IMMUNOLOGY

THIRD GENERATION HYBRID VACCINES

HOUSTON—"An ideal immunogen is a polymer of multiple antigenic determinants (epitopes) assembled into a high molecular weight complex that has the maximum number of its epitopes properly exposed." With this in mind, Pablo Valenzuela of Chiron Corp. (Emeryville, CA) described very recent experiments that seek to exploit the hepatitis B surface antigen (HBsAg) as a matrix for antigen presentation.

Valenzuela and coworkers developed a model system to test this concept by taking a segment of the gene coding for the herpes simplex-1 (HSV-1) gD protein (an immunogenic surface component of the virus) and inserting it into the pre-surface protein segment of the HBsAg gene. The inserted fragment codes for 300 amino acids of the gD protein, but lacks the region encoding the signal sequence at the N-terminus and the hydrophobic membrane-anchor region in the C-terminus domain. The hybrid gene was flanked by sequences required for expression and introduced into a plasmid that could be selected in yeast. Extracts were shown to contain HBsAg and HSV-1 gD epitopes in the same molecule.

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Left: **The hepatitis B virus.** *Right:* **Hepatitis B surface antigen particle. The highly immunogenic surface particle is overproduced in patients infected with virus, mostly as spheres approximately 22 nm in diameter.**

Although Valenzuela has not yet examined this material by electron microscopy, evidence indicates that the hybrid antigen is being assembled into particles. The hybrid antigen behaves as a high molecular weight material when examined by gel filtration, and has a bouyant density in CsCl gradients similar to the native particle.

Whether this hybrid is an improved vaccine remains to be established. However, Valenzuela believes the concept is sound and can be applied to the presentation of antigenic sites from natural cloned genes as well as synthetic genes derived from work with peptides. **—Harvey Bialy**

MEETING REPORT

BUTTERFLY CELLS MAKE HUMAN INTERFERON

HOUSTON—The expression system of choice for the production of agriculturally and medically useful proteins may turn out to be an insect virus. So implied Max Summers of Texas A&M University (College Station), at the Interface High Tech Route to Viral Vaccines meeting. Summers has exploited baculoviruses to develop an expression system that has already produced human fibroblast interferon in an active, glycosylated, and secreted form at 5 mg per liter of culture supernatant.

Baculoviruses are insect pathogens that produce large quantities of a protein called polyhedrin. The gene for polyhedrin is expressed in cultured insect cells to levels that represent about 70 percent of total cell protein (1 gm/l), and is nonessential for virus replication.

Using rDNA techniques, Summers cloned the gene for polyhedrin and modified it to retain only its promoter region. In his initial studies, the gene for human fibroblast interferon was fused to the promoter and the hybrid inserted into the baculovirus by substitution for the natural polyhedrin gene. "The fusion of any foreign gene with the polyhedrin promoter should result in the high level production of that gene's product," says Summers, who reported that he has successfully tested this supposition with other animal and prokaryotic genes.

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A thin section of a nuclear polyhedrosis virus inclusion body from infected cells of the lepidopteran insect *Trichoplusia ni*. The electron-dense rod-shaped nucleocapsids are embedded in a protein crystal that is primarily composed of polyhedrin.

Summers also pointed out that this system, or variations of it, has potential for the development of viral pesticides, since many baculoviruses are highly infectious for insect pests of agricultural importance.

—Harvey Bialy