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The Effects of Salt Intake in the Induction of Influenza Virus-Specific Adaptive Immune Responses

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Summary

Influenza A virus, a negative-stranded RNA virus that belongs to the *Orthomyxoviridae* family, is responsible for annual epidemics that cause severe morbidity or death in approximately 5 million people worldwide. The constant pandemic potential of novel influenza subtypes remains a serious threat to public health, as illustrated by the recent pandemics involving swine H1N1 and avian H7N9. Therefore, there is an urgent need to develop effective vaccines against influenza viruses. The innate immune system, the first line of defense against pathogens, relies on pattern recognition receptors (PRRs) to detect pathogen-associated molecular patterns (PAMPs). For example, influenza genomic RNA is recognized by Toll-like receptor (TLR)-7, which is expressed in late endosomes, whereas the cytosolic sensor, retinoic acid inducible gene-I (RIG-I), detects 5'-triphosphates within the influenza viral genome in infected cells. Signaling via these receptors activates antigen-presenting cells (APCs). These cells produce type I interferons (IFNs) and proinflammatory cytokines, which help to establish an antiviral state, recruit additional immune cells, and direct the adaptive immune response. The type I IFNs not only limit viral replication but also act as a natural mucosal adjuvant for intranasally administered influenza vaccines. Many studies show that mucosal immunity induced by natural respiratory influenza infections is more cross-protective against subsequent infection by variant viruses than systemic immunity induced by parenteral immunization with inactivated vaccine. Therefore, to develop an effective vaccine, it is desirable to mimic the process of natural infection that bridges the innate and adaptive immune responses. For example, intranasally inoculated formalin-inactivated influenza virus vaccine induces protective immunity against both homologous and heterologous viruses; this is probably because the vaccine retains the viral genomic RNA that stimulates TLR7/8. By contrast, a split influenza vaccine does not induce antigen-specific immunity when the vaccine is introduced intranasally. Recent studies have demonstrated that microbiota critically regulates the virus-specific adaptive immune responses following influenza virus infection. In addition, several studies have indicated that high salt intake triggers enteric dysbiosis. Thus, we examined the effects of high salt intake on induction of the virus-specific adaptive immune responses following influenza virus infection. To this end, we fed mice 2% NaCl in drinking water continuously for 2 weeks before influenza virus infection. However, we did not see any significant differences in the virus-specific CD8T cell responses in the lung or survival rate of high salt-fed mice compared with control mice. Further studies are required to determine the effects of high salt intake on gut microbiota composition and the induction of mucosal immune responses against influenza virus infection.