Improve Purification Process Efficiency

Optimizing AAV manufacture, overcoming the challenges of purifying mRNA vaccines, and more. Experts give their views on enhancing downstream purification.

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A Shot in the Arm for mRNA Vaccines

Optimizing AAV Manufacture

Capturing Value in Changing Times

A Shot in the Arm for mRNA Vaccines

Standard methods of preparing mRNA require multiple purification steps, sometimes-costly single use resins, and various chemicals. At the commercial scale, such methodology is impractical; at the vaccine scale (hundreds of millions of doses per annum), it is impossible.

The concept of mRNA therapy has gone from concept to realistic prospect with remarkable speed, but not everyone was taken by surprise. Scott Zobbi (Senior Business Development Manager, Thermo Fisher Scientific) first saw a significant increase in research into RNA therapeutics several years ago, particularly with regard to using mRNA as an alternative to recombinant proteins. But the really exciting development, according to Zobbi, is the application of mRNA to vaccination – not only in cancer immunotherapy, but also for infectious diseases.

In fact, mRNA vaccination constitutes an entirely new immunization modality. Administration of mRNA rather than protein antigens induces the body to produce antigenic proteins internally, eliminating some of the more expensive and time-consuming components of traditional vaccine manufacture. Similarly, the mRNA approach permits more rapid and responsive vaccine development: a simple RNA sequence change will quickly accommodate viral strains that have mutated away from the original vaccine, and entirely new vaccines can be promptly developed when dealing with a novel virus pandemic, such as COVID-19.

Broad commercial application of mRNA vaccines, however, assumes availability of appropriate supporting technology; for example, cost-effective, scalable mRNA purification methods. As Kelly Flook (Senior Product Manager, Purification Products, Thermo Fisher Scientific) puts it: "The move towards mRNA therapeutics and vaccines demands methods to achieve high purity mRNA in as few steps as possible, at the lowest cost possible."

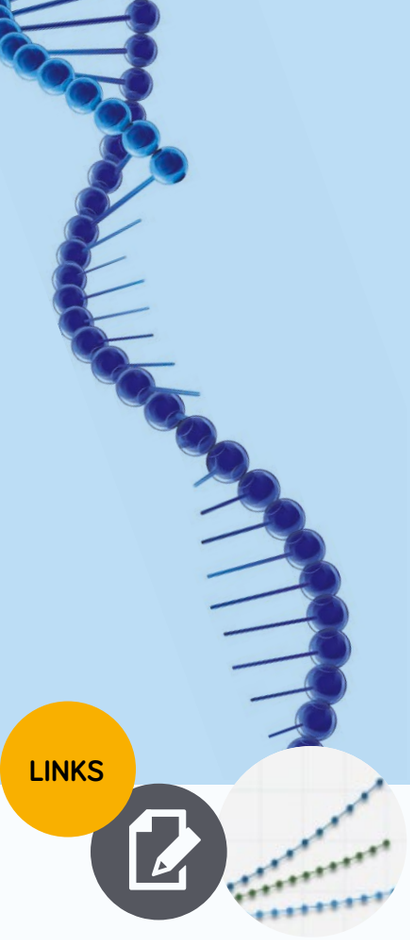
Cleaner capture at lower cost

Flook explains that there are a number of deficiencies with existing methods. "Usually, mRNA is purified with ion pair reversed-phase chromatography, or similar techniques, which rely on ion-pairing reagents," she says. Reagent disposal and elimination of toxins from the drug product comes at a cost – a cost that becomes significant during scale up. "Manufacture of mRNA for COVID-19 mass vaccination would involve the production of millions of doses – hundreds of grams of mRNA – and purification steps requiring hundreds of liters of resin," says Flook. "Costs would be higher still if it turned out that each vaccine course required multiple shots, or if annual vaccinations were necessary. The industry needs a scalable product that can efficiently accommodate such demand."

How did Thermo Fisher Scientific address the need? "It wasn't always straightforward," says Zobbi, who notes that a critical part of the process was screening the different base beads that Thermo Fisher Scientific uses for its affinity capture products. "We found the best performance was provided by our POROS polystyrene divinylbenzene bead at the largest pore size, which wasn't the obvious answer when we started out," he says.

Similarly, the length of the poly-T capture ligand required optimization for efficient capture of the mRNAs of interest. "Eventually, we found a 25- mer poly-T to be ideal, but this took a lot of work. For example, we had to test various coupling chemistries so that the poly-T behaved appropriately in the resin," says Zobbi. "Similarly, a balance had to be found between maximum mRNA capture and the quantity of poly-T ligand on the resin. We want to capture as much mRNA as possible, but increasing the poly-T concentration beyond a certain point does not provide an economically defensible increase in yield."

