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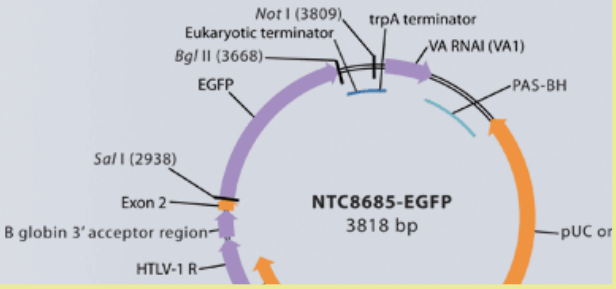



# NTC Spring Newsletter May 2012

## Eurogentec and NTC partner for clinical and commercial-grade plasmid DNA production.

Eurogentec has recently licensed NTC's high yield fermentation process for the GMP production of clinical and commercial plasmid DNA. The combination of NTC's HyperGRO upstream fermentation process with Eurogentec's downstream plasmid purification technology provides the best possible clinical and commercial-grade nucleic acids for gene therapy and DNA vaccination. "The combination of the two technologies provides a very high yield of production together with the lowest cost of goods, all without compromising quality" said Ingrid Dheur, Director of Eurogentec's Biologics division. The combined high yielding fermentation and purification technologies have already been used to produce a plasmid designed by NTC for a European biotech company that will soon perform clinical trials in Europe. This plasmid was made in one of NTC's antibiotic free plasmid backbones.

The advent of nucleic acids based drugs necessitates a scalable plasmid DNA production process, according to Clague Hodgson, President of Nature Technology Corporation. "Eurogentec has established itself as a leader in Europe. The FDA approved CMO has manufactured over 400 batches of highly-purified clinical-grade biologics, including nucleic acids up to 100g in a single batch," he said, adding, "NTC is pleased to be able to offer this service worldwide in partnership with this excellent organization".

Pharmaceutical grade plasmid DNA is bacterial cells grown to high density using NTC's high yield HyperGRO fermentation process. Modern plasmids have been devised by NTC specifically for use in pharmaceutical products, combining regulatory compliance with improved performance at expressing antigens and therapeutic proteins in living cells and tissues.

Over 100 clinical trials have been conducted using nucleic acids-based drugs (Ref.: http://clinicaltrials.gov/ct2/results?term=plasmid+DNA) . The first human DNA vaccine is now in Phase III clinical trials (Vical, San Diego, CA), and many more vaccines and therapeutics are in the pipeline, necessitating industrial scale production to fill anticipated future use in humans and animals, according to Dheur.

# Coridon Coordinates with NTC and VGXI on Herpes Vaccine

Australia's Allied Healthcare Group (ASX: AHZ) announced an update on the progress of Coridon, its investment company founded by Professor Ian Frazer and working on developing the next generation of vaccines. Included in these activities, Cordon has entered into a license agreement with Nature Technology Corporation (NTC) and has contracted VGXI Inc in the US for production of clinical material for the Phase I study scheduled to begin later this year.

NTC has specifically designed safe, minimalised and antibiotic-free selection vectors, which offer superior expression of recombinant proteins in mammalian cells. These vectors have been designed to comply with US Food and Drug Administration (FDA) and European Medicines Agency (EMA) regulatory guidance. The use of this vector improves the overall benefit of the vaccine by driving the in vivo transcription and translation of the genetic material.

"Access to this technology will allow the Coridon vaccine to fully maximize its gene expression and therefore improve the performance of the vaccine" stated Allied Healthcare CEO Mr Lee Rodne "these are important steps forward to the initial Phase I study for Coridon which will provide validation of the Coridon technology".

Coridon's Herpes vaccine, which was recently announced to be 100% effective in protecting animals against Herpes Simplex Virus 2 infection, incorporates the NTC8485 antibiotic-free expression vector. The guidance from US and European regulatory bodies seeks to eliminate non-essential sequences and to avoid use of antibiotic resistance genes where feasible.

In addition to the vector technology, Coridon also receives access to use NTC's HyperGRO fermentation technology, which provides for high yield and cost effective DNA production. The manufacturing of the Herpes vaccine utilising the HyperGRO technology has now commenced with VXGI Inc.

The Phase I study for Coridon's herpes vaccine is scheduled to begin later this year.
Neil Finlayson, Coridon CEO said: "This is an important agreement for the company to be able to access this leading technology and cements the relationship we have built up with NTC dating back to late 2009."

