CASE STUDY

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CPI (High Value Manufacturing Catapult)

The Challenge

Researchers at UCL are developing a new way to make synthetic DNA - the kind used in cutting-edge genomic therapies. Their goal is to build a compact, automated device that can manufacture these therapies on demand, opening up new treatment possibilities for people with ultra-rare diseases.

For this to work, the DNA produced must be extremely pure and high-quality. That means the device needs a reliable purification step: one that can separate the desired DNA from all the other leftover materials in the reaction - including other, very similar strands of DNA.

The researchers identified chromatography as the best method for this job. It's precise, can be automated, and provides valuable quality control data. But there's a catch: there are many types of chromatography resins and protocols out there, and not all are suited to purifying synthetic DNA. The team needed to test and compare a wide range of options to find those capable of consistently isolating the right DNA - no easy task given how chemically similar the different strands can be.

Innovation Launchpad Network+

Innovation

To tackle the challenge of finding the best purification method, the Researcher in Residence (RiR) teamed up with experts at CPI and made use of their advanced high-throughput screening tools. These technologies allowed the team to test many different options quickly and efficiently - something that would have taken much longer using traditional lab methods. Central to this process were tools like the Janus liquid handling robot, which automates the preparation and handling of tiny liquid samples with speed and precision, and the Lunatic plate reader, which can rapidly measure the concentration and quality of DNA samples. By using these instruments, the RiR was able to rapidly narrow down a wide pool of resins and protocols to just a few high-performing candidates. This approach didn't just save time - it brought a level of consistency and scalability that's essential for future automation. Instead of trial-and-error testing by hand, the RiR could screen a broad landscape of purification conditions systematically, identifying combinations that showed real promise for reliably isolating high-purity DNA.

Result

With hands-on support and training from the CPI team, the Researcher in Residence learned how to operate the Janus liquid handling robot and specialized robocolumns - miniature chromatography columns designed for automated testing. These tools enabled the RiR to systematically explore bind-elute purification protocols, where DNA is first captured (bound) and then released (eluted) under controlled conditions. The RiR tested a wide range of purification methods taken from existing scientific literature. However, many of these protocols failed when applied to synthetic DNA *not* produced in E. coli. This is likely because E. coli introduces chemical modifications to the DNA *that were key to these purification protocols functioning* - an important insight that could inform future approaches in the field. Despite these challenges, the work yielded promising results. The RiR successfully identified three chromatography resins that were able to bind the target DNA. In addition, five purification protocols were found that could potentially separate very similar plasmids - circular pieces of DNA used in therapy production - even when those plasmids are nearly identical in size. With further refinement, these protocols could form the basis for robust, automated purification steps in future genomic therapy manufacturing devices.

Impact

The potential of synthetic DNA production routes is substantial, including for a more rapid and reliable process that can be automated and run (fully closed) in a wide range of environments. This compared to the existing E.coli cell-based DNA production method which is time consuming, requires specialised facilities and staff and where cells may adapt to grow without the plasmid DNA product or make unexpected changes to the plasmid sequence.

This technology has particularly high potential to facilitate treatment of ultra-rare diseases and, in the longer-term, personalisation of genomic therapies. Any production process which may be applied to therapeutics requires a highly purified and high-quality product. The work done through the RinR scheme has allowed us to start developing a purification method which will sit naturally within an automated system, alongside our existing (patent pending) DNA amplification reactor.

CPI - HVM Catapult

"This collaboration provided several benefits to CPI and our staff. It enabled us to continue to grow our relationship with UCL, specifically Dan Bracewell and Beattie Melinek. Several members of staff gained exposure as to how research is conducted in academia and were able to see how that differs to industry as well as gaining valuable experience in training, supporting and guiding others. Beattie also presented her work to the wider team given them an overview of the concept to where the application is now, this was great for our team to see and understand the stages and work put in to generate this type of concept and potential to market product."

Beatrice Melinek

"Imagine a coffee pod machine that produces DNA – with similar size and ease of use. A similar capsule-based approach will allow the user to pick their own flavour without any significant change in the production protocol they follow. In the future we hope to build up to a system with the flexibility of 3D printing."

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