

Sequence Specific Knockdown of the mRNA-binding Protein IGF2BP1 Switches Hemoglobin Production in Cultured Human Erythroleukemia Cells

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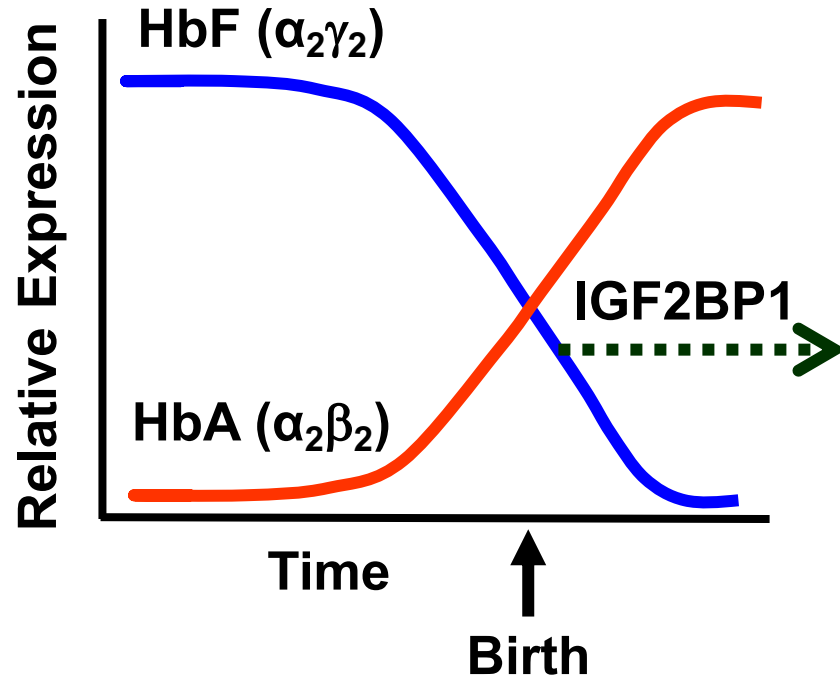
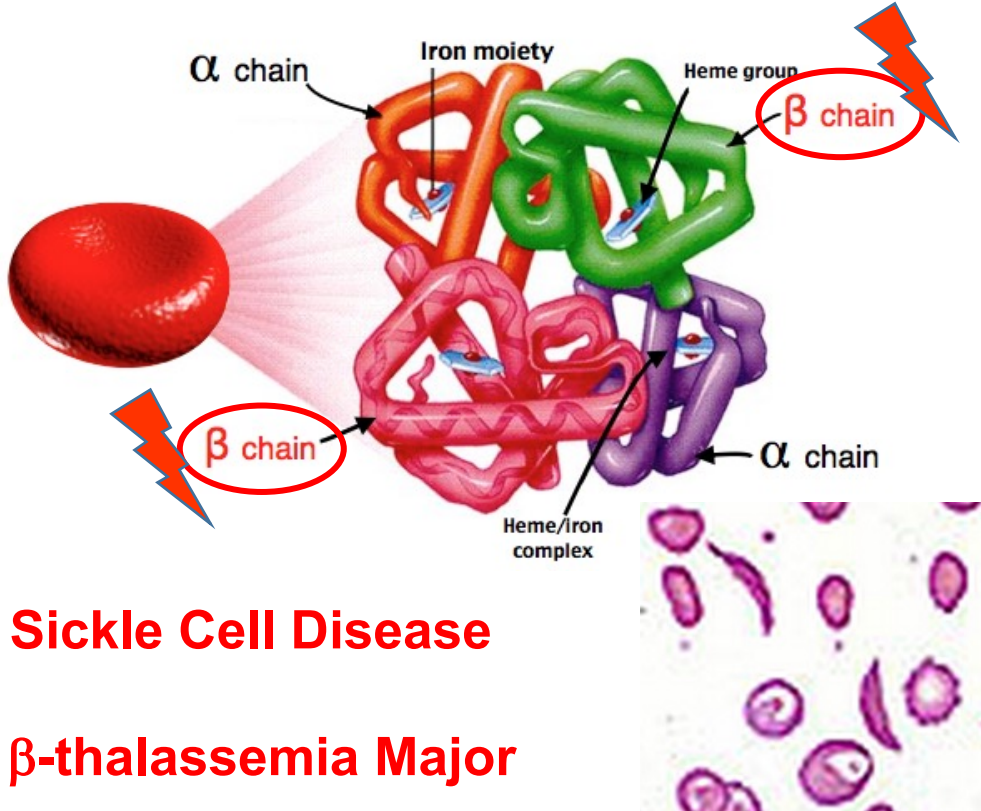
Abstract