Coridon is developing the next generation of vaccines for the prevention and treatment for a range of infectious diseases and cancers in humans. Coridon's DNA vaccine technologies differ from conventional vaccines in that they offer both preventative and therapeutic value.

# Immunomix Shines it's LAMP Technology on Allergy Therapy with NTC Vectors

Immunomic Therapeutics, Inc., ("ITI," Lancaster, PA) a privately-held biotechnology company with laboratories in Rockville, MD, announced that the U.S. Food and Drug Administration (FDA) has completed its review of the Investigational New Drug Application ("IND") filed for the allergy immunotherapy, JRC- LAMP-vax(TM). On April 12th, the FDA notified ITI that there will be no clinical hold and that ITI may now proceed with its clinical trial in June for JRC-LAMP-vax in Atlanta with subjects sensitive to Japanese Red Cedar pollen.

*Immunomic Therapeutics Receives IND Authorization for Phase I Study of JRC-LAMP-Vax Vaccine to Treat Japanese Red Cedar (Sugi) Allergy*

JRC-LAMP-Vax is a plasmid-based DNA vaccine, based on the NTC '8' series plasmid DNA backbone, which will be studied for the treatment of patients with rhino-conjunctivitis (runny nose) symptoms caused by allergic reaction to Japanese red cedar pollen. Almost 45% of the Japanese people are allergic to Japanese red cedar pollen. In North America, there is allergic rhinitis to mountain cedar pollen, which is 80% cross-reactive with Japanese red cedar pollen allergen. ITI intends to partner with a Japanese pharmaceutical company for studies in Japan and will seek FDA approval of the vaccine in the US.

ITI provided FDA with animal studies of JRC-LAMP-Vax, showing no alteration of the routine clinical pathology, body weight, food consumption, temperature, ophthalmology, dermal irritation or the histopathology of any tissue examined microscopically. Overall, JRC-LAMP-Vax caused no abnormal safety issues in biodistribution and toxicology studies in animals. This data was consistent with other reported animal and human studies of components of its vaccine.

Animal safety studies and human clinical studies have documented that LAMP DNA vaccine induces a protective antibody immune response consistent with a preferential MHC-II immune system presentation induced by the LAMP component. LAMP-based vaccines hold potential for the development of potent vaccines for treatment of allergies, infectious disease and cancer. Previous research has specifically indicated that LAMP in the DNA vaccine molecule induces IgG protective antibodies and greatly diminishes the production of the allergy antibody, IgE. This represents a shift of the immune response to the vaccine from Th2 to Th1, the underlying concept for classic allergy desensitization. This re-education of the immune system response is the basis of the medically accepted paradigm for treating allergy by conventional allergy immunotherapy.

Dr. William G. Hearl, CEO of Immunomic Therapeutics, Inc., stated, "The IND authorization is the result of the long-term commitment and support of ITI and the continuous efforts contributed by its researchers and regulatory team. It cannot be overstated what a significant accomplishment this is for our Company. The expeditious FDA review and approval of our Phase I study plan is a testament to a strong scientific foundation and well-planned regulatory strategy."

ITI has begun enrollment for the open label, Phase I, clinical study designed to establish the safety of the LAMP-vax platform and to provide important immune response data as it applies to allergy patients. The study will be conducted in allergy clinical centers based in Atlanta, GA and is expected to begin in June 2012. The primary objective of this Phase I Study is to evaluate both the safety and immunological response of therapeutic doses and the dosing regimen of JRC-LAMP-Vax vaccine.

## *Immunomix Shines it's LAMP Technology, Cont.,*

The NTC '8' series plasmid vector used in the ITI LAMP-vax product combines regulatory compliant, antibiotic-free vector with high-copy plasmid backbone and enhanced gene expression (transcription and translation), for maximal safety, potency and effectiveness.

## NTC Announces Swap Services to Enhance Plasmid Vector Performance.

For investigators developing gene therapeutics or DNA vaccines, "It is most important to design and manufacture vectors for effective expression, safety, and regulatory compliance," according to Dr. Jim Williams, NTC's Chief Scientific Officer, speaking at a recent presentation (http://www.youtube.com/watch?v=zKLpRufcy0k). Jim emphasized that end users should rightly be focused on testing and evaluation, not cloning or vector design, which are services available from NTC.

