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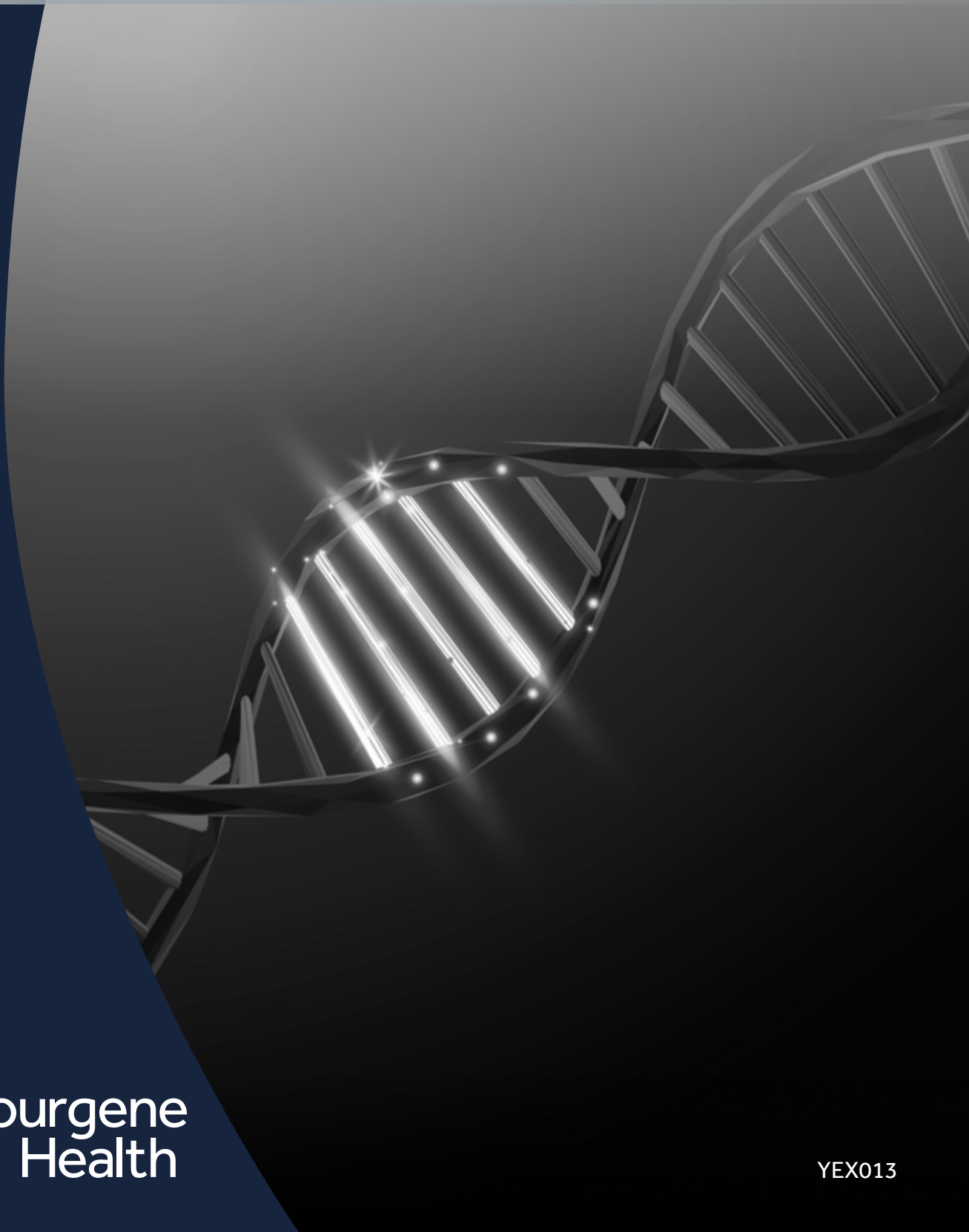
Your Expert