Flook notes how each aspect of the development process was driven by demand: "We optimized raw materials characteristics so that the resulting product fitted the market need – efficient, scalable mRNA purification." The outcome of the development process is the latest addition to the Thermo Scientific POROS family of products, Oligo(dT) 25 Affinity Resin. Comprising base beads with a hydrophilic coating, formed from a highly robust, structurally rigid backbone, the Oligo(dT) resin permits sample loading in high



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Article
Get in the mRNA Vaccine Race with Affinity Purification

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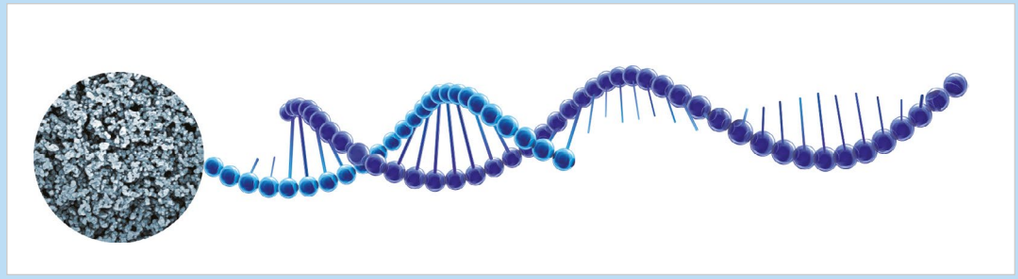
The Customer View

AmpTec manufactures pharmaceutical grade nucleic acids for diagnostic and therapeutic applications. We asked CEO, Peter Scheinert, for his views on the evolution of mRNA manufacture.

AmpTec has been manufacturing nucleic acids for fifteen years; today, the growth in mRNA applications – such as cancer immunotherapy and genome editing – is one of our strongest drivers. But we are particularly excited about the field of mRNA vaccines.

Standard vaccine production involves time-consuming steps, such as virus propagation and antibody generation. By contrast, the mRNA approach – injecting viral antigen mRNA – gets the body to produce the vaccine. It's much more flexible than standard vaccine approaches in that we can rapidly and easily modulate mRNA to reflect new mutations or to respond to new viral threats. But this speed and flexibility demands equivalently rapid and robust purification methods. Routine HPLC methods are associated with toxic reagents – requiring specialized ventilation and waste disposal systems – and scale-up difficulties. Our search for better upscaling solutions led us to a partnership with Thermo Fisher and the opportunity to work with them on the development of the Oligo(dT) resin, an easy-to-handle product that gives excellent mRNA yield. And it works equally well with all mRNAs; efficiency is unaffected by sequence or length. Furthermore, it binds the poly-A tail, and so returns full-length mRNAs, not truncated RNAs, which simplifies purification. Finally, it uses toxin-free reagents, thereby reducing method costs and complexity.

In brief, there is a dramatic and continuing increase in large-scale mRNA production, with mRNA vaccines being a key driver. We believe Oligo(dT) will be a critical manufacturing tool, not least for COVID-19 vaccine trials. Furthermore, the ease of use of this product, and the absence of toxic reagents, means that it can be used in the lab without any special safety or clean-up requirements. AmpTec is now assessing Oligo(dT) in large-scale processes, and I am confident that it will become our standard large-scale purification option. I think it's a fantastic tool!



Large pore bead with increased binding capacity for the efficient capture of mRNA.

salt solution – to favor mRNA-polyT annealing – and elution with reduced salt buffer or water. Key advantages of the system include:

- Efficient use of space and material – the polymer's structural attributes enable dense column packing
- Ligand stability at extremes of temperature (70 °C) and pH permit column clean-up and re-use over multiple cycles, thereby saving material costs
- Hydrophilic bead coating resists non-specific binding, thereby reducing purification cost and complexity
- Elimination of toxic reagents helps reduce operating risk, as well as cost and complexity of waste disposal
- Universal approach (applicable to all mRNAs) enables manufacturers to apply a single platform to all mRNA products Easy to use, simple to scale-up; cost savings become highly significant at commercial scale

And Thermo Fisher Scientific's clients back up these claims (see The Customer View). Flook adds, "Customers have reported plasmid DNA removal to below detectable limits, and binding capacities of 5 mg RNA per mL of resin for a 4000 base pair mRNA, which is excellent!"

Opportunity knocks

Manufacturers have a unique opportunity to take advantage of the cost and time advantages associated with Oligo(dT) – and the adoption process is simple. "We are always happy to have conversations with clients regarding optimization and scale-up," says Zobbi. Those who wish to evaluate the product can benefit from the technical expertise of Thermo Fisher Scientific's field sales force, which routinely provides clients with detailed support during process development and scale-up. "Our f ield-based application support team has global reach and can assist with the complete range of Thermo products for mRNA preparation," says Flook.