A number of NTC vectors are now in approved clinical trials. After a decade of pioneering improvements in mammalian expression vector design, regulatory compliance, and manufacturing, NTC's '8' Series vectors offer what has come to be regarded as the current gold standard in plasmid vectors.

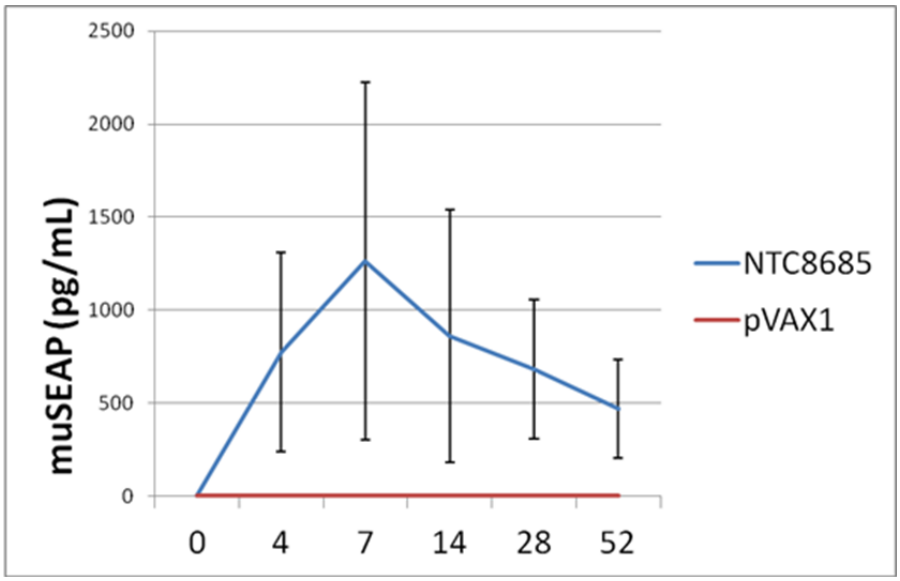
Now, for those who have their own vectors but desire to incorporate attributes of NTC vectors, (such as antibiotic-free selection and tissue specific promoters). "We offer seamless integration of NTC design elements, into customer-developed vectors," Dr. Williams said.

NTC's swap services are fast and economical, providing clients with formulated DNA ready for testing in as little as two weeks. For example, using NTC's RNA-OUT sucrose selectable marker (150bp), *vs.* kanamycin (900bp) reduces the plasmid size by ~750bp, increasing potency, purity, yield, and regulatory compliance, while reducing manufacturing cost.

"Antibiotic resistance genes should not be used in humans, according to EMA guidance, and these genes also put a metabolic burden on production host cells, reducing yield and purity," Dr. Williams said. "Why spend resources on GMP manufacturing of low yield plasmids, wherein 1/3rd of the DNA is essentially junk that can easily be gotten rid of, resulting in high-yield, more pure and potent plasmids?"

*Swap Services Cont.,*

Dr. Williams points to recent data (Fig. 1), which indicated dramatically elevated expression of electroporated plasmids in muscle cells *in vivo*, using a minimalized NTC vector (NTC8685) compared to the commonly utilized pVAX1 vector. "High levels out to 52 days was due to the optimized minimalized vector backbone design compared to the control vector," he said.




To obtain more information about NTC'S swap services, call today to speak to a representative: (402) 323-6289.

## Featured Article:

**High-Yield Plasmid DNA Production: *Genetic Engineering News, Tech Notes***: Apr 15, 2012 (Vol. 2, No. 80).GEN tutorial. Biotechnology News:

GEN Genetic Engineering & Biotechnology News

*Tech Notes:Apr 15, 2012 (Vol. 2,No. 80*
High-Yield Plasmid DNA Production

NTC's Aaron Carnes and Jim Williams discuss the secrets to success in gene based medicines manufacturing in this new GEN tutorial.

## NTC Meetings for 2012

**World Vaccine Congress**
Washington, DC
April 10-13
**American Society for Gene and Cell Therapy (ASGCT)**
Philadelphia, PA
May 16-19, 2012
**Vaccine Technology IV**
Albufeira, Portugal
May 20 – 25, 2012
**BIO2012**
Boston, MA, (Nebraska Booth)
June 18-20, 2012
**DNA Vaccines**
San Diego, CA
Dec 3-5