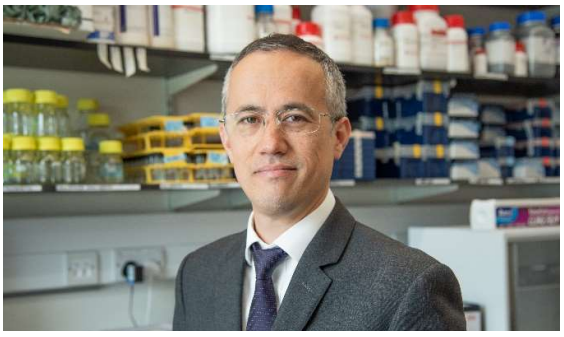
Informatics for Effective Management of Herbicide Screening Data

Agritech companies developing new herbicides generate and analyze huge amounts of data. Data from high-throughput screens, chemical optimization work, plant genomics, bioefficacy and crop safety testing have to be combined to pick candidates for development. Promising candidates must later pass stringent mammalian toxicology and environmental safety evaluations.

Start-up and virtual companies commonly outsource synthetic chemistry, field, glasshouse, physicochemical and regulatory studies to contract research organizations (CROs). This adds another layer of complexity to data management. Ultimately, outsourcing works best if CROs and other collaborators have access to secure two-way information flow without compromising IP, data security or data quality. Digitization of data management is imperative from practical, logistic and regulatory perspectives. Organizations rely heavily on the ability of their informatics infrastructure to manage a wide range of data, seamlessly accommodate in-house workflows and integrate projects with third parties.

MoA Technology was established in 2017, spun out from Oxford University's Department of Plant Sciences with a mission to find and commercialize safe herbicides with novel modes of action. Weeds can reduce crop yields by one third and with no significant new modes of action commercialized for more than thirty years herbicide resistance now threatens global food security. Resistance is present in more than 250 weed species infesting nearly 100 crops and affecting most current herbicide modes of action.[1,2,3]



Dr Shuji Hachisu, Chief Technology Officer, MoA Technology

"Developed by Prof. Liam Dolan and Dr Clément Champion, MoA Tech's innovative approach is

based on an in vivo whole plant model and artificial intelligence," explained Shuji Hachisu, CTO, MoA Technology. "Our technology uses high-throughput screening previously only used with in vitro systems and with disappointing results. Actually seeing herbicidal symptoms on whole plants enables us to quickly identify promising candidates, elucidate their precise mode of action and find unexplored families of safe and effective chemistry."

"No other herbicide screening platform can generate high quality data at the population, individual plant, cellular and subcellular levels simultaneously."
Shuji Hachisu, CTO, MoA Technology

MoA Tech's unique approach includes a fusion of three complementary platforms known as MoA Galaxy™, MoA Target™ and MoA Select™. When used sequentially the three platforms allow progression from initial screening of potentially millions of compounds to glasshouse testing and global field trials within months.

Herbicide needles in a high-throughput haystack

At the forefront of MoA Tech's approach to discovery is MoA Galaxy™, a proprietary platform that makes it possible to carry out high-throughput in vivo screening of potentially millions of compounds per annum. The key is a plant model with a unique profile including a rapid life-cycle. Cutting-edge imaging technology, digitization and machine learning capture and analyze the spectrum of symptoms produced. While traditional high-throughput herbicide discovery screens typically allow a simple progress or reject decision, MoA Galaxy™ is a data-rich screen generating phenotypic data at the population, single organism, cellular and subcellular levels. "This gives us an unprecedented early view of compound potential and an indication of mode of action, including previously unknown mechanisms," Hachisu said.

Identifying compound targets helps design safer herbicides

A second platform, MoA Target™ is used to identify the protein targets of lead compounds. An ideal herbicide would act on a protein only found in plants, e.g. in photosynthesis. At this stage, genomic studies and a novel bioinformatics tool developed in-house can rapidly identify the specific mode of action guided by information on the general area of plant physiology and biochemistry highlighted by MoA Galaxy™.

