cryobio

Additional Agreement to Use Donor WL 430-H

We, _____ (Recipient), and _____ (Partner, if applicable), specifically request and accept frozen semen from Cryobio donor WL 430-H. We understand that this Additional Agreement is an additional part of the Sperm Use Agreement specific to donor WL 430-H. WL 430-H had expanded genetic carrier screening to determine their carrier status for 283 recessive genetic conditions. We have received genetic test results on this sperm donor, and we understand that donor WL 430-H has been found to be a carrier of the following recessive genetic condition:

Neuronal Ceroid-Lipofuscinosis (*TPP1*-Related).

Why carrier status is important: Carriers of genetic diseases have changes, called pathogenic variants or mutations, in a specific (or multiple) gene(s). 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 typically show symptoms of the disease, i.e., they are asymptomatic, although there are rare exceptions. 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 or 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.

Neuronal ceroid-lipofuscinosis (*TPP1*-related) (*TPP1* gene): Neuronal ceroid-lipofuscinosis (NCL) is a term used to identify a group of genetic conditions that primarily affect the nervous system. In general, NCLs typically involve symptoms such as seizures (epilepsy), some type of dementia, and vision loss. Symptoms and age of onset can vary based on the subtype of NCL, and subtypes are determined based on the underlying genetic defect that causes them, *TPP1*-related neuronal ceroid-lipofuscinosis is inherited in an autosomal recessive pattern and is caused by pathogenic variants in the gene *TPP1*. While it is found in different ethnicities around the world, it is most prevalent in individuals from Newfoundland, Canada due to the presence of a founder mutation (i.e.-a genetic variant observed with high frequency in a group that is or was geographically or culturally isolated).

Most *TPP1*-caused neuronal ceroid-lipofuscinosis results in the late infantile form, in which symptoms begin between 2 and 4 years of age. Clinical features include progressive visual loss and neurologic symptoms, including seizures, loss of control of body movements (ataxia), loss of brain tissue and neurons/brain connections (cerebral atrophy), and loss of skills that were previously obtained (developmental regression) such as loss of the ability to walk and talk. Affected individuals do not survive beyond adolescence. Although enzyme replacement therapies have been shown to slow progression of disease, there is no cure. Additionally, any neurodegeneration prior to diagnosis and

therapies is irreversible. Rarely, patients may be diagnosed with a later-onset form. It is not currently possible to predict the age of disease onset based on the patient's specific genetic mutations (genotype).

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 can be requested from Cryobio.

Neuronal ceroid-lipofuscinosis (*TPP1*-related) (*TPP1* gene) carrier status frequency in different ethnicities from Sema4's website:

Worldwide	1 in 379
African	1 in 833
Ashkenazi Jewish	1 in 1268
East Asian	1 in 1480
Finnish	1 in 354
European (Non-Finnish)	1 in 266
Native American	1 in 568
South Asian	1 in 2199

Recommendation: Cryobio recommends that the recipient, or egg source if different than recipient, be tested for neuronal ceroid-lipofuscinosis (*TPP1*-related) carrier status and consider genetic counseling. Please contact Cryobio with any general questions, information about how to get tested, or to arrange genetic counseling. Cryobio strongly recommends 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 had positive results from genetic testing looking at carrier status for 283 conditions. These results indicate that the donor is a carrier for neuronal ceroid-lipofuscinosis (*TPP1*-related).	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 neuronal ceroid-lipofuscinosis (*TPP1*-related), 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 the individual's ethnicity. When an individual tests negative for carrier status, it does not 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 by can vary significantly. For more detailed information regarding the sensitivity of testing and remaining risk after negative screening, please contact us.	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 neuronal ceroid-lipofuscinosis (*TPP1*-related).	Initials: _____ Initials: _____
A negative genetic test result in the egg source 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: _____
Expanded genetic carrier screening is continuing to evolve, and at the time this donor entered the program this was the screening available. My health care provider may recommend an expanded carrier screen that includes/included more than the 283 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: _____
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 through Cryobio, 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 430-H 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 430-H.

We have read and had the chance to ask questions, and we understand and agree to the terms of this Additional Agreement to use donor WL 430-H.

_____

Recipient Date

_____

Partner, if applicable Date

William C. Baird, PhD. 08-15-2022

Cryobio Date