cryobio

Additional Agreement to Use Donor CB 497

We, _____ (Recipient), and _____ (Partner, if applicable), specifically request and accept frozen semen from Cryobio donor CB 497. We understand that this Additional Agreement is an additional part of the Sperm Use Agreement specific to donor CB 497. We reviewed the genetic test results on this sperm donor, and we understand that donor CB 497 has been found to be a carrier of the following recessive genetic condition:

Congenital Disorder of Glycosylation, Type Ia

Congenital disorder of glycosylation, type Ia (PMM2 gene):
Congenital disorder of glycosylation (CDG), type Ia is an autosomal recessive syndrome caused by pathogenic variants in the gene PMM2. While patients have been reported from multiple ethnicities, this disease is more common in the Ashkenazi Jewish and Caucasian populations. CDG Type Ia is a multi-system disease (meaning it can affect many parts of the body), and clinical manifestations are broad and highly variable. However most cases have an important neurologic component. There are three types of CDG type Ia, and they vary depending on types of symptoms and when symptoms develop: the infantile multisystem type, the late-infantile and childhood ataxia-intellectual disability type, and the adult stable disability type. In infants, the disease may present as failure to thrive as a result of feeding problems; later, the disease may manifest as encephalopathy, hypotonia, delayed language and motor development, intellectual disability, stroke-like episodes, and retinitis pigmentosa. Severely affected individuals may die in early childhood, but more mildly affected individuals may survive into adulthood with variable intellectual disability, spinal abnormalities, endocrine dysfunction and coagulopathy. Several specific variants have been associated with milder or more severe disease, and therefore the disease severity may be predicted in some patients based on genetic test results.

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.

Congenital disorder of glycosylation, type Ia (PMM2 gene) carrier status frequency in different ethnicities, from Sema4's website:

African	1 in 245
Ashkenazi Jewish	1 in 66
East Asian	1 in 133
Finnish	1 in 58
Caucasian	1 in 58
Latino	1 in 114
South Asian	1 in 278
Worldwide	1 in 80

Recommendation: Both Sema4 and Cryobio recommend that the recipient, or egg source, if different than recipient, be tested for congenital disorder of glycosylation, Type Ia 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 had positive results from genetic testing. These results indicate that the donor is a carrier for congenital disorder of glycosylation, Type Ia.	**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 congenital disorder of glycosylation, Type Ia 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 gene/condition 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 congenital disorder of glycosylation, Type Ia.	**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 this condition. 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 a genetic disorder. We are making the choice to use donor sperm from donor CB 497 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 497.

We have read, had the chance to ask questions, understand, and agree to the terms of this Additional Agreement to use donor CB 497.

_____
Recipient

_____
Date

_____
Partner, if applicable

_____
Date

William C. Baird, PhD
_____
Cryobio

10-18-2020
_____
Date