CDD VAULT®
Complexity Simplified

Customer Case Study

"CDD Vault ELN has helped a lot to increase efficiency, it also means that we don't lose lab data, as well as reducing the likelihood that mistakes are made."
- Michel Westermann, M.Sc. Chemie

iGEM

NOSQUITO
iGEM Münster 2024

Advancing Sustainable Mosquito Repellent Production: The iGEM-Münster NOsquito Project with CDD Vault

The iGEM Competition is an annual, worldwide synthetic biology event, established by the non-profit iGEM Foundation, through which hundreds of multidisciplinary teams of high school and university students collaborate to conceptualize, build and test genetically engineered systems designed to help address key global issues. Celebrating its 20th year in 2023, the competition showcases innovative concepts for harnessing synthetic biology to make the world a better place, in fields as diverse as biomanufacturing, healthcare, food and nutrition, environment, climate, fashion and cosmetics, and space. The 2024 iGEM contest included projects from more than 400 multidisciplinary teams – nearly 9500 participants – in more than 50 countries and regions.

Collaborative Drug Discovery (CDD) welcomed the opportunity to support the 2024 team of the University of Münster, providing the 27 young scientists with year-long access to CDD Vault and ELN for their mosquito repellent NOsquito project. Headed by student project coordinators Cara Jaeckel, Louis Schanzmann and Annika Potthoff, the investigators aimed to establish an efficient, economically and environmentally sustainable biosynthetic pathway for producing N-benzoylpiperidine (NBP), a key mosquito repellent that is a structural analogue of DEET. The student team was supported by guidance from principal investigator Prof. Dr. Ing Jochen Schmid, together with advisors and postdoc instructors.

The Problem with NBP Production, and a Solution

Like most insect repellents NBP is traditionally manufactured from fossil fuel via a synthetic route. The University of Münster NOsquito researchers wanted to develop a biosynthetic pathway that could then form the basis of a biotechnological approach to NBP manufacture using renewable resources.

Producing NBP by existing synthetic methods has been problematic. Central to the pathway is a piperamide synthase (PAS) enzyme that catalyzes one of the final molecular conversion steps. But the enzyme has low activity, making the process inefficient and slow. “Another problem is that the synthetic route creates a lot of halogenated intermediates, and so is not sustainable,” Louis Schanzmann noted. “And NBP manufacture requires large scale chemical manufacturing facilities, so decentralized production isn’t possible.”

Through NOsquito the researchers aimed to design and validate a more efficient PAS, as part of an enzyme cascade that would allow NBP production from natural sugar feedstocks, rather than via a synthetic chemistry route. This new, more efficient pathway could then be exploited to produce NBP using two different bio-based strategies – one using precision fermentation, and the other enabling production in an engineered crop plant. Both approaches remove reliance on fossil fuels, and were investigated by the team in parallel with their work on optimizing the piperamide synthase enzyme.

For the enzyme identification work, and further research on the biomanufacturing side to the project, the team drew on preexisting knowledge and connected with outside groups that could offer valuable experience.

To find a more efficient PAS enzyme the iGEM researchers harnessed different computational methods to identify mutations and predicted protein structures that might improve enzyme effectiveness. They developed a software tool, 'seq-mutator', which bridges the gap between AI-assisted protein engineering and real-world data. Using these tools the team designed more than 50 novel variants of the rate-limiting PAS enzyme, which they then tested in the lab, identifying a final candidate that exhibited 5.5 times greater enzyme activity than the native enzyme. The investigators demonstrated that the enzyme construct could be used as part of a biosynthetic pathway for NBP.

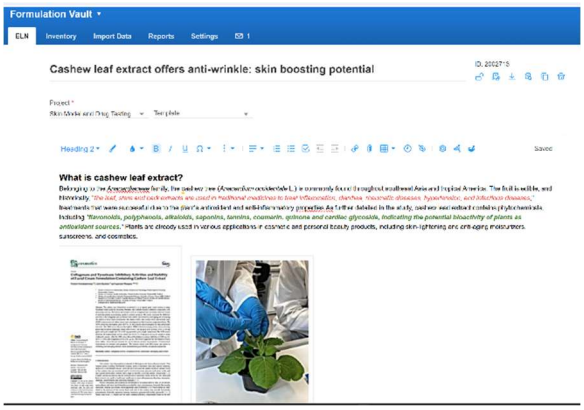
Role of CDD Vault in the Project

Supporting their work, and aided by the CDD team, the University of Münster iGEM group set up the Vault ELN, protocols and their templates, which would make it relatively easy for all of the students to set up protocols, document and manage all experimental data. As well as saving time, this meant that the recording and documentation process was consistent for everyone.