The clinical benefit of fetal hemoglobin (HbF, $\alpha_2\gamma_2$) in the severity of hemoglobin disorders is well documented. Understanding the mechanisms controlling this developmental switch is critical to new treatment options. My studies intended to explore the role of a fetal-specific mRNA binding protein, IGF2BP1, in this process.



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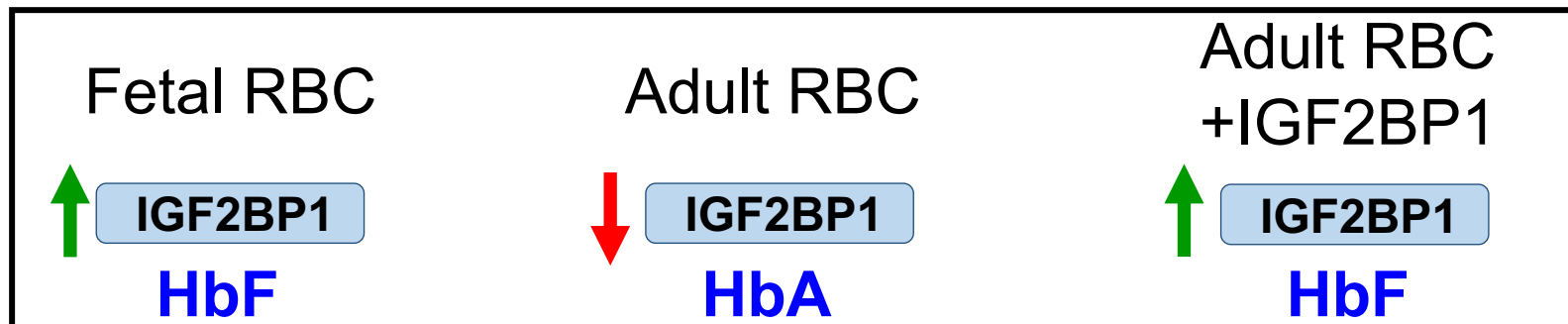
Patients Who Continue to Produce Fetal Hemoglobin have Reduced Symptoms or No Disease



