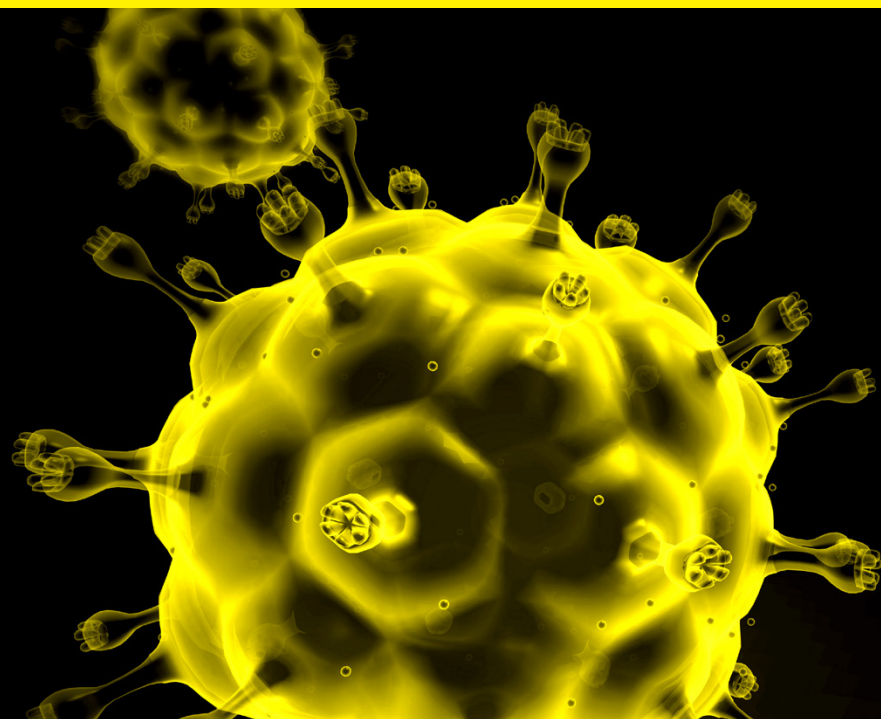


No Llamas, No Lottery: How Tozaro Is Using Octet® BLI and Smart Polymers™ to Rethink Viral Vector Purification

An Interview With Emma Daniels, Head of Development Chemistry, Tozaro

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Overview

Viral vector manufacturing remains one of cell and gene therapy's biggest cost and scalability constraints, held back by inefficient purification workflows and complex analytical requirements. Octet® Bio-Layer Interferometry (BLI) has long been a workhorse for viral vector titer measurement, but Tozaro, a young company developing Smart Polymer™ ligands, is showing that its role can extend much further.

Tozaro is using the Octet® BLI platform as the engine of a discovery and workflow-optimization process aimed squarely at one of the field's toughest bottlenecks: efficient, high-yield viral vector purification paired with robust, fast QC. By combining in silico design, large monomer libraries, and rapid BLI screening, Tozaro is building synthetic ligands that can both quantify and purify complex vectors such as AAV and lentivirus. Their analytical reagents already show picomolar-level performance on Octet® systems across multiple AAV serotypes, while linear Smart Polymers™ are being engineered for gentle, high-capacity lentiviral capture and release. Together, these technologies point toward a more integrated approach, where the same design principles support faster discovery, streamlined development, and sharper QC and analytics across the viral vector lifecycle.

Q: Viral vector manufacturing is often described as one of the biggest constraints on wider adoption of cell and gene therapies. Where are the bottlenecks today?

Emma: I'd say it really comes down to two things: purification and analytics. On purification, a lot of the industry still relies on expensive, often single-use anion exchange chromatography columns that give you a limited yield of functional product, and that really drives up the cost of lentivirus. AAV's a bit different. There are some affinity reagents available, like AAVX, but separating full and empty capsids is still challenging, and it's hard to keep up with just how many new engineered serotypes are coming out. Then the analytics side is also expensive and time-consuming. p24-based assays often overestimate titres, and getting good in-line quantification is tricky too.

