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September 19, 2016

VIA E-MAIL [redacted]

The Honorable Jan Schakowsky
Ranking Member
Select Investigative Panel on Infant Lives
Energy and Commerce Committee
United States House of Representatives
2367 Rayburn House Office Building
Washington, DC 20515-6115

Dear Representative Schakowsky:

On behalf of the University of California, Los Angeles ("UCLA"), I have attached UCLA's response to your letter of July 28, 2016, requesting that UCLA provide the Select Investigative Panel on Infant Lives with information to better understand the importance of and risk to fetal tissue research.

UCLA conducts research using fetal tissue that is vital to an understanding of human biology and to efforts directed toward new treatments for a wide variety of adult and childhood diseases and medical conditions. Our research is conducted in full compliance with federal and state law and in accordance with our tripartite mission of education, research, and public service. The information provided below answers the five specific requests made in your letter.

Please note that UCLA has omitted identifying information from the enclosed documents based on concerns for the safety and security of individuals conducting research. Should you have any questions regarding this response, please contact me at [redacted]

Sincerely,

[redacted]

UCLA Health / David Geffen School of Medicine

cc: Honorable Marsha Blackburn c/o Matthew Tallmer
(via e-mail, [redacted])

1. **Past benefits of fetal tissue research.**

Since the 1930's, fetal tissue has been used in a broad range of research that has led to lifesaving discoveries. The Association of American Medical Colleges (AAMC), of which UCLA is a member, has previously noted that human fetal tissue research has been critical in establishing permanent cell lines for use in vaccine research for diseases such as polio, hepatitis A, measles, mumps, rubella, chickenpox, and rabies. These established cell lines are currently being used to develop an Ebola vaccine[1].

Fetal tissue proved to be necessary for the production of consumer vaccines against measles, rubella, rabies, chicken pox, shingles and hepatitis A. According to the journal Nature, at least 5.8 billion vaccine doses have been derived from fetal tissue lines.[2]

2. **Potential future benefits that might be gained through continued fetal research.**

Biomedical research continues to benefit from the use of new fetal tissue. According to the U.S. Department of Health and Human Services, "fetal tissue continues to be a critical resource for important efforts such as research on degenerative eye disease, human development disorders such as Down syndrome, and infectious diseases, among a host of other diseases.[3]"

As noted in the journal Nature, "In the past 25 years, fetal cell lines have been used in a roster of medical advances, including the production of a blockbuster arthritis drug and therapeutic proteins that fight cystic fibrosis and haemophilia." Yet, existing fetal material and cell lines "…are of limited use for scientists because they do not faithfully mimic native tissue and represent only a subset of cell types…. The lines can also accumulate mutations after replicating *in vitro* over time." New fetal material is critical if we are to continue to pursue vaccines for HIV and other diseases as well as create treatments and cures for devastating illnesses such as Parkinson's and Alzheimer's Disease, blinding eye disorders such a macular degeneration, diabetes, and schizophrenia. [4]

Our response to question 4 below cites a diverse range of diseases being studied by UCLA laboratories whose research requires the use of fetal tissues. These research activities are critical for the development of new therapies for the treatment of these diseases.

3. **Unique aspects of fetal tissue in research, in comparison with adult cells or other cellular organisms that might be used for research purposes**

As described in the following summary of research performed in UCLA laboratories (response to question 4), human fetal tissues are critical for current and future research activities for multiple

[1] AAMC Statement (March 18, 2016)
[2] http://www.nature.com/news/the-truth-about-fetal-tissue-research-1.18960
[3] HHS Letter to Senators Joni Ernst and Roy Blunt, August 14, 2015.
[4] http://www.nature.com/news/the-truth-about-fetal-tissue-research-1.18960

reasons. First, human fetal tissues exhibit biological properties that are distinct from those of tissues derived from children or adults, and these properties, often related to an enhanced capacity for growth and regeneration, can be highly desirable for the development of novel therapies. It therefore is critical to understand the unique properties of fetal tissues, which can be accomplished only through a direct analysis. Some therapies under development would require the direct use of fetal cells, such as recent clinical trials using fetal neural cells to treat patients with spinal cord injury or Parkinson's Disease. Most therapies, however, will emerge from the study of fetal tissues rather than directly including the cells in the ultimate drug product.

