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Cystic Fibrosis Research News

Title:

Phages as immunomodulators and their promising use as anti-inflammatory agents in a *cftr* loss-of-function zebrafish model

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What was your research question?

Phage therapy uses viruses called bacteriophages (phages) that kill bacteria like *Pseudomonas*. What happens when phages interact with human cells is still unclear. We asked whether phage therapy affects the cells of the immune system.

Why is this important?

The goal of our research is to increase safety and effectiveness of phage therapy in the treatment of recurrent/chronic bacterial infections. Understanding the interaction between phages and human cells might open new possibility in phage manipulation and administration for therapeutic benefits, especially in diseases such as Cystic Fibrosis (CF).

What did you do?

In this work we used a zebrafish model of CF because, although without lungs, it reproduces some of the features presented by patients with CF and can be easily manipulated with low experimental costs. This CF zebrafish model presents a hyper-inflammed state as seen in CF lungs, in the absence of exogenous bacterial infections. We injected a cocktail composed of four different phages into the zebrafish embryos and observed its effects on immune system activation. Activation was measured by analysing the expression of inflammatory markers and the recruitment of host-immune cells in response to phage injection.

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What did you find?

Our results demonstrate that phages lessen inflammation in zebrafish by reducing the recruitment of host-immune cells toward the site of inflammation. We speculate that the immunomodulatory action of phages may be elicited through the interaction between phage proteins and receptors of an important pathway in human cells that is generally activated following infection , namely the Toll-like receptor pathway.

What does this mean and reasons for caution?

This indicates that phages not only counteract the bacterial infection, but also play a role in host immune modulation. They could ease high inflammatory states, such as those present in patients with CF. A reason for caution is that other groups have reported that phages can increase inflammatory activity, making urgent to better understand their interaction with the immune system before their introduction as therapeutic option in CF.

What's next?

Future works are necessary to further describe how phages interact with the host-immune system and especially which phage components are able to modulate immune cells. This is important for the use of phages as therapeutic agents.

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