

# Phage-Cured Lactobacillus Strains for Therapeutic Delivery

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Assigned to WARF as biological material.

**The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in a modified strain of *L. reuteri* permanently cured of two prophages without DNA damage, and demonstrably more robust *in vivo*.**

## OVERVIEW

In addition to key roles in food and biofuel production, probiotic strains of lactic acid bacteria are being exploited in medicine as therapeutic delivery vehicles. One obstacle is that bacteriophages pervasive in the lactobacilli genome can be induced/reactivated as a result of various environmental (stress) factors, which compromises viability and robustness.

Several methods have been developed to delete phages from bacterial genomes *in vitro*, including treatment with ultraviolet light and the chemotherapy drug mitomycin C. But these approaches are known to damage DNA and cause mutations. Furthermore, these approaches generally do not make the strains resistant to future bacteriophage incorporation in the genome.

## THE INVENTION

Using a newly developed counterselection method and promoter construct, UW-Madison researchers have created a modified strain of *L. reuteri* cured of two prophages and variations thereof. In the process of deleting the phages from the genome the researchers also deleted the recognition site (*attB*), thereby preventing future phage integration at the site.

The approach used to develop the novel strain does not induce DNA damage and effectively eliminates bacteriophages that could otherwise reactivate and lyse the host cell. The strain is more robust for surviving transit through the gastrointestinal tract, which the researchers envision will enhance its ability to deliver therapeutic proteins *in vivo*.



## THE WARF ADVANTAGE

Since its founding in 1925 as the patenting and licensing organization for the University of Wisconsin-Madison, WARF has been working with business and industry to transform university research into products that benefit society. WARF intellectual property managers and licensing staff members are leaders in the field of university-based technology transfer. They are familiar with the intricacies of patenting, have worked with researchers in relevant disciplines, understand industries and markets, and have negotiated innovative licensing strategies to meet the individual needs of business clients.



## APPLICATIONS

- Available as a biomaterial
- Probiotic use, therapeutic delivery vehicle, production host for enzymes or biofuels

## KEY BENEFITS

- The strain is expected to be more robust and resistant to stress-induced phage induction/lysis.
- Improved survival *in vivo*
- Unlike other methods, no DNA-damaging agents were used.
- Modified recognition site should prevent phage reintegration.

## STAGE OF DEVELOPMENT

The researchers confirmed bacteriophage deletion using PCR, and sequenced the strain to confirm that both *attB* sites were modified. Mouse experiments confirmed that the prophage-deletion strain is more robust in its ability to survive gastrointestinal survival. *In vitro* experiments demonstrated the strain is more resistant to exposure to low pH.

## ADDITIONAL INFORMATION

### Tech Fields

Food & Supplements - Ingredients

Drug Discovery - Drug delivery

## CONTACT INFORMATION

For current licensing status, please contact Joshua Carson at [jcarson@warf.org](mailto:jcarson@warf.org) or 608-960-9844.