cryobio

Additional Agreement to Use Donor CB 566

I, (_____ (Recipient), and _____ (Partner, if applicable)), specifically request and accept frozen semen from Cryobio donor CB 566. I understand that this Additional Agreement is an additional part of the Sperm Use Agreement specific to donor CB 566. CB 566 had expanded genetic carrier screening to determine their carrier status for 502 recessive genetic conditions. Please note that Cryobio thoroughly evaluates each donor's results and assesses potential risks of any identified results before allowing donors to remain in our donor program.

I have received genetic test results on this sperm donor, and I understand that donor CB 566 has been found to be a carrier of the following recessive genetic conditions:

Deafness, autosomal recessive 3; and
Lamellar ichthyosis, type 1.

Purpose of genetic carrier screening: Carriers of genetic conditions have changes, called pathogenic variants or mutations, in a specific (or multiple) gene(s). Most of the genetic conditions that the Cryobio donors are tested for are inherited in an autosomal recessive pattern (see Figure 1). Typically, we all have two copies of every gene---one from the egg source and one from the sperm source. Autosomal recessive conditions require a mutation in both copies of the same gene in order for it to cause the condition. Therefore, individuals who carry just one mutation in a gene that causes recessive genetic conditions are 'carriers' of that specific condition. Carriers of most of the genetic conditions Cryobio donors are tested for do not typically show symptoms of the condition, i.e., they are asymptomatic, although there are rare exceptions. Most individuals are carriers for at least one if not multiple recessive genetic conditions.

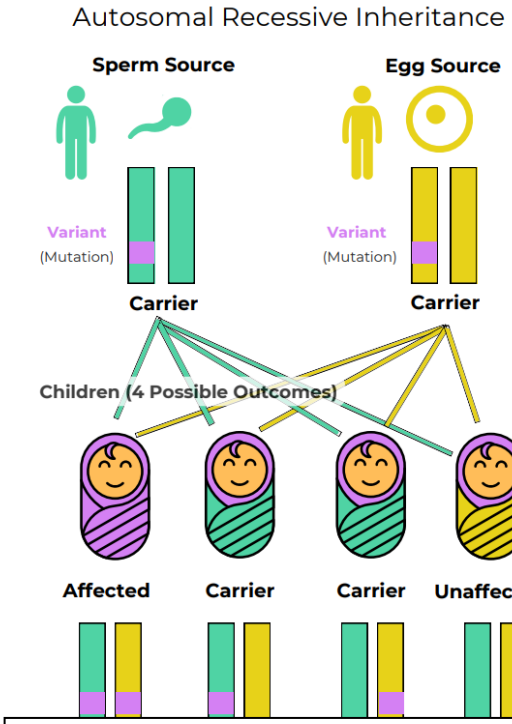

Figure 1. Graphic representing autosomal recessive inheritance of two carrier gametes.

Carrier status is helpful to know because if both the egg source and the sperm source are carriers for pathogenic variants or mutations in the same gene, then there is a 1 in 4 chance of the resulting child having that specific condition; a 2 in 4 chance of the resulting child being a carrier for that specific condition; and a 1 in 4 chance of the resulting child being neither a carrier or having that specific condition. Some of the conditions Cryobio donors are tested for have genotype-phenotype correlation, meaning that specific genetic pathogenic variations (the genotype) in a specific gene can be predictive of the type/specific features of a condition that may present in the individual (the phenotype), but not all do. Additionally, some of the genes can be linked to dominant conditions, meaning having a mutation in just one gene may increase the risk of a specific condition. If a specific change in a gene is linked to a dominant condition, it will be noted in this consent form.

Deafness, autosomal recessive 3 (*MYO15A* gene): Deafness, autosomal recessive 3 is a condition caused by pathogenic variants in the *MYO15A* gene. Affected individuals have profound, sensorineural

hearing loss that is present from birth. Importantly, this hearing loss is non-syndromic, meaning it occurs in isolation without accompanying symptoms, and affected individuals can typically expect a normal lifespan.

Lamellar ichthyosis, type 1(*TGM1* gene): Lamellar ichthyosis, type 1 is an autosomal recessive condition caused by pathogenic variants in the *TGM1* gene. Individuals with this condition have atypical skin, and are usually born with a tight, shiny layer of skin known as a collodion membrane, which is shed within the first two weeks of life. Other skin manifestations may include widespread plate-like brown scales, thickening of the skin on the palms and soles, hair loss, and scarring. Due to the tightness of the skin, some individuals may experience inversion of the eyelids (ectropion) and lips (eclabium), making eye closure challenging even after the collodion membrane has been shed. The severity varies, but individuals often contend with lifelong skin shedding and tightness, managed with topical skin barrier treatments. While there may be some complications like risk of infection or heat intolerance, life expectancy remains largely unaffected.

