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Research Progress on TR-Flu, an Intranasal Flu Vaccine in Dry Powder Form **(First Report)**

Shin Nippon Biomedical Laboratories, Ltd. (SNBL) is currently developing TR-Flu, an intranasal influenza vaccine, utilizing SNBL's novel intranasal drug delivery system (μco^{TM} System). SNBL today announces its progress in researching TR-Flu to induce increases in the production of mucosal sIgA¹, an important antibody in the first line of defense in the prevention of viral infections.

As a first step, SNBL developed a new method for the powderization of injectable liquid form human influenza vaccines, creating solid form fine particles while retaining the activity of the original vaccines. TR-Flu in intranasal dry powder form was then prepared using powdered human influenza vaccine antigen.

TR-Flu was administered intranasally to cynomolgus monkeys in order to compare antibody production induced by TR-Flu with that induced by traditional subcutaneous injection. No adjuvant² was added to TR-Flu in this study. Compared to subcutaneous injection, intranasal TR-Flu induced 50 times the levels of nasal mucosal sIgA. In contrast, as expected from existing research, the immune response induced by subcutaneous injection was primarily production of serum IgG³; subcutaneous injection led to approximately 5 times the levels of serum IgG when compared to TR-Flu. Mucosal sIgA, the antibody primarily induced by TR-Flu, is considered to be the first line of defense in the prevention of viral infections, as it attacks the virus on the mucosal membrane before it enters the body (Asahi Y. *et al.*, J. Immunol. 2002 Mar 15; 168 (6): 2930-2938). By contrast, serum IgG works either by controlling disease onset by fighting off viruses that have already entered the body, or by preventing infections from increasing in severity.

Furthermore, in the study, compared to a liquid intranasal spray, which are relatively easy to formulate, intranasal TR-Flu induced more than 3 times the levels of both nasal mucosal sIgA and serum IgG. As TR-Flu induced increases in the production of both nasal mucosal sIgA and serum IgG compared to the liquid intranasal spray, TR-Flu is expected to be highly effective as the first line of defense in the prevention of viral infections.

It is strongly expected that intranasal delivery of influenza vaccines is very cost-effective, as neither a needle nor a syringe are required; QOL is also improved due to the potential for pain free self administration. In addition, it is strongly expected that nasal mucosal sIgA will be effective in preventing both seasonal influenza virus infections and pandemics⁴ caused by mutant viruses (such as new variant influenza) (Asahi Y. *et al.*, J. Immunol. 2002 Mar 15; 168 (6): 2930-2938). The safety and effectiveness of μco^{TM} System, the breakthrough technology utilized in TR-Flu, have already been demonstrated in the development of SNBL's lead product candidate, an intranasal formulation of granisetron (development code: TRG), through its Phase 2 clinical study. Going forward, SNBL is planning to focus further on the research and development of TR-Flu by optimizing its formulation and conducting clinical studies.

The effect of this new venture on the earnings of SNBL's current term is minimal.

Notes:

- ¹ sIgA: A secretory antibody that exists on the mucosal membrane. Plays an important role as the first line of defense against bacteria and viruses that attempt to invade the body through mucosal membranes such as the membranes of the respiratory tract.
- ² Adjuvant: A substance administered with a vaccine if the necessary immune response cannot be achieved by administration of the vaccine alone; increases the immune response, such as antibody production, when administered with a vaccine.
- ³ IgG: The most abundant antibody in serum. Plays an important role in the body's immune response to invading bacteria and viruses.
- ⁴ Pandemic: An infectious disease spread on a global scale.