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Pseudo particules de rotavirus : propriétés et perspectives d'utilisation

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► **To cite this version:**

J Cohen, A Charpilienne, M Labbé, S Crawford, M Estes. Pseudo particules de rotavirus : propriétés et perspectives d'utilisation. *Veterinary Research*, 1995, 26 (3), pp.208-209. <hal-00902333>

HAL Id: hal-00902333

<https://hal.science/hal-00902333v1>

Submitted on 11 May 2020

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whereas the mucosal immunity was not evaluated.

Immunity conferred by Ad-vectored vaccines seems to be long-lasting (at least 8 months after a unique injection in adult or 1-day-old mice). Some drawbacks still exist, for example the need to inoculate a high level of virus in order to elicit a strong immune response (10^8 to 10^9 TCID₅₀). Nevertheless, we have shown that the protective doses in mice were greatly reduced when the virus was formulated in oil adjuvants. Moreover, our recent work showed that the simultaneous inoculation of a recombinant adenovirus and a plasmid coding for IL2 by the intramuscular route led to an enhancement of the immune response. We have also compared protective doses of an Ad-gD, a replication-defective adenovirus expressing the *gD* gene of pseudorabies virus, and Ad-gD-E1a, in which a functional E1A transcription unit has been restored. The protective dose of Ad-gD-E1a was 1 000-fold lower in cotton-rats, an Ad5 permissive species, than that of Ad-gD. In mice, a species restricted for Ad5 replication, the protective dose of Ad-gD-E1a was still 16-fold lower than that of Ad-gD. In both species, Ad-gD and Ad-gD-E1a induced similar antibody responses for each dose tested. Recently, experiments in pigs with oil-formulated Ad-gD showed good evidence of efficacy, close to that of adjuvanted live vaccines which express all the glycoproteins of PRV.

We are also investigating one of the main limitations of vaccination of new-born children or animals, *ie* the interference of maternal antibodies. Experiments are currently being conducted in mice and pigs by injection of naked DNA or recombinant adenovirus, each expressing *gD* under the control of the same regulatory sequences, to litters of mothers vaccinated or not against PRV. Several trials are currently being undertaken or planned, to evaluate recombinant viruses expressing genes from PRV,

FIV, FIP and canine distemper viruses inoculated by various routes. On the other hand, several experiments have been or are currently being carried out to evaluate the safety of replication defective adenoviruses. First, the dissemination of deletion mutants of Ad5 and wt virus was evaluated in cotton rats and mice (respectively permissive and non-permissive for wild-type Ad5), using several routes of administration. Secondly, cotton rats were coinoculated with 2 recently constructed defective adenoviruses expressing either the betagalactosidase or the luciferase gene, by the intramuscular or the intravenous route and later infected with a wt Ad5. No transcomplementation of the defective E1a/E1b genes was evidenced *in vivo*, in contrast with *in vitro* experiments. We are also studying the capacity of the E1 gene of several animal adenoviruses to provide phenotypic transcomplementation of their counterparts in Ad5. Finally, several modifications of the encapsidation signals are being made in order to design adenovirus genome vectors with reduced ability to be encapsided when mixed with a wt virus.

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Pseudo particules de rotavirus : propriétés et perspectives d'utilisation. J Cohen ¹, A Charpilienne ¹, M Labbé ¹, S Crawford ², M Estes ² (¹ INRA, unité de

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La capsidie des rotavirus est relativement complexe. Elle peut être représentée par un modèle de 3 couches concentriques. Elle est constituée de 4 protéines majeures (VP2, VP6, VP7, VP4) et de 2 protéines minoritaires (VP1, VP3). Chacune de ces protéines a été clonée et exprimée dans le système baculovirus–cellules d'insectes. L'expression de VP2 conduit à la formation de particules sphériques correspondant à la couche interne de la capsidie. La co-expression de VP2 et de diverses protéines structurales conduit à des pseudo particules stables (VLP : *virus like particles*) faciles à purifier. La co-expression de VP2 et VP6 permet d'obtenir des VLP2/6 qui sont morphologiquement identiques aux particules dont la couche externe a été solubilisée par chélation de calcium. De même, la co-expression des protéines VP2, VP6, VP7 (que VP4 soit co-exprimée ou non) conduit à des particules qui sont superposables en microscopie électronique aux particules virales complètes et infectieuses.

La stochiométrie des différentes VLP coïncide assez bien avec celle des particules virales infectieuses. Ces différentes VLP conservent aussi les caractéristiques antigéniques et fonctionnelles des virions authentiques. En particulier les VLP sont capables de fusionner avec des vésicules membranaires ou entrer en compétition avec des virus lors de mesure de l'attachement sur des cellules sensibles. Il est aussi possible d'obtenir des particules chimériques contenant des protéines provenant de souches virales appartenant à des sérotypes ou à des sérogroupes différents. Cette capacité des protéines virales de s'auto-assembler d'une façon précise (et cepen-

nant assez souple) permet d'aborder l'étude des interactions entre protéines de structure, le rôle de chaque protéine dans les différentes étapes de l'infection ou de la morphogénèse, et aussi les propriétés vaccinales de chaque protéine. Enfin ces VLP sont potentiellement utilisables pour vectoriser des antigènes (ou des drogues) et les cibler vers l'entérocyte.

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Surface bacterial antigen CS31A as a tool to design new recombinant vaccines displaying heterologous antigenic determinants. C Martin, JP Girardeau, M Der Vartanian, MC Méchin, F Bousquet, Y Bertin, H Laude *, M Contrepois (*INRA-Theix, laboratoire de microbiologie, 63122 Saint-Genès-Champanelle; * INRA, laboratoire de virologie et immunologie moléculaires, domaine de Vilvert, 78352 Jouy-en-Josas cedex, France*)

New recombinant vaccines composed of a genetic fusion between an immunogenic bacterial protein and a foreign antigenic determinant (epitope) are currently under investigation. Such vaccines would present considerable advantages such as safety, low production cost, and ease of transport. The carrier proteins fimbriae have the advantage of being readily accessible to the host's immune system since