Carrier status frequency: Carrier status frequency is the chance of an individual being a carrier for a genetic condition based on general population risks or based on reported ethnicity prior to any genetic screening. If an individual tests negative as a carrier for a condition or conditions, then the chance of being a carrier is significantly decreased. There is still remaining risk called residual risk. Residual risk means the risk of being a carrier even after negative genetic testing for a condition. Residual risk data on the conditions the donor tested negative for can be requested from Cryobio. The carrier frequency provided is from the test provider. As with all genetic information, these carrier frequency numbers may change over time, and may slightly vary from lab to lab depending on the data used to curate them. Therefore, the carrier frequencies from this additional agreement are based on the numbers available from the performing laboratory on the date the donor's test results were reviewed by the lab.

Deafness, autosomal recessive 3 (*MYO15A* gene) carrier status frequency in different ethnicities as reported by SEMA4:

Worldwide	1 in 81
African	1 in 138
Ashkenazi Jewish	1 in 173
East Asian	1 in 44
Finnish	1 in 178
European (Non-Finnish)	1 in 87
Native American	1 in 100
South Asian	1 in 115

Lamellar ichthyosis, type 1 (*TGM1* gene) carrier status frequency in different ethnicities as reported by SEMA4:

Worldwide	1 in 237
African	1 in 209
Ashkenazi Jewish	1 in 620
East Asian	1 in 279
Finnish	1 in 179
European (Non-Finnish)	1 in 194
Native American	1 in 562
South Asian	1 in 467

Recommendation: Cryobio recommends that the recipient, or egg source if different than recipient, be tested for deafness, autosomal recessive 3 (*MYO15A* gene) and lamellar ichthyosis, type 1 (*TMG1I* gene) carrier status and consider genetic counseling. Please contact Cryobio with any questions or to arrange

genetic counseling. Genetic counseling services can also be found through the National Society of Genetic Counselors. We also strongly recommend that you discuss the donor's genetic carrier status results with your health care provider. Finally, we recommend that any future child be notified of this donor's carrier status once they are of reproductive age, as even if they do not have a recessive disease, they could be a carrier and their carrier status could help them identify risks related to their own reproductive future.

Cryobio has advised me of the following:	Please initial to show your understanding and agreement:
The donor I have chosen has positive results from genetic testing looking at carrier status for 502 genes. These results indicate that the donor is a carrier for deafness, autosomal recessive 3 and lamellar ichthyosis, type 1.	Initials: _____ Initials: _____
The genetic conditions tested for are inherited in recessive patterns. This means that if both the egg source and the sperm source are carriers for the same condition, there is a significantly higher chance of the resulting child having that genetic condition.	Initials: _____ Initials: _____
By the donor testing positive as a carrier for deafness, autosomal recessive 3 and lamellar ichthyosis, type 1, the risk to a resulting child would now be higher than that of the general population.	Initials: _____ Initials: _____
When an individual tests negative for carrier status, it does not completely eliminate their chance of being a carrier for that condition, however their remaining risk is greatly reduced. This remaining risk is called residual risk, and the residual risk can vary significantly from person to person. For more detailed information regarding the sensitivity of testing and remaining risk after negative screening, please contact Cryobio.	Initials: _____ Initials: _____
As genetic testing evolves and more data becomes available, I understand that there is the possibility of updated genetic information that may be uncovered for this donor for a variety of reasons. It is my responsibility to check back with Cryobio to see if any new genetic information is available for this donor.	Initials: _____ Initials: _____
Genetic testing for me (or the egg source, if different) can also be done to better understand and further reduce the risk to offspring.	Initials: _____ Initials: _____
Genetic testing is *strongly recommended* for me (or the egg source, if different) to see if I am a carrier for deafness, autosomal recessive 3 (*MYO15A* gene) and/or lamellar ichthyosis, type 1 (*TGM1* gene).	Initials: _____ Initials: _____

Expanded genetic carrier screening is continuing to evolve, and at the time this donor entered the program this was the screening available. This donor had genetic testing with SEMA4 in 2022. My health care provider may recommend an expanded carrier screen that includes/included more than the 502 genes screened for in this donor. It is my responsibility to share this information with my health care provider and review the risks and benefits of being screened for more (or fewer) genetic conditions.	Initials: _____ Initials: _____
The genetic testing done on the donor does ***not*** screen for all known genetic conditions.	Initials: _____ Initials: _____
While genetic testing can lower the likelihood for certain genetic conditions, no amount of genetic testing can guarantee that a child will be free of all genetic conditions.	Initials: _____ Initials: _____
Genetic counseling is available to me if I have additional questions regarding these test results and potential risks of using this donor.	Initials: _____ Initials: _____
Both the donor's carrier status and whether the donor is acceptable for my use should be discussed with my health care provider.	Initials: _____ Initials: _____

I have read the above material and assume the risk of using donor sperm from a donor who has been found to be a carrier of genetic conditions. I am making the choice to use donor sperm from donor CB 566 willingly and agree to release any legal claims, including negligence, that may arise from or are related to insemination or assisted reproduction using donor sperm from donor CB 566.

I have read and had the chance to ask questions, and I understand and agree to the terms of this Additional Agreement to use donor CB 566.

_____

Recipient Date Email

_____

Partner, if applicable Date Email

William C. Baird, PhD, HCLD 12-26-2023

Cryobio Date