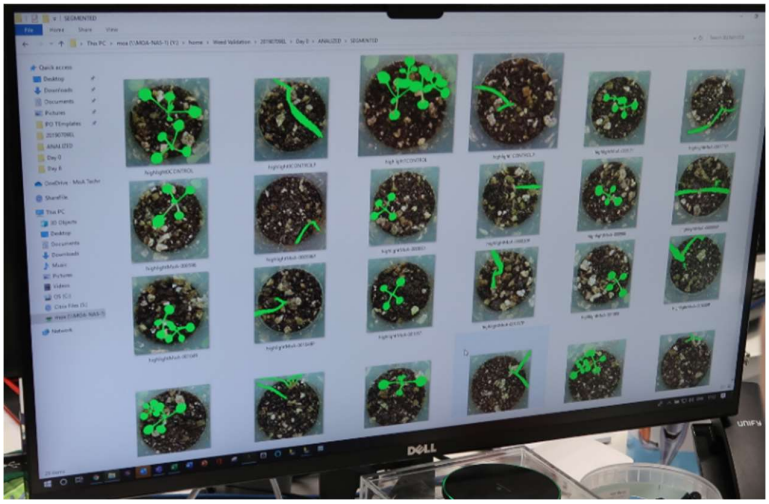
"With just one screening system we can discover herbicide chemistry with novel modes of action."
Shuji Hachisu, CTO, MoA Technology

This information provides important insights into potential toxicity to people, animals and the environment, plus activity across different weed types. Typically, identification of promising leads is followed by optimizing the chemistry to achieve higher potency, better crop safety or a superior environmental profile.

"The beauty of our approach is that it is not only data-rich, but delivers high quality, insightful data. We believe this gives our lead compounds a much higher chance of success when progressed to glasshouse and field trials."
Shuji Hachisu, CTO, MoA Technology

Smart data management for huge datasets

Critically, as a fast-moving young company, MoA Tech required a flexible, scalable web-hosted informatics platform that could help manage multiple data streams. "We were looking for a user-friendly platform that would work out-of-the-box," Hachisu noted. "We wanted a solution capable of handling huge amounts of data, offering an ELN (electronic lab notebook) and able to cope with rapid growth."



It was a tall order. MoA Galaxy™ generates huge data sets that need contextualizing with other data. Then there are also chemical optimization data and results from later regulatory studies.

Third parties are important too. Plant genome sequencing, glasshouse testing and regulatory work is outsourced to CROs; compound management providers supply libraries; and synthetic chemists synthesize batches of the most promising compounds for further testing. Information flow to and from multiple actors must be kept secure and allow the company to protect its IP. MoA Tech had to be confident that it could create access for third party off-site users, offer a user-friendly interface and retain complete security.

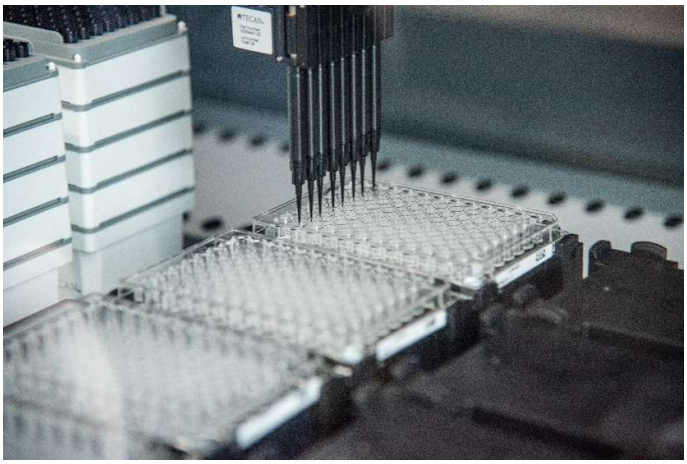
Ticking all the boxes

After reviewing a number of potential technologies MoA Tech tested a CDD Vault and quickly realized its advantages as an informatics platform. "Without any expert help on installation or routine use, we were able to set up and start using the hosted CDD Vault platform as a database for managing the huge volumes of data that our technologies generate," Hachisu added.

"We needed an informatics infrastructure that could offer a database to hold vast numbers of images and other screening data, act as a compound management platform, offer an ELN and give us a safe, secure system through which to communicate and share data with our CROs and other partners. It was a tall order that CDD Vault has fulfilled impeccably, whatever we throw at it."

Shuji Hachisu, CTO, MoA Technology

MoA Tech has set up a primary CDD Vault that acts as the central repository for the data and metadata generated by MoA Galaxy™, MoA Target™ and MoA Select™ screens, and from downstream glasshouse and field trials, plus all synthetic chemistry workflows.



While pharma companies focus on the efficacy and safety of new drug compounds specifically on humans, crop protection companies not only have to assess the efficacy of candidate herbicides on target weeds, they also have to assess crop selectivity and potential toxicity to non-target organisms including mammals, fish, insects, even to other plants - and to the environment, including aquatic safety. Some of this work is conducted in-house, but much of the experimental and predictive health and environmental toxicity and safety work is carried out by specialist CROs.