Continued Production of HbF into adulthood

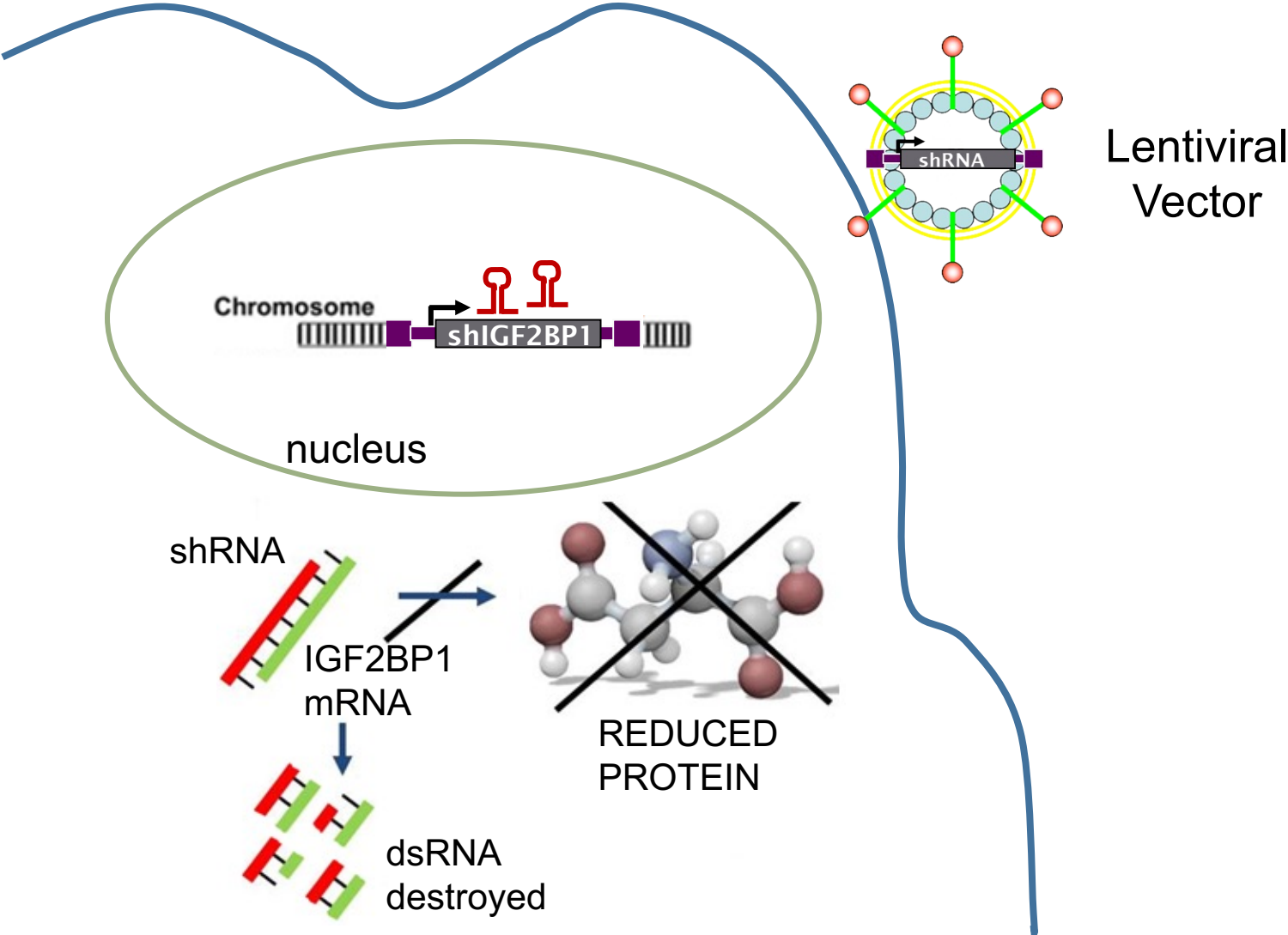
Completely Asymptomatic if HbF \geq 30% of total Hemoglobin

