cryobio

Additional Agreement to Use Donor WL 4005

We, _____ (Recipient), and _____ (Partner, if applicable), specifically request and accept frozen semen from Cryobio donor WL 4005. We understand that this Additional Agreement is an additional part of the Sperm Use Agreement specific to donor WL 4005. We reviewed the genetic test results on this sperm donor, and we understand that donor WL 4005 has been found to be a carrier of the following recessive genetic condition:

Cystic Fibrosis

Why carrier status is important: Carriers of genetic diseases have changes, called pathogenic variants or mutations, in a specific gene or multiple genes. Most of the genetic diseases that the Cryobio donors are tested for are inherited in an autosomal recessive pattern. Typically, we all have two copies of every gene---one from the egg source and one from the sperm source. Autosomal recessive diseases require a mutation in both copies of the same gene in order for it to cause disease. Therefore, individuals who carry just one mutation in a gene that causes recessive disease are 'carriers' of that specific disease. Carriers of most of the genetic diseases Cryobio donors are tested for do not show symptoms of the disease, i.e., they are asymptomatic. Some diseases tend to occur more in certain ethnicities, and some tend to occur evenly in all ethnicities. Most individuals are carriers for at least one if not multiple recessive genetic diseases.

Carrier status is important 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 disease; a 2 in 4 chance of the resulting child being a carrier for that specific disease; and a 1 in 4 chance of the resulting child being neither a carrier nor having that specific disease. Some of the diseases 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 of specific disease that may present in the individual (the phenotype), but not all do.

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, where there is a carrier frequency of about 1 in 25. Mutations in the CFTR gene result in thickened secretions (mucus) in structures throughout the body. The most common clinical presentation of cystic fibrosis includes thick mucus accumulation in the lungs, leading to progressive damage to the respiratory system, which results in breathing difficulties and infection. Many individuals with cystic fibrosis also have significant digestive issues related to mucus build up in the pancreas. Most men with cystic fibrosis also have congenital bilateral absence of the vas deferens (CBAVD), leading to male infertility. Some genotype/phenotype correlations exists, meaning specific genetic mutations can help predict the clinical picture of the disease. Individuals with two "classic" pathogenic variants in CFTR are expected to present with a more severe disease phenotype. The average life expectancy for individuals with "classic" forms of cystic fibrosis used to be childhood, but with advanced treatments, it is now in the 30s-40s. Non-classic variants in CFTR may lead to less severe forms of disease or specific phenotypes, such as individuals presenting only with male infertility as a result of CBVAD or hypoplasia of the vas deferens.

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:

Worldwide	
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

Recommendation: Both Sema4 and Cryobio recommend that the recipient, or egg source if different than recipient, be tested for cystic fibrosis 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 for 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.	**Initials: _____ Initials: _____**
This genetic condition is inherited as a recessive trait. 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, 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.	**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 4005 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 4005.

We have read, had the chance to ask questions, and we understand and agree to the terms of this Additional Agreement to use donor WL 4005.

_____
Recipient

_____
Date

_____
Partner

_____

Date

William C. Baird, PhD

_____

Cryobio

10-06-2021

_____

Date