BIOTECH USA

CONFEREES DISCUSS BIOREACTORS, SEPARATIONS

SAN FRANCISCO—Few events give as great an appreciation of the biotech universe's diversity as a general industry conference, and Biotech USA, held here last November, was no exception. The three-day event attracted nearly 1,700 scientists, engineers, managers, equipment manufacturers, patent lawyers, and financial consultants. It included not only technical and business seminars, but also a trade show, a seminar on U.S.-Japan relations, and a spectacular computer-generated molecular modeling video ("Terms of Entrapment" by Arthur Olson of the Scripps Clinic, La Jolla, CA).

About 100 people were on hand for a session on novel high precision separations. Chairman John Smart of Hoffmann-La Roche (Nutley, NJ) described a scheme for purifying interleukin-2 (IL-2) by using its own receptor. His group uses immobilized IL-2 receptors—produced by genetically engineered Chinese hamster ovary (CHO) cells and attached to a polymeric support within a column—for separating IL-2 from cell culture fluids. This approach, Smart pointed out, has the advantage (over conventional immunoaffinity techniques) of capturing almost exclusively the monomeric, active form of IL-2, with no detectable endotoxin associated with the purified compound. It will be especially valuable for purifying molecules that are difficult to re-fold: receptors have epitopes that recognize correctly-folded molecules.

A full day's discussion of bioreactor technology highlighted the pros and cons of high-density, continuous culture designs versus more traditional batch-mode suspension cultures. Chairman Malcolm Rhodes of Celltech (Slough, U.K.) noted that his company has successfully grown a wide range of cell types in large (thousands of liters) stirred tanks and airlift reactors. Such reactors support the growth of attachment-dependent cells on microcarriers, he said. Rhodes pointed out that economies of scale are vital for the commercial success of lower-value mammalian cell products—those that cannot command exorbitant prices. And producing such compounds in large batches reduces two major components of production cost: labor and quality control testing.

Other speakers detailed the advantages—in productivity and product quality—of growing cells in dense, compact, immobilized colonies. Setec's (Livermore, CA) James Robinson discussed how his company's Tricentric™ hollow fiber bioreactor encourages cells to channel their energy into producing desired product instead of into cell growth. John Vournakis presented an overview of Verax's (Lebanon, NH) fluidized bed bioreactor, in which native bovine type I collagen forms novel microporous microcarriers. According to Vournakis, this system produces undegraded, properly glycosylated recombinant proteins and monoclonal antibodies.

Rounding out the bioreactor program, Kim Nelson of United Engineers & Constructors (division of Stearns Catalytic, Philadelphia, PA) stressed that planners should coordinate the design of building support systems (purified water, clean-in-place facilities, and sterile piping) with unit bioreactor and harvesting processes. **—Pamela Knight**

BIOTECH USA

BIOBLOOD: BUSINESS AND SCIENCE

SAN FRANCISCO—The nation's blood supply has never had to satisfy as many demands as it does today. Not only has the need for transfusable blood increased annually—currently about 16 million units—but that blood also has to be safe to use—a profound scientific challenge. Not surprisingly, this multi-billion-dollar segment of the healthcare industry also affords significant commercial opportunities. And a series of sessions on the biotechnology of blood at Biotech USA here in November made it clear it is possible to solve blood-banking problems by providing new means to increase the safety and utility of donated blood or by designing and building its components.

Jack Goldstein's (New York Blood Center, New York, NY) approach for providing blood's cellular components is to convert any red cells to universal donors by enzymatically removing or altering their "typing" antigens. Goldstein has already transformed blood group antigen B erythrocytes into universal donors by treating the terminal sugar groups with exoglycosidase. These cells survive, function normally, and have produced no untoward effects in human volunteer recipients. Goldstein's group continues to produce typeless cells from all A-cell donors via exo- and endoglycosidases. This technology lends itself to large-scale commercial production based on genetically engineered converting enzymes. Implementing this strategy could solve problems of supply, inventory management, outdating, and safety—as well as cut overall costs for human red cells.

If quantities of hemoglobin are the goal, then it should be possible to bioengineer *in vitro* production systems. But not yet. According to Joseph A. Walder (Integrated DNA Technologies, Iowa City, IA), there are 450,000 kilograms of hemoglobin in 10 million units of whole blood. And there are *no* recombinant DNA-based production systems today—regardless of the product—that come anywhere near to generating such vast quantities. Those amounts might be better produced by transgenic animals than by the usual bacterial or yeast fermentation methods, he suggested.

There's more than one way to provide tissues with oxygen—including C. Anthony Hunt's (University of California, San Francisco, UCSF) method of using hemoglobin-containing liposomes as synthetic red cells. Alternatively, genetically engineered stem cell-stimulating proteins (such as erythropoietin) can increase the numbers of available red cells. It may even be possible to produce chemicals without biological equivalents—such as perfluorocarbon emulsions—to act as oxygenating solutions (an approach taken by HemaGen Associates, St. Louis, MO) or to modify hemoglobin from outdated blood.

Biotechnology's potential impact on the blood market doesn't stop there. In therapeutics, clotting factors are a ripe opportunity, as well. UCSF scientists are producing platelets *in vitro*, and several groups are in hot pursuit of factors VII, IX, and X, as well. In diagnostics, monoclonal antibodies and genetically engineered antigens have yet to come into their own as screening assays for donated blood. While Cetus' (Emeryville, CA) polymerase chain reaction (PCR) technology has already increased the sensitivity of tests for the human immunodeficiency virus (HIV), Chiron's (Emeryville, CA) recent success in cloning and expressing non-A, non-B hepatitis virus antigen should lead to a new diagnostic test—providing blood banks with the tools to effectively detect this dangerous contaminating virus.**—Thelma H. Carter**