"So, at MoA Tech, we use CDD Vault to communicate directly with many CROs, including, synthetic chemists, toxicology assay specialists, glasshouse and field trial partners," Hachisu added. All of these data are also housed directly in the primary CDD Vault. "CROs are given authorized access to the Vault, by project. MoA Tech scientists can easily create and share detailed experimental protocols with CROs through the in-house ELN used to generate and record experiments and SOPs (standard operating procedures). The CROs then carry out the requested experiments using the compounds and protocols provided. All their results, including plant symptoms and images, and other experimental data, are uploaded back into the CDD Vault directly and securely. CDD Vault acts as a secure, easy-to-use data repository from which data can then be viewed or analyzed via third party tools."

Importantly, the primary CDD Vault also acts as MoA Tech's dedicated compound management platform. Screening libraries are ordered and tracked, and batches of specified compound structures requested for synthesis by the firm's chemistry providers in Europe and China are ordered and registered. The system can also alert key personnel when sufficient numbers of ordered compounds have been received to initiate glasshouse trials by third party CROs, keeping delays to a minimum.

"Because CDD Vault and the ELN are so secure, we can set up user accounts for our CRO partners through which they can directly access experiments that our scientists have designed for them to carry out and report back their results and images."

Shuji Hachisu, CTO, MoA Technology

Managing plant husbandry

While MoA Tech has demonstrated the versatility of CDD Vault for its R&D data management requirements, the company has also been innovative in its application of the CDD Vault technology. A second, separate Vault has been set-up by the company as a 'sandbox' giving scientists and new users a way of practicing with the system safely. A third Vault manages all MoA Tech's plant husbandry practices used in genomic work. "It shows the versatility of the CDD Vault infrastructure that we were able to configure a plant husbandry Vault that acts as a kind of inventory for the plants themselves," Hachisu said. "This means we can effectively record and oversee tracking of each plant strain, to the timing and outcome of breeding and other genetic experiments, and even plant watering and disposal."

"CDD Vault is so flexible that we have even been able to set up a separate vault that we use to oversee and manage plant husbandry."
Shuji Hachisu, CTO, MoA Technology

MoA Tech today and tomorrow

As of mid-2020, MoA Tech's lead herbicide candidates, identified less than 12 months ago, were sent to their CRO partner for early field trials with results expected by the end of the year. The company projects continued growth and expansion over the next couple of years. "We are hoping to hire additional scientists so that, as well as continuing to progress existing compounds through R&D, we can start new discovery projects and design new compounds based on the wealth of structural and activity data already held in the Vault," Hachisu commented.

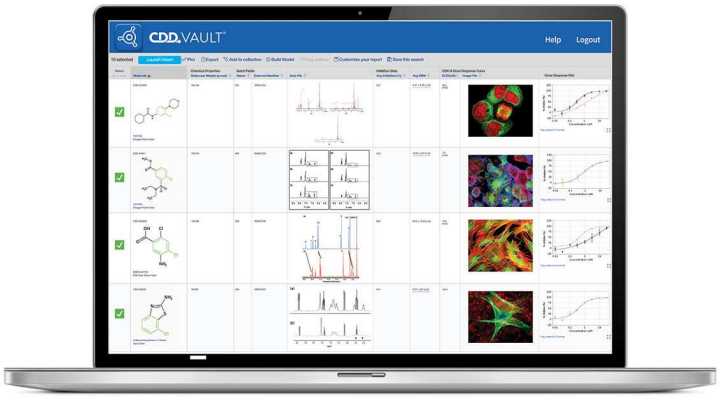
MoA Tech also hope to further automate and augment its screening library construction, chemical target design and image phenotyping workflows by applying cutting edge AI and machine learning tools being developed in collaboration with both academia and industry to select the most promising hits from the Vault for further study. "It's an exciting period for MoA Tech," Hachisu commented. "CDD Vault is now an integral part of our operation, giving us a safe and secure platform for managing and accessing the vast amount of data that we generate from so many different types of experiments, without any loss of content or context. Whether it's storing thousands of images, giving our CROs access to the data and experimental protocols that they need, or giving us an overview of all of our compounds and plants, CDD is easily configured without highly specialist IT knowledge, easy to use and has proven to be highly flexible."

References

1. International Survey of Herbicide Resistant Weeds www.weedscience.org

2. Duke, S O (2012). Why have no new herbicide modes of action appeared in recent years. Pest Management Science, 68, 505-512

3. Oerke, E C (2006). Crop losses to pests. Journal of Agricultural Science, 144, (1), 31-43



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