**The Effect of Bacterial Oligoribonucleotides on Stimulating the Immune System**

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**Abstract**

Oligoribonucleotides (ORNs) are small chains of ribonucleotides. ORNs are used to detect complementary RNA and can change to function of the RNA they bond to. Previous studies recently have demonstrated the anti-viral, anti-bacterial and anti-inflammatory properties of ORNs. However, not enough research has been done to determine the specific interactions between ORNs and the immune system to cause such effects. This study will compare ORNs released by Lactobacillus casei to the L. casei genome to determine what type of RNA transcripts are released. Each ORN will be aligned to a similar area in the genome and the number of ORNs that match to each sequence in the genome will be recorded. The type of RNA transcript could help formulate a hypothesis on interactions between ORNs and the immune system. Previous studies in both mice and humans have shown modified ORNs were able to stimulate the immune system by activating receptors 7 and 8, which means the ORNs likely stimulate the toll like receptors. Future studies should continue to study the effects of ORNs on the immune system and explore the interactions between them. A future goal of this study would be to create a dietary probiotic or nasal spray using ORNs to reduce infection and symptoms of respiratory diseases.

**Introduction**

Bacterial RNA could one day protect you from viruses. Bacterial oligoribonucleotides (ORNs) are small pieces of bacterial RNA and have been shown to have anti-inflammatory and anti-viral properties (Eigenbrod et. Al). One study by Melnichuk et. Al showed that modified ORNs can inhibit hemagglutinin activity of influenza viruses, preventing infection. Bacterial ORNs are released by bacteria when under stressful conditions, such as when being ingested by an animal. In a previous study by Melnichuk et. Al, modified ORNs were found effective in causing an immune response and preventing infection by the parainfluenza virus type 3. Patients were given either a common flu medicine or ORNs as treatment and the group given ORNs experienced shorter duration of symptoms and hospital. Another study by Forsbach et. Al demonstrated bacterial RNA was able to stimulate an immune response by activating the toll like receptors 7 and 8. Another study by Grigorov et. Al found that a methylated ORN was able to inhibit reverse transcription of the HIV DNA. Further research could create new treatments and medicines for increasing innate immunity, hopefully preventing or reducing the severity of respiratory diseases and other pathogenic diseases.

Previous studies have shown that ORNs are effective in inhibiting pathogenic activity and stimulating an immune response. A study by Eigenbrod et. Al found toll like receptors 7 and 8 are stimulated by detection of pathogenic genetic material and release type 1 IFN causing an immune response. Kandimalla et. Al created synthetic oligoribonucleotides that were able to activate toll like receptors 7 and 8. Similarly, research by Lan et. Al found a synthetic ORN was able to induce an immune response in mice using toll like receptors 7 and 8. Another study by Forsbach et. Al found comparable results in humans, where modified ORNs activated an immune response by stimulating toll like receptors 7 and 8. Forsbach et. Al modified a ORN and found it bypassed toll like receptor 7 and instead stimulated toll like receptors 8 and 9 to release type one IFN. Marchyshak et. Al used thioacetamide on mice to induce hepatotoxicity, which is drug induced liver damage. They found that a modified ORN, similar to the ORNs used in Melnichuk’s study, was able to reduce the damage by its anti-inflammatory properties. This shows the wide applications of ORNs to protective effects in animals. Studies even suggest ORNs could help develop improved cancer treatments. Fujita et. Al found that ORNs could be used to detect mutations and activate the immune system to fight tumors. Wang et. Al found that activating the immune system by synthetic ORNs causes strong immune responses with the ability to fight against tumor growth in mice. Although these studies were able to show ORNs were able to stimulate the immune system, it is not completely known how ORNs are able to interact with innate immune cells to activate them.

Lactobacillus casei is a harmless dietary bacterium that releases RNA fragments (ORNs) when in stressful environments. When L. casei bacteria release ORNs, the ORNs then interact with the immune cells in a way that is currently unknown. This study will analyze what types of RNA transcripts are being released as ORNs in order to formulate a hypothesis on how ORNs interact with the immune system to cause an immune response. Finding what type of RNA is released by L. casei when under stressful conditions will help determine how future studies can create ORNs that will most effectively stimulate the immune system.

The sequences of ORNs released by L. casei will be compared to the L. casei genome in order to find areas in the genome that match to many of the released ORNs. An area in the genome with many alignments from the RNA fragments could indicate a connection between the specific gene and the RNA fragment released to cause an immune response.

Previous studies have been able to find evidence that ORNs are able to stimulate the immune system and inhibit viral and bacterial activity, however, have not been able to find how ORNs interact with the immune system to do so. This study will analyze RNA sequence data from Lactobacillus casei, a harmless dietary bacterium. RNA fragments released by L. casei under stressful conditions have been found to stimulate innate immune response in animals and prevent subsequent infection from pathogens. This study will analyze the ORNs released by L. casei to the L. casei genome in order to determine what types of RNA transcripts are released and how they interact with the immune system.

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