GeneMedi Nanobead Technology White Paper

Cell Sorting: 50 nm Interference-Resistant Anti-Biotin Nanobead Technology and Integrated Supply Chain Solutions

1. Executive Summary

Reshaping Cell Sorting Standards: Precision, Safety, and Supply Stability

With the rapid development of Cell and Gene Therapy (CGT) and single-cell multi-omics technologies, the upstream cell preparation process faces unprecedented challenges: How to obtain high-purity cells from complex tissues with high endogenous biotin backgrounds? How to maintain the native physiological state of cells while ensuring a high recovery rate? How to ensure the supply stability of key reagents throughout the entire life cycle of clinical translation?

This white paper details the technological innovations and application value of the newly launched column-based cell isolation system by GeneMedi. Approaching from **chemical, physical, and industrial** dimensions, we propose a comprehensive solution for human immune cell isolation:

1、Chemical Dimension - Anti-Biotin Nanobeads: In terms of underlying molecular design, GeneMedi employs engineered anti-biotin monoclonal antibodies to replace traditional streptavidin (SA) as the surface capture ligand, thereby avoiding SA's susceptibility to interference from endogenous free biotin in complex samples. To adapt to downstream application research, we have deeply optimized the antigen-antibody binding kinetics, introducing two anti-biotin nanobead product lines:

Interference-Resistant Anti-Biotin Nanobeads (Non-releasable): These possess extremely high affinity and can potently resist competitive interference from high concentrations of free biotin in whole blood or plasma. They exhibit outstanding structural stability and high biological inertness in *in vivo* physiological environments, meeting the requirements for

processing complex samples such as whole blood and even direct clinical-grade reinfusion.

Releasable Anti-Biotin Nanobeads: While ensuring the efficient capture of rare cells, these allow for the controlled elution of nanobeads *in vitro* using mild competitive reagents. The releasable design enables the acquisition of pure, bead-free cells, maximally preserving the cells' original phenotype and functionality, and providing extremely high research flexibility for single-cell sequencing, *in vitro* cell expansion, and cell function studies.

2、Physical Dimension - 50 nm Nanobeads: Based on a 50 nm superparamagnetic nano-matrix , the nano-sized beads eliminate the mechanical stress imposed on cells by larger-diameter beads, ensuring that the isolated cells maintain high viability and functionality.

3、Industrial Dimension - Stable Supply Chain: Relying on the GM-ExBeads™ Microsphere Engineering & Modification platform , the GM-LIBRA™ AI-Driven Ligand Evolution platform , and the GM-ExImmune Integrated Immune Cell Verification platform , GeneMedi has achieved vertically integrated in-house research and production, from nanobead synthesis to antibody discovery. This not only eliminates the batch instability and supply disruption risks associated with the OEM model but also provides regulatory compliance support for Investigational New Drug (IND) applications for industrial clients.

Through validation data and principle analysis, this white paper reveals how the SOLIDEX™-ISOEx system achieves three core breakthroughs: attaining **"zero background interference" via anti-biotin technology , guaranteeing "high cell purity, high recovery rate, and high viability" with 50 nm nanobeads , and establishing "supply chain security"** through a fully integrated R&D process. Consequently, it provides a superior cell isolation solution for CGT and human immune cell research.

2. Validation of the Outstanding Performance of the SOLIDEX™-ISOEx System

GeneMedi provides three highly efficient column-based sorting strategies: Positive Selection, Negative Selection (Untouched), and Depletion. These exceptional sorting solutions are based on the core 50 nm Anti-Biotin Nanobeads and rely on GeneMedi's three proprietary core technology platforms (GM-ExBeads™, GM-LIBRA™, and GM-ExImmune). They achieve a perfect balance of high cell purity, high recovery rate, and high viability across a variety of complex sorting scenarios.

2.1 Negative Selection (Untouched): Acquiring Unlabeled Native Cells

Negative selection imposes extremely high requirements on controlling the non-specific adsorption of magnetic beads. GeneMedi specifically depletes unwanted cells using a biotinylated antibody cocktail, leaving the target cells completely untouched.

Taking the SOLIDEX™-ISOEx Untouched Human NK Cell Isolation Kit as an example, in an experiment isolating CD56+ NK cells from human peripheral blood mononuclear cells (PBMCs), the purity of the target cells prior to isolation was merely 3.45%, which surged to 96.0% post-isolation. Similarly, when processing cryopreserved PBMC samples using the SOLIDEX™-ISOEx Untouched Human Classical Monocyte Isolation Kit , the purity of CD14+ classical monocytes in the flow-through fraction increased from an initial 21.7% to 92.1%. These two sets of empirical data fully demonstrate that this series of kits can efficiently deplete non-target cells, providing high-purity NK cells and monocytes that perfectly preserve their native physiological state for downstream experiments.