Steinberg et al, Blood 2014

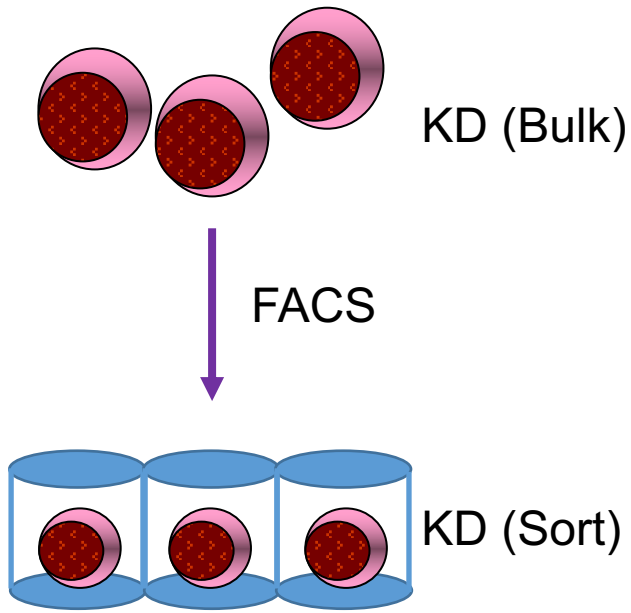


RNA-Specific Knockdown of IGF2BP1

shRNA knockdown

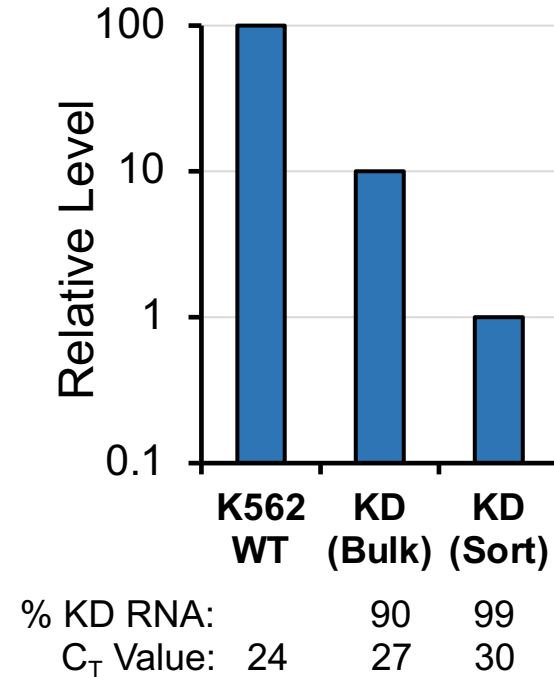


FACS Sorting of K562 Human Erythroleukemia Cells with IGF2BP1 KD

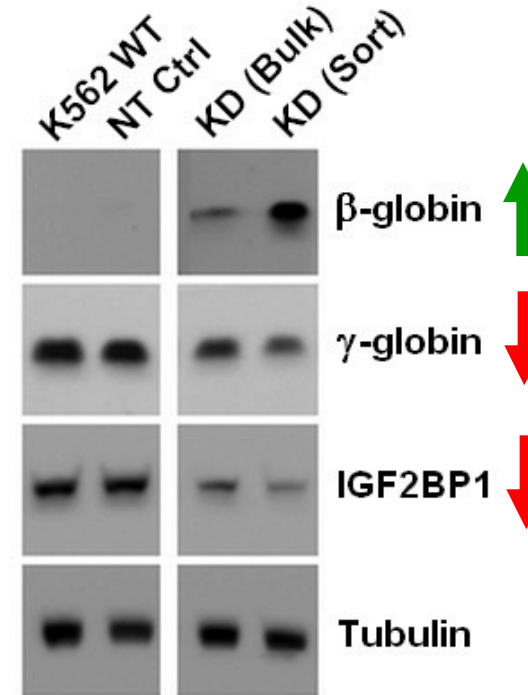


Screen Clones for Reduction in IGF2BP1 mRNA

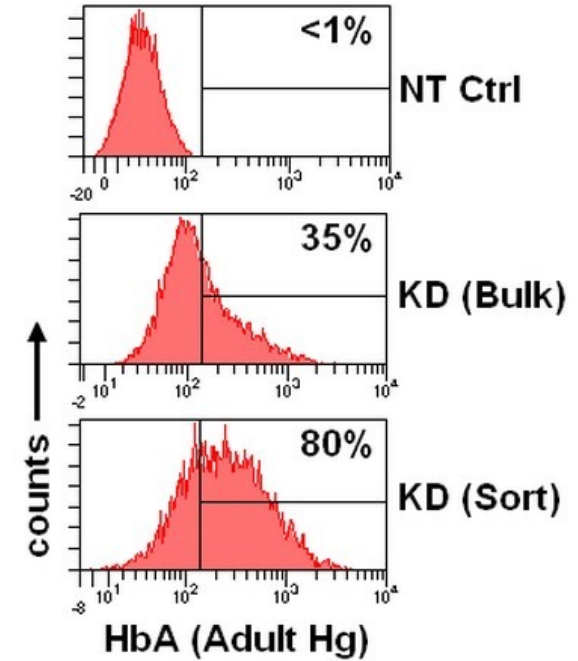
IGF2BP1 mRNA



Globin protein level as a function of IGF2BP1



Adult Hb Production as a function of IGF2BP1



TAKE HOME MESSAGE

What I found from my experiments...

- **shRNA knockdown of IGF2BP1 to levels $\leq 1\%$ of that in wild type K562 human erythroleukemia cells is sufficient to reverse hemoglobin production from the fetal (HbF, $\alpha_2\gamma_2$) to adult type (HbA, $\alpha_2\beta_2$).**
- **Creates a useful model system to define the mechanism(s) by which IGF2BP1 functions in hemoglobin switching.**



Acknowledgements

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