Possible progress against Parkinson's and good news for stem cell therapies

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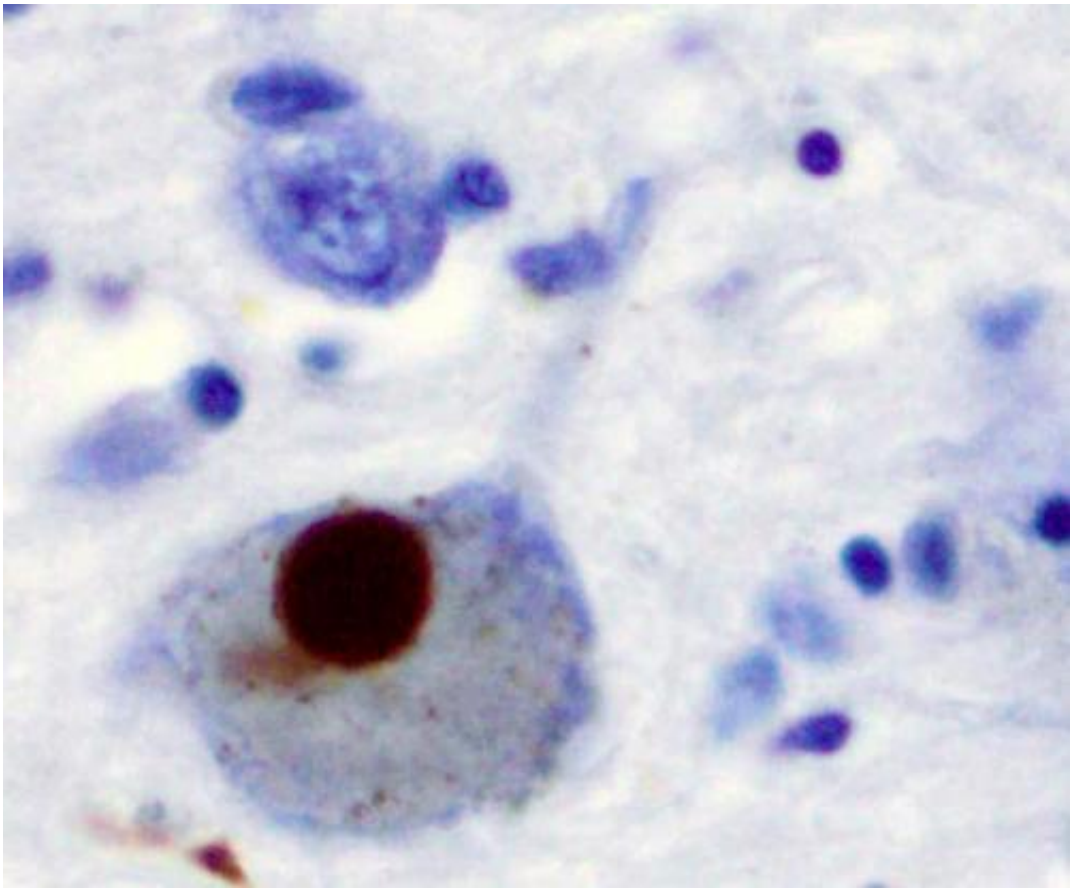

Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneural Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

Brazilian researchers at D'OR Institute for Research and Education

(IDOR) and Federal University of Rio de Janeiro (UFRJ) have taken what they describe as an important step toward using the implantation of stem cell-generated neurons as a treatment for Parkinson's disease. Using an FDA approved substance for treating stomach cancer, Rehen and colleagues were able to grow dopamine-producing neurons derived from embryonic stem cells that remained healthy and functional for as long as 15 months after implantation into mice, restoring motor function without forming tumors.

Parkinson's, which affect as many 10 million people in the world, is caused by a depletion of dopamine-producing neurons in the brain. Current treatments include medications and electrical implants in the brain which causes severe adverse effects over time and fail to prevent disease progression. Several studies have indicated that the transplantation of embryonic stem cells improves motor functions in animal models. However, until now, the procedure has shown to be unsafe, because of the risk of tumors upon transplantation.

To address this issue, the researchers tested for the first time to pre-treat undifferentiated mouse embryonic stem cells with mitomycin C, a drug already prescribed to treat cancer. The substance blocks the DNA replication and prevents the cells to multiply out of control.

The researchers used mice modeled for Parkinson's. The animals were separated in three groups. The first one, the control group, did not receive the stem cell implant. The second one, received the implant of stem cells which were not treated with mitomycin C and the third one received the mitomycin C treated cells.

After the injection of 50,000 untreated stem cells, the animals of the second group showed improvement in motor functions but all of them died between 3 and 7 weeks later. These animals also developed intracerebral tumors. In contrast, animals receiving the treated stem cells

showed improvement of Parkinson's symptoms and survived until the end of the observation period of 12 weeks post-transplant with no tumors detected. Four of these mice were monitored for as long as 15 months with no signs of pathology.

Furthermore, the scientists have also shown that treating the stem cells with mitomycin C induced a four-fold increase in the release of dopamine after in vitro differentiation.

"This simple strategy of shortly exposing pluripotent stem cells to an anti-cancer drug turned the transplant safer, by eliminating the risk of tumor formation", says the leader of the study Stevens Rehen, Professor at UFRJ and researcher at IDOR.

The discovery, reported on April in the journal *Frontiers in Cellular Neuroscience*, could pave the way for researchers and physicians to propose a clinical trial using pluripotent stem cells treated with mitomycin C prior to transplant to treat Parkinson's patients and also other neurodegenerative conditions.

"Our technique with mitomycin C may speed the proposal of clinical trials with pluripotent cells to several human diseases", says Rehen. "It is the first step to make this kind of treatment with stem cells possible".

More information: M. Acquarone, T. Melo, F. G. Meireles Ferreira, J. Brito-Moreira, G. Oliveira, S. Ferreira, N. Castro, F. Tovar-Moll, J. C. Houzel, S. K. Rehen. Mitomycin-treated undifferentiated embryonic stem cells as a safe and effective therapeutic strategy in a mouse model of Parkinson's disease. *Frontiers in Cellular Neuroscience*. Available online. journal.frontiersin.org/articl … .2015.00097/abstract

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