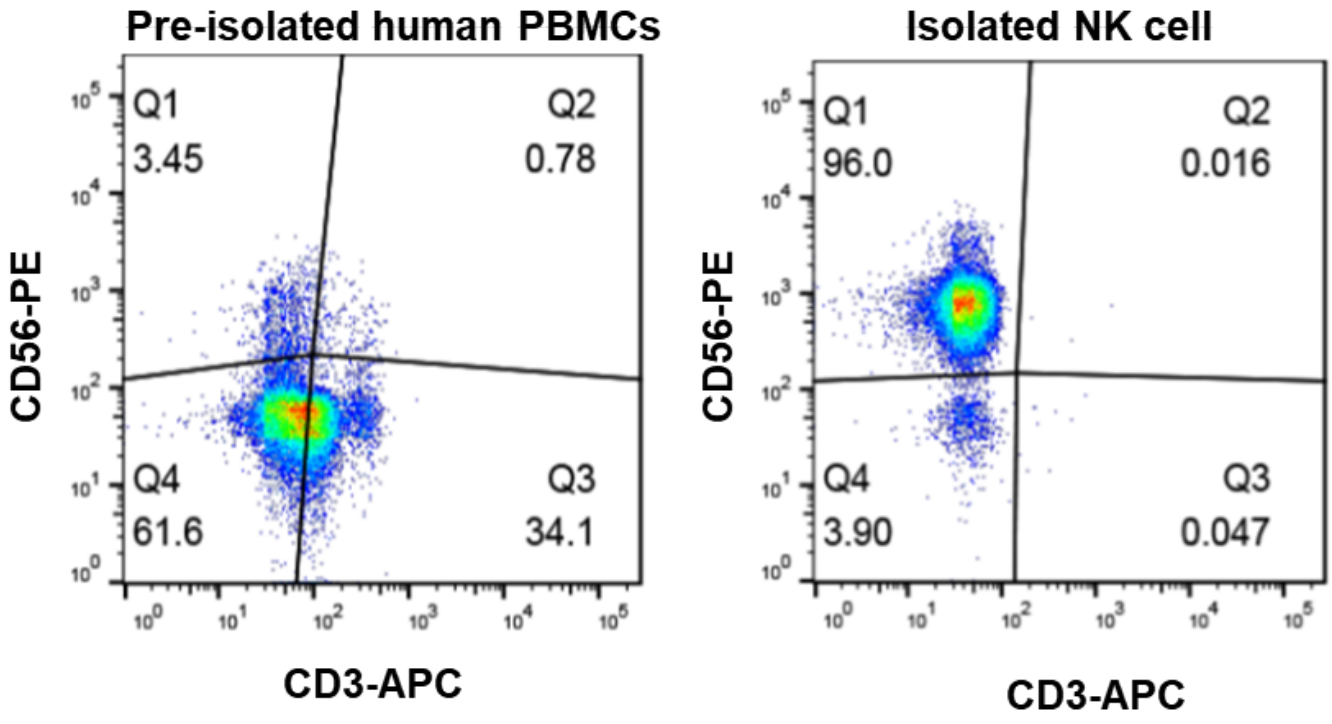

Figure 1. SOLIDEX™ -ISOEx Untouched NK Cell Isolation Kit (Column-Based): Achieving the isolation of high-purity NK cells.

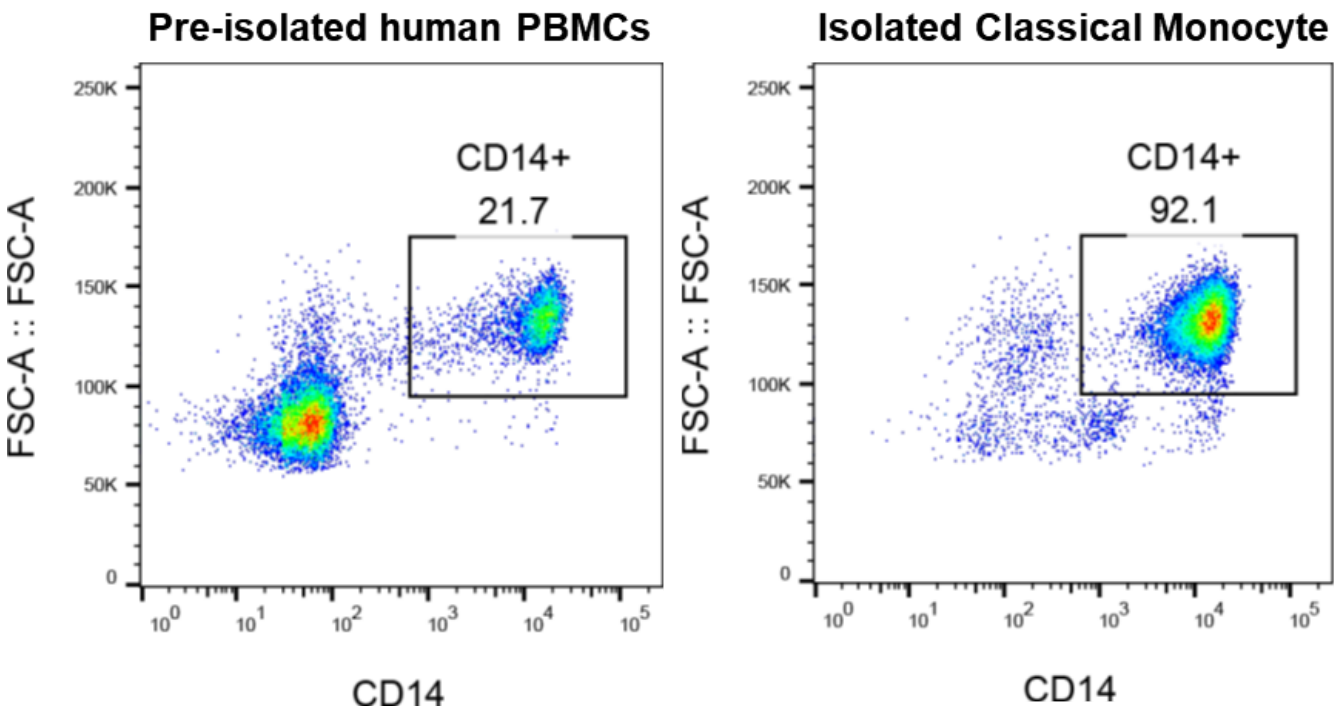

Figure 2. SOLIDEX™-ISOEx Untouched Human Classical Monocyte Isolation Kit: Achieving the isolation of high-purity classical monocytes.

2.2 Positive Selection: High-Affinity Precision Capture of Target Cells

Positive selection utilizes the high specificity of nanobeads to directly bind and enrich target cells, making it particularly suitable for the efficient recovery of rare cells. In tests using SOLIDEX™-ISOEx Human CD3 Isolation Nanobeads to directly isolate CD3+ T cells from human PBMCs, the proportion of CD3+ cells in the pre-isolation sample was 52.6%. After rapid column-based isolation, the purity of CD3+ T cells reached 95.0%, and the isolated cells maintained exceptionally high viability.

