Genomic Antibody Technology™
The Best Tool for Antibody Research

GAT™ in a Nutshell

Antibodies are widely used today for diagnostic and therapeutic research of proteins and associated diseases. The race for publications in the academic realm and pursuit of new drugs in the pharmaceutical industry produce a compelling necessity for efficient products. One major challenge of antibody research is the poor quality and design of antibody reagents. The process of designing antigens in order to generate and characterize antibodies is complex and prone to many mistakes – it is simply impossible for the average researcher to catch every flaw throughout the complicated process.

Strategic Diagnostics, Inc. (SDIX) recently developed Genomic Antibody Technology™ (GAT™), a unique, effective way to create custom antibodies (Figure 1). This technique is superior to its traditional counterparts because it relies on the idea of genetic immunization. Instead of typical protein immunization to generate antibodies, GAT™ applies a proprietary bioinformatics approach to create genetic antigens, since DNA is easier to generate than proteins. After encoding antigens in DNA expression plasmids, the transformational plasmid is delivered to an animal, which makes the antigen *in vivo*. The effectiveness of the process of immunization, as well as the precision of SDIX's bioinformatics antigen design, make GAT™ one of the most efficient custom antibody tools currently available on the market.

Challenges of Traditional Antibody Development Methods

Traditional methods of custom antibody production include protein purification, recombinant protein production and purification, and peptide synthesis and conjugation. In practical terms, all of these methods share the qualities of being time consuming, low-yielding, and inaccurate. Protein purification involves purifying proteins from a known source. Not only is the protein usually found in small concentrations, but there also lies a risk of denaturing the proteins in the purification process, producing imprecise results. The process of recombinant protein production and purification, (i.e. when the DNA sequence is known and is used to express proteins in another bacterium or animal) holds similar disadvantages as protein purification (low yield and inaccurate results). The third traditional method of antibody production involves finding the most immunogenic region of a protein and synthesizing

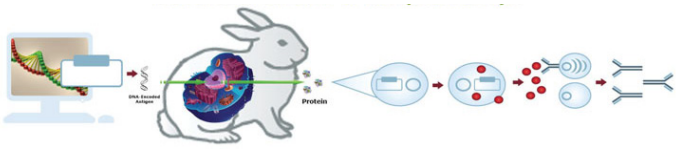

Figure 1: SDIX's new Genomic Antibody Technology™

peptides that will be conjugated to carrier proteins for reacting in immunization. Drawbacks to this process include inaccurate software to find peptide regions, the expense of synthesizing some peptides, and the expertise needed for conjugation. It is clear that creating custom antibodies in a researcher's lab can pose many problems during the process.

These three traditional methods of antibody development are used to produce synthetic peptides. However, such peptides cannot fold properly, often impeding their function. This limitation is due to a short peptide sequence, which also prevents the presence of epitopes for the same immunogen and the ability to recognize a diverse array of epitopes. Larger peptide sequences possess these traits and form more stable structures, but their production is not feasible under traditional methods of antibody manufacturing. The new GAT™ method of producing antibodies eliminates all of these hurdles of past antibody development (See Figure 2 for additional Advantages of GAT™).

Important Considerations of GAT™ to Optimize Genetic Immunizations

GAT™ operates by a similar mechanism to create both polyclonal and monoclonal antibodies. After designing an antigen, DNA encoding this antigen is transformed in a bacterial plasmid. When producing polyclonal antibodies, an animal (e.g. rabbit) is immunized with the plasmids and the protein antiserum is produced. The plasmids are also used to express the specific proteins in *E. coli* cells in order to produce an affinity column for the protein antiserum. Passing the antiserum through the column manufactures affinity-purified polyclonal antibodies. Similarly, in monoclonal antibody production, an immunized animal produces hybridoma cells, which are screened using recombinant protein from the original DNA plasmids in order to produce purified monoclonal immunoglobulins.

