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Researchers connect severity of 'kissing disease' to T-cell population

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Acute infectious mononucleosis (AIM), also known as mono or the "kissing disease," is caused by the Epstein-Barr Virus (EBV). In a paper published this week in *mBio*, researchers connect the onset and severity of mono to T-cells that react to both EBV and the influenza A virus, which causes the flu. The study represents one of the first reported links between how a person's immune system responds to infection and receptors on T-cells, which instigate the immune response.

A person's immune system remembers the disease-causing microbes it encounters over a lifetime. Each time a person is infected with some pathogen - like the influenza virus - T cells retain information. "You develop memory cells every time you have any infection," says pathologist and study leader Liisa Selin at the University of Massachusetts Medical School in Worcester, Mass. As a result, individuals develop memory cells with a heterogeneous mix of receptors that evolves during their lifetime.

"Everybody has different memory cells with different T cell receptors on them," says Selin, "even genetically identical twins." A person's repertoire of receptors, she says, "determines whether you get infectious mono or not."

Not everyone does. According to the Centers for Disease Control and Prevention, almost everyone - 95 percent of the world population - is infected with EBV by the time they reach 30. However, children infected with the virus rarely suffer the debilitating symptoms of mono,

like fatigue, fever, and sore throat. Even some adults barely notice the infection. That may be because of their immune history: They don't have the specific receptors in those cross-reactive memory T cells that trigger a severe immune response, Selin says.

She and her colleagues studied blood samples collected over a decade from college students: 32 diagnosed with mono, separated into two groups by severity of the disease, and 17 healthy controls who had tested positive for EBV. People with severe cases of mono had 25 times more T-cells that reacted to both Influenza A and EBV, per volume of blood, than the healthy controls. Similarly, people with mild cases had 10 times more of the cross-reactive T-cells than the EBV+ participants.

EBV is a tricky virus that can hide quietly for years - or even decades - in the tonsils, says Selin. The new work may help explain how a person's history of disease exposure can influence their susceptibility to disease.The findings suggest, for example, that a previous flu infection may make mono worse.

"If you have a lot of these flu memory T-cells in your tonsils and you get EBV, instead of silently hanging around, it activates those memory cells," says Selin. She hypothesizes that if young adults can avoid the flu, as by getting vaccinated, they might have fewer memory T-cells that were cross-reactive to influenza. As a result, they may be less likely to develop severe mono after EBV infection.

The findings reach beyond the kissing disease: EBV is associated with many autoimmune diseases, though the reasons why remain a mystery. Having infectious mono, for example, may increase a person's risk of developing multiple sclerosis.

The study adds to a growing body of research aimed at understanding the connections among T cell receptors, infectious disease outcomes and

autoimmunity. A clear understanding this relationship, Selin says, may enable researchers to identify T-cells with specific receptors that can worsen the symptoms and pathology during an infection and may even sometimes lead to autoimmunity.

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