Stellar Biotechnologies

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Megathura crenulata Post Larval Culture - Bottleneck for a Valuable Medical Resource

Commercial Impact

Introduction

The Giant Keyhole Limpet, *Megathura crenulata* (*M. crenulata*) is a scarce sea mollusk and the sole source for KLH, an immune-stimulating protein vitally important in vaccine and immunodiagnostic practices. Unable now to rely on natural resources, Stellar provides a sustainable biopharmaceutical source of KLH through reliable culture methods that produce *M. crenulata* at a scale sufficient to support the commercial demand for KLH. This has been the focus of our NSF funded Phase-I/II research efforts.

Sustainable supply of KLH through a unique land based aquaculture system for *M. crenulata*

Through the support of SBIR Phase-I/II funding, Stellar has developed and optimized methods to control reproduction and growth of this important species .Using innovations and discoveries from Phase I research, the team was successful in developing hatchery and nursery facilities that effectively control all phases of the lifecycle of the mollusc and , for the first time, boasts multiple generations onsite that will produce commercial quantities needed to sustain the future supply of pharmaceutical grade KLH. The methods and systems developed through this Phase II/IIB research optimized first generation culture systems, exceeding production forecasts and improving KLH productivity. Horizontal studies have further identify KLH in early larval tissues by PAGE and Western blot with polyclonal anti-KLH antibody, as early as 7 days post-fertilization, indicating that: a) KLH is produced in early larval development, as well as, b) the potential viability of identifying KLH producing cells and the possibility of growing them in cell-culture-based system for production of KLH.

Successful extraction and purification of pharmaceutical grade KLH in commercial quantity

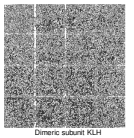
Establishing comparability and uniformity of KLH isotype distribution between wild-capture and aquaculture, as well as non-lethal collection methods, paved the way for commercial preparation of pharmaceutical grade KLH. The extraction of KLH hemolymph from controlled/cultured keyhole limpet colonies allows Stellar to deliver an unprecedented level of control over lot to lot traceability, quality and performance; benefits valued by vaccine manufacturers and drug developers using KLH. This positions Stellar as the only company that will be capable of supplying GMP grade KLH that can meet the anticipated long-term demand within the pharmaceutical industry. In early 2013, the Company has submitted a Type IV Biologics Master File (BB-MF) to the U.S. Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER) for its subunit KLH. These files, contain the proprietary information regarding the manufacture and safety of a drug components, allow Stellar to provide customers controlled access to reference as part of their product applications.

Demonstration best-in-class performance and quality

KLH is relatively unique in its ability to engage C-lectin receptors on antigen presenting cells in a manner that leads to downstream class-I antigen cross-presentation to Th1 T-cells, while at the same time engaging strong class-II (Th2) mechanisms promoting antibody production by B-cells. However, variability in immunogenicity among different forms, preparations and commercial sources of KLH has been reported, suggesting that data generated across laboratories may be challenging. In collaboration with a commercial partner, Stellar recently completed studies characterizing different Stellar and commercial KLH preparations biochemically and immunologically in a T-dependent antigen response (TDAR) rat animal model system with results showing greater anti-KLH antibody stimulation for Stellar's HMW-KLH and su-KLH than for other commercial preparations. In the vaccine arena, two of the Stellar vaccine partners have advanced KLH conjugated vaccines in multiple Phase II and III trials for breast cancer and autoimmune diseases (e.g. lupus and rheumatoid arthritis).

The Product and Value Proposition

Sustainable supply and proprietary formulations of KLH for active immune therapy and immunodiagnostic markets

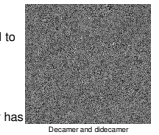


Dimeric subunit KLH

Stellar has successfully advanced both HMW-KLH and su-KLH toward commercialization in both vaccine and immunodiagnostic markets. These products include:

a) KLH formulations for use in preclinical and human clinical trials to enable routine uses in toxicology testing to monitor immune functions;
b) Immunoassays in ELISA format (Enzyme linked immunoabsorbant assay) for assessing antibody levels to KLH in preclinical models;
c) KLH as carrier and adjuvant for therapeutic vaccines with a range of clinical indications including cancer, autoimmune, dimentia and infectious diseases.

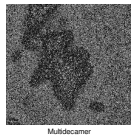
Scientific innovations through internal R&D and external collaborations



Decamer and didecamer

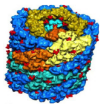
KLH based adjuvant platform: Stellar submitted a provisional application for a patent to the U.S. Patent and Trademark Office for new innovations related to Stellar's Keyhole Limpet Hemocyanin ("KLH")-based combinatorial adjuvant technology. The application included claims for pharmaceutical grade adjuvant compositions, manufacturing processes and uses in a wide range of vaccine therapies. Stellar's KLH-based adjuvant platform has the potential to improve vaccine potency, reduce toxicities and offer highly targeted Th1 and Th2 immune activation.

***Clostridium difficile* carbohydrate KLH conjugated vaccine**: Through strategic research partnership with the University Of Guelph (ON, Canada), Stellar has identified vaccine targets containing unique polysaccharide (PS) antigens that may target *C. difficile* colonization in intestine. The overall goal is design and development of a KLH-PS conjugate vaccine that promotes mucosal innate immune mechanisms and evokes adaptive immune responses effective in clearing residual infection and limiting re-colonization.

