The adjuvant effect of Gantrez®AN nanoparticles on oral vaccination of pigs and mice with F4 fimbriae is strongly influenced by polymer degradation.

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We analysed the adjuvant effect of Gantrez nanoparticles NP on oral immunisation of pigs and mice with F4 fimbriae. The animals were vaccinated with F4, F4 encapsulated in Gantrez NP, called gF4 NP, or F4 + empty Gantrez NP, called F4 + gNP, and intragastrically infected with F4+ ETEC.

In pigs, a clear F4-specific serum IgA and IgG response following vaccination could only be observed in the F4+g NP group. After infection with F4+ ETEC, a secondary antibody response was observed in the F4 group. Adding Gantrez NP to F4 or encapsulation of F4 in Gantrez NP enhanced this response. In mice, the strongest response could also be seen in the F4 + g NP group. In contrast to the results in pigs however, encapsulation of F4 in NP reduced the response. An important difference between mice and pigs is that pigs have an intestinal F4 receptor, whereas mice don’t have this receptor.

Taken together, in both mice and pigs, the best adjuvant effect was seen by adding empty NP to the fimbriae. These data suggested that offering gastro-intestinal protection and a depot effect are not the main properties of the Gantrez polymer responsible for the adjuvant effect but that functional groups at the surface are more likely to play a significant role.

To analyze if the adjuvant effect of the empty NP was sufficient to protect suckling pigs, the experiment was repeated 6 months later on pigs of 8 days old. A secondary response could be seen after the ETEC challenge infection in the F4 and the F4 + g NP group, indicating a good priming. However, the response in the F4 + g NP group was not improved compared to the F4 group. In the gF4 NP group, serum antibodies were induced later, and only the IgA and IgM response were increased compared to the negative controls.

To explain the discrepancy between the studies, the polymer was characterized again and a second mice experiment was performed to analyze the influence of storage on the polymer properties. Changes in polymer weight and polymer weight distribution occurred. In addition, the adjuvant effect of empty NP on F4 in mice was lost. Nevertheless, this could be restored by crosslinking the NP more strongly, 0.22mg diaminopropane DP/mg NP instead of the 0.01mg DP/mg NP used previously, and hence, stabilizing the resulting anhydride groups more strongly. As a result, the immunisation profile of F4 + highly crosslinked NP was comparable to that of F4 + slightly crosslinked NP in the first study.