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FROM 5 WEEKS TO JUST 2 DAYS:

# Streamlining the yeast display antibody screening workflow with fluorescent-magnetic MagDots

## Key Takeaways:

- Yeast surface display antibody discovery workflows are complex, tedious, time-consuming, and expensive.
- MagDots provide dual magnetic-fluorescent properties in a single nanoparticle, enabling magnetically-separated cells to go directly into fluorescent analysis, streamlining the workflow.
- MagDots demonstrate highly efficient target cell recovery, reducing the number of selection rounds needed to obtain high purity target cell suspensions in YSD workflows.

Yeast surface display (YSD) has revolutionized antibody discovery by enabling efficient screening of large libraries while maintaining genotype-phenotype linkage. However, conventional YSD workflows are hindered by complexity, requiring multiple rounds of sequential magnetic labeling, magnetic-activated cell sorting (MACS) separation, fluorescent labeling, and fluorescence-activated cell sorting (FACS) sorting to achieve adequate antibody purity **(Figure 1)**. This multi-step approach raises the risk of losing rare antibodies, increases costs through additional reagents and equipment, and extends discovery timelines.

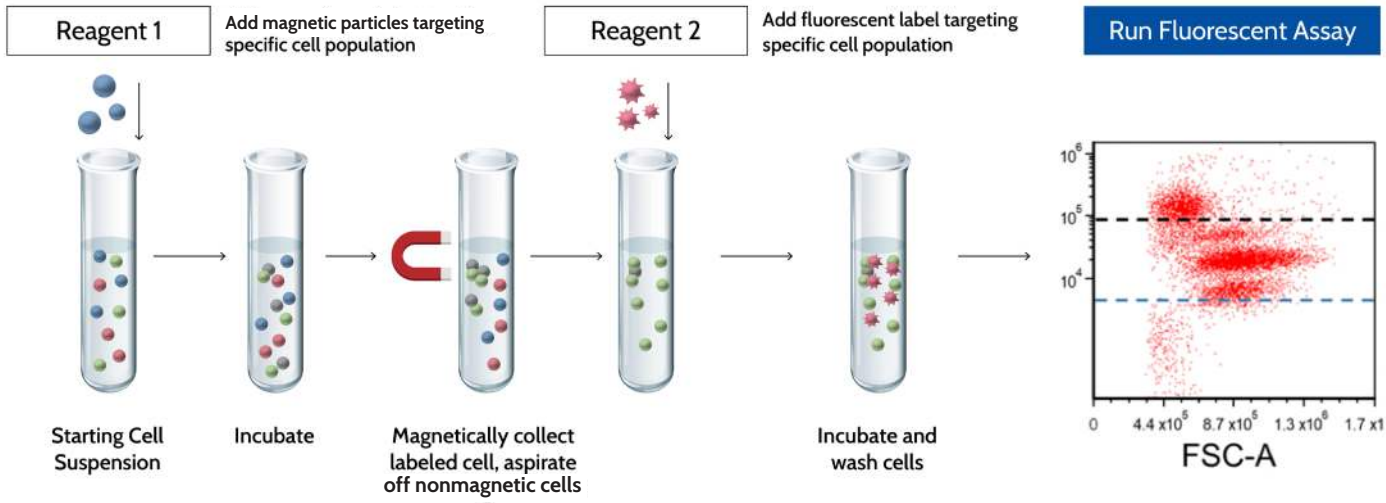


**Figure 1.** Typical YSD workflow using sequential magnetic cell separation and fluorescent labeling steps.



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www.corequantum.com
info@corequantum.com

Core Quantum Technologies' MagDots offer an attractive solution by combining magnetic and fluorescent properties in a single label. This integration allows researchers to magnetically separate antibodies from complex YSD libraries and immediately proceed to FACS sorting without additional labeling steps **(Figure 2)**. This streamlined approach delivers highly pure cell suspensions while reducing processing time, minimizing sample loss, and decreasing discovery costs.