Second, the direct study of human fetal tissues is essential for an understanding of human development. This understanding is necessary for the advancement of fundamental biology, for the pursuit of therapies for the treatment of developmental diseases, such as Down syndrome and the microcephaly associated with Zika virus infection, and for the pursuit of therapies for the treatment of many other diseases that have been linked to developmental defects, including several cancers.

Third, human fetal tissues are critical for the establishment of mouse models for the study of human diseases and for the testing of potential new drugs and other therapies. For example, rodents are highly valuable for biomedical research, but they are inadequate for many studies of human disease and for the advanced testing of new therapies (e.g. HIV does not infect rodent cells). To circumvent the limitations of rodents, human fetal tissues can be implanted into immunocompromised mice, thereby generating an invaluable model system for studies that require the use of a living animal, such as the testing of new drugs. Importantly, human fetal tissues are essential for the establishment of these models due to their unique properties in comparison to tissues from children and adults.

4. Summary of any research conducted since 2010 that UCLA has been involved in that used fetal tissue or relied upon other studies that used fetal tissue

Research laboratories at UCLA studying a wide array of human diseases have used fetal tissues for their medical research projects since 2010. A survey of these researchers resulted in a consistent response that the use of fetal tissues has been, and will continue to be, essential for progress in their fields. While much remains to be learned about the specific properties of fetal tissues, it has been well-established that their properties are distinct from those of adult tissues. Fetal cells often differ from other cells because the fetal cells need to support the rapid growth and maturation of the tissue during fetal and neonatal development; in contrast, the functions of cells from children and adults are usually restricted to maintenance of the physiological functions of the tissue. An understanding of the unique properties of fetal cells and tissues is likely to be of great value for the development of new treatments for a number of devastating human diseases.

We provide here a summary of seven representative research efforts at UCLA that rely on fetal tissues and for which the research is strongly dependent on continued availability of fetal tissue

CANCER: One project focuses on an effort to improve the treatment of a form of lymphocyte leukemia in young children. Although the survival rate of these patients has improved dramatically, approximately 15% of pediatric patients with the most aggressive forms of the leukemia continue to die. A growing body of evidence suggests that these fatal leukemias may be unusually aggressive because they emerged from a unique type of B cell progenitor (B cells are white blood cells that secrete antibodies) generated only during fetal development. Research recently completed at UCLA has shown that the genetic regulation of fetal and adult B cell development is distinct. The aim of the ongoing research is to identify genes expressed only in fetal B-cell progenitors that contribute to the development of the aggressive forms of leukemia observed in young children.

IMMUNITY: Another UCLA research laboratory is immersed in an analysis of fetal T cells, another important type of white blood cell generated in the thymus. A primary goal of this laboratory is to develop improved strategies for rejuvenation of the immune system in cancer patients and in HIV patients whose immune systems have been compromised by chronic virus infection. Human fetal T cell progenitors have been found to be completely different from progenitors found in children and adults in their ability to rejuvenate the immune system. This laboratory has been performing detailed comparisons of the molecular properties of the fetal and adult cells in an effort to understand how to speed up immune system rejuvenation and make the immune system healthier.

As exemplified above, one general reason several UCLA laboratories rely on fetal tissues for their research is that an examination of the properties of the fetal tissues is needed to understand how they differ from older tissues and from tissues derived from induced pluripotent stem cells (iPSCs). iPSC are cells with embryonic stem cell like properties that can be generated from a patient's own skin cells (by a method developed less than 10 years ago), and then matured into any of a wide variety of human tissues; these cells hold great promise for the treatment of many degenerative and chronic diseases. One goal of the researchers is to engineer adult cells and iPSC to possess the unique, beneficial properties of fetal cells. This goal can be achieved only if the molecular features of the fetal cells have been clearly defined.

LUNG DISEASES: A UCLA laboratory is pursuing new treatments for a form of lung disease in infants. A long-term goal is to treat this disease by generating iPSC from a patient and then converting the iPSC into therapeutic lung cells. The ultimate therapy would not require the use of fetal cells. However, successful development of the therapy depends on an understanding of the unique properties of fetal lung cells, which have been found by the UCLA laboratory to grow and divide far more robustly than comparable cells from children or adults. The laboratory has developed a disease model that is being used to understand the unusual growth properties of he fetal cells and how these properties can be harnessed for therapeutic benefit.

