**Part 3: *What can we learn from genetics?***

The patient's father had also had transient neonatal cyanosis, with hemoglobin oxygen saturation of approximately 80% at birth, despite the use of supplemental oxygen and adequate arterial oxygenation. Extensive testing for infections and metabolic abnormalities were all negative. His cyanosis resolved within 1 to 2 months, and he was subsequently healthy. The patient had an older brother and mother who were not cyanotic at birth.

1. Which gene(s) (be specific) in the happy blue baby patient would you examine for a mutation? Why?

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1. Sketch a little pedigree that describes the phenotype of the happy blue baby, her father, her uncle, and her grandmother. Paste your pedigree sketch or JPG here:
2. If this family’s infantile cyanosis exhibits simple Mendelian inheritance, can you predict if the defect is dominant vs. recessive? X-linked? Y-linked? Autosomal?

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1. A screenshot of a cell phone

   Description automatically generatedAs part of her genetic testing, the patient’s β-globin gene cluster on chromosome 11 was sequenced, producing the depicted results for codons encoding amino acids 65-69 in fetal Gγ-globin. Based on the DNA sequence, what is the mutation in the newborn (e.g. X##Y, where X is the original amino acid, ## is the position of that amino acid in the protein chain, and Y is the mutated amino acid)? Is the mutated residue side chain similar to or different from that found in the wild type protein? Explain your answer in terms of the size and physicochemical properties.

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**Part 4: *Is there a 3D structure of a protein that can explain the molecular basis of the happy blue baby’s cyanosis?***

Knowing a point mutation is a good starting place, but it is not sufficient to explain how the baby became blue. To explore the molecular basis of the newborn’s cyanosis, search the Protein Data Bank (at [www.rcsb.org](http://www.rcsb.org)) for one or more structures of this mutant protein. You can start your search using the protein name or other details that you know. (Hint: search by the name of the mutation, or the mutation itself, e.g. X##Y, where X is the original amino acid, ## is the position of that amino acid in the protein chain, and Y is the mutated amino acid). Examine the search results and refine as necessary to collect the most relevant.

For the PDB ID that you wish to explore, open the structure explorer page for the entry by entering the PDB ID in the top search box on [www.rcsb.org](http://www.rcsb.org). You can learn many things by exploring the page that opens (the structure summary page). Explore the box below to learn about what you can find on this page, review the contents of the page and complete the following table with information about the entry.

*Box 1: Navigating the Structure Summary Page*

1. **Title** - that tells you what the structure is about

2. **Snapshot** - of what the structure of the molecule/complex looks like.

3. **Authors** – who solved the structure

4. **Literature** –access the article that describes the structure. This section also includes links to PubMed page and the abstract of the article describing this structure, when available.

5. **Macromolecules** – All proteins and nucleic acids present in the structure are listed here. Each unique type of macromolecule or molecular chain is listed as a separate entity. There may be multiple copies of each molecule in the structure.

6. **Small molecules** – All ligands, ions, cofactors, inhibitors that are present in the structure are listed here. You can find links here to explore the interaction of this ligand with the target protein.

7. **Experimental details** – describe details about how the structure was determined

8. **Structure quality** – shows a slider that provides insights about the quality of the structure and its agreement with the experimental data and geometric standards.

See <http://pdb101.rcsb.org/learn/guide-to-understanding-pdb-data/introduction> for details

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| PDB ID |  |
| Author(s) of entry |  |
| Year when the structure was published/released |  |
| Structure determination method |  |
| Number of protein chains in the entry |  |
| Names and number of copies of ligands (Small Molecules) present in the structure |  |