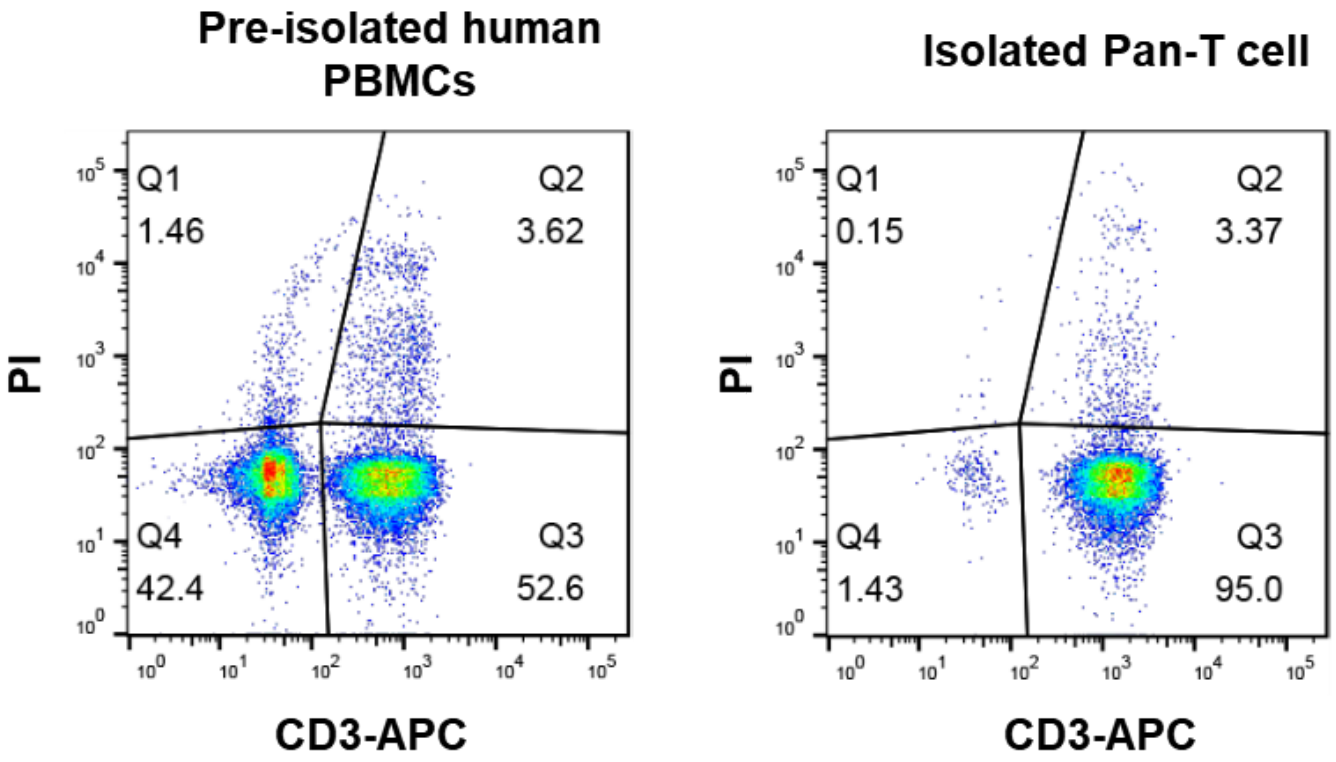

Figure 3. SOLIDEX™-ISOEx Human CD3 Nanobeads (Column-Based): Achieving the isolation of high-purity T cells.

2.3 Depletion: Efficient Removal of Non-Target Cells

The depletion method is specifically designed to remove distinct cell populations, requiring extremely high depletion efficiency without damaging non-target cells. We tested this using the SOLIDEX™-ISOEx Indirect Human TCRα/β+ T Cell Depletion Kit. In the initial human PBMC sample, the proportion of TCRα/β+ cells was as high as 54.7%. After processing through the separation column, the residual rate of these cells in the flow-through fraction dropped to 0.079%, demonstrating a depletion efficiency exceeding 99.3%. This data confirms that the kit achieves efficient depletion without causing non-specific loss of non-target cells.

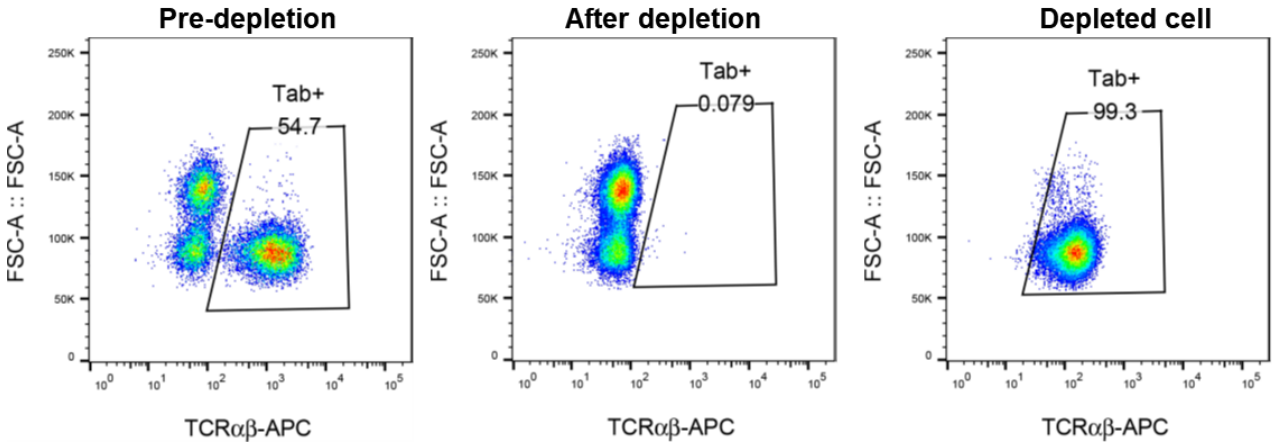

Figure 4. SOLIDEX™-ISOEx Indirect Human TCRα/β+ T Cell Depletion Kit (Column-based): Achieving efficient depletion of TCRα/β+ cells from human PBMCs.