In conclusion, Zobbi adds, "We welcome new collaborators, and are very familiar with the variety of needs they may have."

Pharmaceutical Grade Reagent. For Manufacturing and Laboratory Use Only.

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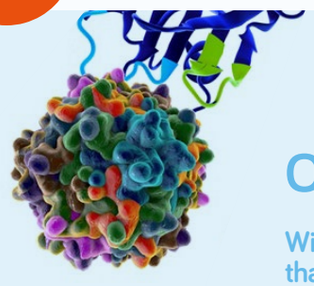


Optimizing AAV Manufacture

With the potential to cure genetic disorders rather than alleviate symptoms, gene therapies look set to revolutionize the field of medicine. Adeno-associated viruses have emerged as the vector of choice for delivering therapeutic genes to target cells, but manufacturing processes need to be improved and optimized to unlock their full potential.

By Orjana Terova and Zoltan Gulyas

Over the last decade, significant progress has been made in our ability to deliver therapeutic genes to target cells. Medicines that are able to replace faulty and missing genes are genuinely life-changing.

Despite the relative immaturity of the field, two gene therapies have already been approved by the FDA (Luxturna® and Zolgensma®), and the pipeline looks strong; the FDA expects that approvals for cell and gene therapy products will rise to 10–20 per year by 2025. Right now, gene therapies are targeting orphan diseases, especially in children, but they have the potential to treat central nervous system related disorders, such as Alzheimer's, Parkinson's or Huntington's disease.

Expectations are high, but there are many challenges on the road ahead; as gene therapies are looking to treat larger patient populations, there is a concomitant need to increase the manufacturing scale, and improve productivity and process control.

The vector of choice

Selected viruses have been successfully engineered into smart vehicles to deliver DNA to target patient cells. These viral vectors lack any viral genes but contain DNA sequences of interest for various therapeutic applications. In particular, recombinant adeno associated viruses (AAVs) have emerged as the vector of choice for many therapies for several reasons.

First and foremost, AAVs are generally considered safe, as they are non-pathogenic and non-toxic, and have inherently low immunogenicity, when compared with other viruses. Scientists have identified 13 naturally occurring serotypes so far, and each of them has different tropism (i.e., ability to target specific cell types), which enables selective transduction of specific tissues and organs. Companies are actively developing novel, engineered capsids to further improve tropism, and thereby increase the potency.

From a more practical standpoint, AAVs are relatively simple to manufacture, and these vectors have no lipid envelope as found on retroviruses and lentiviruses, so they are more stable, and able to withstand the typical process conditions used for protein purification such as low pH and high salt.

The potential of AAVs to treat wider patient populations and target more common disorders is somewhat limited due to the manufacturing and scale-up related challenges. The majority of gene therapies in late clinical phases are the result of first-generation processes that started as research projects in academia or hospitals years ago. In these settings, vector production is often performed by the classical tools and methods such as adherent cell cultures on plates or cell factories, sonication for cell disruption and ultracentrifugation for purification. Most of these techniques are either not scalable or can only be scaled out.

