Study sheds light on cellular interactions that lead to liver transplant survival

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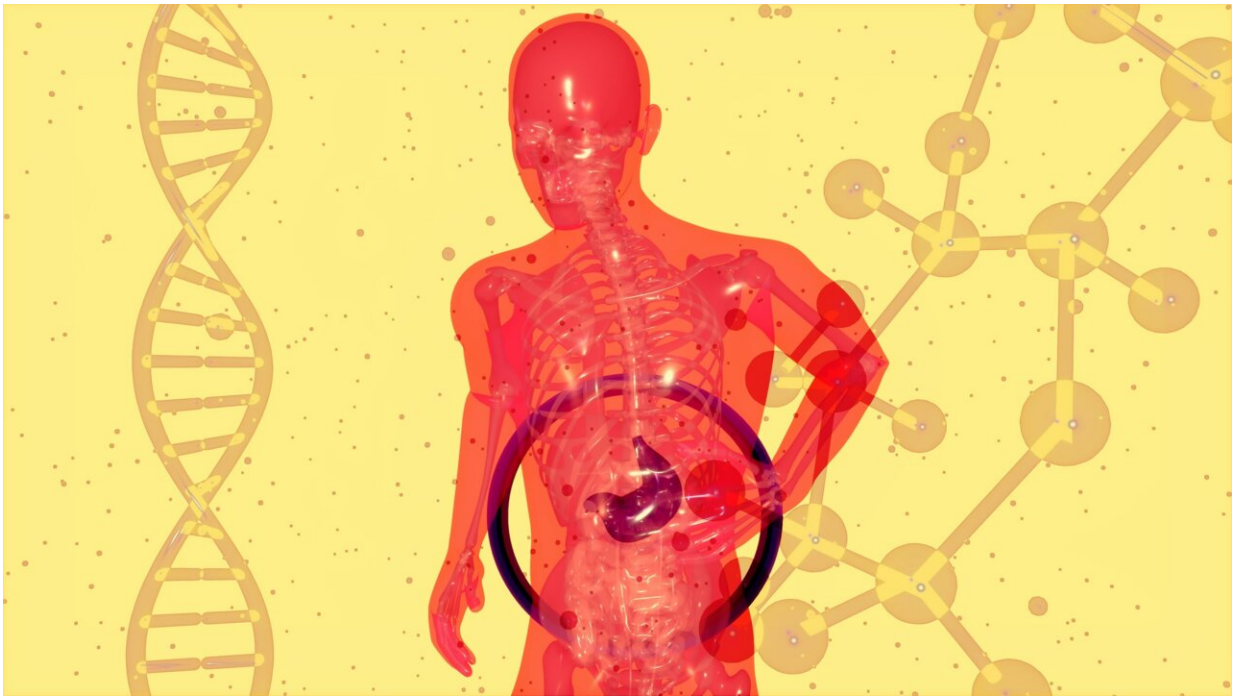

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A new study in *Gastroenterology* identifies how certain proteins in the immune system interact and lead to organ rejection. The study, which involved experiments on mice and human patients, uncovered an important communication pathway between two molecules called CEACAM1 (CC1) and TIM-3, finding that the pathway plays a crucial role in controlling the body's immune response during liver

transplantation.

When an organ is transplanted from a donor to a recipient, the recipient's immune system recognizes the transplanted tissue as foreign, activating an immune response that can lead to rejection. T cells play a significant role in this response.

To prevent or manage transplant injury caused by T cell-mediated rejection, immunosuppressive medications are commonly prescribed. These drugs suppress the immune response and reduce the activity of T cells, helping to prevent rejection and preserve the function of the transplanted organ.

Advancements in surgical techniques, immunosuppressive medications, and post-transplant care have significantly improved liver transplant survival rates, which exceed 90% at one year and around 70-75% at year five. Survival can vary depending on factors, including the recipient's immune response.

In the new study, scientists led by Dr. Jerzy W. Kupiec-Weglinski, director of the Dumont-UCLA Transplantation Research Center, investigated the role of a specific type of immune cell, called CD4+ T cells, along with proteins called CEACAM1 (CC1) and TIM-3, in how the immune system responds to a transplanted liver. They conducted experiments using mice while also analyzing data from human patients who had undergone liver transplantation.

In the mouse experiments, the scientists transplanted livers from normal mice into mice that lacked the CC1 protein. They found that the livers transplanted into mice without CC1 suffered more liver injury compared to livers transplanted into mice with CC1. They also noticed that there were more special immune cells called TIM-3+CD4+ T cells in mice with CC1.

To understand this better, the scientists introduced T cells lacking CC1 into mice that were missing other immune cells. They observed that this led to more liver damage. However, when they made these T cells produce more TIM-3 and put them into the mice without CC1, the liver damage was reduced.

They also reviewed outcomes of human liver transplants and indeed found that when the levels of CC1 increased during the transplant procedure, the transplanted livers were less damaged, and there were fewer complications and rejections.

"This study gives us an important insight into the essential beneficial role of these factors in liver transplant outcomes," said Dr. Kupiec-Weglinski. "By focusing on how CC1 and TIM-3 work together in T cells, we can potentially protect the liver transplant and improve the overall success of the procedure."

While the findings are an important step, the authors say more research is needed to understand these interactions and how that knowledge can potentially impact the success of liver transplants.

More information: T cell CEACAM1—TIM-3 crosstalk alleviates liver transplant injury in mice and humans, *Gastroenterology* (2023).

Provided by University of California, Los Angeles