3. Advantages of the Anti-Biotin System

3.1 Technical Background: Evolution of Indirect Sorting Strategies

In Magnetic-Activated Cell Sorting (MACS) technology, indirect labeling is widely adopted due to its flexibility. Traditional magnetic beads rely on the binding of streptavidin (SA) to biotinylated antibodies. However, as the requirements for purity and viability in cell therapy and rare cell sorting increase, the inherent limitations of the SA system have gradually become apparent.

Once SA binds to the magnetic beads, it is extremely difficult to dissociate without damaging the cells (e.g., via extreme pH, high temperatures, or denaturing agents). Consequently, the isolated cells permanently carry magnetic beads and antibody complexes on their surface. This not only causes receptor blockade but may also trigger non-specific signaling pathway activation, severely interfering with downstream immunological functional assays, single-cell sequencing, or clinical reinfusion.

Therefore, GeneMedi has introduced anti-biotin nanobeads. The GeneMedi SOLIDEX™-ISOEx series cell isolation system includes two types of anti-biotin nanobeads to meet the demands of different experimental scenarios:

(1) SOLIDEX™-ISOEx Interference-Resistant Anti-Biotin Nanobeads (Non-releasable):

Suitable for routine positive/negative selection, flow cytometric analysis, nucleic acid extraction, and other protocols insensitive to cell surface remnants. Their high affinity ensures robust capture, while the nanoscale size reduces cytotoxicity.

(2) SOLIDEX™-ISOEx Releasable Anti-Biotin Nanobeads: Specifically designed for scenarios with stringent requirements for the native state of cells, such as functional studies, cell therapy, and single-cell sequencing. Through competitive elution with D-biotin, the magnetic bead and antibody complexes can be completely removed to obtain "scarless" (bead-free) cells, avoiding receptor blockade and non-specific activation.

3.2 GeneMedi's Innovation: Kinetics Regulation Based on Anti-Biotin

The GeneMedi SOLIDEX™-ISOEx system discards the traditional SA system, instead utilizing anti-biotin monoclonal antibodies as the capture molecules on the surface of the magnetic beads. Antigen-antibody interactions are inherently reversible non-covalent bindings. By screening and modifying the antibody variable region (Fv), GeneMedi has successfully developed two nanobead product lines with distinct kinetic profiles to meet diverse research and clinical needs.

Under normal human physiological conditions, the concentration of free plasma biotin is typically very low (< 1 ng/mL), but it can rise to > 100 ng/mL in populations taking high-dose biotin supplements. This poses a significant interference background. Addressing this challenge, GeneMedi's R&D team established strict screening criteria: ensuring that even against a free biotin background reaching the human physiological limit (> 100 ng/mL), the magnetic beads are neither prematurely blocked by free biotin nor allow the competitive displacement of captured targets. This guarantees the accuracy and reliability of clinical sample sorting.

Figure 5 illustrates the residual signal of different antibody clones in the presence of gradient concentrations of free biotin. Anti-biotin antibody G maintains the highest signal under free biotin competition, demonstrating extremely tight binding. Anti-biotin antibody G tolerates biotin interference far exceeding the human physiological limit, indicating its suitability as an **interference-resistant anti-biotin nanobead**. Conversely, anti-biotin antibody A is sensitive to free biotin; its curve shifts significantly to the left, enabling efficient and rapid elution using lower concentrations of biotin, making it ideal as a **releasable anti-biotin nanobead**.

Relying on their superior tolerance and stability, the **interference-resistant anti-biotin nanobeads** are not only capable of high-purity cell sorting in the research field but also pave the way for clinical cell therapy manufacturing processes; their "bead-removal-free" characteristic dramatically simplifies GMP production workflows. In addition, the **releasable anti-biotin nanobeads** are specifically designed for scenarios demanding ultimate sample purity. Whether for single-cell sequencing and flow cytometry on the research side or special pipelines requiring multiplex labeling or "foreign-body-free preparations" on the

clinical side, their mild and rapid elution capabilities ensure the acquisition of highly viable "bead-free cells."

