

# Oral Targeted Multivalent Vaccine, Intestinal Dendritic Cells are Directly Activated

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## Introduction

Recent concerns about pandemic diseases, bioterrorism, and particular disease eradication initiatives have increased the demand for an efficient needle-free vaccine. Due to its quick and simple administration, enhanced safety, lower cost, and diminished discomfort associated with immunisation, a needle-free vaccine could aid in mass vaccination, increasing compliance. The creation of an effective oral vaccine faces two significant challenges: safeguarding the target antigen from the low gastric pH and digestive enzymes; and delivering the target antigen to Dendritic Cells (DCs), which are expert antigen-presenting cells [1]. Two strategies were used to overcome these obstacles. First, *Lactobacillus* species, such as *L. acidophilus* or *L. gasseri*, bacteria that can survive and thrive in the gastrointestinal tract, were altered to produce the target antigen in the gut. This was done to protect the antigen from harsh stomach secretions. Second, a twelve amino acid long tag was added to the immunogenic vaccine subunit to help in the transport of antigen to the professional antigen presentation cells.

### Antigen delivery vehicle using the *Lactobacillus* Species

Most disease-causing organisms enter the body primarily through mucosal surfaces. Therefore, vaccines able to elicit a mucosal immune response can boost the mucosal layer's defences and offer infection protection. For ages, several species of lactobacilli have been included in human diets as nutritional supplements and are thought to be safe to eat. The typical gut microbiota also includes several *Lactobacillus* species. Utilizing *Lactobacillus* species as a vaccine delivery vehicle shields the vaccine component from the harsh acidic environment and enhances vaccine bioavailability since *Lactobacillus* species thrive in the low pH of the stomach. Researchers have also created lactobacilli species-effective constitutive and inducible expression vectors to deliver immunogenic antigens [2]. While immune tolerance to a commensal inhabitant of the gastrointestinal mucosa was once a worry with this method, lactobacilli like *L. gasseri* are able to overcome tolerance probably due to their potent innate adjuvant characteristics. Our research has been successful in giving vaccinated mice the Protective Antigen (PA) of *Bacillus anthracis* to help them fight off this potential bioterrorist agent using *L. gasseri*. In addition, another team successfully delivered Salmonella antigens using *L. gasseri* [3].

### Dendritic cells to boost immune response

With their exceptional capacity to deliver antigen and activate naive T lymphocytes, Dendritic Cells (DCs) are the most efficient antigen-presenting cells in both humans and domestic animals. As such, they are essential for the induction of particular initial

immunological responses. These cells can effectively bind antigens due to the expression of numerous surface receptors, including C-type lectins (such as mannose R, DC-SIGN, and DEC-205), Toll-like Receptors (TLRs), receptors for the Fc Component of Antibodies (FcRs), and Complement Receptors (CR3, CR4) [10]. Due to the constitutive expression of class II MHC molecules and co-stimulatory/regulatory molecules, including as *CD40*, *CD86*, and *B7-H1* on mature DCs, captured antigens are subsequently processed and effectively delivered to rare antigen specific T cells. Consequently, antigen was only transmitted to DCs, not to B lymphocytes or macrophages, because reduces the amount of antigen needed to stimulate the immune system and has the potential to be used as a vaccination strategy to trigger protective immunological responses. Traditional receptors, such as class II MHC molecules, CD11c, and TLRs, can be used to target antigens selectively to DCs without causing ineffective antigen delivery because many other cell types also express similar receptors and would compete with DCs for vaccine binding. A phage display library was successively absorbed by monocytes, T cells, B cells, and Langerhans cells and then screened for the capacity to bind human myeloid-derived DCs in order to find a specific DC-targeting peptide moiety. By fusing this DC targeting peptide to PA of *Bacillus anthracis*, the resulting sequence was then evaluated for its in-vitro binding capability and its use in antigen delivery in a mouse model of oral vaccination [4].

For *Bordetella bronchiseptica*, the primary causative pathogen of the contagious respiratory disease complex, infectious tracheobronchitis or "kennel cough," which is frequently seen in dogs housed together in pet stores, kennels, and animal shelters, oral vaccine strategies are currently being developed or are already in use. Cats and infrequently immuno-compromised people can contract this disease. In order to prevent or lessen Newcastle disease, fowl cholera, and avian encephalomyelitis in poultry, oral therapeutic strategies are also employed in rabies control programmes that target ownerless pet populations in enzootic areas. They also protect new-born calves from scours and diarrhoea caused by *E. coli*, and foals are vaccinated orally against *Rhodococcus equi* pneumonia [5]. In reality, chickens are perhaps the most heavily immunised domestic species, and the intensity of production is anticipated to rise considerably over the next few decades as chicken consumption and the wealth of nations like China and India rise. We examined this targeting peptide's capacity to bind DCs from other species of significant veterinary value in order to broaden the scope of its applicability as an antigen delivery agent in domestic animals. We discovered that DC-peptide significantly binds to DCs from all tested species more strongly than a nonspecific peptide, indicating that this peptide binds to highly conserved areas of its receptor. These findings favourably point to the potential application of this particular approach in the future creation of multivalent vaccinations for animals.

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