

December 13, 2018

The Honorable Jim Jordan  
Chairman  
House Oversight and Government Reform  
Subcommittee on Healthcare, Benefits, and  
Administrative Rules  
2056 Rayburn HOB  
Washington, DC 20515

The Honorable Raja Krishnamoorthi  
Ranking Member  
House Oversight and Government Reform  
Subcommittee on Healthcare, Benefits, and  
Administrative Rules  
515 Cannon House Office Building  
Washington, DC 20515

Th Honorable Mark Meadows  
Chairman  
House Oversight and Government Reform  
Subcommittee on Government Operations  
1024 Longworth HOB  
Washington, DC 20515

The Honorable Gerry Connolly  
Ranking Member  
House Oversight and Government Reform  
Subcommittee on Government Operations  
2238 Rayburn HOB  
Washington, DC 20515

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

On behalf of the millions of patients throughout the nation and around the world, as well as the scientific and medical communities dedicated to advancing human health, the undersigned organizations and institutions write to express our collective and strong opposition to restrictions that would further impede fetal tissue research. Any new restriction on this critical work would obstruct research that is necessary for the development of new treatments for a wide range of serious diseases.

Public policy that facilitates ethically responsible research is in the best interest of patients worldwide. Decades of thoughtful deliberation on fetal tissue research has provided an ethical and policy framework for valuable medical research to progress, leading to the discovery of new treatments. We believe the ethical considerations fall heavily in favor of permitting federally supported fetal tissue research to continue, in accordance with current federal rules. To do otherwise would be disruptive to biomedical research and devastating to patients.

### **Fetal tissue research cannot be replaced with existing alternative research models**

It has been incorrectly claimed that other cells can be used to replace fetal tissue in biomedical research. In fact, cells in fetal tissue have unique and valuable properties that often cannot be replaced by other cell types. Cells from fetal tissue are more flexible and less specialized than cells from adult tissue and can be more readily grown in culture. The study of human fetal tissue also helps researchers understand how birth defects arise and how they can be prevented. It provides an unparalleled window into the complexity of human tissue development, including why serious congenital defects sometimes arise. While there have been some advances in recent years that have reduced the need for fetal tissue in certain areas of research, it remains critically important in many other areas. As representatives of the scientific and medical communities we are obligated to correct the record.

### Induced pluripotent stem cells (iPSCs) and organoids cannot replace fetal tissue research

It has been inaccurately stated that iPSCs and organoid models can replace fetal tissue research. These cells and model systems may reduce the need for fetal tissue to address certain questions, but they cannot replace it. Organoids can only be used to model certain aspects of human development that can be studied in culture (growing in laboratory dishes). There are many disease processes or therapies for which studies in tissue culture are not sufficient - in vivo studies are required. This is particularly true of diseases that involve interactions between different tissues or complex combinations of cell types.

- Organoids lack immune cells and tend to mimic early fetal development, making them inadequate for modeling immune responses to infection, inflammation, or later stages of fetal development.
- There is a general inability to form a functional human immune system with organoids or with iPSCs, or to model the complex interactions between different kinds of immune cells and supporting cells in lymphoid organs. For this reason, diseases that affect the immune system, such as HIV, are studied by transplanting human hematopoietic and lymphoid tissues into mice, creating a functional human immune system in vivo.
- iPSCs are an inadequate substitute for fetal tissue because the cells generated from iPSCs lack the complex environment and signaling between different cell types that leads to complete tissues and organs. For this reason, we are unable to generate human organs from these cells, making it impossible to study disease processes that involve the interaction of different cell types within human organs.
- The cells derived from iPSCs or organoids grown from adult tissues do not replicate cells that can be obtained from fetal tissue. The cells derived from iPSCs are too developmentally immature and the cells derived from adult tissues are too developmentally mature. This makes it impossible to study congenital diseases, like zika virus, that affect fetal tissues in the latter half of gestation.

There are cases in which diseases can be studied with cells derived from iPSCs or organoids. But even in those cases, the results have to be validated using fetal tissue as the “gold standard” reference material. As a result, fetal tissue remains critically important to understand human development and to validate iPSCs or organoid models.

### Established fetal cell lines are not adequate substitutes for fetal tissue research

While we support the continuation of research using established fetal cell lines, these cell lines are not a substitute for fetal tissue research. The existing fetal cell lines are limited to a small number of fetal cell types and stages. These cell lines can never obviate the need to study fetal tissue for the same reason that organoids and iPSCs could never completely replace fetal tissue: some diseases can only be studied in vivo where there are complex interactions among different cell types. Researchers cannot study the entire fetal development period or complex tissues without access to fetal tissue.

### The NeoThy mouse model cannot replace the BLT mouse model

It is not correct that the NeoThy mouse model (in which neonatal human thymic tissue and cord blood cells are transplanted into mice to form human blood and immune cells) can replace the BLT mouse model (in which fetal human bone marrow, liver, and thymic tissue are transplanted

into mice to form human blood-forming and immune systems). The BLT mice have human blood-forming stem cells that are maintained and that give rise to diverse types of human blood and immune system cells within human blood-forming tissues (liver and bone marrow). In contrast, the NeoThy mouse has only human thymic tissue in which one component of the human immune system can develop. Cord blood cells can be transplanted into NeoThy mice to transiently form other components of the blood forming system but in the NeoThy mouse this occurs in mouse blood-forming tissues, not in human tissues. Consequently, the NeoThy mouse does not fully model human blood cell production within human tissues. The NeoThy mouse may be adequate for some applications, but the BLT mouse more fully models the formation of human blood and immune system cells in human tissues and therefore is a more realistic model for many diseases. The NeoThy mouse is also still a new model that has yet to be fully vetted by the scientific community.