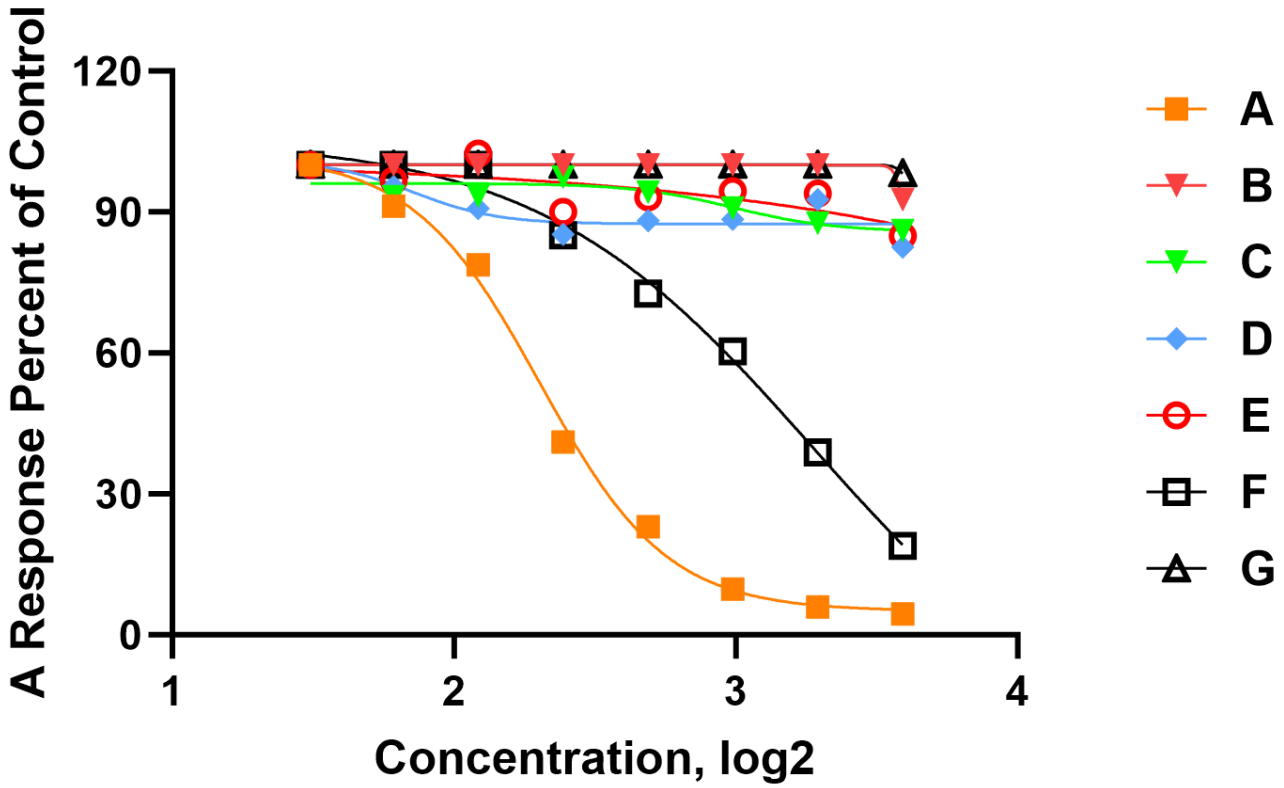

Figure 5. The free biotin competition assay reveals significant performance differences between the interference-resistant anti-biotin nanobeads and the releasable nanobeads.

3.3 Core Technology Comparative Analysis

Compared to the "irreversible" binding limitations of traditional streptavidin (SA) magnetic beads, the GeneMedi anti-biotin magnetic bead system utilizes antibody kinetics regulation technology to achieve a technological leap from singular "strong capture" to flexible "release."

While traditional methods may lead to cellular receptor blockade or non-specific activation caused by the residual magnetic beads, GeneMedi's interference-resistant series maintains high affinity and recovery rates comparable to traditional products while significantly reducing cytotoxicity and steric hindrance by virtue of its biodegradable nano-matrix. This provides a superior and safer alternative for routine experiments. Furthermore, the releasable series breaks through technological barriers, thoroughly resolving the pain point of "magnetic bead residue" through a competitive dissociation mechanism. This achieves truly scarless sorting and zero activation throughout the entire process.

The fundamental differences in the biological source, spatial structure, and binding kinetics of the core ligands dictate the application scenarios of the final magnetic bead products. Traditional SA, limited by its exogenous background and physical properties that make it highly susceptible to interference from endogenous biotin, is difficult to apply directly in complex clinical scenarios such as whole blood isolation or direct cell reinfusion. In contrast, the anti-biotin system, meticulously designed through antibody engineering, endows the binding and dissociation processes with "tunable" characteristics.

To more intuitively demonstrate this performance translation from "underlying ligands" to "top-level magnetic beads," we will first compare the molecular attributes of the three core ligands (**Table 1**) and then deeply analyze the performance differences of the resulting finished magnetic beads in real-world cell sorting scenarios (**Table 2**).

Table 1. Comparison of the three core ligands.

Comparison Dimension	Streptavidin (SA)	Anti-Biotin Antibody (Interference-Resistant)	Anti-Biotin Antibody (Releasable)
Biological Source	Exogenous (bacterial-derived protein)	Humanized	Humanized
Molecular Nature	Tetrameric protein	Immunoglobulin (IgG or fragment thereof)	Immunoglobulin (IgG or fragment thereof)
Affinity for Biotin	Ultra-high affinity	High affinity	Moderate affinity
Binding Reversibility	Irreversible	Extremely difficult to reverse	Highly reversible
Immunogenicity Risk	High	Extremely low	Extremely low

Table 2. Comparison of the application performance of magnetic beads corresponding to the three ligands.

Comparison Dimension	Streptavidin Magnetic Beads	Anti-Biotin Magnetic Beads (Interference-Resistant)	Anti-Biotin Magnetic Beads (Releasable)
Applicable Sample Types	Washed samples only (e.g., PBMCs)	Complex samples such as whole blood, plasma, tissue homogenates	Washed samples (e.g., PBMCs)

Comparison Dimension	Streptavidin Magnetic Beads	Anti-Biotin Magnetic Beads (Interference-Resistant)	Anti-Biotin Magnetic Beads (Releasable)
Resistance to Free Biotin Interference	Not resistant	Resistant	Not resistant
Effect of Free Biotin	Causes bead failure	No effect	Acts as an elution agent
Bead Release State	Permanently bound, not released	Firmly bound, not released	Released on demand, yielding bead-free cells
Impact on Cell Function	May cause steric hindrance or non-specific activation	Minimal size and biologically inert, no significant impact on cell function	No significant impact

4. The Physical Dimension Innovation: 50 nm Superparamagnetic Nanotechnology

4.1 Why 50 nm? — Redefining "Cell-Friendly" Sorting

In magnetic cell sorting, the size of the magnetic bead is not merely a physical parameter; it directly dictates how the bead interacts with the cell. Commercially available magnetic beads span a wide range of sizes, from the nanoscale (~50 nm) to the microscale (1-4.5 µm).

After extensive screening and validation, GeneMedi ultimately settled on the golden size of 50 nm. Compared to bulky microscale magnetic beads, the SOLIDEX™-ISOEx 50 nm nanobeads bring a qualitative leap to cell sorting:

(1) "Invisible" Binding (Zero Physical Stress): Relative to cells (typically 7-15 µm in diameter), microscale magnetic beads exert significant mechanical stress on the cell membrane upon binding, potentially even altering cell morphology. In contrast, a 50 nm bead is merely the size of "dust" relative to a cell.