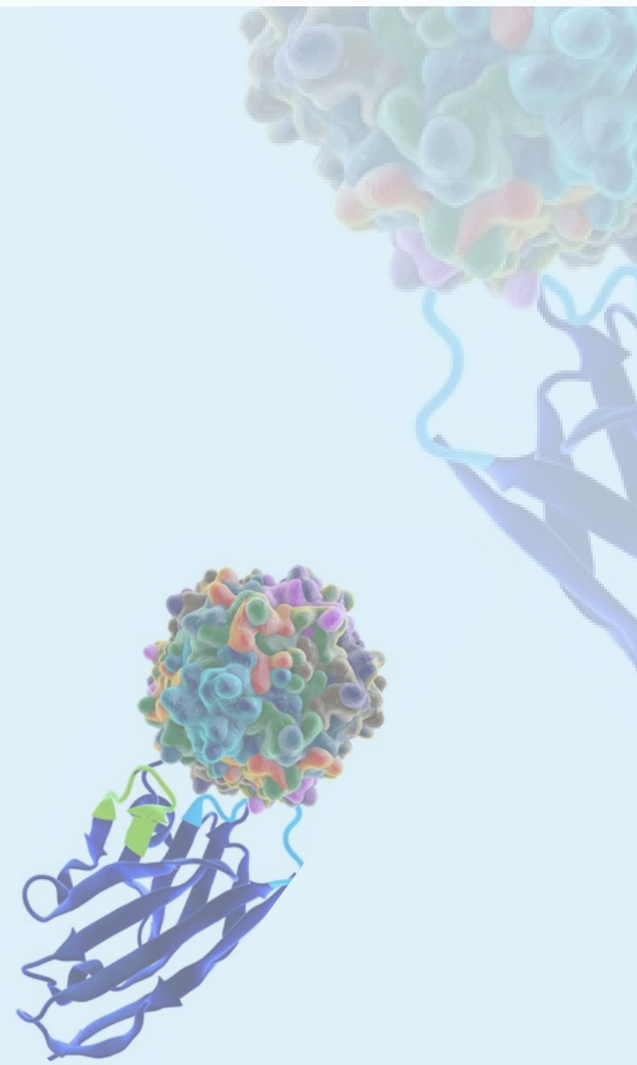
Essential evolution

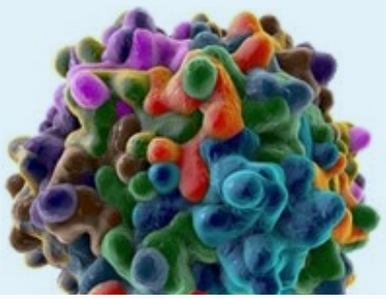
Today's gene therapy developers are using scalable techniques from the beginning of development, and recognize the need to not only improve productivity, but also process robustness and reproducibility. At the same time, regulatory agencies are expecting increasingly established product control and product characterization.

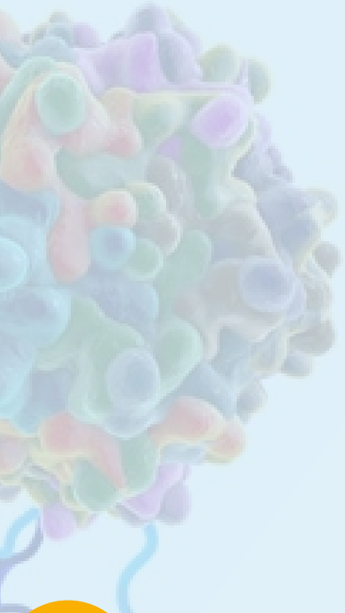
The monoclonal antibody (mAb) field was in a similar position not so long ago. It, too, had to evolve and mature, and can serve as a "role model" to the gene therapy field. Today, suspension cultures are used with high cell density to achieve high titers, and purification is performed by multiple chromatography steps including the highly selective affinity capture and the orthogonal polishing steps. All tools and methods are GMP-compliant, and the product is extensively characterized for its safety and efficacy.

Broadly speaking, the gene therapy field needs to follow a similar path, which requires significant investment of time and resources, while meeting speed-to-market needs. Though the path is similar, we must recognize that we cannot simply "copy and paste" solutions from the biopharma industry as these were designed with a different mind-set for different molecules. When it comes to optimizing AAV processes, there is much work to do.

In terms of upstream processing, gene therapy developers are still seeking reproducibility and looking to push productivity orders of







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Webinar

AAV downstream processing for industrial scale production - moving towards commercial manufacturing

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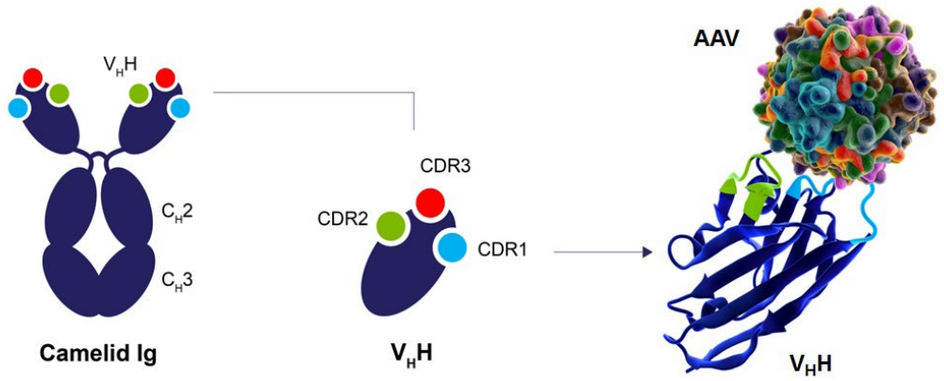

CaptureSelect technology is based on the single N-terminal domain of Camelid IgG, the V_HH fragment. Camelid-derived immunoglobulins are naturally devoid of light chains. The small size of the V_HH fragments allows for binding to epitopes of the target molecule which are difficult to access by larger immunoglobulins. Overall, the V_HH fragments offer high specificity, affinity and stability.

magnitude higher than the current standards. Improved packaging mechanisms are also needed to boost the percentage of full capsids (those that contain genetic material) versus empty capsids (which have no therapeutic value).

Turning our attention downstream, developers need scalable purification methods with high selectivity towards the molecule of interest, and high recovery to make sure not to lose the produced material.

Surrounding these elements is the need for accurate and reliable analytics that enable DoE-based process development, product characterization and quality control.