Q: Could you explain Tozaro's Smart Polymer™ platform and what unmet needs you initially aimed to address in viral vector manufacturing?

Emma: Smart Polymers™ are non-biological, synthetic affinity reagents, and we design them rationally, using a combination of advanced in silico modelling, machine learning, and *in vitro* epitope discovery and screening. Because they're chemically produced, they come with some real advantages over biological affinity reagents such as antibodies, and they're free of any animal-derived components. What we really want to do with the platform is create novel affinity reagents for viral vector purification and for detection and quantification. There just aren't many good options out there for that in the industry right now.

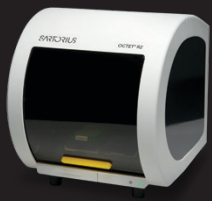
Q: The requirements for effective analytical reagents are quite different to those for purification reagents. How can Smart Polymers™ be tailored to complement each other across the discovery, development, and QC lifecycle for AAV and lentivirus?

Emma: Our design platform lets us tailor the properties and binding affinities of our Smart Polymers™ to suit whatever application we're going for. For purification, we actually want reagents that don't bind their target too strongly, so we can elute and collect the product. That matters even more for something like lentivirus, which is quite fragile; we want gentle elution conditions there, to maximise the yield of functional product.

For analytical reagents it's almost the opposite: we tend to target higher binding affinities, because that gives us a bigger dynamic range for detection. Being able to think about all of that from the very start of our design and modelling process and having such a wide range of chemical space to draw on through our monomer library, is what lets us build Smart Polymers™ with so many different properties.

Q: The use of Octet® BLI screening is central to your development workflow. Can you walk us through how Octet® technology specifically accelerates the discovery and optimization of your Smart Polymers™?

Emma: Honestly, the Octet® is a workhorse for us when it comes to screening our Smart Polymers™. Unlike solution-based techniques, it lets us probe how each Smart Polymer™ behaves on a solid support. In a typical screen we'll immobilise one Smart Polymer™ onto each biosensor and test it against its target, and our current Octet® lets us screen up to eight polymers in as little as an hour. We use that not just to spot promising initial candidates, but also to probe and optimise how we synthesise our lead reagents. Before we had the Octet®, we were doing this kind of screening using surface plasmon resonance, or SPR, and the throughput was so much lower. What takes us under an hour on the Octet® used to take about seven hours with SPR!



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Dr Emma Daniels

Head of Development Chemistry, Tozaro

Emma gained a PhD in Sustainable and Circular Technology from the University of Bath where she focused on the development and application of sustainable polymers. At Tozaro, she leads the Development Chemistry team to drive the development of Smart Polymers™ to improve the efficiency and quality of AAV and lentiviral manufacturing.

Q: What advantages do your Smart Polymers™ offer over traditional viral vector quantification methods, especially in terms of speed, cost-effectiveness, and accuracy?

Emma: The big thing is that our quantification reagents are designed to target the intact viral vector itself, not a fragment of it, and that gives us an immediate advantage over something like a lentivirus ELISA. Those assays target p24, which can lead to overestimated titres because you're also picking up soluble p24 that isn't part of a functional particle. On top of that, both AAV and LV need to be lysed for the ELISA process, so it's slow, and you lose any information about how much intact vector was in your sample to begin with. Our early data suggests an Octet®-based quantification assay using our Smart Polymers™ would be much quicker than running an ELISA; we're talking results in as little as an hour. There are serotype-agnostic ELISA kits out there for AAV titering, but they're less effective for certain serotypes, like AAV9, and they may not work at all for new, engineered capsids. Because we can develop Smart Polymer™ ligands quickly for each serotype, we could offer quantification tools that are properly tailored to each viral vector.

