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**Title: Conditional Creation and Rescue of Nipbl-Deficiency in Mice Reveals Multiple Determinants of Risk for Congenital Heart Defects**

**Introduction:** The most common human birth defects are congenital heart defects or CHDs which occur and mainly arise through multiple genes. There isn’t just one leading cause, but many distinct sources that lead to CHDs that has been found. Another birth defect that delays growth and maturation, neurological deficits, is called Cornelia de Lange Syndrome or otherwise known as CdLS, are seen in 30% of people with CHDs. The main cause for CdLS is for NIPBL which is Nipped-B-homologue. Animals, particularly with zebra fish and mice, CdLS that have mutant traits in Nipbl-deficient, are models for CHDs

**Reason for research:** During the procedure and the experiment, was to rescue and to see if there was, in a sense, a cure for Nipbl-deficiancy. Using a method called Nipbl FLEX (flip-excision), which is a new allelic series.

Mice are the main study during this experiment and embryos through In vitro fertilization. To show how a unique mouse with Nipbl and CdLS and their genetics cause birth defects as well as how soon do heart defects take place while in embryo and the size of the heart.

**Method and Materials:** To obtain the embryos, male mice that were positive for Nipbl, were bred naturally with female mice. once embryos were injected with FLEX they were then dissected for tissue collection and for it to be processed for results. While still in Embryo, they were injected with the FLEX serum to inactivate Nipbl. Female mice were tested for heterozygous in cre-expressing transgenes so that it was possible to revert the Nipbl effect upon mice. Dissected embyros then went through microscopy, MRI, and optical projection tomography.

**Results:** Half of the Nipbl-deficiancy mice, displayed defects in the heart in the artrial septum between the gestational days of 15.5 and 17.5. Nearly 100 genes have been found that are linked to the production of heart defects that begin during the early embryonic stages as the heart is developing. The development in heart defects happen earlier on with mice that are Nipbl positive. Mice that received the FLEX treatment could be used to determine in which of the cells or tissues the Nipbl-deficiancy would be a cause for heart defects while the embryo is developing.

**Discussion:** A mouse positive for Nipbl-deficiancy that has CdLS, the genes are small minor adjustments that make the difference. In Nipbl-deficient mice, in the heart, the atrial spetum is delayed but also the right ventricle is reduced in size, which suggests that these Nipble-deficient mice, starts as early as gasturation while in the embryo.

During the study, it was speculated that heart size may be a determinant. Nipbl-deficient embryos were significantly smaller to those who didn’t have it as well as the heart size. The idea was also presented that the risk of CHDs is a smaller risk with a smaller heart.

**Conclusions:** During the early stages of the emryo development, there are many factors that lead to CHDs and ways to help control that. There is also many determinants to the size of the heart as well as the genes and alleles of the makeup of each individual mouse. Through the FLEX technology, some were able to show signs of improvement while others didn’t show signs. During the MRI’s and other scans and tests, Nipbl-deficiant mice and their ventricles in the heart were slower to develop.

**Limitation of this study:** This study was on mice and while mice are still in embryo. Congenital Heart Defects also start developing at such a young stage while in embryo and to start at a younger stage while the embryo is developing. With the results, it starts with the alleles and how everything develops.

**Bibligraphy:**

**http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.2000197**