Product Feature: Excellent maintenance of cell viability and morphology. This microscopic size ensures that the sorting process is "gentle" on the cells, preventing cell rupture or activation caused by mechanical pulling.

(2) True Suspension State (Uniform Binding Kinetics): Large-sized magnetic beads are prone to sedimentation due to gravity, requiring users to constantly mix them during incubation; otherwise, uneven binding will occur, negatively impacting the recovery rate. The 50 nm nanobeads form a stable colloidal suspension system in solution.

Product Feature: High operational fault tolerance and excellent batch stability. Users do not need to perform cumbersome shaking or rotary mixing during antibody incubation; the magnetic beads can automatically and evenly seek out target cells, eliminating experimental fluctuations caused by human operational differences.

(3) Interference-Free Downstream Analysis: Because their size is close to that of bacteria or small cells, microscale magnetic beads easily scatter lasers, interfering with the optical path of flow cytometers.

Product Feature: Excellent flow cytometry compatibility. The 50 nm nanobeads are far below the detection threshold of a flow cytometer and are invisible on Forward Scatter/Side Scatter (FSC/SSC) dot plots.

After positive selection, cells can be directly analyzed on the machine without the need to dissociate the magnetic beads, vastly simplifying the quality control workflow.

4.2 The Perfect Integration of Purity and Speed: The Efficacy Leap of GeneMedi's Column-Based Nanobead Sorting

Because the single magnetic moment of nanobeads is relatively weak, they cannot be directly attracted by a magnetic rack like large magnetic beads (which use column-free methods); they must be used in conjunction with a high-gradient magnetic separation column. Traditional wisdom holds that column-based operations are complex and time-consuming. However, separation columns can effectively wash away non-specifically adsorbed unwanted cells through a physical barrier, thereby providing high purity unattainable by column-free methods.

To resolve the contradiction between "high purity" and "time-consuming" processes, GeneMedi has optimized the operational workflow:

(1) Optimized Binding Buffer: Accelerates antigen-antibody binding kinetics, shortening the required incubation time.

(2) High Flow Rate Column Design: While ensuring capture efficiency, the matrix pore size has been improved to increase the liquid flow-through rate.

This improvement compresses the standard operation time of the GeneMedi SOLIDEX™-ISOEx column-based nanobeads to **25 minutes**. In comparison, standard protocols for similar column-based sorting products on the market typically require 30-40 minutes. We have not only retained the high-purity advantage of column-based sorting but also increased efficiency by 20%-40%, truly achieving "uncompromised purity with doubled speed."

4.3 Core Comparative Analysis: 50 nm Nanobeads vs. Traditional Microscale Magnetic Beads

4.3.1 Microstructural Characterization: Ultimate Uniformity and Regularity The core of the SOLIDEX™-ISOEx sorting technology lies in its unique nanobead matrix. We employ a precision synthesis process to prepare superparamagnetic nanobeads with a strictly controlled particle size of 50 nm.

As shown in **Figure 6**, SOLIDEX™-ISOEx nanobeads exhibit a highly regular spherical structure and an extremely narrow particle size distribution. The SOLIDEX™-ISOEx nanobeads utilize superparamagnetic nanobeads with high uniformity and a particle size of 50 nm, which can rapidly respond to magnetic fields and have no significant impact on cell viability or activity. Experimental results demonstrate that compared to Company M's products, the SOLIDEX™-ISOEx nanobeads are more consistent in size and more regular in shape.

This high degree of size uniformity is crucial. It ensures that the magnetic response speed of every single bead is consistent, thereby avoiding non-specific cell capture caused by magnetic bead aggregation. Concurrently, the regular spherical surface provides more stable antibody conjugation sites, minimizing steric hindrance to the greatest extent and ensuring inter-batch stability.

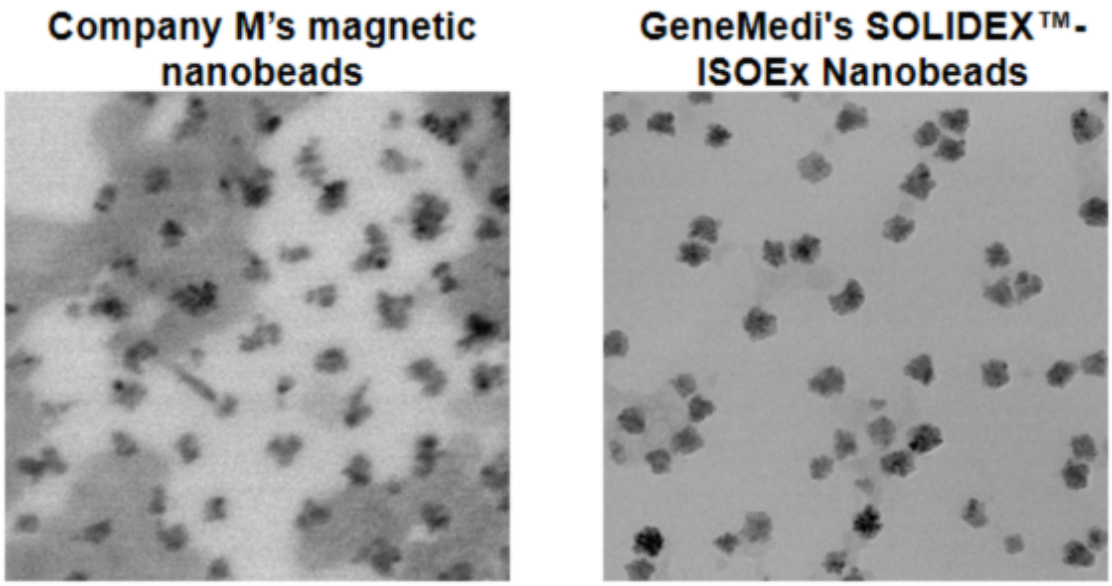

Figure 6. GeneMedi's SOLIDEX™-ISOEx Nanobeads: Uniform size and regular shape.

