Understanding Target Proteins in Various Selections

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Abstract

mRNA Display, a selection technique invented by Professor Richard Roberts, develops peptide binders that target specific proteins. In mRNA display, peptides are linked to their encoding genetic information, enabling the in vitro selection of specific binders.

Our lab has begun to identify specific factors that effective target proteins have in common, in order to see if there is a way to prescreen targets and identify if they will be optimal for mRNA selection. We also learned about the diagnostic and therapeutic applications of mRNA display.

Application of mRNA Display

Autoimmune Diseases

Autoimmune diseases often require malfunctioning antibodies (**autoantibodies**) to recognize your own healthy proteins and tissues as foreign substances instead of invading pathogens. mRNA display could develop specific peptides that bind to autoantibodies.

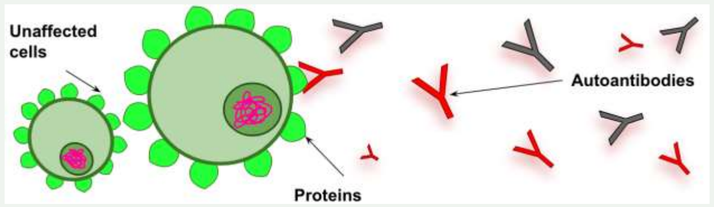


Figure 1: Autoantibodies attacking healthy cells in the body.

Diagnosis: Currently, these diseases are extremely difficult to diagnose, as they can only suggest the presence, but cannot confirm or identify the specific disease.

Using mRNA display as a diagnostic tool:

- Identify the specific autoantibody using a specific binding peptide and detect its presence
- Quantify the presence of autoantibodies to diagnose progression or severity of disease

Treatment: By using mRNA display, the selected binders which specifically bind to the autoantibodies could:

- Bind to the autoantibodies and inhibit their function
  - Slows the progression and spread of the disease

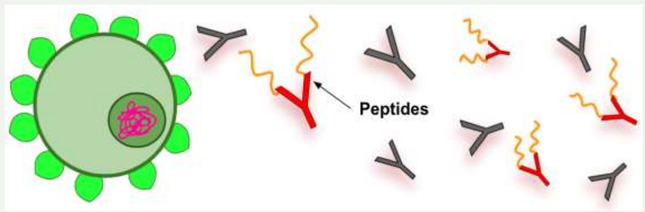


Figure 2: Peptides selected through mRNA display attaching to the autoantibodies, inhibiting their function.

mRNA Display Methodology

Why mRNA Display?

1. Covalent and highly stable
2. Entirely in vitro
3. Large upper limit for library
4. Aids in identifying proteins

mRNA Display Cycle:

1. PCR
2. Transcription
3, Ligation
4. Translation
5. Selection
6. PCR
7. Re-selection

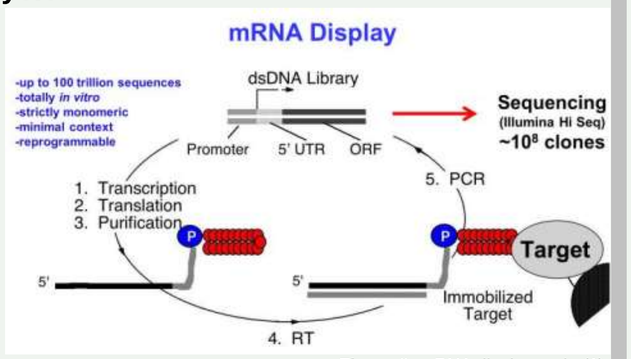
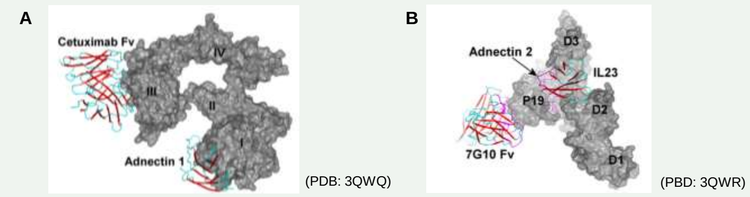


Figure 3: mRNA display cycle (1)
Image from USC Roberts Research Lab

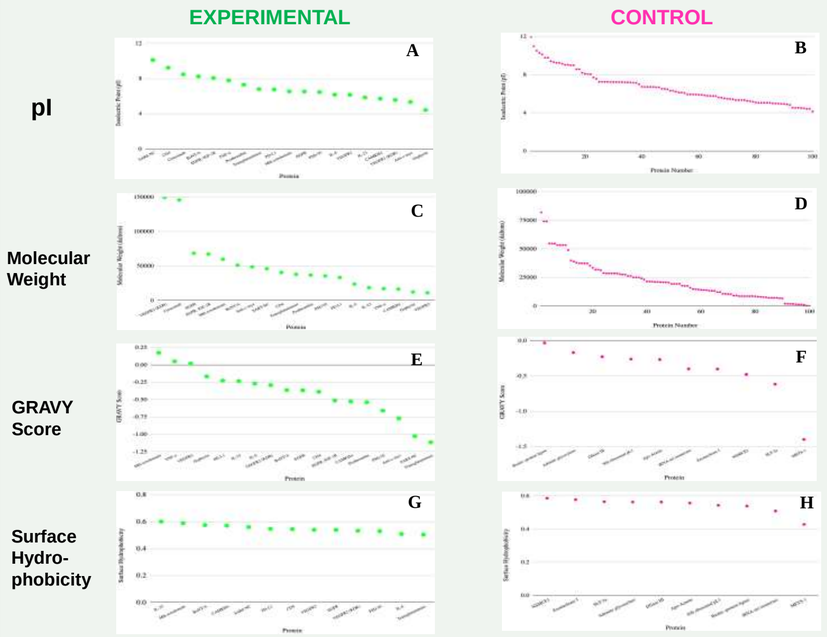
Binders Developed by mRNA Display

Figure 4: (A) EGFR is shown as surface representation (gray) with Fibronectin binder, (Adnectin 1, shown as cartoon representation). **(B)** IL-23 is shown as surface representation (gray) with a Fibronectin binder (Adnectin 2 in cartoon representation). [2] Both Adnectins have a different binding site from its antibody, Cetuximab and 7G10.



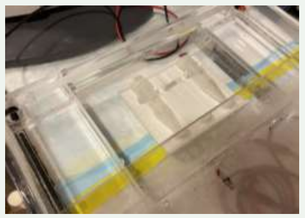
Protein and Peptide Binder Analysis

Figure 5 (A-H): Experimental (green) and Control (pink) Protein Analysis of Isoelectric Point, Molecular Weight, GRAVY score and Surface Hydrophobicity. [3]



How This Relates to Your STEM Coursework

mRNA Display is a very important tool for understanding more about protein-peptide binding complexes. Protein-peptide complexes are relevant in biology and chemistry in order to understand the interaction between these important molecules.

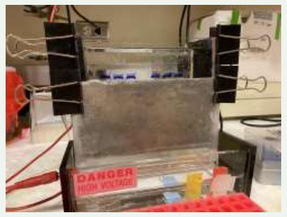


Learning about mRNA display and other selection techniques used in the will be extremely useful and applicable in my science and medical courses next year and in the future!

Advice To Future SHINE Students

To future SHINE students:

- Allow yourself to struggle
- Reach out for help,
- Don't doubt yourself; You earned your spot here!
- Make the most of it and enjoy your time at SHINE!!



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