A Ranger® Technology Application: Synthetic Biology and Gene Synthesis



Yourgene Health

YEX013

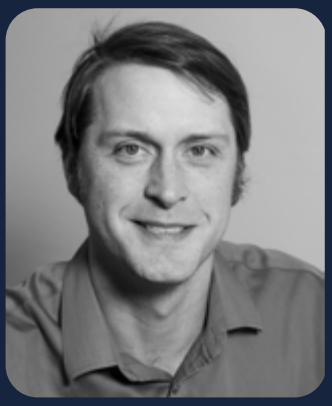
In this edition of Your Expert, Yourgene Health interviewed **Matthew Nesbitt,** one of the developers of our breakthrough Ranger® Technology to discuss how its **size selection function is revolutionising the approach to Gene Synthesis** and how dozens of organisations are already benefitting from this function in the manufacture of their deliverables.

Matt has expertise in automated, scalable solutions for electrophoresis and over 16 years experience in sample preparation.

Matthew Nesbitt

Co-Creator of Ranger® Technology

Yourgene's Product Specialist Director



Introduction

Biotechnology harnesses cellular and biomolecular processes to develop technologies and products. These products already improve our lives and also show great potential for enhancing the health of our planet.

In recent years and especially during the COVID-19 pandemic, the critical role of biotechnology and biomanufacturing in developing life-saving diagnostics, therapeutics and vaccines has been demonstrated and looks poised to progress on stratospheric trajectory, if we can successfully refine the technique to suit its myriad applications.

Where does size selection come in? Where does size selection help?

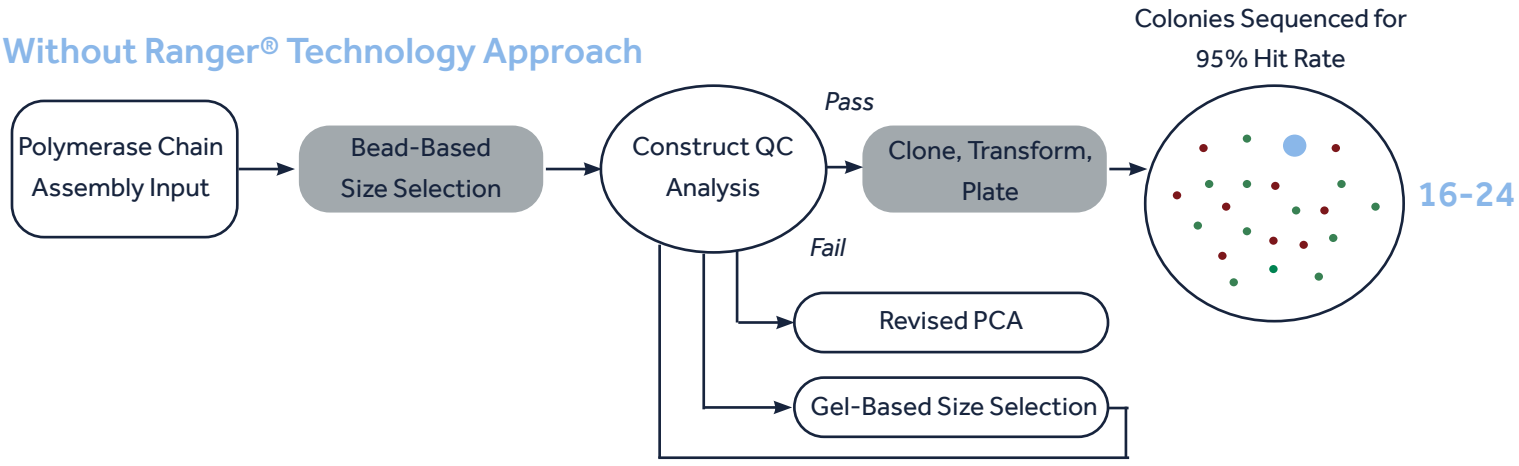
I think one of the exciting areas for me is the clinical, pharmaceutical and other technology sectors struggling with sample purity. When considering the work done in that arena, everything is highly dependant on the ability to manufacture new drug candidates in new ways. This actually relies to an increasing extent on synthetic biology, which is an application that we have really good utility overlap with. Size selection is about enriching and purifying, in other words getting rid of the stuff that you don't want and keeping the stuff that you do want by differentiating based on size.