In the field of cell sorting, the size of the magnetic beads directly determines the sorting mechanism and the final state of the cells. To elucidate the design advantages of the SOLIDEX™-ISOEx 50 nm nanobeads, we conducted a multidimensional performance comparison between GeneMedi's nanobeads and commonly available microscale magnetic beads on the market. The table below details the differences in product performance between GeneMedi's 50 nm beads and common microscale (>1 μm) beads on the market.

Table 3. Comparison of the impact of magnetic bead size on cell sorting efficacy.

Comparison Dimension	Traditional Micron-Sized Beads (Non-50nm Microbeads, >1μm)	GeneMedi SOLIDEX™-ISOEx Nanobeads (50nm Nanobeads)
Bead Size and Morphology	Large (close to bacterial size) Visible under microscope, prone to physical obstruction.	Extremely small (virus-sized) Invisible under microscope, does not alter cell appearance.
Physical Stress on Cells	High Mechanical shear forces from large particle binding may damage fragile cells.	Extremely low Behaves like a solute molecule, imposes minimal mechanical load on cell membrane, preserving cell viability.

Comparison Dimension	Traditional Micron-Sized Beads (Non-50nm Microbeads, >1μm)	GeneMedi SOLIDEX™-ISOEx Nanobeads (50nm Nanobeads)
Incubation Handling Experience	Cumbersome Beads settle easily; requires continuous use of a rotator or manual mixing during incubation.	Simple Colloidal suspension properties; after mixing, static incubation is sufficient, no monitoring required.
Sorting Principle	Column-free Simple operation, but prone to impurity carryover	Column-based Magnetic field is amplified by magnetic matrix for rigorous washing to remove impurities
Flow Cytometry Compatibility	Poor Large beads scatter light, interfering with cell population gating; removal is recommended before analysis.	Excellent Beads are "invisible" to the optical path, enabling clear flow cytometry plots directly (positive selection) without the need for bead removal.
Total Processing Time	Fast (~15-20 min) Fewer steps due to no column requirement.	GeneMedi Optimized Protocol (~25 min) Although column-based, the process is kinetically optimized, taking only slightly longer than column-free methods and significantly faster than competitor column-based methods (30-40 min).
Key Advantages Summary	Fast, suitable for rough selection.	High cell purity, minimal cell damage, preserved cell viability and functionality, consistent results, suitable for demanding applications.

5. Supply Chain: An Integrated, Fully In-House R&D and Production System

In the fields of biopharmaceuticals and basic research, the stability and supply security of reagents are not merely related to the success or failure of experiments, but also to the controllability of project cycles. Many magnetic bead products on the market are constrained by complex Original Equipment Manufacturer (OEM) networks, where core raw

materials (magnetic bead carriers or antibody ligands) heavily rely on external procurement. This often leads to significant inter-batch variations and the risk of supply disruption.

GeneMedi has disrupted this industry norm by building a closed-loop ecosystem spanning from nanobead synthesis to ligand development, and further to large-scale production and functional validation. We rely on three core technology platforms: GM-ExBeads™, GM-LIBRA™, and the GM-ExImmune Integrated Immune Cell Verification platform.

5.1 GeneMedi's Solution: Three Proprietary Core Technology Platforms

GeneMedi has abandoned the traditional "assembly" model and established a vertical integration strategy of "in-house research of underlying raw materials + in-house control of core processes." We do not rely on any third-party suppliers for core raw materials. Relying on our three proprietary core technology platforms, we have achieved closed-loop control from nanobead synthesis and ligand discovery to final functional validation.

5.1.1 GM-ExBeads™ Microsphere Engineering & Modification Platform

Magnetic beads are not merely carriers; they are constructors of the micro-physical environment. Relying on the GM-ExBeads™ platform, GeneMedi has eliminated its dependence on external magnetic materials, achieving full-scale synthesis capabilities ranging from large-pore chromatography resins to nano-scale magnetic carriers.

(1) Precise Synthesis of the 50 nm Core: We have independently constructed 50 nm superparamagnetic beads optimized specifically for cell sorting. By strictly controlling the magnetic bead production process, we ensure an extremely low particle size distribution coefficient, guaranteeing the consistency of the magnetic response.

(2) Oriented and Ordered Arrangement of Surface Chemistry: Traditional conjugation processes often lead to the random lodging of ligands, resulting in the masking of active sites. The GM-ExBeads™ platform, combined with proprietary surface chemistry, achieves oriented ligand arrangement on the surface of the magnetic beads.

(3) Steric Hindrance Optimization: We precisely regulate the hydrophilicity and charge distribution of the surface modification layer from a physicochemical perspective. This effectively constructs an "anti-non-specific adsorption barrier," eliminating non-specific aggregation at the source and ensuring an extremely high signal-to-noise ratio.

5.1.2 GM-LIBRA™ AI-Driven Ligand Evolution Platform

The core of capturing cells with magnetic beads lies in the specificity of the ligand (antibody). Unlike competitors who directly procure generic antibodies, GeneMedi redefines "biorecognition" through the GM-LIBRA™ platform.

(1) AI-Driven Epitope Prediction: This platform leverages artificial intelligence algorithms to focus on precise epitope prediction. We target "isolation epitopes" that are fully exposed on the cell surface and have minimal impact on cell function.

(2) Directed Ligand Evolution: Based on the targeted epitopes, we discover and evolve highly adaptable ligands. This strategy not only fundamentally enhances capture efficiency but also significantly minimizes non-specific adsorption.

(3) Humanized Fc Backbone Design: As an important supplementary strategy, we engineer the ligands by introducing a humanized Fc backbone. This not only improves protein stability but also significantly reduces the immunogenicity risks potentially caused by heterologous proteins, thereby achieving high product reproducibility and stability.

