



November 27, 2018

Jill Escher
Escher Fund for Autism
1590 Calaveras Avenue
San Jose, CA 95126

Dear Ms. Escher:

Thank you for writing to Dr. Francis Collins, Director of the National Institutes of Health (NIH), and other NIH Institute directors about your idea for a research program on the heritable effects of general anesthesia. As Director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), I am responding to your letter. An important part of NICHD's scientific mission is to ensure that every person is born healthy and that all children have the chance to fulfill their potential to live healthy and productive lives.

It is well established that Autism Spectrum Disorder (ASD) is a complex developmental disorder that affects how a person behaves, interacts with others, communicates, and learns. There is not one single cause of ASD. Although it has a genetic component, as certain genes may increase the risk that a child will develop autism, the disorder also appears to have an environmental component (exposure to toxicants, parental age) as various environmental factors may further increase autism risk (epigenetic factors). Furthermore, pregnancy and birth complications (e.g., prematurity, low birth weight) may lead to an increased risk of ASD in the child.

At present, there are limited scientific data to support your hypothesis that general anesthesia given to the mother during gestation, to a child in early life, or to the father at the time of puberty, may increase risk of ASD. We know that general anesthetics can strongly affect neuronal activity and can induce functional changes when administered during critical periods of brain development. A recent 2018 study¹ in rodents showed that neonatal exposure to sevoflurane (a common pediatric anesthetic) can affect the next generation of males through epigenetic modification (changes in DNA methylation). Interestingly, considering autism affects males more than females, female rodents were at diminished risk of affected neuronal activity.

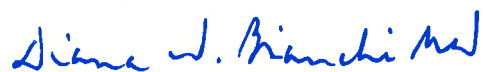
Although intriguing, it is difficult to evaluate the human relevance of this study due to long intergenerational times leading to numerous confounding variables. Nevertheless, investigator-initiated anesthesia-related basic research would help to understand complex biological events as they pertain to multi-generational heritability. As Dr. Matynyuk and colleagues noted in the above-mentioned study, "additional animal studies using different neonatal anesthesia paradigms that more broadly model stages of human postnatal brain development at the time of anesthesia

¹ <https://www.sciencedirect.com/science/article/pii/S0007091218303738?via%3Dihub>

exposure and during anesthesia exposure in human patients will be needed.” NIH welcomes submission of grant applications proposing such studies, which will be given full consideration during the rigorous peer review process.

Thank you again for writing and for your continued interest in the research activities supported by NIH.

Sincerely,

A handwritten signature in blue ink that reads "Diana W. Bianchi M.D." The signature is written in a cursive style.

Diana W. Bianchi, M.D.

Director

Eunice Kennedy Shriver National Institute of
Child Health and Human Development