#### Tissue from spontaneous abortions cannot replace tissue from elective abortions

Tissue from spontaneous abortions is not a reliable substitute for tissue from elective abortions. Spontaneous abortions, commonly called miscarriages, often result from profound genetic defects, developmental abnormalities, or other conditions that undermine the usefulness of the tissue for research. Finally, spontaneous abortions generally do not occur in settings where the tissue can be adequately preserved for research.

#### **Fetal tissue research is critical for researching early human development**

Fetal tissue allows researchers to more fully understand congenital defects such as those of the heart or nervous system and to understand how viruses like the Zika virus impact fetal development. The use of donated fetal tissue has been critical for understanding how Zika virus crosses the placenta and impacts human brain development. The insights gained through studies of Zika virus in human fetal tissue are already guiding the development of therapies to prevent transmission of the virus. These examples illustrate how legislation that limits human fetal tissue research would hinder the development of critical new treatments and potentially cost lives.

#### **There are well-established and rigorous regulatory frameworks for fetal tissue research**

Rigorous legal and ethical oversight of fetal tissue research has been in place for decades. This research has garnered bipartisan support in the U.S. Congress and has been funded by the National Institutes of Health (NIH). Numerous federal panels and reviews, conducted under both Republican and Democratic congressional majorities and presidential administrations, have evaluated human fetal tissue research and have concluded 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. Legal and ethical frameworks that are already in place ensure appropriate oversight, and that the tissue is obtained legally and with donor consent. The fetal tissue that is used for research would be discarded if not donated for research.

#### **Fetal tissue research improves human health, and saves lives**

Historically, fetal tissue research has been critical for scientific and medical advances that have saved the lives of millions of people, including the development of vaccines against polio, rubella, measles, chickenpox, adenovirus, rabies, and treatments for debilitating diseases such as rheumatoid arthritis, cystic fibrosis, and hemophilia. Fetal tissue was also essential for the

development of a therapy to prevent the transmission of HIV (Truvada). It remains critical for ongoing clinical research for Amyotrophic Lateral Sclerosis (ALS), spinal cord injury, and Parkinson's disease. Fetal tissue is medically important to understand human development, to test new therapies, and as a source of cells for new cell therapies that offer the potential to improve the treatment of major public health problems.

If fetal tissue research had been prohibited decades ago, vaccines that have saved millions of lives would never have been developed, or their development would have been delayed. How many lives would have been lost? How many lives will be lost in the future if other lifesaving interventions are prevented or delayed by restricting future fetal tissue research?

We urge you to support the continuation of this important research to support the families who are relying on biomedical research to develop new treatments for diseases that affect their loved ones and millions of other people around the world.

Sincerely,

AIDS Action Baltimore  
Axis Advocacy  
AIDS Foundation of Chicago  
AIDS Treatment Activist Coalition  
Alliance for Aging Research  
American Academy of HIV Medicine  
American Association for the Advancement of Science  
American Association of Anatomists  
American Association of Colleges of Pharmacy  
American Association of Immunologists  
American Physiological Society  
American Society for Cell Biology  
American Society for Investigative Pathology  
American Society for Reproductive Medicine  
American Society of Hematology  
American Thoracic Society  
Americans for Cures  
Association of American Medical Colleges  
Association of American Universities  
Association of Independent Research Institutes  
Association of Public and Land-grant Universities  
AVAC  
Bailey House, Inc.  
Christopher & Dana Reeve Foundation  
Coalition for the Life Sciences  
Columbia University Irving Medical Center  
Council on Governmental Relations  
Endocrine Society  
Federation of American Societies for Experimental Biology (FASEB)  
Global Healthy Living Foundation  
Harvard University

HIV Medicine Association  
HIV+Aging Research Project-Palm Springs  
Housing Works  
International Rectal Microbicide Advocates  
International Society for Stem Cell Research  
ISCT, International Society for Cell & Gene Therapy  
Lupus and Allied Diseases Association  
Massachusetts General Hospital  
Nashville CARES  
NASTAD  
National Multiple Sclerosis Society  
New York University  
NMAC (Formerly known as the National Minority AIDS Council)  
Project Inform  
Research!America  
Rutgers Biomedical and Health Sciences  
Society for Neuroscience  
Stanford University School of Medicine  
Texans for Cures  
The Michael J. Fox Foundation for Parkinson's Research  
The Nebraska Coalition for Lifesaving Cures  
The State University of New York System  
The University of California System  
Treatment Action Group  
Tuberous Sclerosis Alliance  
University at Buffalo Jacobs School of Medicine and Biomedical Sciences  
University of Michigan  
University of Minnesota  
University of Pittsburgh  
University of Wisconsin-Madison  
Weill Cornell Medicine  
Yale University