5.1.3 GM-ExImmune Integrated Immune Cell Verification Platform

To ensure product applicability in complex clinical scenarios, this platform breaks through the limitations of single-cell therapies. Addressing the specific demands of advanced immunotherapies, including T-Cell Engagers (TCE) and NK Cell Engagers, it conducts panoramic immunophenotyping analysis, multimodal functional verification, and in-depth biological evaluation (such as signal pathway integrity and receptor conformation verification) on the sorted cells. This step ensures that every batch of magnetic beads produced by GeneMedi undergoes stress testing simulating real-world drug mechanisms before delivery to the customer.

5.2 In-House Production: Linear Scale-Up from Milligrams to Grams

Possessing technology is only the first step; scalable manufacturing capability is the cornerstone of supply chain stability.

(1) Dual Autonomy: GeneMedi is an enterprise equipped with large-scale production capabilities for both magnetic bead synthesis and ligand production. We do not rely on upstream suppliers and can flexibly adjust production capacity according to market demand.

(2) Guarantee of Batch Consistency: Because the core raw materials (magnetic beads and antibodies) are produced internally, we can implement strict Quality Control (QC) standards right at the raw material source, eliminating fluctuations in end-product performance caused by changing raw material suppliers.

5.3 Supply Chain and Quality Control Comparison

The following table provides an in-depth analysis of GeneMedi's advantages from the perspective of industrial chain security:

Table 4. Controlling Risks from the Source: Strategic Differences Between GeneMedi's Fully Integrated In-House R&D System and the Traditional OEM Model.

Comparison Dimension	Traditional Assembly/OEM-Dependent Manufacturers	GeneMedi (Integrated Manufacturer)	Market/R&D Risk Analysis
Bead Source	External procurement / OEM	In-house R&D and production (GM-ExBeads™)	External bead sourcing risks include variability in particle size and potential supply disruptions; GeneMedi ensures batch-to-batch consistency and supply chain stability.
Antibody/Ligand Source	Procurement of generic antibodies	In-house screening and evolution (GM-LIBRA™)	Generic antibodies are not optimized for bead conjugation, leading to high batch-to-batch variability in affinity; GeneMedi enables in-house R&D of antibodies/ligands.
Antibody/Ligand Production	Hybridoma or ascites	Proprietary large-scale recombinant expression using serum-free mammalian cell systems	Assemblers are highly dependent on hybridoma or ascites-based processes, which often face challenges in antibody sequence batch stability, limited scalability, and animal-derived compliance risks; GeneMedi achieves precise control of ligand sequences and exceptional batch-to-batch uniformity.

Comparison Dimension	Traditional Assembly/OEM-Dependent Manufacturers	GeneMedi (Integrated Manufacturer)	Market/R&D Risk Analysis
Cell Function Validation	External platform validation	In-house cell function validation (GM-ExImmune)	Assemblers rely on external platforms for functional validation; GeneMedi enables comprehensive multimodal functional assessment of isolated cells.
Product Iteration Speed	Slow	Fast	Assemblers must wait for upstream innovations; GeneMedi can rapidly adapt ligands for new targets.
Batch-to-Batch Consistency	Inconsistent	Excellent	Assemblers are subject to upstream variability, making quality control challenging; GeneMedi maintains control over QC standards, ensuring batch consistency.
Supply Stability	Unstable	Stable	Assemblers face risks of batch-to-batch quality fluctuations and sudden supply disruptions ("bottleneck" risks); GeneMedi ensures autonomous control and stable supply, enabling scalable production capacity.
Customization Capability	Simple conjugation only	Deep customization: core + ligand + validation	Assemblers lack this capability; GeneMedi can tailor bead surface chemistry for specific cell types.

5.4 Market Insights: Why is Supply Chain Stability Crucial?

In the current biopharmaceutical market environment, supply chain stability has transcended mere commercial considerations to become the lifeline of scientific research and industrial translation.

(1) Consistency Requirements for IND/NDA Applications: For cell therapy enterprises, changes in the manufacturing process (including raw material changes) require extremely cumbersome validation. Selecting a supplier like GeneMedi, which possesses control over the entire industrial chain, means that the risk of raw material changes is minimized, providing solid compliance assurance for clinical applications.

(2) Stability in Responding to Sudden Demand: Whether addressing the surging demands of epidemiological research or the production scale-up following enterprise expansion, GeneMedi's proprietary production lines ensure the provision of sufficient and stable products within short lead times, preventing the loss of market windows due to "waiting for reagents."

6. Conclusion

Through an in-depth analysis of molecular binding mechanisms, nanophysical properties, and the supply chain system, this white paper presents validation data demonstrating the highly efficient isolation of target cells or depletion of unwanted cells by GeneMedi SOLIDEX™-ISOEx cell isolation nanobeads. It also demonstrates how underlying technological reconstruction systematically resolves the challenges faced by traditional magnetic bead sorting:

Reconstructing Chemical Precision: The anti-biotin system completely ends the issues of endogenous interference and receptor blockade caused by streptavidin. Through antibody optimization, it provides researchers with two types of anti-biotin nanobeads—interference-resistant and releasable—achieving zero-background capture of target cells.

Redefining Physical Compatibility: The 50 nm superparamagnetic nanobeads not only resolve the mechanical stress damage inflicted on cells by microscale magnetic beads but also achieve seamless integration with flow cytometry through their exceptional colloidal suspension properties and optical invisibility.

Fortifying the Industrial Foundation: Relying on the three core platforms—GM-ExBeads™, GM-LIBRA™, and GM-ExImmune —GeneMedi has broken the industry's reliance on the OEM assembly model. What we provide are not merely reagents, but a commitment to supply chain security based on fully independent intellectual property rights across the entire process. This complete controllability, from raw materials to finished products, provides solid compliance assurance for pharmaceutical companies' IND/NDA applications and mitigates the risk of supply disruptions caused by geopolitics or commercial mergers and acquisitions.

In summary, GeneMedi's nanobead technology is not just a product iteration, but a redefinition of cell sorting process standards. We are dedicated to providing more authentic biological data for basic research, supplying safer and more stable critical raw materials for clinical translation, and collaborating with our partners to advance life science research.