Recognizing the need for progress across the board, the Thermo Fisher Scientific bioproduction team is active in all these areas (see sidebar: "Innovation for All").

AAV Affinity Chromatography – the game changer

Focusing on purification, many companies have moved away from ultracentrifugation over the past few years and established multiple chromatography steps including ion-exchangers and hydrophobic interaction resins to achieve the required purity. In addition to the lengthy processing time and raw material cost, however, such multi-step processes generate cumulative yield losses. Moreover, process development lead times increase, hindering speed-to-market.

Affinity chromatography can overcome most of these challenges, as it can selectively capture the product of interest from crude material, providing high purity and yield in a single step, and robust methodology with less need for process optimization. This highly specific separation delivers significant improvements to downstream processing by reducing the number of purification steps and maximizing productivity.

Affinity chromatography is already a key element of the purification platform for monoclonal antibodies (consider Protein A), and specifically from Thermo Fisher Scientific's standpoint, our CaptureSelect™ team has been developing affinity solutions for over 15 years, enabling a similar paradigm shift in the purification of antibody-derivatives, recombinant proteins and now viral vectors. Due to the larger size of viral vectors, the affinity ligands are immobilized on Thermo Scientific™ POROS™ base beads, which are extremely suited for the purification of larger molecules (see box: CaptureSelect and POROS Up Close).

We currently offer three POROS CaptureSelect AAV affinity resins – AAV8, AAV9 and AAVX. As their name suggest the POROS CaptureSelect AAV8 and AAV9 resins were developed for the indicated serotypes, while the POROS CaptureSelect AAVX resin works for all naturally occurring serotypes as well as engineered capsids. This allows our customers to use it as a platform capture step in all their AAV projects (similarly to Protein A for mAbs). Based on the feedback we received since it launched, the AAVX resin is largely

Realities in the Field

Our dedicated team of field applications specialists are more than happy to answer questions and help solve problems. Here are some advices and points to consider regarding affinity capture of AAVs.

1. Process steps between harvest and capture chromatography are often neglected or not properly optimized, but the feed-stream quality can have a profound impact on purity, yield and process performance. Removal of all insoluble components by depth and membrane filters is important to avoid backpressure issues and column clogging. We also recommend soluble impurity reduction by various techniques (such as endonuclease treatment, flocculation, tangential flow filtration, and/or various chemistries on solid support) as much as possible prior to affinity capture.
2. Low product concentration in the load can cause earlier break-through and thereby resin capacity loss. Feed-streams can be concentrated by TFF, which also provides impurity clearance and reduces the loading time.
3. If capsids are present in the flow-through, increasing the residence time may be able to mitigate this.
4. Root causes for low recovery of the capture step could be caused by under-loading the column due to insufficient product quantities (loading around 1E12 vg/mL resin or below, which is 2-3 logs lower than the AAVX capacity), lack of elution efficiency, and/or overestimation of load concentration. Column volume reduction, eluting in upflow and optimizing the elution (evaluating different buffers, pH and additives) can mitigate the product loss.
5. Insufficient eluate purity can be resolved by incorporating and optimizing intermediate washes between load and elution.
6. If the affinity resin is meant to be reused, cleaning optimization should be performed to avoid carry-over issues. We recommend an acidic strip followed by cleaning with a chaotropic agent, such as guanidine hydrochloride. Concentrations and contact times are process dependent, but upflow direction is always recommended. Please note that our AAV affinity resins are compatible with up to 25mM NaOH only.

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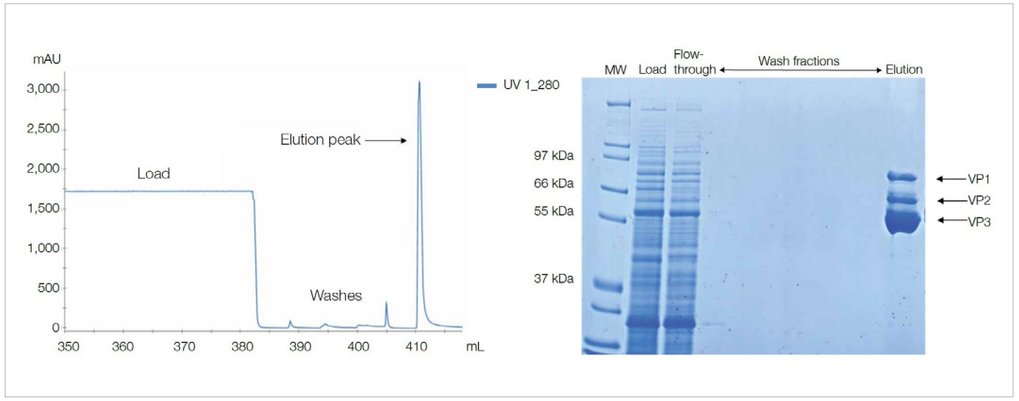


Chromatogram showing elution peak of rAAV6 purified on POROS CaptureSelect AAVX affinity resin (left). Fractions from AAV6 purification run on a Coomassie stained gel. The capsid proteins VP1, VP2, and VP3 are indicated (right).

fulfilling the industry's expectations, enabling high purity in a single step, offering process consistency from lab to production scale. Lastly, the performance of POROS CaptureSelect AAV affinity resins is maintained even at high flow rates, thereby enabling increased productivity and process flexibility.