Putting information directly into the ELN also made the data accessible to users in real time, and on any device. “A digital platform means that we can access all and any of the information we need from the Vault ELN, whether we are using a laptop at home or are working on a laboratory PC,” explained Cara Jaeckel. “We can look at experiments individually, or contrast and compare.”

Michel Westermann, who headed the protein engineering work for the NOsquito project said, “The ELN has helped a lot to increase efficiency, it also means that we don’t lose lab data, as well as reducing the likelihood that mistakes are made.” This is a huge benefit, Michel Westermann noted, and contrasts with more rigid digital, or error-prone paper-based reporting methods that may not be applied universally or consistently across a project. “The CDD platform is also easily scalable, and while our project remained relatively small, this ability to scale can be really important as projects grow and expand,” Westermann continued.

"Using the Vault ELN templates made it relatively quick and easy to correctly document our lab work," Jaeckel added. ""There are quite a number of people involved in this project who require access to the data, and the ELN made it easier for us to keep all our information organized, accurate, and up-to-date. We were running a lot of experiments based on repetitive protocols. Having standard templates into which you only have to input specific variables for that particular experiment, and without having to write everything else down every time, is a huge time saver."



Importantly, the researchers found the platform to be very user friendly, Jaeckel continued. "Once you have a basic grasp of how everything works it's really straightforward. There are some particularly helpful features, such as the ability to build different projects. This allows us to organize lab work in those different projects, but still look at all the projects in parallel, without mixing them up. Subgroup properties and data filtering capabilities are also useful."

Success and Future Steps

The NOsquito project was a great success, winning the team a gold medal and an award for the best software tool. The initiative was also nominated for best modeling, and best plant synthetic biology awards. Westermann noted. "We generated some results that represented firsts in this field. We proved that the newly engineered enzyme was effective and could make the pathway more efficient."

The University of Münster group's achievements through iGEM have been recognized by leading scientists in relevant fields, and their results represent a key resource for continued development. With the iGEM project now completed, the scientists are sharing their results and data with other interested groups. "Additional studies will of course be needed to progress beyond proof of concept, demonstrate that the NBP produced is effective as a mosquito repellent, and confirm safety," Westermann acknowledged. Work will need to continue to test and scale production of NBP by precision fermentation, and through crop engineering.

So how did CDD and the University of Münster scientists first connect? It was a meeting at a trade show during 2023, explained Mel Berg, CDD Marketing Specialist. "The University of Münster scientists saw our booth and were interested in what we had to offer. We sat

down with them and the more we found out, the more we realized there was the potential for CDD to really help. It was a great opportunity for us to make a valuable contribution to the success of this project in the context of the international iGEM competition. And although the competition has now finished, the team will continue to have access to their data in the Vault."

Using CDD Vault also gave the students valuable experience working with a digital platform that might otherwise not be available to them in an academic setting, Berg continued. "The ability to familiarize young scientists with these tools is really important, because eventually they'll be going out into industry, and they need to have some knowledge about and confidence in using digital platforms … The assumption that our products are outside the Academic budget range is often false. This project has been a great example of how getting together to discuss possibilities can lead to some really positive collaborations."

For more information, visit us at www.collaborativedrug.com.

Key Takeaways

Sustainable Innovation: The NOsquito project showcased a pioneering biosynthetic approach for producing N-benzoylpiperidine (NBP) using renewable sugar feedstocks instead of fossil fuels, addressing both economic and environmental sustainability.

Enhanced Enzyme Efficiency: Through the use of computational tools and protein engineering, the team developed a variant of the piperamide synthase (PAS) enzyme with 5.5 times greater activity than its native form, significantly improving production efficiency.

Digital Transformation in Laboratory Management: The implementation of CDD Vault and its Electronic Lab Notebook (ELN) streamlined data documentation and protocol management, ensuring real-time data accessibility, consistency, and scalability across the project.

Collaborative Success and Skill Development: The partnership between the University of Münster and Collaborative Drug Discovery not only accelerated the research but also provided valuable hands-on experience for the participating students, equipping them with digital and technical skills relevant to modern biotechnological practices.

Recognition and Future Prospects: The project's innovative approach and technical achievements earned awards and recognition at the iGEM competition, setting a solid foundation for further research, scale-up efforts, and potential industrial applications.