Cleft Lip and Palate

Name: ____________________________

Cleft lip and palate is a disorder caused by problems during embryonic development. The structures that form the upper lip and the roof of the mouth typically fuse during the first three months of fetal development. In cleft lip and palate, these structures do not join. The result is a gap or a split in the roof of the mouth, the upper lip, or both. The effect can be as simple as a small notch in the lip or as complicated as a large opening that runs into the roof of the mouth and nose (Figure 1). Cleft lip and palate is one of the most common birth defects in the world, occurring in about 14 out of every 10,000 births.

**Figure 1. Cleft lip and palate.** This infant has a cleft lip and palate. Multiple surgeries within the first year of life are often required to help children born with this condition.

The causes of cleft lip and palate are complex. Many genes play a role in coordinating embryonic development. More than 42 genes are involved in the development of the head and face alone. Genes control the pathway of development that causes the upper lip and roof of the mouth to fuse. Mutations in these genes can cause cleft lip and palate. When genetics is part of the cause of cleft palate, sometimes mutations in many genes are involved, but other times a mutation in only one gene is the cause.

A growing embryo is also very sensitive to changes in its environment. Environmental effects, such as the lack of certain nutrients at specific times during development, can also cause cleft lip and palate. Most cases of cleft lip and palate are the result of interactions between genetics and the environment. In some cases, the exact cause is never determined.

Scientists are making headway in understanding some causes of cleft lip and palate. Some patients who develop a cleft lip and palate have a condition called Van der Woude syndrome. Evidence shows that this syndrome is caused by mutations in just one gene, called the *Irf6* gene. *Irf6* stands for “interferon regulatory factor 6,” but it is easier to just call it *Irf6*. 
*Irf6* is a gene that codes for a protein that controls other genes. That is, the protein from this gene turns other genes on or off. This protein is required for normal development. In mice, this gene is active in the cells that line the two sides of the forming mouth. The gene is turned on and makes protein just before and during fusion of the two sides of the mouth.

Genetic studies in humans show that some mutations to *Irf6* cause one form of cleft lip and palate (Van der Woude syndrome). Cells with these mutations don't make enough of the protein from this gene. This means that other genes don't get turned on or off at the right time. Mutations to *Irf6* act in many ways like a dominant allele. Only one of the mutated alleles is needed to cause cleft lip and palate.

To better understand this syndrome, scientists would like to know how specific changes to the gene affect the phenotype. However, the *Irf6* gene is very large, more than 18,000 nucleotides long. It would be very helpful to use evidence to identify sections of the gene that may be especially important for gene function.

**Questions**

Use the information you just read to answer the following questions. Work together as a group to share what you have learned.

1. Calculate the number of babies expected to be born with cleft lip and palate in the United States each year:
   
   a. The worldwide incidence of cleft lip and palate is 14 out of every 10,000 births. Calculate the frequency of cleft lip and palate by dividing the number of babies with the condition by the number of births.
   
   b. Assume that there are 4,000,000 births per year in the United States. Multiply the number of births by the frequency of cleft lip and palate you calculated in Question 1a to determine the expected number of babies born with cleft palate each year in the United States.

2. How could a change to a gene cause cleft lip and palate? How might a change in an environmental signal cause cleft lip and palate?

3. Assume that one parent has an allele of the *Irf6* gene with a mutation that causes cleft lip and palate and a second allele that is normal. Also assume that the second parent has two normal alleles for this gene. What is the probability that a child born to this couple will have a cleft lip and palate? Mutated *Irf6* alleles act in a dominant fashion.

4. Explain how studies from mice are helpful to scientists trying to understand cleft lip and palate in humans.

**Sources:**

http://www.patient.co.uk/doctor/Cleft-Lip-and-Palate.htm