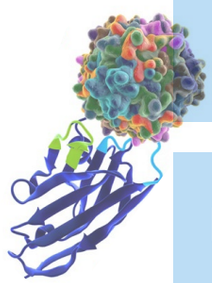
Team players

Even when using affinity chromatography, users still need to perform process optimization to ensure high purity and recovery. This work is more crucial in the gene therapy processes, where the current product and process understanding is limited, and the "plug and play" approach often leads to lackluster process performance. The importance of optimization goes beyond the affinity capture step (see sidebar: "Realities in the Field").

In this rapidly evolving and challenging field – and with such high expectations – teamwork is more important than ever. Upstream, downstream and analytical experts need to be in constant communication, and combine efforts to move the needle. This is why our team of field application specialists is keen to engage and collaborate with gene therapy developers on technical matters – to discuss recommended conditions, troubleshoot problems, and brainstorm on challenges. We are eager to learn, and as our knowledge base grows, we become better equipped to provide more efficient support and develop next-generation solutions that can help companies overcome the productivity and scalability challenges.

At Thermo Fisher Scientific, we provide the tools and services needed to manufacture AAV drug products, smoothing the path to commercialization and helping to bring life-changing gene therapies to the clinic faster.

Orjana Terova is Senior Product Manager, Purification, and Zoltan Gulyas is Senior Field Applications Specialist, Purification, both at Thermo Fisher Scientific.



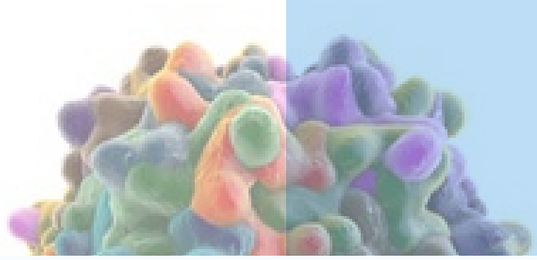
CaptureSelect and POROS™ Up Close

CaptureSelect technology is based on a strong foundation of over 15 years of experience in developing affinity ligands and producing resins for GMP manufacturing. The platform uses the variable domain of the heavy-chain-only camelid antibodies called V_HH – a single domain with a size of 15 kDa that provides full functionality in antigen specific recognition and high affinity binding. Their compact structure and the lack of light chains also results in increased stability, which allows them to withstand a wide variety of process conditions when applied as affinity ligands.

For large target molecules such as AAV, the CaptureSelect ligands are immobilized on the POROS backbone, which is a rigid, polystyrene-divinylbenzene based solid support with large pore structure for high binding capacity and a more efficient purification process. The large pore structure of the POROS resins results in reduced mass transfer resistance and as linear velocity increases, capacity and resolution decline very little. This leads to improved process productivity.

Innovation for All

In Thermo Fisher Scientific's BioProduction Division, all business units are devoted to bring solutions to the gene therapy field. The cell culture team is focused on the development of suspension cell lines, media and additives needed for high productivity upstream. The single-use team develops bioreactors for suspension culture (both in batch and continuous mode), and highly-customized single-use bags that are gamma irradiated for immediate use in clean rooms for closed processing. The purification team is focused on highly specific affinity resins to establish platform capture for AAVs. We also offer ion exchange resins to enable full capsid enrichment and additional impurity clearance. Finally, the pharma analytics team have developed highly sensitive assays for process-related impurity and advantageous agent detection. We have just launched a residual DNA detection kit for HEK-293 cells, and an Sf9 specific kit is in the works. Lastly, our dedicated viral vector services team has extensive expertise in clinical and commercial manufacturing of AAV, to progress programs from early to late phase development and commercialization.