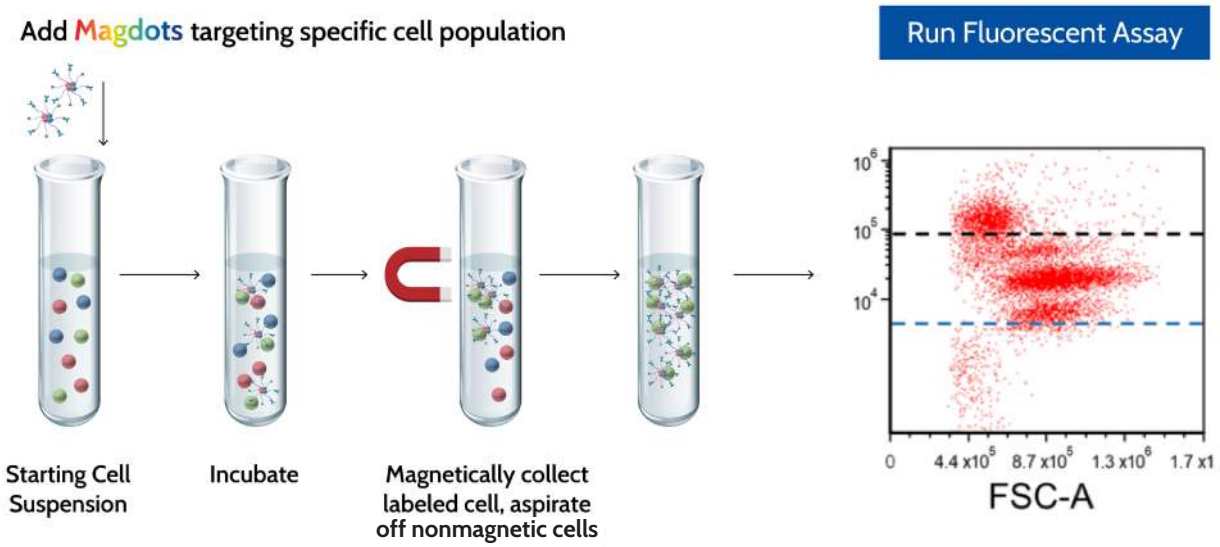


**Figure 2.** MagDot YSD workflow leveraging a single, combined magnetic-fluorescent labeling step.

**Here, we demonstrate how one researcher used MagDots to simplify the YSD workflow and reduce screening time from 5 weeks to just 2 days.**

## Case Study: Simplifying and accelerating YSD nanobody screening

A high throughput YSD library laboratory evaluated the use of MagDots - nanoparticles comprised of both quantum dots and magnetic iron oxide particles - to simplify the YSD nanobody screening workflow in his laboratory.[1] Using MagDots, targeted cells are magnetically enriched (or depleted) and immediately analyzed using the integrated fluorescent quantum dots in a single step.

This proof-of-concept study utilized a yeast display anti-ALFA nanobody screening library to test the MagDot workflow efficiency. A MagDot (MagDot610 anti-biotin) was used to label a biotinylated ALFA-tagged fluorescent protein (mEos3.1) bound to yeast cells displaying anti-ALFA nanobody **(Figure 3)**.

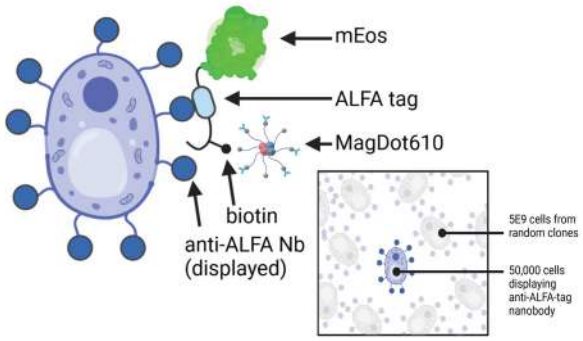


**Figure 3.** Illustration of the binding scheme used in the study. A MagDot (MagDot610 anti-biotin) binds to biotinylated ALFA-tagged fluorescent protein (mEos). A yeast strain expressing anti-ALFA nanobody (positive control) was mixed with yeast cells from random clones to create a complex library.

MagDot-labeled yeast cells were magnetically separated from unbound yeast cells (those without anti-ALFA nanobodies) using a CoreMag2T open magnetic system. Recovered yeast cells were first stained with propidium to label dead cells then immediately added to FACS for sorting and analysis, bypassing the need for a separate fluorescence labeling step.

Flow cytometry analysis showed that in a single magnetic separation step using the CoreMag2T magnet, yeast displaying an anti-ALFA nanobody were enriched from a level of 1% in the original yeast library suspension to a level of 70% in the magnetic fraction.

