cryobio

Additional Agreement to Use Donor WL 4003

We, _____ (Recipient), and _____ (Partner, if applicable), specifically request and accept frozen semen from Cryobio donor WL 4003. We understand that this Additional Agreement is an additional part of the Sperm Use Agreement specific to donor WL 4003. We reviewed the genetic test results on this sperm donor, and we understand that donor WL 4003 has been found to be a carrier of the following recessive genetic conditions:

Cystic Fibrosis

Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies

Cystic Fibrosis (CFTR gene):
Cystic fibrosis is an autosomal recessive disorder caused by pathogenic variants in the gene CFTR. It may be diagnosed in individuals worldwide, but has the highest prevalence in the Caucasian population in individuals with Northern European ancestry with a carrier frequency of about 1 in 25. The clinical presentation includes thick mucus accumulation in the lungs leading to breathing difficulties and infection, poor digestion, and male infertility. The average life expectancy is in the 30s. Although some genotype/phenotype correlations exist, individuals with two classic pathogenic variants in CFTR are expected to present with a more severe disease phenotype. Non-classic variants in CFTR may lead to less severe forms of disease or specific phenotypes, such as male infertility as a result of congenital absence or hypoplasia of the vas deferens.

Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies (CEP290 gene):
CEP290-related ciliopathies include four different overlapping disorders, known as Leber congenital amaurosis, Bardet-Biedl syndrome, Joubert syndrome and Meckel syndrome. All diseases are inherited in an autosomal recessive manner and are caused by pathogenic variants in the gene CEP290.

- Leber congenital amaurosis manifests with vision loss at birth or in early infancy. Patients have profound loss of vision at an early age, and some have been reported to have intellectual disability.
- Bardet-Biedl syndrome is characterized by obesity, intellectual disability, kidney disease, genital abnormalities, and loss of vision beginning with loss of night vision and progression to tunnel vision and blindness.
- Joubert syndrome presents with intellectual disability, brain malformations (known as the molar tooth sign), low muscle tone (hypotonia), ocular problems including uncontrollable eye movements and loss of vision, and kidney cysts leading to end-stage renal disease.
- Meckel syndrome often manifests before birth and is characterized by occipital encephalocele, brain malformations, facial dysmorphism, renal agenesis, and extra digits. Because of their serious health problems, most individuals with Meckel syndrome die before or shortly after birth.

Life expectancy varies according to the phenotype; it is not reduced in patients with Leber congenital amaurosis, but death in infancy is expected in patients with Meckel syndrome. Currently, it is not possible to predict which phenotype a patient will have based on the variants inherited.

Carrier status frequency:
Carrier status frequency is the chance of an individual being a carrier for a genetic condition based on their ethnicity alone 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. This remaining risk is known as residual risk, meaning what is the risk of being a carrier even after negative genetic testing. Residual risk data is available directly through sema4's website, sema4.com, or can be requested from Cryobio.

Cystic fibrosis (CFTR gene) carrier status frequency in different ethnicities, from Sema4's website:

African	1 in 58
Ashkenazi Jewish	1 in 24
East Asian	1 in 277
Finnish	1 in 75
Caucasian	1 in 23
Latino	1 in 40
South Asian	1 in 73
Worldwide	1 in 33

Leber congenital amaurosis 10 and other CEP290-related ciliopathies (CEP290 gene) carrier status frequency in different ethnicities, from Sema4's website:

African	1 in 131
Ashkenazi Jewish	1 in 461
East Asian	1 in 32
Finnish	1 in 713
Caucasian	1 in 97
Latino	1 in 199
South Asian	1 in 222
Worldwide	1 in 120

Recommendation: Both Sema4 and Cryobio recommend that the recipient, or egg source if different than recipient, be tested for cystic fibrosis carrier status and Leber congenital amaurosis 10 and other CEP290-related ciliopathies carrier status and consider genetic counseling. Please refer to Sema4's website, sema4.com, for more information and contact Cryobio with any questions or to arrange genetic counseling. Because the donor was tested by Sema4, Cryobio recommends that the recipient or egg source should be tested by Sema4 as well. 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 be important to identify risks related to their own reproductive future.

Cryobio has advised us of the following:	**Please initial to show your understanding and agreement:**
The donor we have chosen has positive results from genetic testing. These results indicate that the donor is a carrier for cystic fibrosis and Leber congenital amaurosis 10 and other CEP290-related ciliopathies.	**Initials: _____ Initials: _____**

These genetic conditions are inherited as recessive traits. 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 for carrier status for cystic fibrosis and Leber congenital amaurosis 10 and other CEP290-related ciliopathies, the risk to a resulting child would now be higher than that of the general population.	**Initials: _____ Initials: _____**
Both the risk of being a carrier and the sensitivity of the genetic testing can vary depending on an individual's ethnicity. When an individual tests negative for carrier status, it ***does not completely eliminate*** their chance of being a carrier for that disease. Instead, their remaining (residual) risk of being a carrier is determined by their ethnic background. While a negative result decreases the likelihood that an individual is a carrier, how much that risk is reduced can vary significantly. For more detailed information regarding the sensitivity of testing and remaining risk after negative screening, please see Sema4's website.	**Initials: _____ Initials: _____**
Genetic testing looking at a large panel of genes, including the genes/conditions that the donor has tested positive for, is available and could be done.	**Initials: _____ Initials: _____**
Genetic testing is ***strongly recommended*** for me (or the egg source, if different) to see if I am a carrier for cystic fibrosis and Leber congenital amaurosis 10 and other CEP290-related ciliopathies.	**Initials: _____ Initials: _____**
A negative genetic test result in me (or the egg source, if different) significantly reduces the likelihood that the resulting child could be affected with these conditions. However, we fully understand that the risk cannot be completely eliminated.	**Initials: _____ Initials: _____**
While genetic testing can lower the likelihood for certain genetic diseases, no amount of genetic testing can guarantee that a child will be healthy or free of genetic disease.	**Initials: _____ Initials: _____**
Genetic counseling is available to us, either through Cryobio or Sema4, if we have additional questions regarding these test results and potential risks.	**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: _____**

We 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 disorders. We are making the choice to use donor sperm from donor WL 4003 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 WL 4003.

We have read, had the chance to ask questions, understand, and agree to the terms of this Additional Agreement to use donor WL 4003.

_____
Recipient

_____
Date

_____
Partner

_____
Date

William C. Baird, PhD
_____
Cryobio

10-18-2020
_____
Date