1. What do the oxygen binding studies tell you about the V67M mutant’s oxygen binding and release ability, as compared to the wild type protein? Quote relevant binding constants to support your answer.

**Part 7: *What is the consequence of the (fetal) gamma globin V67M mutation?***

In addition to solving the 3D structure of V47M, the authors examined the biochemical consequences of the hemoglobin mutation. They expressed the recombinant hemoglobin F (α2γ2) protein in an *Escherichia coli* expression system. The mutant hemoglobin F was produced at yields similar to those for wild-type hemoglobin F. Initial studies indicated that the oxygenated hemoglobin tetramer (α2γV67M2) was not excessively prone to oxidation, heme loss, or denaturation, as compared with wild-type hemoglobin F. The authors used partial laser photolysis and rapid mixing methods to measure the association (k′o2) and dissociation (ko2) rate constants for the last step of oxygen binding to individual globin subunits in wild-type and V67M γ-hemoglobin F. Data from the experiments are included in the table below:

A screenshot of a cell phone

Description automatically generated

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1. Relate the oxygen binding studies to your structural explorations. Explain in 2-3 sentences the structural basis of the oxygen binding properties.

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1. What does the author’s experience with the production of the protein imply about whether the mutation affected protein folding? Explain how it is possible for a protein to be fully folded but unable to bind its ligand.

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1. Was the happy blue baby cured of her genetic disease? (Hint: read <https://patch.com/new-jersey/tomsriver/genetic-mutation-named-for-toms-river-may-shed-light-49e5fd1947> and refer to the NEJM article at <https://www.nejm.org/doi/full/10.1056/NEJMoa1013579>)

**Part 8: *How did things turn out for the happy blue baby?***

The infant received erythrocyte transfusions, which raised her hemoglobin oxygen saturation from approximately 80% to more than 90%. She was discharged home at 6 days of age, with oxygen saturation in the range of 90 to 95%. Her clinical course was unremarkable, and by 2 months of age, her hemoglobin oxygen saturation was consistently higher than 95%.

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1. The NEJM article summary mentions a condition that may arise in the mutant proteins leading to denaturation and anemia. What is that condition? Explain your answer based on the structure that you have visualized. Include a figure to support your explanation.

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