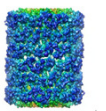


Multidecamer

Value Proposition



KLH 1 Didecamer (8 MDa)



KLH 2 Didecamer (4 MDa)

100 Å

World leader of sustainable, renewable and scalable pharmaceutical grade KLH supply
Proprietary manufacturing methods for highly immunogenic KLH for Immune Function Testing in TDAR protocol
Innovative design of KLH and KLH based multivalent adjuvants for different vaccine targets
Innovations in KLH conjugated vaccines to promote mucosal immunity against pathogens or cancers

Lineage

1900
Illingsworth the first and only thesis describing the anatomy and physiology of Megathura *crenulata*

1950-1990
Hemocyanin from *M. crenulata* (KLH) is found to stimulate the immune system in mammals

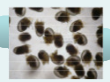
1995
KLH becomes available for use in humans and marketed as a readily available clinical reagent

1997
Safety and sustainability of KLH for drug products from wild harvested limpets in doubt

1999
Stellar Biotechnologies is founded to resolve the constraints on the supply of KLH as a sustainable drug product

2004
NIH supports Stellar research to show consistency of KLH between captive and wild limpets

2007
NCI supports Stellar research to develop pharmaceutical grade KLH from captive limpets



2008
NSF supports Stellar research to eliminate the constraints on production of M. crenulata from controlled aquaculture

2009-10
Stellar leverages NSF Phase IIB to secure partnerships and funding for commercialization

2010
Stellar Biotech becomes a publicly traded company through reverse merger

Stellar was founded in 1999 (Port Hueneme) as a Private company to address the urgent need for sustained commercial-scale supplies of high quality keyhole limpet hemocyanin (KLH). Through multiple grants from the National Institutes of Health (NIH) and the National Science (NSF), the company developed leading practices, facilities and proprietary capabilities to address this need. The founders included leading aquaculture executive Frank Oakes (CEO) formerly of The Abalone Farm, Inc., and eminent scientist, Daniel E. Morse, Ph.D. of the University of California at Santa Barbara. In April 2010, Stellar went public via merger with a TSX Venture Exchange company and simultaneous financing transaction in Canada.

Stellar specializes in production of KLH (keyhole limpet hemocyanin) and has generated important intellectual property (IP). This IP relates to aquaculture technologies, spawning, selection and maintenance of the limited natural source of this important pharmaceutical material (*Megathura crenulata*), as well as processing, purification and engineering of specific stabilized formulations of this valuable protein. Stellar has generated revenues since 2001 and its customers and partners include multi-national pharmaceutical companies, world-renowned laboratories and research centers, as well as biotechnology companies and vaccine developers.

KLH is a potent immune-stimulating protein used in a new class of drugs known as conjugate vaccines. KLH is refined from the hemocyanin of the rare ocean mollusk, *Megathura crenulata* (the California giant keyhole limpet). The extreme complexity and very large size of KLH glycoprotein make it unsuitable for synthetic production; therefore it must be purified from its natural source, which is rare and diminishing in population. KLH is used as an essential carrier protein in vaccines being developed for use in oncology, cardiology (e.g. hypertension), rheumatology (arthritis), neurology (Alzheimer's), and other important clinical indications. KLH is also widely used as a standard antigen in diagnostic applications such as immunotoxicology and assessment of immune status.

Stellar Biotechnologies' core competencies include: The Stellar team includes experts in marine science, immunology, molecular biology, pharmaceutical manufacturing and aquaculture. Stellar has the world's only demonstrated aquaculture technology for sustainable growth and cultivation of *M. crenulata* and production of KLH. Patented hemolymph extraction methods that enable sustainable, controlled supply of KLH protein. Proprietary purification methods for GMP-grade KLH (patents pending). Product specifications tailored to meet pharmaceutical standards and custom dose forms. Deep knowledge base of KLH biochemistry and immunology.

The Stellar Team

Frank Oakes - Chairman of the Board, President & Chief Executive Officer
More than 36 years of management experience in biotechnology and aquaculture, including a decade as CEO of The Abalone Farm, Inc. He led that company through the R&D, capitalization and commercialization phases of development to become the first profitable and largest abalone producer in the U.S.

Darrell Brookstein - Director, Executive VP, Corporate Development & Finance
Managing Director of The Nanotech Company, LLC and a director of CAG Capital. He has founded, built to profitability and been CEO of investment firms involved in securities, commodities, mining, natural resource and advanced technologies venture capital

Herbert S. Chow, Ph.D. - Chief Technology Officer
25+ years in business management and product development of biologics, therapeutic devices, clinical diagnostic and consumer diagnostic markets. He held key senior management positions with start-up biotechnology companies, as well as Abbott Labs and Johnson & Johnson

Catherine Brisson, Ph.D. - Chief Pharmaceutical Officer
More than 14 years of experience in biotech, pharmaceutical and medical devices in Quality Assurance and Global Regulatory Affairs providing leadership and direction over GMP, GLP & GCP operations. She held key senior management positions with start-up biotechnology companies, as well as Sicor Pharmaceuticals, Inc. (currently Teva Parenteral Products).

Brandon Lincicum M.S. – Executive Director of Aquaculture and Facilities
10+ years experience in the Aquaculture Industry including 6 years of research directly with *M. crenulata*. He has been responsible for the developing the company's methods for culture of M. crenulata at commercial capacity from larvae to extractable adult.

The Giant Keyhole Limpet – *Megathura crenulata*
A rare ocean mollusk found only from Northern Baja California to Monterey Bay; the epicenter of the population occurring in Southern California, this species is the ONLY source of Keyhole Limpet Hemoycyanin (KLH).