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Immunity Revolution

Training Innate Immunity for Enhanced Defense

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Immunity is defined as the body's ability to resist an attack from a particular infectious disease or pathogen. Immunity can be developed naturally or by prior exposure to harmless versions of disease or pathogen. Diving deeper into immunity knowledge, we find that natural immunity is called innate immunity, the first line of defense. Epithelial cells, mucus flows, and tears are all examples of innate immunity. Adaptive immunity is the secondary defense inside our bodies with the recruitment of antibodies, found in vaccines. While innate immunity can deal with all kinds of pathogens, adaptive immunity comprises specialized, systemic cells and functions to eliminate specific pathogen growth. The B-cells, antibody-producing factories, can generate memories of the pathogen's attack for faster pathogen recognition in the next fight. Previously, researchers thought that memory has always been the unique feature of adaptive immunity. However, scientists recently found that we could train innate immunity. In reality, more organisms lack adaptive immunity in advance, making innate immunity's role in protecting an organism's survival ever more substantial; ultimately, this is what has led to research on trained immunity.

The common concept of training the innate immune system is to have early exposure of disease or pathogens at a harmless level. This is to aid in pathogen recognition before our bodies meet the harmful ones, called by the funny name 'real pathogens.'

One familiar example of training the immune system is using a vaccine from degraded viruses — weakened or harmless pathogens from specific diseases — to prevent infections. For instance, let us say that a child was injected with tuberculosis vaccines in the first ten days after birth. This does not mean the child had tuberculosis soon after birth. Rather, when injecting tuberculosis vaccines, the child's immune system could recognize the virus causing tuberculosis and "analyze" it. Most importantly, the child's immune system learns how to fight against the tuberculosis virus. The child's immune system then could defeat the viral attack if a new tuberculosis challenge were to happen. Vaccines are an early prevention method for this child's survival.

With a similar mechanism of early exposure to the pathogen's sources, some scientists discovered we could train innate immunity by giving the intended approach to diseases multiple times. When conducting this research, scientists chose *Drosophila melanogaster*, or fruit flies, as the ideal object organism before they concluded about the benefit of trained immunity in human health. Fruit flies do not have adaptive immunity; they only possess innate immunity. Furthermore, more scientists immerse themselves in researching trained immunity because they can observe human immunodeficiency disorders related to T-cell and B-cell deficiencies. Thus, scientists want to boost the innate ability of defense to prevent patients' deaths and prolong survival rates.

Recently, a group of Japanese scientists established experimental systems for detecting the trained immunity in *Drosophila melanogaster* through training exposure to low-pathogenic bacteria, *Micrococcus luteus* and *Salmonella typhimurium*. Then, in continuous days, living flies trained with exposure would compute into a secondary test, with a challenge by a lethal bacteria dose of *Staphylococcus aureus* or *Pseudomonas aeruginosa*.

Scientists used the *Drosophila melanogaster* strain Orgeron-R from Bloomington *Drosophila* Stock Center raised on

standard cornmeal medium at 25 degrees Celsius. Only male flies aged four to seven days were split into two groups to participate in the systems. The first male flies' generation was collected and continued for four to seven days before training progressed. Scientists prepared a bacteria solution of MI or St drawn into a glass needle and injected it into the body cavity of the fly thorax by using the micromanipulator. After six days incubating at 25 degrees Celsius, the male flies were exposed to the lethal challenge of bacteria to evaluate the training quality. Scientists used high-concentration of Sa or Pa bacteria for a secondary challenge. Data from the survival assay were calculated by the percentage of flies living after the lethal challenge.

Both MI and St systems showed that *Drosophila melanogaster* flies with training in low-pathogenic bacteria could better survive the high-pathogenic bacteria. Roughly 35 percent of male flies with training in MI systems survived throughout day six after the lethal challenge, compared to none of the flies in the group without training being able to survive through the dose shock. This positive trend was similarly observed in the St system. Remarkably, 100 percent of experienced male flies survived after suppressing the *P. aeruginosa* lethal dose, while naive male flies from the control group would have died after 24 hours. In summary, the Japanese scientists successfully generated trained immunity for innate defense in *Drosophila melanogaster*, then concluded that the early training process benefited the *Drosophila melanogaster* survival rates toward pathogens.

In developing trained immunity to help boost innate immunity in animals, especially humans, scientists propose to test other animals whose genomes share a close relationship to the human genome after the successful experiment in *Drosophila*

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melanogaster. Further research investigates trained immunity in mouse models, in which animals possess both innate and adaptive immunity. When adaptive immunity malfunctions, innate immunity with better training experience will benefit patients' health, patching up the loss of antibodies and adaptive mechanisms. In discovering trained immunity, scientists give hope to patients having immunodeficiency disorders to prolong survival. ●●●