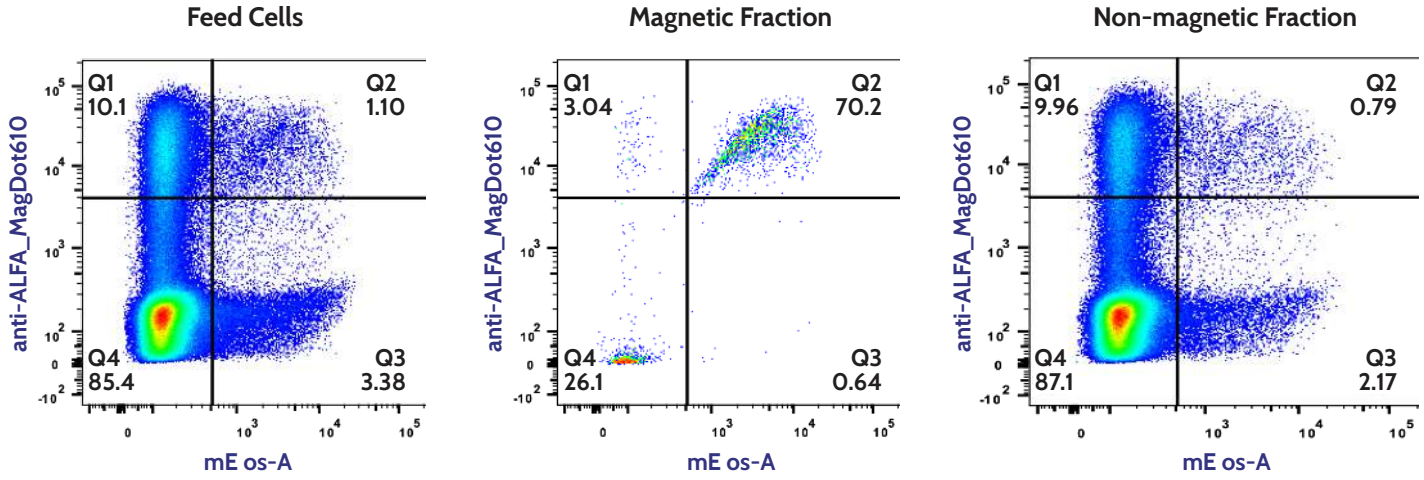


**Figure 4.** Flow cytometry analysis of 1% spiked ALFA-Nb displaying cells. Feed cells, magnetic fraction, and non-magnetic fraction are shown.

A second test was conducted to assess sensitivity and purity of magnetically isolated cells. A positive control anti-ALFA nanobody strain was seeded into a background of negative yeast cells at a 0.001% concentration. Positive-control cells were again magnetically enriched and immediately sorted by FACS; live cells were recovered and sequenced to screen for the clones of interest. NGS revealed that the positive control strain was the top hit recovered and present at a level 3X that of the next most-prevalent clone, evidence of highly efficient target recovery. With a high level of cell separation efficiency, MagDots offer the potential for reducing the number of selection rounds needed to obtain high purity target cell suspensions in YSD workflows.

This study successfully demonstrated the potential for MagDots to simplify and accelerate complex YSD nanobody screening workflows. MagDots eliminated the need for a separate fluorescence labeling step and enabled direct fluorescent analysis of magnetically-captured cells, improving laboratory workflow efficiency and reducing reagent costs. For this application, MagDots enabled the high throughput YSD library laboratory to save a significant amount of time, reducing a 5-week nanobody library screening process to only 2 days.

## MagDots: Multiple configurations to streamline laboratory workflows

By combining magnetic and fluorescent properties in a single nanoparticle, MagDots are a 2-in-1 laboratory powerhouse, reducing hands-on sample manipulation and instrument time, and simplifying workflows. MagDots are available in various combinations of fluorescent nanocrystals (spanning the emission spectrum) and modifications (ex. PEG, antibodies, biotin, streptavidin, etc.) and can be customized for use in any application. Additional benefits of MagDots include a unique spectral signature, high signal intensity, resistance to photobleaching, and an improved shelf-life stability compared to traditional fluorescent dyes. Further, MagDots are easily conjugated to any protein or antibody of interest to accelerate research and discovery.

Are you ready to discover how MagDots can streamline your laboratory workflows? **Contact us** to discuss solutions for your specific application.

# Reference

1. Whitepaper: **Yeast Surface Display Antibody Screening using MagDot Anti-Biotin**. Core Quantum Technologies.