



UNIVERSITY OF CALIFORNIA, DAVIS

PAUL S. KNOEPFLER, PH.D.
ASSOCIATE PROFESSOR
DEPARTMENT OF CELL BIOLOGY & HUMAN ANATOMY
COMPREHENSIVE CANCER CENTER
GENOME CENTER
SCHOOL OF MEDICINE
ONE SHIELDS AVENUE
DAVIS, CALIFORNIA 95616
TEL: (916) 453-2289
FAX: (916) 453-2290
knoepfler@ucdavis.edu

February 6, 2015

Dear Lord Alton,

I am writing to you regarding the Mitochondrial Regulations related to mitochondrial transfer or so-called "3-parent IVF" technology, approved by the UK House of Commons this week and pending vote in the House of Lords.

As you are aware, I am an opponent of the approval of this technology for use in humans at this time.

I favor continued study to produce additional data regarding safety and efficacy. I should also point out that I support cutting edge biomedical research such as human embryonic stem cell research and I am pro-choice so I am writing definitely not as some kind of extremist, but rather as a concerned scientist speaking for myself and not my university.

I understand that at a meeting at the House of Lords that Chief Medical Officer of Health Dame Sally Davies referred to my reported comment in the Daily Telegraph regarding my concerns over risks such as cancer in the children who might be produced by this technology as "bunk".

I would like to respectfully respond to her dismissal of my concerns. Please forward this letter on to her and to the Minister. This letter may be made public.

There are concrete reasons for concerns over safety regarding mitochondrial technology.

Both animal studies and unapproved human assisted reproduction experiments largely undertaken in the US in the late 1990s have bearing on this situation.

While of course animals are not humans, stem cell and developmental biologists such as myself often find that they can prove useful and highly relevant. A variety of animal studies similar to the mitochondrial transfer technology have given mixed results including some negative outcomes such as altered cognition, aging, and other problems.

Perhaps even more relevant are the unapproved human reproductive experiments in the 1990s with human egg cytoplasm transfer. Although some healthy children were born of such methods, there were also very serious negative outcomes: (1) a miscarriage and (2) an abortion of a fetus (in both cases having the chromosomal/developmental disorder Turner Syndrome), (3) at least two children

with heteroplasmy (mixed mitochondria that studies linked with cognitive dysfunction and obesity), and (4) a child born with a severe developmental disorder. (just one of many sources: <http://www.independent.co.uk/news/science/medical-dilemma-of-threeparent-babies-fertility-clinic-investigates-health-of-teenagers-it-helped-to-be-conceived-through-controversial-ivf-technique-9690058.html>).

As a scientist myself, I find these data concerning and not so easy to dismiss.

If anything the mitochondrial procedures proposed in the UK today are far more invasive to the human egg or embryo than those used for the experiments from the 1990s that led to developmentally disabled fetuses and children. Thus, there is a reasonable likelihood that the same kinds of outcomes could occur with mitochondrial transfer if approved by the UK.

There is a logical reason why the US FDA has not approved this technology and that is that the risks and unknowns are too high. Of course the UK can and has in the past diverged on cutting edge biomedical technologies or has innovated in ways that US scientists did not and that's admirable.

The notable example of IVF is a good one.

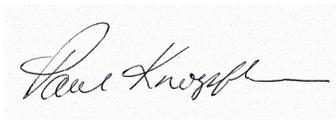
However, another example of past divergence is more concerning and that is the case of thalidomide.

While the US FDA banned thalidomide, it was used in Europe and the UK as a sedative including in pregnant women with horrible consequences of severely developmentally disabled children, widely considered one of the most disastrous events in medical history.

Of course mitochondrial transfer might be proven safe, but then again it might not. From my perspective as an impartial observer not personally or professionally tied to this issue and if anything putting myself at some risk by publicly opposing this technology supported by so many distinguished scientists that I deeply respect, its approval at this time would be a very risky gamble with children's health and lives on the line. I understand that the goal of mitochondrial IVF is to help prevent health problems in children due to mitochondrial diseases and that is noble, but the first rule of medicine is "do no harm".

I believe there is substantial risk of harm here and that these concerns are not "bunk." I respectfully ask that the House of Lords not approve this technology at this time until at the very least further studies in primates are conducted that are more conclusive on safety and completed in a manner that is more relevant to mitochondrial disease prevention in humans via this kind of technology.

Sincerely,

A handwritten signature in black ink, appearing to read "Paul Knoepfler", written in a cursive style.

Paul Knoepfler