High-throughput phage display screening

**KEY FEATURES**

- Enables higher throughput while freeing up manual labor and increasing the walk-away time
- Provides consistent, objective colony picking instead of subjective, manual picking
- Accommodates a broad range of different applications, such as fluorescence screening and liquid handling
- Tracks data electronically, allowing for well-documented data control

**Screen 3000 clones per hour with automated colony picking**

A typical phage library contains about $10^9$–$10^{11}$ variants individually expressed in *E. coli*. Due to this large number of clones, searching for the right candidate phage requires a huge amount of effort. The process of picking manually poses a substantial bottleneck because it is subjective, laborious, and time consuming.

The automated QPix™ 400 Series Microbial Colony Pickers can significantly reduce the bottleneck with its ability to pick up to 3,000 clones per hour, increasing speed, throughput, and walk-away time.

**Significance of phage display**

Phage display was initially described over 30 years ago, and the concept was further developed and improved. The development of phage display revolutionized antibody drug discovery. The method is often used to discover and isolate highly specific therapeutic antibodies used in anti-cancer or anti-inflammatory therapeutics. Today, many other selection techniques exist based on this concept, including mRNA display and yeast display.

**How does phage display work?**

In phage display, individuals from a library of billions of antibody variants are uniquely expressed on the outside a phage, while the genetic material encoding each variant resides on the inside. The phage library is infected into *E. coli*, creating a diverse pool of phage-containing cells. The presence of both the amino acid sequence and the DNA encoding it within the same virus particle creates a physical bridge, allowing for rapid selection based on binding affinity to a given target molecule by an *in vitro* selection process called panning (Figure 1), which consists of 4 steps:

- **Bind**—Displayed peptide from phage library binds to an immobilized target protein
- **Wash**—Wash non-binding phage
- **Elute**—Collect high-affinity-bound phage
- **Amplify**—Eluted phage pool is re-infected into *E. coli*, constituting an enriched mixture
Target identification and library generation
(Infect phage into E. coli)

Bind

Amplify

Panning 3-5 rounds

Wash

Elute

Reinfection of E. coli

Re-infect phage library into E. coli

High-throughput screening

Select colonies for analysis

Automated plating and picking

Characterizing binding affinity and cross reactivity

Converging consensus sequences are typically identified that bind to target molecule

After 3-5 panning rounds, eluted phage pool is infected into bacteria and plated. Phage-forming colonies are grown and characterized.

Phage display libraries contains billions of variants uniquely expressed in individual colonies of E. coli. For clones to be characterized, they must be picked following an iterative selection process. Manual picking of clones can be a laborious and time-consuming process, which creates a significant bottleneck.

### Microbial colony pickers
- Specialize in picking microbes such as E. coli
- Avoid cross-contamination with organism-specific pins
- Broad applications span synthetic biology, metagenomics, biofuels, blue/white colony screening, etc.

The QPix 400 Series Microbial Colony Pickers allow automated picking up to 3000 clones per hour, significantly increasing speed, throughput and walk-away time. Additionally, clones can be screened in white light or fluorescence, and the system can select clones based on user-defined parameters such as compactness, axis ratio, size, proximity, and fluorescence level (Figure 2).

In addition, many other tasks in phage display can be automated, including plating, screening, picking, replicating, gridding, and re-arraying (Figure 3).

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