THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

December 13, 2018

Committee on Oversight and Government Reform

Chairman Jim Jordan
Ranking Member Raja Krishnamoorthi
Subcommittee on Healthcare, Benefits, and Administrative Rules

Chairman Mark Meadows
Ranking Member Gerald Connolly
Subcommittee on Government Operations

Dear Chairman Jordan, Chairman Meadows, Ranking Member Krishnamoorthi, and Ranking Member Connolly:

As you hold a hearing exploring alternatives to fetal tissue research, please consider how this research benefits patients across the country, including Americans living with Parkinson's disease. Federal policy that supports scientific freedom and facilitates the responsible investigation of every promising therapeutic approach is our best hope for accelerating the development of improved treatments and cures. Unnecessarily impeding such research hurts people living with disease and their families.

Fetal Tissue Research Is Vital to Advancing Parkinson's Breakthroughs
Since launching in 2000, The Michael J. Fox Foundation for Parkinson's Research has funded more than $800 million in research to speed a cure for Parkinson's disease, a degenerative brain disease that impacts an estimated 1 million Americans, second only to Alzheimer's disease in prevalence. Available Parkinson's medications inadequately treat symptoms while the underlying progression continues; a disease-modifying therapy remains patients' greatest unmet medical need.

Parkinson's disease occurs when the brain cells that make dopamine, a chemical that coordinates movement, stop working or die. As such, restoring or replacing damaged dopamine neurons in the brain has been a long-sought goal in Parkinson's research. Fetal tissue and related regenerative approaches are among those areas of investigation that have fundamentally moved our field forward since the 1980s.

The use of fetal tissue transplants in the 1980s and 1990s furnished proof of principle that it was possible to replace some dopamine cells in the brains of people with Parkinson's. First,

preclinical research demonstrated that transplanting the fetal cells significantly improved motor symptoms in rodents.[1] Researchers subsequently conducted rigorous clinical trials in humans across the world, including countries such as China[2], the Czech Republic[3], Poland[4], Sweden[5], the United Kingdom[6] and others. While these early trials were not able to replace all lost dopamine cells in people with Parkinson's, they provided a critical framework for improving the next generation of stem cell-based transplants, some of which are now in clinical testing. Without the early trials, stem cell approaches to Parkinson's treatment would not be where they are today.

These same fetal tissue trials led to a groundbreaking discovery in 2008, when posthumous examination of brain tissue from trial participants unexpectedly demonstrated that dysfunction in the protein alpha-synuclein spreads from one cell to another in the brain.[7] (In Parkinson's, alpha-synuclein clumps together to form aggregates called Lewy bodies, which scientists believe are toxic and lead to disease symptoms.) Researchers discovered that alpha-synuclein can move from original brain cells into transplanted brain cells made from fetal tissue. This stunning finding shifted the field's understanding of Parkinson's pathology and transformed researchers' ability to target this protein, which now represents the most promising therapeutic strategy to stop Parkinson's in its tracks.

Today, fetal tissue research is the "gold standard" for scientists seeking new insights into neurodevelopment, and specifically the development of the dopaminergic system. Its flexibility, rapid ability to replicate and decreased chance of rejection make it essential for modeling dopamine cell development. This activity cannot be satisfactorily recapitulated by any other tissue or cell. (When dopamine cells are created using other materials, such as induced pluripotent stem cells derived from adult skin cells, researchers must validate these results using fetal tissue.) Without access to fetal tissue, researchers would be deprived of an irreplaceable tool by which to advance understanding of vital neurodevelopment processes. It

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[1] Perlow MJ, Freed WJ, Hoffer BJ, Seiger A, Olson L, Wyatt RJ. Brain grafts reduce motor abnormalities produced by destruction of nigrostriatal dopamine system. Science. 1979;204:643–647.
[2] Jiang NJ, Tang Z, Zhang F, Li S, Jiang D. Human fetal brain transplant trials in the treatment of Parkinsonism. Acta Acad Med (Shanghai) 1987;14:77; Ben R, Ji-Chang F, Yao-Dong B, Yie-Jian L, Yi-Fang Z.; Transplantation of cultured fetal adrenal medullary tissue into the brain of Parkinsonian. Acta Neurochir Suppl (Wien) 1991;52:42–44.
[3] Subrt O, Tichy M, Vladyka V, Hurt K. Grafting of fetal dopamine neurons in Parkinson's disease. The Czech experience with severe akinetic patients. Acta Neurochir Suppl (Wien) 1991;52:51–53.
[4] Zabek M, Mazurowski W, Dymecki J, Stelmachów J, Gawur B, Trautsolt W, Zawada E. Transplantation of fetal dopaminergic cells in Parkinson disease Neurol Neurochir Pol. 1992;Suppl 1:13–19.
[5] Lindvall O, Brundin P, Widner H, Rehncrona S, Gustavii B, Frackowiak R, Leenders KL, Sawle G, Rothwell JC, Marsden CD. Grafts of fetal dopamine neurons survive and improve motor function in Parkinson's disease. Science. 1990;247:574–577.
[6] Hitchcock ER, Kenny BG, Henderson BT, Clough CG, Hughes RC, Detta A. A series of experimental surgery for advanced Parkinson's disease by fetal mesencephalic transplantation. Acta Neurochirurgica Suppl. 1991;52:54–57.
[7] Li J-Y, et al. Lewy bodies in grafted neurons in people with Parkinson's disease suggest host-to-graft disease propagation. Nat Med. 2008;14:501–503.

is impossible to know what future discoveries may be missed in the event of a withdrawal of federal funding for fetal tissue research.

Fetal Tissue Research Enjoys Bipartisan Support and Is Well Regulated
Fetal tissue research enjoys bipartisan support in the U.S. Congress and has been funded by the National Institutes of Health for decades. Multiple federal panels and reviews, conducted under both Republican and Democratic congressional majorities and presidential administrations, have evaluated fetal tissue research and concluded that it is critical for lifesaving biomedical research. This research has long been viewed as good public policy to improve human health and has proceeded with public support. Oversight of fetal tissue research adheres to rigorous legal and ethical standards. Fetal tissue is obtained exclusively through highly regulated research processes, and only with donor consent.

Patients Have the Right to Insist on the Responsible Pursuit of Every Promising Therapeutic Approach
Basic scientific research at the federal level is vital to the discovery of new treatments and cures for life-threatening illnesses, including Parkinson's disease. The Michael J. Fox Foundation exists to leverage this federal investment. We deploy philanthropic capital with a keen focus on bridging the translational gap — chaperoning more good ideas into clinical testing. As federally funded research does more, we can do more, and together we can accelerate real results to the American families putting their faith in us. But we can do so only if we know that federal investment in basic science will be premised on the potential to help people with disease, and not on politics.

It is a human right — if not a human obligation — to insist that all paths of research be followed toward potentially life-transforming treatments for disease. The number of people living with Parkinson's is only rising as our population ages. Now is not the time to hold back federal funding for any promising avenue of inquiry. We urge the Members of the Committees to take every action available to ensure that fetal tissue research may continue to be thoroughly interrogated for the benefit of Americans living with disease.

Thank you for the opportunity to supply information.