in house electronic laboratory notebook (ELN) for recording their assay protocols, but a secure link directly from the ELN to the compound structure and assay data stored in CDD Vault makes it easy to view all the relevant research data side by side, said Zettor, who is one of the few scientists with authorization to import into the Vault new compound library data and assay data generated by the research teams.

#### Tropical diseases and SARS-CoV-2

Emerging infectious diseases is one major focus area for research carried out at Institut Pasteur, with interests spanning tropical diseases including Dengue, chikungunya, and Zika viruses. PF-CCB's facilities and expertise were harnessed to assist in research and

development for SARS-CoV-2 treatments. "Thanks to collaboration with research teams experienced in virology, we were able to quickly set up a platform for compound screening against SARS-CoV-2 from the beginning of the pandemic," Chiaravalli said. Proof of concept does need to be carried out on the native virus, it's not possible to rely on screening compounds against reporter assays in pseudo viruses. "But there aren't many institutional organizations such as ours that have the required BSL level 3 with automation and access to the virus. This meant that we received a lot of requests from small biotech companies and academic labs with interesting molecules they wanted to evaluate."



Credit : Institut Pasteur/François Gardy

The automated 384-well plate pipeline that was developed now allows Institut Pasteur to work end to end on antiviral compound screening. "We have this whole pipeline in place and it's relatively easy to adapt to other viruses. We are working to expand the model to other viruses, especially tropical diseases or respiratory diseases in the context of a pandemic preparedness program.

"In the coming years, PF-CCB could play a pivotal role in the establishment of a future Center for Drug Discovery and Development, suggested Zettor. "By facilitating highthroughput in vitro and in silico screening of chemical hits, it will serve as a crucial entry point in the drug development pipeline." Added Chiaravalli, "This center will integrate advanced methodologies, such as AI-driven approaches and structural biology insights, to identify promising compounds efficiently. It will support subsequent stages, including hit-to-lead optimization and lead characterization, ensuring a streamlined and innovative path toward preclinical evaluation and therapeutic breakthroughs."

#### About Collaborative Drug Discovery

Collaborative Drug Discovery provides a modern approach to drug discovery informatics that is trusted globally by thousands of leading researchers. Our CDD Vault is a hosted informatics platform that securely manages both private and external biological and chemical data. It provides core functionality, including chemical registration, structureactivity relationship analysis, inventory management, visualization, and electronic lab notebook capabilities. For more information, visit us at <u>www.collaborativedrug.com</u>.



Credit : Institut Pasteur/François Gardy