

## What are the limits of adjuvanticity?

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### Abstract

Vaccines developed traditionally following empirical approaches have often limited problems of immunogenicity, probably due to the low level of purity of the active component(s) they contain. The application of new technologies to vaccine development is leading to the production of purer (e.g. recombinant) antigens which, however, tend to have a poorer immunogenicity as compared to vaccines of the previous generation. The search for new vaccine adjuvants involves issues related to their potential limits. Since the introduction of aluminium salts as vaccine adjuvants more than 70 years ago, only one adjuvant has been licensed for human use. The development of some of these new vaccine adjuvants has been hampered by their unacceptable reactogenicity. In addition, some adjuvants work strongly with some antigens but not with others, thus, limiting their potentially widespread use. The need to deliver vaccines via alternative routes of administration (e.g. the mucosal routes) in order to enhance their efficacy and compliance has set new requirements in basic and applied research to evaluate their efficacy and safety. Cholera toxin (CT) and labile enterotoxin (LT) mutants given along with intranasal or oral vaccines are strong candidates as mucosal adjuvants. Their potential reactogenicity is still matter of discussions, although available data support the notion that the effects due to their binding to the cells and those due to the enzymatic activity can be kept separated. Finally, adjuvanticity is more often evaluated in terms of antigen-specific antibody titers induced after parenteral immunization. It is known that, in many instances, antigen-specific antibody titers do not correlate with protection. In addition, very little is known on parameters of cell-mediated immunity which could be considered as surrogates of protection. Tailoring of new adjuvants for the development of vaccines with improved immunogenicity/efficacy and reduced reactogenicity will represent one of the major challenges of the ongoing vaccine-oriented research.