Dear [redacted]

Thank you for utilizing Existence Genetics' genetic testing services. We received your daughter's saliva sample, extracted her DNA from the saliva, and processed her DNA successfully on Existence's proprietary Nexus® DNA chip. We then analyzed thousands of her genes using our patent-pending technology and used that information to produce the attached genetic report.

The included bullet-point summary is written specifically for her healthcare providers and is a unique, additional report provided by Existence Genetics. While her healthcare provider may be interested in reviewing her entire report, he or she may find the information in the healthcare provider summary pages most helpful in efficiently learning about the most important findings. Your daughter's healthcare provider is also welcome to contact us with any questions at [redacted] or [redacted]

Thank you,
Brandon Colby, MD
[redacted]
[redacted]

Confidential Identification Number: [redacted] [redacted]2011

Genetic Testing Results Summary for Your Healthcare Provider

Rare Diseases & Syndromes Screen. Based on a screen for more than 1,200 rare diseases, conditions, and traits detected the following:

- Fumarylacetoacetase Pseudodeficiency: Carrier. Due to a mutation in her FAH gene (referred to in genetic terms as R341W) this patient is a carrier of, but is not affected by, this condition. When this mutation occurs on its own, it usually produces no clinical abnormalities (the individual with this mutation is healthy). If this mutation occurs with a second mutation in the FAH gene, however, then symptoms similar to Tyrosinemia, Type I may occur.
    - This condition is related to Tyrosinemia, Type I ("hepatorenal tyrosinemia") and if this patient has a second rare mutation in her FAH gene (that may not have been detected via this genetic test) then this patient may be at risk of Tyrosinemia, Type I. While this is very unlikely, if the patient does have symptoms associated with Tyrosinemia, Type I, then a workup for this disorder should be conducted.
        - Symptoms of Tyrosinemia, Type I include failure to thrive, progressive liver disease, renal tubular dysfunction, hypophasphatemic rickets, progressive somnolence, peripheral neuropathy, extensor hypertonia, vomiting or paralytic ileus, and muscle weakness.
            - Onset of symptoms can vary from infancy to adolescence.
        - Tyrosinemia, Type I is a *recessive* disorder: If both parents are a carrier then each child may have a 25% chance of being affected by this condition <u>but if only the patient is a carrier</u> then each child the patient has will have close to a 0% (zero percent) chance of being affected by this condition but may have a 50% chance of being a carrier like the patient.
        - If symptoms suggest possible Tyrosinemia, Type I, consider referral to a pediatric geneticist. Urine and blood testing may show increased succinylacetone levels as well as increased plasma concentrations of tyrosine, methionine, and phenylalanine. Treatment with Nitisinone may be warranted.

- Hirschsprung Disease: Increased Risk Detected. Due to a mutation in her RET gene(referred to in genetic terms as IVS 1, ds, +9277 and also as +9349 relative to MET) this patient has a 2.1 fold increased risk of Hirschsprung Disease. This disease results in absence of nerves at the end of the large intestine, which can cause abnormalities with bowel function.
    - This does *not* mean the patient has Hirschprung Disease, only that she is at increased risk compared to the general population due to a change in one of her genes.
        - Symptoms of Hirschprung Disease include failure to pass meconium, constipation, watery diarrhea, poor feeding, poor weight gain and slow growth, and abdominal distention.
        - While this disease is usually identified when the patient is a newborn, some patients may not be diagnosed with this condition until later in childhood or, sometimes, not even until adulthood.
        - If symptoms suggest possible Hirschprung Disease, consider abdominal x-ray and referral to gastroenterologist.
            - Based upon her genes, this patient is <u>not</u> at increased risk of radiation-induced breast cancer.