Gene synthesis is hard! Traditionally, when we talk about gene synthesis we're talking about a process that uses a lot of old bench techniques that have been around for decades. I don't know if anyone else ever did much cloning when they were in university, but I certainly did and it is painful!

The process is predicated on synthesising a construct which is as pure as possible and then you've got to clone the thing. **Of the many risks and difficulties associated with the process, this is the largest hurdle in a market which demands complex, quality DNA on increasingly tight turnaround times.**

There are many stages in which impurities and error can be introduced early during the building of the construct, and several steps further down the line which jeopardise the chances of isolating your construct at all, not least when transforming it into a bacterial host – hopefully you don't kill everything when you do that! Then you've got to let it grow for a while once it's plated out, and finally begin the laborious task of sampling dozens of colonies before you find the exact construct of interest.

Without Ranger® Technology Approach

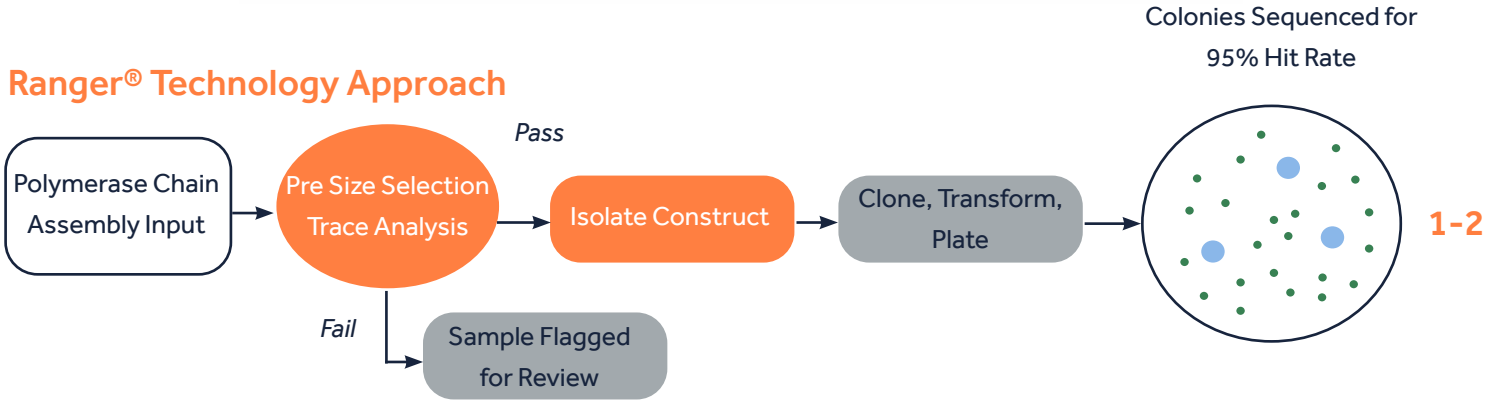


The problem is that off-targets get produced much more often than desired products: when taking a sample from your construct to clone, it's often not of adequate purity because the processes used to synthesize it are imperfect. Additionally, **the presence of a lot of concomitant truncation products frequently results in a success rate below 10% in complex synthetic reactions, meaning that fewer than 10% of the bacterial colonies from which construct is harvested actually contains the exact construct which is desired.**

Ranger® Technology size selection can bump that up to as high as 90%. If you can do that; you don't need to check as many colonies before you find your true positive construct.

RANGER® TECHNOLOGY

Ranger® Technology Approach



For longer DNA constructs, Ranger® Technology can help greatly reduce the signal-to-noise issue. In the context of gene synthesis, we can use size selection to get rid of the noise associated with truncation products and recover the full length construct of interest, which is a valuable input for manufacturing new therapeutics for pharmaceutical entities.

To be clear, this is perhaps less applicable for simple processes like synthesizing of short constructs or meeting a simple PCR amplicon, but it is certainly applicable for situations where you require larger and more complicated constructs.

What does this mean for the gene synthesis industry?

Being able to generate these larger constructs has more **economic value** for groups like pharmaceutical companies; think about vaccine manufacturers as a topical example. The gene synthesis industry as a whole is really trending towards taking this and trying to turbocharge it to be able to make it work well at scale.

