

TECHNOLOGY FOR USING rDNA CONSTRUCT AND THE EXPRESSED CHIMERIC PROTEIN AS A VACCINE AGAINST BRUCELLOSIS

Biotech Consortium India Limited (BCIL) is seeking companies interested in commercializing a technology for using a rDNA construct consisting of 3 immunodominant antigens and the expressed chimeric protein as a candidate for *Brucella* vaccine, developed by Scientists at Indian Veterinary Research Institute, Izatnagar, Uttar Pradesh, India.

BCIL was incorporated as public limited company in 1990 under the Indian Companies Act 1956. It is promoted by the Department of Biotechnology, Government of India and is financed by several all India financial institutions, venture capital funds and the corporate sector. BCIL has been actively involved in technology transfer, project consultancy, fund syndication, information dissemination, and manpower training & placement related to biotechnology over the last decade and half. BCIL has transferred more than 15 technologies in the last 5 years using its expertise in facilitating licensing agreements that allows a healthy and productive cooperation between the inventor and the licensee.

INTRODUCTION

Brucellosis is a major zoonotic disease widely distributed in both animals and humans, especially in developing countries (Young, E.J., 1983; Young, E.J., 1988). Bovine brucellosis is mainly caused by *Brucella abortus*, a gram negative, facultative intracellular bacterium. Vaccination using live attenuated smooth *Brucella* strain S19 is the most commonly used method and has proven effective in controlling brucellosis in many countries over several decades. This method, although gives the highest level of protection, but at the same time, suffers from drawbacks in terms of safety and interference in sero-diagnosis of clinical infection. More recently, a rifampicin-resistant mutant strain RB51 has been approved for use as vaccine in the U.S.A. and a few more countries, but tends to be weaker antigen than S19. However, in view of the drawbacks of live attenuated vaccines, the use of *Brucella* immunogens as recombinant antigens to induce a protective immune response in animals is being investigated by several groups across the country and abroad. Recombinant antigen can be even be used in adult animals including pregnant one and vaccination does not interfere with sero-diagnosis of infection.

TECHNOLOGY

The present technology involves the use of a multigenic construct encompassing 3 different immunodominant antigens (viz., Cu-Zn Superoxide dismutase (SOD), P39 antigen and L7/L12 ribosomal protein) of *Brucella abortus* as a vaccine candidate against Brucellosis. The multigenic construct has been expressed in *E.coli* system to produce the chimeric antigen. Vaccination in experimental animal models (BALB/c mice) was performed using the multigenic construct



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(DNA Vaccine) followed by administering the chimeric antigen and also through the E.coli cells harbouring the expressed chimeric antigen. Both groups of vaccines were found to elicit high level of protection to immunized mice against virulent challenge by *Brucella abortus* 544 strain and were also found to be safe when studied in pregnant guinea pigs. The Log₁₀ Protection using E.coli cells harbouring the chimeric protein was found to be as high as 1.72 vis-à-vis the maximum value of 2.13 for live attenuated S19 strain as detailed in the table below:

Vaccine Group	Brucella cfu / Spleen	Log ₁₀ Brucella / spleen	Log ₁₀ Protection
DNA Vaccine followed by chimeric antigen	3.2 X 10 ³	3.50	1.54
E.coli cells harbouring chimeric protein	2.1 X 10 ³	3.32	1.72
Live attenuated S19 strain	8.3 X 10 ²	2.91	2.13
PBS control	1.1 X 10 ⁵	5.04	0

SCALE OF TECHNOLOGY DEVELOPMENT

The technology has been developed at laboratory scale in which approximately 15-20 mg of purified chimeric antigen per litre of culture could be obtained.

Approximately 1.5 to 2.0 mg of plasmid DNA could be harvested per litre of culture.

A cost effective vaccine can be developed using live recombinant E.coli cells (expressing the chimeric protein) as vaccine candidate.

REQUIREMENTS FROM INDUSTRIAL PARTNER

We look for an industrial partner to evaluate the effectiveness of chimeric antigen in the target animals, i.e., cattle and buffalo (in collaboration with the concerned scientist).

PATENT(S)

Patent application filed in India for "Fusion protein and nucleotide as *Brucella* vaccine" (Application No. 2190/DEL/2006, Dated 4/10/06).