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(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT OF HEMOGLOBINOPATHIES

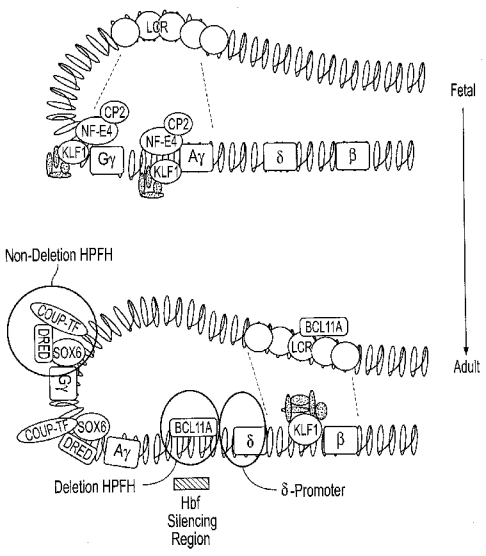


FIG. 1

Non-Deletion HPFH... HPFH non de délétion
Fetal ... Fœtal
Adult ... Adulte
Deletion HPFH... HPFH de délétion
δ-Promoter... δ promoteur
HbF Silencing Region... Région d'inactivation de HbF

(57) Abstract: Provided are compositions and methods for the treatment of hemoglobinopathies such as thalassemias and sickle cell disease. Compositions and methods include one or more endonuclease(s) or endonuclease fusion protein(s), including one or more homing endonuclease(s) and/or homing endonuclease fusion protein(s) and/or CRISPR endonuclease(s) and/or CRISPR endonuclease fusion protein(s): (a) to disrupt a Bell la coding region; (b) to disrupt a Bell la gene regulatory region; (c) to modify an adult human β-globin locus; (d) to disrupt a HbF silencing DNA regulatory element or pathway, such as a Bell la-regulated HbF silencing region; (e) to mutate one or more γ-globin gene promoter(s) to achieve increased expression of a γ-globin gene; (f) to mutate one or more δ-globin gene promoter(s) to achieve increased expression of a δ-globin gene; and/or (g) to correct one or more β-globin gene mutation(s).

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