Complicated DNA needs to be turned around on a on a tight timeline. But it normally takes months from the time that it's ordered until the construct is delivered and so this kind of turnover time is incompatible with a research and development environment, which is what a lot of pharmaceutical is. If you have an idea about how to make a new therapeutic, you need to have X number of genes made in order to be able to have them transcribed in order to make the product, you have to iterate on that cycle many times. But if it takes months every time you iterate, then it's not conducive to coming up with new therapeutics.

So you need to be able to make these long stretches of DNA on a turnaround which is quick.

Ranger® Technology can be used to help clear that hurdle. The reason for that is because it's able to clean up a lot of those reactions that end up being heavily polluted with truncation or concatenated products which are concomitant with the target product.

Achieving this drops your sequencing costs, and a whole bunch of other costs necessary to identify a synthetic construct that has the desired sequence.

The potential of size selection is being seen by our customers at both ends of the adoption curve.

One of our early adopters of Ranger® Technology has some real moon-shot ideas as to where gene synthesis is going to be in the future. They're utilising our high throughput NIMBUS Select to reduce the turnaround time for the delivery of their complicated DNA products for the Pharmaceutical Industry. They deliver gene constructs to their pharma partners who require inputs for their own novel drug pipeline, enabling them to make and test more candidate products than before.

We have another Ranger® Technology adopter; a complex DNA firm who are utilising our size-selection service for their samples. We are supporting them to make much larger DNA synthetically and know that the associated complexities of this can only be solved by making sure there is purity between steps.

We've got lots of customers that have demand for this function and who are coming to the conclusion that Ranger® Technology is the best and most viable option because the volume required can only be satisfied by Ranger® Technology solutions. The additional flexibility of being able to utilise our size selection service in Vancouver as a project-based proof of concept to demonstrate the capabilities of Ranger® and allow customers to test this before they commit to any capex spend has helped us build confidence.

What else does the future hold for Ranger®?

In talking about supplanting industrial products, we can also turn our attention beyond biotherapeutics and mRNA vaccines to the territory of petrochemical and coming incumbents including things like plastics. While the market economics of that have previously been a little bit questionable, that's less and less the case today. The White House itself released a memo in September 2022 talking about how synthetic biology could be used in manufacturing that accounts for about 1/3 of global output, which was an estimated $30 trillion in terms of value.

The White House has laid out plans to initiate programs which will increase biomanufacturing and expand opportunities within this sector. This in turn has led to us seeing a lot more government-based investment in synthetic biology, which will surely drive the demand for these gene synthesis products that Ranger® Technology can be turned to ensure the effective delivery of.

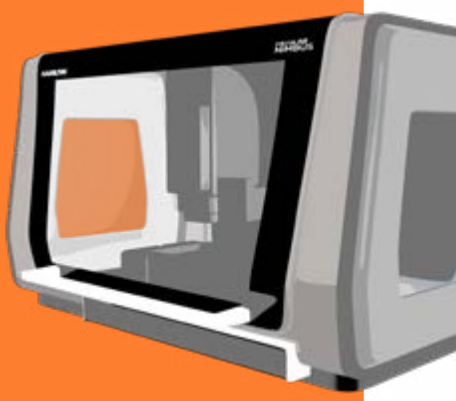
"Where speed, complexity and cost matters, we are allowing groups to take advantage of size selection in a way that should be the least disruptive out of any option available to the market. That's because we offer the highest degree of automation; we can process more samples per unit time than anything else that's out there. This is a technology that's relied upon by blue chip vaccine manufacturers as well as in other applications to great scale and efficacy."

Resources:

Click to read the White House Exec Order

Interested in Ranger® Technology for Gene Synthesis?

Contact us at **info@yourgenehealth.com**



Scan the QR code to learn more about Ranger® Technology for Gene Synthesis

About YOURGENE HEALTH

Yourgene Health is an international molecular diagnostics group which develops integrated genomic technologies and services *enabling genomic medicine*

Yourgene Health
Skelton House
Lloyd Street North
Manchester Science Park
Manchester
M15 6SH
United Kingdom

Yourgene Health

yourgenehealth.com