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Effective Lyme Disease Chimeric Recombinant Vaccine

Main Inventor

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Overview

Richard Marconi, PhD, Professor, Department of Microbiology and Immunology, Virginia Commonwealth University, a recognized expert in the study of Lyme disease, has developed a unique Lyme disease chimeric recombinant vaccine that has a dual synergistic mechanism of protection.

Utilizing for the first time a specific region of OspA and addressing the variability of OspC, this vaccine provides a targeted and broad response. **This unique combination of protective epitopes kills *Borelli burgdorferi* in feeding ticks, thus inhibiting their transmission to mammals. Spirochetes that do transmit from tick to mammals are then eliminated by anti-OspC antibody responses. Should any cross into the mammal it will be killed before it can cause disease.**

Lyme disease is the most prevalent vector-borne disease in North America and Europe. Previously underreported, the CDC has now revised its estimates to 350,000 annual cases in the U.S. alone. The great majority of the Lyme disease cases still occur in the Eastern U.S., but due to climate change, it is rapidly spreading to the mid-western states. Symptoms are diffuse and there is no reliable diagnostic. The VCU-developed chimeric recombinant vaccine has the potential to provide an effective way to prevent this disease and the debilitating effects that occur when left untreated.

Key features

- First chimeric recombinant vaccine containing OspA protein and specialized chimeric protein composed of antigenic material from 7 OspC variants
- Multiple OspC antigens yields a broadly protective vaccine
- Kills *B. burgdorferi* in feeding ticks and can block transmission of the disease to host
- Canine studies with vaccine showed 93.7% reduction in the incidence of *B. burgdorferi* infection *
- Low rate of adverse events post-vaccination in a canine multi-site safety study*
- Clinical canine data - ready to progress to human clinical trials
- Single engineered protein - minimal extraneous material administered in the vaccine
- Inexpensive to produce - recombinant protein produced in *E. coli*

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Patent estate

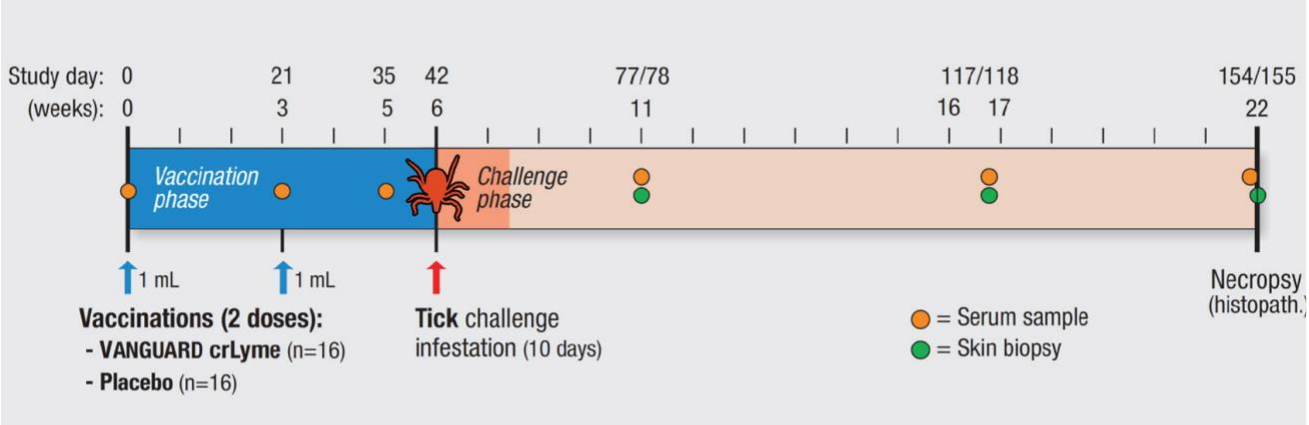
The Lyme disease vaccine is protected by an extensive international patent estate. Issued patents and patent applications ensure patent protection until 2025 at a minimum with the potential for additional protection through 2035. The patent estate claims cover both compositions of matter and methods of use:

- A variety of novel sequences of OspA, OspC and OspE proteins
- Constructs consisting of specific combinations of specific protein fragments that make the vaccine effective against multiple strains
- Methods of use

Additional information about the patent estate is available upon request.

Clinical efficacy as demonstrated in the canine model*

Summary of study design and timeline – challenge experiment demonstrates efficacy of vaccine



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Histopathological Evaluation

Histopathology results		
Inflammation graded 2 or higher in…	**Control**	**VANGUARD^{C} crLyme**
Subdermis (%)	87.5	0
1 joint (%)	81.3	0
2 or more joints (%)	56.3	0

Lesion severity grades of 0=absent (no lesion found), 1=minimal (very few or very small), 2=mild (few or small), 3=moderate (moderate number or moderate size), 4=marked (many or large), 5=severe (extensive number or extensive size)

Safety data from canine studies*

Results of safety studies conducted by Zoetis using Vanguard®crLyme in 620 healthy canines and reported in their Technical Bulletin December 2015, demonstrated a low incidence of post- vaccination adverse effects from the vaccine. The health events were as expected for vaccines that are a single engineered protein and contain minimal extraneous materials. The major event was swelling at the injection site (3.81% 47/1232 vaccinations)*.

Frequency of adverse reactions.	
Abnormal health event	**Percent of injections**
***Immediate** post-vaccination reactions* *(<30 min post-vaccination; n=1231 injections)*	
Injection site edema	0.08%
Injection site paraesthesia	0.24%
Vocalization at administration	0.73%
***Late** post-vaccination reactions* *(>30 min–10 d post-vaccination; n=1232 injections)*	
Anorexia	0.08%
Diarrhea	0.16%
Hyperthermia	0.08%
Injection site edema	3.81%
Injection site pain	0.32%
Lethargy	0.24%
Muscle tremor	0.08%

***Zoetis Technical Bulletin 2015**

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Selected Publications

- Earnhart CG, Marconi RT. OspC phylogenetic analyses support the feasibility of a broadly protective polyvalent chimeric Lyme disease vaccine. *Clin Vaccine Immun* 2007; 14:628-634.

- Earnhart CG, Buckles EL, Dumler JS, et al. Demonstration of OspC type diversity in invasive human Lyme disease isolates and identification of previously uncharacterized epitopes that define the specificity of the OspC murine antibody response. *Infect Immun* 2005; 73:7869-7877.

- Buckles EL, Earnhart CG, Marconi RT. Analysis of antibody response in humans to the type A OspC loop 5 domain and assessment of the potential utility of the loop 5 epitope in Lyme disease vaccine development. *Clin Vaccine Immun* 2006; 13:1162-1165.

- Earnhart CG, Marconi RT. An octavalent Lyme disease vaccine induces antibodies that recognize all incorporated OspC type-specific sequences. *Human Vaccine* 2007; 3:281-289.

- Earnhart CG, Marconi RT. Construction and analysis of variants of a polyvalent Lyme disease vaccine: approaches for improving the immune response to chimeric vaccinogens. *Vaccine* 2007; 25:3419-3427.

- Earnhart CG, Buckles EL, Marconi RT. Development of an OspC-based tetravalent, recombinant, chimeric vaccinogen that elicits bactericidal antibody against diverse Lyme disease spirochete strains. *Vaccine* 2007; 25:466-480. *Clin Vaccine Immun* 2007; 14:628-634.

- Rhodes DVL, Earnhart CG, Mather TN, et al. Identification of *Borrelia burgdorferi* ospC genotypes in canine tissue following tick infestation: implications for Lyme disease vaccine and diagnostic assay design. *Vet J* 2013; 198:412-418.

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