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Solutions
Cell and Gene Therapy
Purification Solutions

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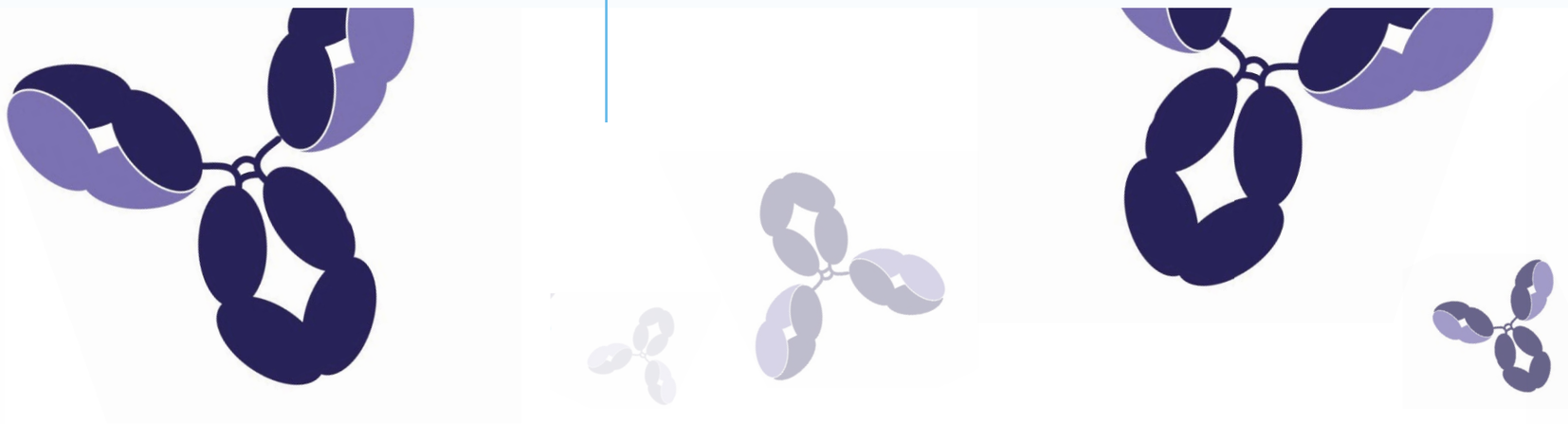

Capturing Value in Changing Times

The increasing complexity of biologics raises significant manufacturing challenges – not least regarding cost control and downstream purification. Thermo Fisher Scientific's answer? To boost capture efficiency with a scalable, broadly applicable platform technology called CaptureSelect™.

Innovative biotherapeutics promise to more fully meet patient needs, but only if manufactured at appropriate cost and quality. Unfortunately, standard purification processes tend to be incompatible with advanced biologics. This mismatch adds time and expense to biotherapeutics development, as manufacturers often must develop a new process using inefficient capture systems. Fortunately, there is a better way. Imagine adopting an affinity resin system that could be customized for nearly any biologic – and rapidly scaled up to cGMP manufacture. We asked Thermo Fisher Scientific's experts to tell us more about CaptureSelect affinity resins.

What changes have you seen in biologics manufacturing?

Laurens Sierkstra: Back in 2003, everybody focused on standard monoclonal antibodies purified with Protein A. In fact, the original business plan for the CaptureSelect technology began its life as a direct competitor for Protein A. But we immediately found that our customers wanted to process molecules for which Protein A was unsuitable, so we developed purification products that customers needed – resins for recombinant proteins, non-standard antibodies, gene therapy vectors, and other innovative biologics.

Pim Hermans: Discovering that customers were moving to biologics incompatible with Protein A was a real eye-opener for us – and this shift in the biologics landscape continues today. Fifteen years ago, customers might have wanted to purify Factor VIII; now they want to purify exosomes, viral vectors, or hard-to-process antibody fragments, while avoiding co-purification of light chains. Clinical pipelines reflect this evolution. Back then, over 90 percent of biologics entering the clinic were monoclonals; today, 25–30 percent comprise entities such as viral vectors, cell therapies, bispecific proteins, antibody fragments, and Fc fusion proteins.

Have other aspects – for example, timelines – also become more challenging?

LS: Well, manufacturers have always wanted to get to the clinic as fast as possible! Fortunately, the CaptureSelect platform has time advantages as it can purify virtually any biologic without needing to develop a whole process from scratch. Just as manufacturers use Protein A and polishing to purify standard monoclonal antibodies, CaptureSelect is a standardized platform for purifying biologics that Protein A cannot accommodate. Thus, CaptureSelect accelerates processes by reducing downstream complexity.

PH: Notably, the technology isn't just for non-antibody products – it also meets antibody purification needs that Protein A cannot address. For example, we can direct ligand specificity to precise FAb or Fc domains, thus enriching for advantageous properties.

What makes CaptureSelect unique?

LS: Firstly, the technology works through antibody-based selectivity, so we can develop an affinity resin for virtually any biologic – indeed, we have never failed to make a purification system for a proteinaceous molecule. Others have tried to make antibody-based affinity resins, but conventional antibodies are somewhat unstable, expensive to produce, and difficult to upscale. CaptureSelect, however, uses single domains from antibody heavy chains: these are robust and compatible with large-scale manufacture. And that's why they are ideal for affinity resins intended for biotherapeutics manufacture.

