ADVERTISEMENT FEATURE

CUTTING-EDGE TOOLS KEEP PACE WITH DRUG DISCOVERY'S DATA DELUGE

SMART DATA MANAGEMENT is more important than ever as drug screening continues to grow in scale and complexity.

Digital tools for data management and visual analytics have been common in pharma for decades, but the nature of those tools has changed dramatically. David Gosalvez, director of strategy and informatics portfolio at Revvity Signals Software, recalls his early career as a bench scientist in academic and startup labs. "I already needed software to cope with all the data," he says. "But many of those software tools were still in their infancy, these command-line things with horrible user interfaces, if any." These various software components were often standalone programmes, each with one use case.

This patchwork approach is no longer an option. Contemporary drug screening workflows often entail high-throughput screening of millions of compounds in a single experiment. Such scale demands rigorous assay planning and data analysis, and the ability to seamlessly share between remote teams.

The latest digital tools, including Revvity Signals Software's cloud-based Signals Research Suite platform, are streamlining the management of even the most cutting-edge biological screening efforts. These platforms accelerate the process of target discovery, lead generation, optimization and toxicology.

NEW CHALLENGES, NEW NEEDS

The benefits of thoughtful laboratory digitalization can be immense, says developmental biologist Daniel Weaver, product manager for lead discovery and screening at Revvity Signals Software. He remembers implementing an end-to-end electronic laboratory notebook (ELN) in a previous role at Array Biopharma. "At the time, it was a way of differentiating the company," Weaver says. "Over 13 years we invented 18 medicines, in no small part because we invested in informatics." But this is no longer an optional investment. "It's just the way you do science," he says.

The sheer volume of data being generated is one of the challenges companies need to grapple with. Many drug discovery programmes rely on high-content and phenotypic screening, in which vast numbers of multi-well plates are used to assess how biological specimens react to different drug candidates, doses or formulations. This typically involves analysing images or videos of each sample to extract data on cell proliferation, apoptosis or other physiological and biochemical parameters.

These multi-dimensional datasets are complicated to manage. "You have to efficiently reduce what might be a few million images down to a coherent set of features," says Weaver. "You could describe these data as this broad and tall but very sparsely populated matrix." This means considerable extrapolation may be required to fill gaps in the data and distinguish promising 'hits'.

New classes of therapeutics exacerbate this challenge. Gosalvez cites the example of proteolysis-targeting chimeras (PROTACs). These are molecules — first described in a paper co-authored by Yale University researcher Craig Crews, founder of the first PROTAC-focused drug developer — that exploit naturally-occurring protein degradation processes to eliminate specific disease-related molecules from cells. These promising drugs remain challenging to research for many reasons, including an unpredictable safety profile (Trapotsi, M. et al. ACS Chem. Biol. 17, 1733-1744; 2022).

This profiling process can be sped up by ultra-sensitive protein-protein interaction in vitro assays and facilitated by emerging assay formats, such as 'cell painting' screens. In cell painting, multiple organelles in each cell are simultaneously labelled with different fluorescent tags, enabling collection of several thousand phenotypic measurements per sample, describing a broad range of biological activities. But these analyses are still labour-intensive. "It's so complicated to find new and safe candidates," says Gosalvez. "That's probably why we still don't have a PROTAC drug on the market."

THE END OF 'COPY AND PASTE'

Revvity Signals Software's solution to these challenges, Signals Research Suite, comprises two main components. The first is Signals Notebook, a cloud-based ELN system that stores and disseminates biological information, experimental protocols and assay workflows, and the data generated by laboratory instruments. The second, Adver tiser retains sole responsibility for contentt — analyses assay data and converts complex results into intuitive graphics.

This second component is particularly critical when working with data from high-content screening experiments, notes Weaver, who highlights a tool within the data processing capabilities called Signals Image Artist. "You can go from the reagents and antibodies for the screens to storing and doing the image processing, to doing the feature selection, to storing those final results, all in one continuous stream," he says. Revvity Signals Software plans to update data processing capabilities within Signals Research Suite to handle temerging assay formats, and Weaver says cell painting is a priority for the team.

Andrew Brookes/Getty Images

▲ The scale and complexity of modern drug discovery demands rigorous assay planning and data analysis.

Efficiency and consistency are key advantages conferred by Signals Research Suite, particularly as the pharma industry embraces the 'FAIR' principles, which assert that experimental data should be findable, accessible, interoperable and reusable. "We are trying to get rid of 'copy and paste' completely," says Gosalvez, referring to the error-prone means by which researchers have traditionally shared their data for collection, analysis and reporting. "With a the data processing capabilities workflow," Weaver adds, "in minutes you can go from the raw instrument files to the final report, all quality-controlled and ready for publication."

Flexibility is another important edge. An overly rigid informatics platform can make it challenging to test or refine assay designs. Signals Research Suite can handle both ends of the spectrum, allowing early experimentation and process optimization before a lab commits to a final procedure. "This interactivity and flexibility is perfect for the early project phases," says Gosalvez. "The system can then shift as the project matures and the workflow becomes automated with the transition from low to high-throughput experimentation."

BROADENING DATA'S REACH

These data management challenges will only grow steeper as pharmaceutical business models become more complicated. "Lab automation in the physical world must go hand-in-hand with data flow automation in the virtual world," Gosalvez says. "This goes beyond the boundaries of a single company."

Many drug companies now rely on contract research organizations (CROs) — some of which may be independent drug companies themselves — to perform much of their discovery and preclinical work. "Currently we are focused on getting biologists working with biologists in one company, or biologists and chemists," says Gosalvez. "The next big thing is to expand this whole collaboration idea to the network of CROs that pharma and biotech companies have access to."

Adapting to these changes in the industry and the research toolkit it employs will keep the Signals Research Suite team busy. Weaver sees many opportunities for the platform to evolve, but says the team will take its time to ensure the resulting software products are targeted at the specific needs of pharma researchers. "I think it's really important to make sure the system comes with science 'in the box'," he says. "That means checking we're not getting so enamored with the technology that we forget what it's for: to help people invent medicine■ to improve human health."

REFERENCE

https://www.nature.com/articles/d42473-023-00003-0

revvity signals

Advertiser retains sole responsibility for content