Letters & Notices

CORONAVIRUS

Is the production of a Covid-19 vaccine using transformed *Pasteurella* plausible?

WE read with interest the letters from Aung Myint and Trevor Jones (*VR*, 28 March 2020, vol 186, p 388 and *VR*, 4/11 April 2020, vol 186, p 419) describing their experience with vaccination of poultry against infectious bronchitis virus (IBV) in Myanmar and the proposal that a similar method could be used to control Covid-19.

While a viable method for the production of a Covid-19 vaccine is of huge interest at the moment, and it is important to adopt the experience and lessons from prophylactic vaccination in veterinary medicine, we feel that some aspects of the underlying science put forward in these letters require supporting evidence and further clarification to demonstrate they are plausible.

The authors speculate that 'administration of a vaccine containing formalin-killed *Pasteurella multocida* cells, prepared as we described, could be effective in therapy if administered early in the course of [Covid-19], by stimulating the production of specific protective antibodies'. Are the authors suggesting that orally administered inactivated *P multocida* cells expressing severe acute respiratory syndrome coronavirus 2 proteins will not be digested in the human stomach and will induce virus-neutralising systemic antibodies?

The authors also state that 'when mixed with cell lysates of virus-infected tissues, *P multocida* took up free viral genes and incorporated them into its genome'. However, since *P multocida* is known to be difficult to transform (even using high-voltage electroporation),[1,2] and natural transformation in Pasteurellaceae requires specific uptake sequences,[3] this seems highly unlikely.

Such a process would not generate a very standardised vaccine, but would likely have large batch-to-batch variations. Furthermore, the process of transformation, if successful, would result in a genetically modified product, and one would have to show quite extensively that it is appropriately inactivated without affecting any vaccine components.

As a coronavirus, IBV has an RNA genome and contains no DNA with which to transform the *P multocida*. How do the authors suggest the viral RNA is converted to DNA before being rapidly degraded inside the bacterial cell?[4]

It is also unclear what steps were taken to verify viral gene expression in the *P multocida*. The authors state that '*P multocida* cells expressing foreign antigens on their surface could be detected by the addition of specific antibody-tagged erythrocytes', but how did they ensure the natural haemagglutination properties of *P multocida* capsule polysaccharide[5] were not responsible for the linkage between 'transformed' *P multocida* and the erythrocytes?

Finally, in the field vaccination of 9000 birds that Myint and Jones reported to be a success, was there a controlled trial comparing unvaccinated birds and birds vaccinated with untransformed *P multocida* with those vaccinated with *P multocida* expressing viral antigens? Such data would be needed to give confidence that the vaccine is indeed effective.

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