Secondly, CaptureSelect is highly efficient. Remember, biologics must be manufactured at an acceptable cost-of-goods, and this requires high yield. Reaching the clinic quickly with an inefficient process only results in a cost-of-goods disadvantage compared with a manufacturer who has a more efficient process. Our capture step provides increased yields, partly because of its intrinsic efficiency and partly because we can design our resins to preferentially select active (rather than inactive) forms of the biologic. Thus, CaptureSelect provides manufacturers not only with high yield but also with a high proportion of functionality.

Thirdly, CaptureSelect reduces the number of purification steps, which helps save time and cost. And finally, fewer columns, in turn, reduces the clean-room footprint, and increases efficiency of clean-room utilization. Together, these four attributes give manufacturers a valuable cost-of-goods advantage.

LINKS

Article
Rapid implementation of novel affinity purification.

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How do you help manufacturers who are struggling with biologics purification?

LS: Our *modus operandi* is highly collaborative and customized. Put simply, we begin by understanding the client's problem, and then we develop a program to solve that specific issue. Often – due to CaptureSelect's high selectivity – we can suggest solutions that manufacturers have not even considered.

PH: Usually, manufacturers assess available purification products and then design a process that fits those products. But we do it the other way around; we work with the client to identify the ideal process, and then we make a resin that fits the ideal. Conventional purification technologies can't provide customized resins that perfectly match the needs of a given client.

How else do you differ from other providers of purification technology?

LS: Firstly, we are a one-stop shop: we can take clients all the way from initial concept to a fully developed affinity resin compatible with GMP manufacture. We have the ability to both produce a ligand of interest and make a scalable, GMP-compliant affinity resin. And that requires excellent infrastructure and expertise. We were fortunate in that we had the right assets from the very beginning. Many companies with good ligand identification technologies have failed because they could not turn ligands into products that can be manufactured at appropriate quality criteria and scale – finding something that binds a particular molecule is the easy part! But with CaptureSelect, we can guarantee development of a GMP-compliant affinity resin within about ten months, scalable from ~1 mL to ~200 liters as necessary. In brief, manufacturers need certainty regarding scale, price and timescale, and we provide all three.

If we only offered ligand discovery technology, and not the ability to make scalable, GMP-compliant affinity resins, we would have to license the affinity ligands to clients. Instead, our model is to make and sell affinity resins for clinical trials and cGMP manufacturing.

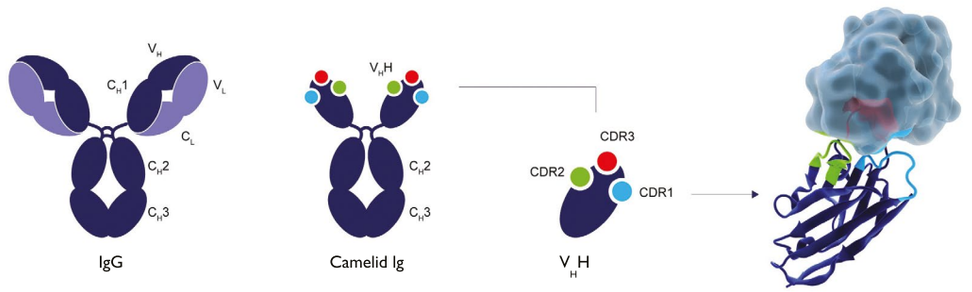
How are you positioned to meet future challenges?

LS: Biologics will continue to become more complex; advanced Fc fusions, fusion proteins, new gene therapy vectors (such as exosomes or red blood cells), or allogeneic cell therapies are key trends. But we too will evolve; we are always adapting the CaptureSelect technology to address more complex products by working closely with customers.

PH: We ensure that we keep track of market developments. Years ago, we realized that adeno-associated virus vectors would become important, and developed products for that niche. Today, we are doing likewise for exosome technology. The goal is always to give customers excellent downstream processing tools – while staying ahead of the technology curve.

Laurens Sierkstra (Business Segment Leader, CaptureSelect Affinity Products) has been involved in CaptureSelect technology from the beginning and has almost 25 years' experience with the technology.

Pim Hermans (Manager, CaptureSelect Ligand Discovery) also worked on CaptureSelect technology during its genesis and today continues to liaise closely with clients to develop the ideal affinity resins for their needs.



CaptureSelect technology is based on the variable domain of Camelid heavy-chain only antibodies (single domain or V_HH fragment). In contrast to conventional IgG molecules, camelid antibodies are devoid of light chains but they maintain the same level of specificity. V_HH fragments are exceptionally small antigen binding fragments (~15kD) which allows binding to alternative epitopes, leading to a unique affinity profile. Compared to standard antibodies, these fragments are very robust and can withstand the harsh conditions used during chromatography.

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Solutions
CaptureSelect Affinity Technology

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