Q: Lentiviral purification is notoriously difficult, with low yields and loss of functional titre. What have your linear Smart Polymers™ shown so far in terms of functional LV recovery, impurity (DNA/HCP) removal, and the potential to replace multi-step, harsh processes?

Emma: Early data from our research-use-scale kits is really promising. We're seeing over 50% recovery of functional lentivirus, along with up to a 1000-fold reduction in DNA and host cell protein impurities. And we're getting that straight from crude harvests, without needing benzonase treatment, while using pretty gentle elution conditions; just subtle pH shifts.

Q: Your workflow combines in-silico modelling, large monomer libraries, and BLI screening in a tight loop. Can you quantify how much faster ligand discovery becomes when in-silico design, monomer libraries and Octet® screening are combined?

Emma: It's hard to put an exact number on it, but if you do the back-of-an-envelope maths, it shows you just how effective this design cycle is. When we set about making new Smart Polymers™ to target VSV-G, we identified seven peptide templates from our in silico models and screened each of those against a library of 91 monomers. That's 637 possible combinations; there's just no way you'd make all of those in the lab. So in the end, we made 50 polymers and screened them by SPR, which took around three months. On the Octet®, we could screen all of those polymers in just a few days.

Q: One of your goals is a "single purification solution" for viral vectors. Based on the data you've generated so far on AAV and lentivirus, how close do you feel you are to that vision, and what are the key scientific or engineering hurdles still to overcome?

Emma: We already have really promising data for lentivirus purification, using membranes and monoliths functionalised with our Smart Polymers™. At research-use scale, we're getting binding capacities and functional recoveries that are on the heels of gold-standard techniques like AEX. So our next challenge is really about improving performance and scaling the technology up, so it can eventually be used at every scale of production. Our AAV programme is progressing well, too. The challenge there is finding a Smart Polymer™ that performs equally well across all the different AAV serotypes, or, alternatively, designing serotype-specific reagents for each one.

Q: From a QC and analytical standpoint, where do synthetic Smart Polymers™ offer clear advantages over antibodies, and where do antibodies still retain strengths today?

Emma: For one, Smart Polymers™ are more stable. They can withstand a much wider range of harsh conditions. We've even sent Smart Polymers™ to space and shown they're still functional when they come back!

I think the bigger issue with biological affinity reagents, though, is how they're made in the first place; it's random. You're relying on an immune response, so you can't predict or control things like the binding region or the binding affinity. I like to call it the "antibody lottery." Smart Polymers™, on the other hand, are rationally designed from the start to meet the exact needs of whatever application we're building them for. And because it's a chemical process rather than a biological one, it's animal-free too. No llamas used in the making of our ligands!

Where antibodies still have the edge is simply that they're trusted. They've been used for years, and that's not nothing. Smart Polymers™ are a disruptive technology, so our data has to be really strong to give people the confidence to make the switch to polymeric affinity reagents.

Q: Finally, what does success look like for you in the context of cell and gene therapy? How would you describe the future viral vector process or QC workflow that Tozaro's Smart Polymer™ platform and the Octet® system are helping to make possible?

Emma: For me, the end goal is really simple: helping make cell and gene therapies more affordable, so more people can be treated. If Tozaro's Smart Polymers™ can help with that—even a little—by making viral vector purification more cost-effective and efficient, or by giving people faster, more accurate quantification tools, then we'll have done our job.

Conclusion

Tozaro's work with Smart Polymer™ ligands on the Octet® platform illustrates how synthetic, computationally designed chemistries could help unlock the next generation of viral vector processes. By uniting analytical and purification polymers within a common BLI-driven workflow, the company is beginning to address today's low-yield, multi-step operations while moving toward a future of simpler, higher-performing viral vector manufacturing and analytics.



Company Profile

Tozaro® is developing a novel suite of reagents to help transform the development and manufacture of viral vectors in cell and gene therapy. Operating at the intersection of chemistry and biology, Tozaro's smart polymers are evolving existing analytical and purification processes to realize a future where advanced therapies are accessible to all.

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