

A time to imagine and dare

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As the number of drug-able targets are limited to protein products of 30,000 odd human genes, many traditional pharmaceutical industries with expertise in discovery of broad spectrum inhibitors to these targets are looking to exploit modern biotechnology for targeted therapies such as peptides and therapeutic monoclonal antibodies. Instead of building expertise from scratch, many pharma majors have started to become biopharma by acquiring small biotech companies with exciting and innovative therapeutic ideas, collaborate with mid-size biotech companies with novel platform technologies and/or merge with biotech companies which have rich pipeline of products at various stages of development.

Unlike major global pharma, Indian pharma industries, transformation into biopharma is through organic growth and mainly by developing similar biologics at much cheaper cost. From the point of discovery of novel molecules there are only few players who endeavor into high-risk long term projects in India. However, in the past few years with rich talent pool of chemist, Indian pharma, biopharma companies and CROs have entered into mode of discovery and development of novel molecules using chemical compound libraries with intention to collaborate with multinational companies for global development.

When it comes to biologics, replacement therapeutic drugs such as insulin, growth hormones and enzymes were the first to

enter market, however, in the past decade more than 20 therapeutic monoclonal antibodies have been approved for marketing and there are more than 400 under clinical trials. The unprecedented success of blockbuster drugs such as Avastin, Herceptin, Rituxan and Humira has catalyzed the interest of major biopharmas to include in their development pipeline, monoclonal antibodies as well. The success of antibody therapy is attributed to its unique properties such as specificity, high affinity, long half-life and safety. Unlike replacement therapy drugs which were discovered by cloning and expressing the genes for its product and developed as drugs, antibodies were initially developed either by conventional polyclonal and monoclonal approaches and later discovered to be used for therapeutic use. The draw back in developing and discovering therapeutic antibodies using the conventional approach is that they are of animal origin (mouse hybridomas) which leads to problems associated with immunogenicity in humans. Recombinant antibody technologies have overcome the immunogenicity issues by converting the mouse hybridoma antibodies to chimeric or humanized antibody variants.

Similar to discovering chemicals by screening compound libraries, human antibodies are being discovered using combinatorial approaches such as phage display technology and later developed as drugs for therapy and diagnosis. In India, in addition to tapping the reagent vessels of chemist for source of drugs, there is scope and opportunities for scientist to make a paradigm shift to discover therapeutic drugs using state-of-the art display technologies such as phage and yeast display for antibodies and peptides.

Antibody and peptide display technologies unleash new opportunities for drug discovery for immunotherapy, as well for diagnosis. In addition, display technologies can also provide opportunities to discover and develop affinity ligands for purification of biologics that are produced using fermentation-based technologies and for removal of enzymes used during upstream and downstream processing of biologics.

There are plenty of opportunities for Indian biopharma to exploit the display technologies with the help of their experienced medicinal chemists; to build antibodies and peptide libraries and screen for drugs, affinity ligands and diagnostic reagents.