

DEVELOPING A VACCINE TO PREVENT STREPTOCOCCUS INIAE INFECTION IN FISH

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The bacterial pathogen *Streptococcus iniae* grows on a blood agar plate. *S. iniae* is closely related to the Strep A and B bacteria that commonly infect children. Photo: Jeff Locke



A juvenile hybrid striped bass used in vaccine studies. Photo: Jeff Locke



Sea Grant Trainee Jeff Locke injects a juvenile hybrid striped bass with *S. iniae.* Photo: Carlo Milani



S. iniae cocci chains visualized using light microscopy. Photo: Jeff Locke

SUMMARY

With Sea Grant support, medical researchers helped fish growers develop a control method for a deadly bacterial infection that costs the global aquaculture industry about \$100 million annually.

BACKGROUND

Twenty-six species of fish, including hybrid striped bass, tilapia and rainbow trout, are known to be susceptible to meningitis (brain swelling) from *Streptococcus iniae*, a bacterial pathogen that is closely related to the Strepococcus strains that cause "Strep throat" in children. Outbreaks are most common at fish farms where warm-water species are raised at very high densities.

PROJECT

The vaccines currently on the market for preventing *S. iniae* infections are classical vaccines based on exposing fish to killed versions of the pathogen. The objective of this project was to combine pharmacology and genetic science to create a live-attenuated vaccine to prevent *S. iniae* infections in fish. Such a vaccine is of interest because it opens the door to being able to inoculate fish orally through feed, instead of having to inject fish individually, which is labor intensive and costly. Viable, cost-effective vaccines also obviate the need to administer antibiotics to diseased fish.

OUTCOMES

Applying techniques developed for human medicine, researchers identified the genes of *S. iniae* responsible for pathogenesis and then mutated these genes to weaken the pathogen's virulence. In a series of laboratory experiments, the scientists then verified that fish exposed to this mutated, weakened pathogen still developed antibodies to the real pathogen. This ultimately led to the creation of a live-attenuated vaccine. The technology for producing the vaccine has since been patented.

COLLABORATORS

STUDENTS

Kent SeaTech Corp. (now Kent BioEnergy Corp.)

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PUBLICATIONS

Locke JB, Ostland VE, Vicknair MR, Nizet V, Buchanan JT. 2010. Evaluation of *Streptococcus iniae* killed bacterin and live-attenuated vaccines in hybrid striped bass through injection and bath immersion. Diseases of Aquatic Organisms 89:117-123.

Milani CJ, Aziz RK, Locke JB, Dahesh S, Nizet V, Buchanan JT. 2010. The novel polysaccharide deacetylase homologue Pdi contributes to virulence of the aquatic pathogen *Streptococcus iniae*. Microbiology 156:543-554.

Buchanan JT, Colvin KM, Vicknair MR, Patel SK, Timmer AM, Nizet V. 2008. Strain associated virulence factors of *Streptococcus iniae* in hybrid striped bass. Veterinary Microbiology 131:145-153.

Locke JB, Aziz RK, Vicknair MR, Nizet V, Buchanan JT. 2008. *Streptococcus iniae* M protein contributes to virulence in fish and is a target for live-attenuated vaccine development. PLoS One 3:e2824.

Locke JB, Colvin KM, Datta AK, Patel SK, Naidu NN, Neely MN, Nizet V, Buchanan JT. 2007. *Streptococcus iniae* capsule impairs phagocytic clearance and contributes to virulence in fish. Journal of Bacteriology 189:1279-1287.

Locke JB, Colvin KM, Varki N, Vicknair MR, Nizet V, Buchanan JT. 2007. *Streptococcus iniae* beta-hemolysin streptolysin S is a virulence factor in fish infection. Diseases of Aquatic Organisms 76: 17-26.

Buchanan UT, Stannard JA, Lauth X, Ostland VE, Powell HC, Westerman ME, Nizet V. 2005. *Streptococcus iniae* phosphoglucomutase is a virulence factor and a target for vaccine development. Infection and Immunity 73:6935-6944.

PROCEEDINGS

Milani C, Aziz RK, Locke JB, Nizet V, Buchanan JT. Role of PDI, a novel deacetylase homologue, in virulence of the aquatic pathogen *Streptococcus iniae*. Lancefield International Symposium of Streptococci and Streptococcal Diseases, Porto Heli, Greece, June 2008.

Locke JB, Colvin KM, Vicknair MR, Carlberg JM, Nizet V, Buchanan JT. Characterization of *Streptococcus iniae* virulence factors for vaccine development. International Meeting of the World Aquaculture Society. San Antonio, TX, February 2007.

Colvin K, Patel S, Timmer A, Van Olst JC, Nizet V, Buchanan J. Strain-associated virulence patterns in *Streptococcus iniae* in hybrid striped bass. Abstract B223. ASM Conference on Streptococcal Genetics, St. Malo, France, June 2006.

Buchanan JT, Patel S, Datta A, Nizet V. Capsule plays a significant role in virulence in the aquaculture pathogen *Streptococcus iniae*. Abstract B221. ASM Conference on Streptococcal Genetics, St. Malo, France, June 2006.

Locke, JB, Colvin KM, Vicknair MR, Nizet V, Buchanan JT. Streptolysin S is required for *Streptococcus inae* infection in fish. Fifth International Symposium on Aquatic Animal Health (ISAAH). San Francisco, CA, September 2006.





This publication is based on research project R/A-124 and is sponsored by NOAA Sea Grant, U.S. Department of Commerce, under grant NA100AR4170060, project C/P-1. The views expressed herein are those of the authors and do not necessarily reflect the views of NOAA or any of its sub-agencies. The U.S. government is authorized to reproduce and distribute for governmental purposes. This document is available in PDF on the California Sea Grant website: csgc.ucsd.edu.

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