

CELL THERAPY

## Cell transplantation for spinal cord injury: sex matters

Pitonak, M. et al. *Nat. Commun.* **13**, 5380 (2022)

A new study highlights the importance of considering the biological sex of both donor cells and hosts in cell transplantation studies for spinal cord injury (SCI) by showing that donor–recipient sex mismatch triggers immune responses in mice.

SCI is a damage to the spinal cord that often causes permanent changes in strength, sensation and other body functions. Cell transplantation is a promising therapeutic strategy to replace damaged nerve cells after SCI, but the true potential of this approach is still under investigation. Although the biological sex of the host is recognized as an important variable affecting outcomes in cell transplantation studies for SCI, to date nothing is known about the effects of the sex of the donor cells.

To address this question, lead investigator Jennifer Dulin and colleagues at Texas A&M University transplanted sex-matched or sex-mismatched neural progenitor cells (NPCs) into the injured spinal cords of

adult male and female mice. The researchers used donor cells and hosts that were both on a C57BL/6 inbred background to ensure sex was the only biological variable across experimental groups. Mouse tissue analysis four weeks post-transplantation revealed that male NPCs transplanted into female mice evoked an immune response, characterized by hypervascularization of grafts, infiltration of T-cells into grafts and increased perivascular cell density. “This doesn’t happen in male mice that receive female cell grafts, so it appears to be a one-way street with female immune rejection of male cells,” comments Dulin.

Several human clinical organ transplantation studies have already described this phenomenon, reporting that female humans are more likely to have adverse events and even reject organs from male donors, including kidneys, liver, lungs, hearts, and even corneas. “To my knowledge, however, this is the first time

anyone in the spinal cord injury field has looked into the issue of the sex of donor NPCs. This could be important, since there are human NPC transplantation clinical trials going on right now, in Japan - and the sex of the cells being tested is male,” says Dulin.

Moving forward, Dulin’s team will focus on identifying the mechanism by which male cells evoke immune rejection in females and determining the long-term effects of graft rejection. “We are interested to find out whether months or even years down the road, this sex mismatch issue could lead to adverse outcomes, such as inflammation, the development of pain, or worsened motor performance,” concludes Dulin.

Alexandra Le Bras

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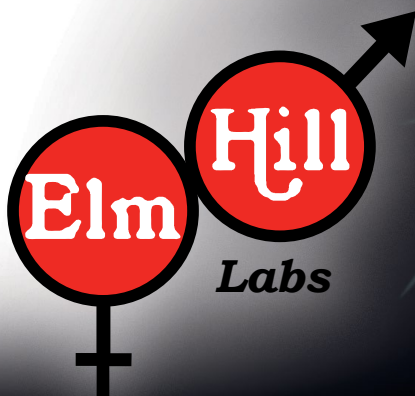
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