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Opinion

Bacterial Vaccine: Potential and Safety Concerns

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Vaccines have had a major impact on the improvement of health and have played an important role in the eradication of certain diseases in countries or on entire continents. Live bacteria vaccines induce cell-mediated immunity, as well as systemic antibody-mediated immunity and hence, are considered highly efficient. However, several attenuated microorganisms were shown to be unstable and occasionally to revert to virulence which raised several safety concern of live bacterial vaccine [1,2]. The pathogenicity must be weakened via attenuation before using pathogenic bacteria for vaccination purposes. This involves inactivation of virulence factors or mutation of genes encoding metabolic enzymes. Inactivation of a metabolic gene has the advantage that the bacteria still express virulence determinants important to elicit a protective immune response [2]. Appropriate stable auxotrophic strains are usually not able to replicate in the human body and can safely be used even in immune compromised individuals. Specific deletions of at least two metabolic essential genes are usually used which decrease the probability of reversion to virulence [2,3]. The use of antibiotic resistance genes as marker genes in vaccines is not encouraged as these genes can transfer to in the end humans and thus hamper the use of therapeutic antibiotics. Different alternatives to antibiotic resistance marker genes have been published and should be used as soon as possible in the developmental process of a vaccine [4-6]. Some of the major safety concerns of vaccine strain are associated with systemicdisturbance, infection, and inhibition of bacterial production of nutrients. They also influence the immune system, Induction of tolerance to pathogen instead of immunity, Production of harmful/undesired metabolites including enzymatic activities. Induction or potentiation of autoimmunity is also another important concern however the risk is certainly lower than after natural infection but the theoretical side effect is the possible induction [7, 8]. However, there is no recommendation to avoid vaccination of people with an ongoing autoimmune disease like rheumatoid arthritis or systemic lupus erythematosus if vaccination otherwise is motivated [9,10]. New ways of further are attenuating bacteria like combining auxotrophy with deletions of virulence genes may find the way to immune-compromised hosts for vaccination [11].

In broad-spectrum, the spread of live bacterial vaccines to the environment is also a matter of concern. Though, attenuated human pathogens are usually not adapted to live outside its host. Therefore, survival in the environment is usually short. Vaccines based on recombinantLactic Acid Bacteria (LAB) may result in the release of these bacteria in nature as they are more suited to survive in nature. Both attenuated bacteria like salmonella and food related LABhas been developed as live vaccines suitable for oral administration. Today, live vaccines based on attenuated *Salmonellatyphi* and *Vibriocholerae* are available. The development of bacterial vaccine vehicles carrying a heterologous gene or a DNA vaccine is more problematic and not yet into the market for use. Several bacteria have been suggested as vaccine vehicles and especially LABis promising. Their safety and immune modulating capacity have been tested using diverse vaccine components like antigens from infectious diseases, allergy-promoting proteins and therapeutic antibodies. However, considerable safety issues against live vaccine vehicles can be raised. We still need a better approachfor overall health and concern about safety during vaccination.

Keywords: *Vaccine; Live bacteria; Lactic acid bacteria; Safety*

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