Breaking the productivity barriers of baculovirus technologies
For decades, the vaccines have been produced in cell cultures or fertile eggs. The huge demand of vaccines and the urgent need to reduce the vaccine production costs, to make them accessible to the whole human population and farm animals, made crucial the development of new production processes.

Four main production platforms are used for the production of the next generation vaccines (bacteria, yeast, mammalian or insect cells). ALGENEX has developed the “fifth production element” to obtain the subunit vaccines, the CrisBio™ technology platform.

ALGENEX has developed and patented this innovative technology platform, which take advantage of a multicellular living organism, the Lepidoptera Trichoplusia ni (T. ni). This highly efficient technology combines T. ni chrysalises with the proprietary improved baculovirus vectors TopBac® for the production of recombinant subunit vaccines. The scientific team at ALGENEX has optimized and industrialized CrisBio™ technology, reaching production yields that exceed 20 times the productivity of insect cells cultured in bioreactors. CrisBio™ technology is currently used by ALGENEX to produce several virus-like particle (VLP) vaccines in collaboration with international veterinary companies.
CrisBio™ advantages

1.- **Fast development times:** less than two months are required to scale-up the production of any recombinant protein (extremely important in pandemic situations). This scaling-up is linear and depends only on the virus vector inoculum quantities and the number of chrysalises infected and incubated at the same conditions (high production consistence among infected pupae). The virus inoculum can be produced in cells or pupae, being the last one more productive (up to \(10^9\) pfu/pupa).

2.- **Productivity and enablement:** cell diversity increases productivity. The pupa tissue heterogeneity, not possible in cell cultures, provides alternate cellular environments for high level expression of even the most difficult-to-produce proteins.

3.- **Semi-automated processes:** Most companies using insects as living biofactories employ insect larvae instead of pupae for protein production. Movement and soft bodies difficult its robotic manipulation such as baculovirus vector inoculation. CrisBio™ overcomes this difficulty because the pupae are inert and can be stacked and stored at 4°C for at least a week before injected with a baculovirus by a specifically designed robot. The storage room needed to incubate the infected pupae is much more smaller than that required for infected larvae. Healthy or infected pupae can be easily transported to vaccine production factories by land or air without any deleterious effect in productivity.

4.- **TopBac® and CrisBio™ synergism:** ALGENEX is proprietary of the patented improved baculovirus expression cassette TopBac®. Baculoviruses modified by this genetic construct increase their productivity up to 6 times in insect pupae. CrisBio™ is the only technology which combines the best baculovirus expression vectors with a living insect. It allows to reach unprecedented productivities, up to gram quantities of recombinant protein per liter of insect extract.
Upstream and downstream processes are extremely simple and can be performed by conventional means by trained personnel. There are no relevant differences in downstream to obtain a purified protein in comparison to cell culture procedures.
In some aspects, the production platform CrisBio™ is similar to the egg-based production, but differs in its versatility. Eggs can be used only for viruses that replicate efficiently in them. In addition, egg supply for vaccine production is limited and also expensive considering the productivity per unit. Egg-derived vaccines frequently contain elements that may cause allergic reactions and eggs may support the replication of unapparent pathogens that could infect the vaccine receivers. In contrast, there are not reports either of allergic reactions produced by T. ni-derived products or about pathogens replicating in this Lepidoptera that may affect mammals. Frequently, a single vaccine dose is obtained from a single egg (e.g. influenza vaccine). In contrast, the T. ni pupae may produce any recombinant subunit vaccine and dozens of vaccine doses can be produced by a single baculovirus infected pupa. The operating procedure of healthy egg and pupa transfer to the vaccine production laboratory is almost the same, but with the difference of space required in such transport and the lability of the material. Insect pupae can be delivered infected and frozen to the vaccine production factory, ready to extract the vaccine antigen.
Our business model

- **Feasibility studies** including optimization of your recombinant protein production

- **Co-development agreements** of protein based products, specially in the fields of diagnostic and vaccines (glycoproteins, VLPs, etc..) and

- **Supply Agreements** bringing the insect biomass (pupae) or clarified extracts to your manufacturing site as raw materials for your Vaccines.