Advantages of GAT™

- *In vivo* production of antibodies – avoids protein production and purification costs
- Antigens with native epitopes – since antigens are produced inside the cell, they are more likely to possess native epitopes
- Naturally pure product – so-called "chaperone" molecules inside the cell assist proteins that cannot fold on their own and get rid of unfolded protein (Figure 2)
- Accommodates larger antigens – increases functionality and prevalance of antigens
- Accurate antigen design – less burden and chance for mistakes for the researcher

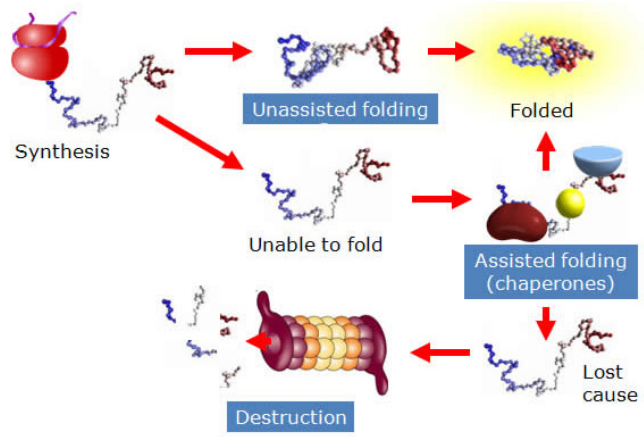

Figure 2: The role of chaperones in protein folding

There are many factors involved in genetic immunization that can easily be overlooked by a researcher. GAT™ takes these factors into consideration to provide the most successful results when utilizing custom antibodies.

One such factor includes antigen design. GAT™ uses an efficient, cost-effective method to design codon optimized synthetic genes. SDIX's proprietary bioinformatics tool addresses the many restrictions involved when selecting an antigen (Figure 3). Long antigens can fold, produce a large response and are easy to make, but have the disadvantages of being expensive, more difficult to express, and potentially cross-reactive with closely related proteins. GAT™ uses a 100-a.a. or more design to optimally balance the aforementioned effects. In an experiment to test whether protein fragments using GAT™ could still fold into native-like structures, Alpha-1 Antitrypsin (AAT) a monomeric, glycosylated serum protein with no restricted regions was used to systematically select ten 100-a.a. sequences across the protein. Interestingly, all of the antibodies produced were successful in ELISA despite non-compact regions of the target being used, which proved that the designs worked equally well and were able to recognize native proteins. Only GAT™ gives the researcher this level of quality and successful results that can often not be matched by a researcher's efforts alone. In addition, a commonly forgotten feature to include when designing an antibody is the ability for the antibody to get outside of the cell in order to react with immune cells. GAT™ takes this property into account and creates antigens that are both functional and abundant. GAT™'s antigen design also optimizes the scaffold to which the antigen will bind, thereby enhancing translation, folding, solubility, and antigen presentation. The adjuvants, expression plasmids to aid antigen function, are included in

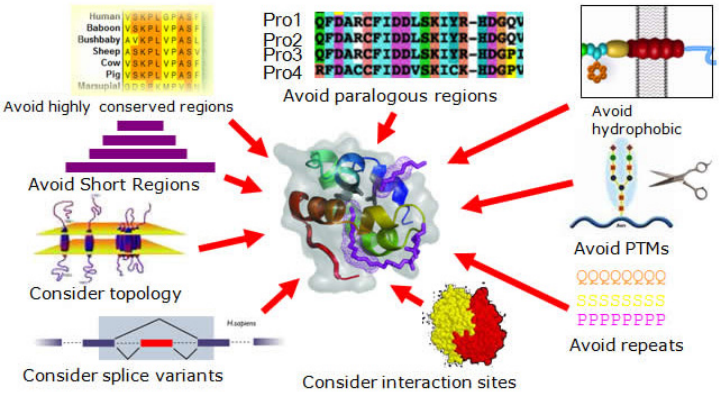

Figure 3: Various restrictions overcome by GAT™ when designing an antigen using SDIX's propriety bioinformatics tool

GAT™'s genetic code to substantially enhance the immune response. All of these aspects, as well as the timing of immunization and SDIX's proprietary recombinant protein folding process for testing and purification, compose details of the immunization process that must be accurate in order to have successful results. Luckily, SDIX's revolutionary technology will eliminate the chances for error from the researcher and ensure more efficient, accurate research.

Conclusion

GAT™ is an innovative and successful way to create polyclonal and monoclonal antibodies for today's scientific research. The hassle and frustration involved with this detailed process can often deter the progress of research. With GAT™, the mistakes and time-consuming procedures are diminished, providing a faster track to advancement and discovery. GAT™'s accuracy is also notable – upon random analysis, GAT™ products have shown remarkable success in a variety of applications including Western Blot, immunohistochemistry, immuno-fluorescence, flow cytometry, and ELISA. SDIX's efficient GAT™ method of producing custom antibodies can be applied to any field of research – GAT™ should be every researcher's primary partner in conducting effective antibody-based assay design.

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