GENETIC AND MUSCLE DISORDERS: Another UCLA laboratory studies diseases of muscle, including muscular dystrophy, toward the goal of regenerating functional muscle in patients. Similar to the findings with fetal lung, this laboratory has found that the regenerative capacity of human fetal muscle cells greatly exceeds that of older muscle satellite cells. Recent studies of the underlying mechanisms have revealed possible molecular explanations for the differences between the fetal cells and older cells. This professor considers fetal muscle cells to be the "gold standard" for all efforts to develop therapies for degenerative muscle diseases, due to the powerful and unique regenerative properties of these cells. Quite simply, for an understanding of the important differences between fetal muscle cells and older muscle cells, which are critical for the development of novel therapies, there is no alternative to the ability to analyze the fetal tissues themselves. It is also noteworthy that several of these studies are moving rapidly toward clinical trials, which necessitates the focus on human cells rather than rodent models.

HIV: Another reason several researchers rely on the availability of fetal tissues is that the fetal tissues can be used to create mice implanted with a specific human tissue, thereby providing an animal model in which potential therapies for the treatment of diseases of that human tissue can be tested. Such mice can eliminate the need for the testing of therapies in non-human primates, and are often preferable to studies of non-human primates because they allow the direct study of human cells.

Some UCLA laboratories use mice containing a human immune system for their studies of potential HIV therapies. These mice, which can be generated successfully only with the use of human fetal cells, are extremely important for progress of the HIV field, as HIV does not infect rodent cells. Currently, these mice are being used to study gene therapy approaches for the treatment of HIV infection, with the studies leading rapidly toward clinical trials.

BRAIN/SPINAL CORE INJURY: Human fetal tissues are also of great value for studies of the unique structure of the human brain, which is dramatically different from that of the mouse brain. UCLA research has used human embryonic stem cell lines to generate brain organoids (collections of neuronal cells that self-assemble into structures that resemble small portions of the brain). A comparison to fetal brain tissue is essential for the researchers to evaluate the validity of their organoid method, which is currently being used to understand developmental diseases of the brain, as well as the impact of Zika virus on brain development. The laboratory hopes to use this model to screen for drugs that may protect the fetal brain from the growth impairment caused by Zika virus infection. This same laboratory is also studying strategies for the generation of spinal cord neurons in the laboratory, for use in determining the underlying causes of neurodegenerative diseases, such as spinal muscular atrophy and amyotrophic lateral sclerosis, and for screening for drugs that could slow disease progression and extend patient lifespan.

INFERTILITY: The final UCLA laboratory discussed in this report uses fetal tissues for studies aimed at the diagnosis and treatment of human infertility. State-of-the-art genomics methods are being used to develop reference maps of germ cells and of fertilized eggs at the earliest stages of embryonic development. One goal of these studies is to better understand the reasons for spontaneous miscarriages. These studies are strongly dependent on human fetal tissues because early embryonic development in mice differs substantially from that in humans. The reference maps being developed by this laboratory are also of great importance for the study of germ cell cancers.

5. Description of any recent changes experienced by UCLA in the availability of fetal tissue for research and the related impact of these changes, including whether or not there have been interruptions and/or delays in research as a result.

Most UCLA researchers surveyed emphasized that recent national events have increased the challenge of obtaining the fetal tissues required for the research projects described above. One reputable company was forced to close due to legal expenses associated with challenges to its operations. This has delayed important studies and has forced laboratories to spend a considerable amount of time and resources searching for alternative suppliers. One laboratory has identified a reliable source of fetal tissues in Germany. Another laboratory has reduced their effort on studies that require fetal tissues, despite the importance of this research, due to concerns about personal safety. Of further note, recent publicity surrounding the procurement of fetal tissue delayed publication of a manuscript submitted by UCLA investigators to a renowned journal by more than seven months. The findings reported in that study have the potential to impact the development of therapies for HIV, cancer, multiple sclerosis, asthma, and organ transplant rejection.