New discovery may lead the way to improved whooping cough vaccine

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Scientists at Trinity College Dublin have made novel discoveries concerning the current vaccine against whooping cough that may lead to the development of an improved future vaccine. The findings could help reduce the incidence of the disease which is increasing in developed countries. The research led by Professor of Experimental Immunology, Kingston Mills has just been published in the leading international journal *PloS Pathogens*.

A new vaccine against whooping cough, caused by the bacteria Bordetella pertussis was first introduced to the routine vaccination schedule for infants and children in most developed countries, including Ireland over a decade ago. Prior to the introduction of this vaccine, children were immunised with a vaccine made from whole bacteria. Although this 'whole cell pertussis vaccine' was effective at preventing the infection, it had been associated with side effects. Dissatisfaction with that vaccine led to the development of an 'acellular pertussis vaccine' made from components of the bacteria combined with an adjuvant to boost immune responses. Following its introduction in the late 1990s, the new vaccine has proved to be very safe and has been effective in controlling the potentially fatal disease of whooping cough in children. However, protective immunity conferred with the vaccine falls quite quickly, necessitating frequent booster vaccinations. This fall off in the immunity may be contributing to the number of whooping cough cases which are increasing with quite dramatic increases reported in certain countries, including the US, Australia and the Netherlands.

Professor Kingston Mills's research team at the School of Biochemistry and Immunology in the Trinity Biomedical Sciences Institute has discovered important mechanistic differences in the type of immune responses induced with the new 'acellular' and old 'whole cell' vaccine. The whole cell vaccine, although much more likely to cause adverse reactions in recipients, was capable of inducing strong cellular immune responses mediated by white blood cells called T cells, in particular a type of T cell called Th1 cells. In contrast, the new acellular vaccine, although safer, was less effective in inducing cellular immunity, but instead induced immunity mediated by antibodies and another type of T cell called a Th17 cell.

Most vaccines include a component called an adjuvant to boost immune responses to the bacterial or viral antigens in the vaccine and the acellular pertussis vaccine uses an aluminium salt, called alum. However, Dr Padraig Ross, Dr Sarah Higgins and Ms Aideen Allen in Professor Mills' laboratory, working in collaboration with Dr Rachel McLoughlin and Dr Ed Lavelle, have shown that the vaccine could be improved further through the use of a different adjuvant.

The current vaccine does not enhance the induction of Th1 cells, required for conferring optimum protective immunity against the bacteria. They showed that by switching the adjuvant from alum to an adjuvant based on bacterial DNA, they could induce the crucial Th1 cells and thereby enhance the efficacy of the vaccine against Bordetella pertussis infection in a murine model. The new vaccine has the potential to protect a higher proportion of immunised children using a lower number of doses.

Commenting on the significance of the findings, Professor Mills said:

"Although it will not be an easy task to implement, our findings should pave the way for an improved vaccine against whooping cough in

children."

The finding from Science Foundation Ireland-funded TCD research was published online last week in the leading peer-review journal *PloS Pathogens*. The challenges with the current pertussis vaccine will be a central theme of the 10th International symposium on Bordetella being organised by Professor Mills in Trinity College Dublin in September of this year.

Provided by Trinity College Dublin