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Chloride Ion Contribution to Leukocyte Activation and Organ Inflammation

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Summary

Recently the relationship between salt and immune function has been rapidly attracting attention. However, the target of research is often the differentiation process of lymphocytes, monocytes, and macrophages. In this study, we examined the role of chloride ion, which is a principle component of salt, in the immune function of neutrophils, which controls non-specific biological defense in the innate immune system. Neutrophils release superoxide and hypochlorous acid in a respiratory burst and exert a bactericidal action, and this dysfunction leads to individual-level susceptibility to infection.

First, neutrophil respiratory bursts were induced in bone marrow neutrophils with phorbol 12-myristate 13-acetate (PMA), which was evaluated using a luminol reaction signal that responds sensitively to hypochlorous acid. The luminol response was significantly reduced in neutrophils pretreated with a neutrophil peroxidase (MPO) inhibitor or MPO-deficient neutrophils. This indicates that the superoxide produced by the respiratory burst is converted to hypochlorous acid by MPO.

Next, we confirmed that the cystic fibrosis transmembrane conductance regulator (CFTR), which is a cell membrane transporter responsible for the intracellular migration of chloride ions, is expressed in neutrophils. We created cells infected with viral vector particle expressing shRNA against *Cftr* gene and *Cftr*-deficient mouse. This allows us to elucidate whether neutrophil dysfunction partly explains refractory chronic bacterial infection in patients with cystic fibrosis.

In the future, we will examine the effects of CFTR on neutrophil function in terms of self defense against infection and aseptic autoimmune diseases.