# Article information:

Therapeutic adenine base editing of human hematopoietic stem cells - PubMed  
<https://pubmed.ncbi.nlm.nih.gov/36639729/>

# Article summary:

1. The study explores the use of ABE8e, an adenine base editor variant, for therapeutic editing of human hematopoietic stem cells (HSCs) in β-thalassemia patients.

2. Efficient on-target adenine base edits were achieved at regulatory regions involved in γ-globin expression, leading to robust induction of fetal hemoglobin.

3. The researchers also developed a near-PAMless ABE variant called ABE8e-SpRY and successfully used it to correct specific mutations in patient-derived HSCs, demonstrating the potential of ABE-mediated base editing for treating inherited blood disorders.

# Article rating:

May be slightly imbalanced: The article presents the information in a generally reliable way, but there are minor points of consideration that could be explored further or claims that are not fully backed by appropriate evidence. Some perspectives may also be omitted, and you are encouraged to use the research topics section to explore the topic further.

# Article analysis:

The article titled "Therapeutic adenine base editing of human hematopoietic stem cells" discusses the potential use of adenine base editing in treating β-thalassemia, a monogenic blood disorder. The authors explore the application of ABE8e, an adenine base editor variant, in patient-derived hematopoietic stem and progenitor cells (HSPCs) to induce γ-globin expression or repair β-globin mutations.

Overall, the article provides a detailed analysis of the efficiency and effectiveness of ABE8e-mediated base editing in HSPCs. The authors present data on the successful introduction of nucleotide substitutions at regulatory regions, resulting in robust γ-globin induction. They also describe the development of a near-PAMless ABE variant, ABE8e-SpRY, and its successful application in correcting specific mutations in patient-derived HSPCs.

The article appears to be well-supported by experimental data and includes figures that illustrate the results obtained. The authors provide statistical analyses and present mean values with standard deviations for their findings. This adds credibility to their claims and supports the reliability of their results.

However, there are some potential biases and limitations to consider in this article. Firstly, it is important to note that this study was conducted using ex vivo models and animal models (mice). While these models can provide valuable insights into potential therapeutic approaches, they may not fully represent the complexities and challenges associated with human patients.

Additionally, the article primarily focuses on the positive outcomes and efficacy of ABE8e-mediated base editing. It does not extensively discuss potential risks or limitations associated with this approach. For example, off-target effects are briefly mentioned but not thoroughly explored or quantified. Further investigation into off-target effects is necessary to fully understand the safety profile of this technique.

Furthermore, while the authors mention that they developed a near-PAMless ABE variant (ABE8e-SpRY), they do not provide a comprehensive comparison of its efficiency and specificity compared to the original ABE8e variant. This information would be valuable in assessing the potential advantages or disadvantages of using ABE8e-SpRY.

The article also lacks a discussion on potential ethical considerations associated with genome editing in human HSPCs. The use of genome editing techniques raises important ethical questions, such as the potential for unintended consequences or the creation of heritable genetic modifications. These considerations should be addressed in order to have a well-rounded analysis of the topic.

In conclusion, while the article provides valuable insights into the potential therapeutic application of adenine base editing in treating β-thalassemia, it has some limitations and biases that should be taken into account. Further research is needed to fully understand the safety and efficacy of this approach, as well as to address potential ethical concerns associated with genome editing in human HSPCs.

# Topics for further research:

* Adenine base editing off-target effects in hematopoietic stem cells
* Comparison of ABE8e-SpRY and ABE8e efficiency and specificity
* Ethical considerations of genome editing in human hematopoietic stem cells
* Challenges and limitations of ex vivo models in studying β-thalassemia treatment
* Potential unintended consequences of adenine base editing in hematopoietic stem cells
* Heritable genetic modifications and genome editing in human hematopoietic stem cells

# Report location:

<https://www.fullpicture.app/item/ab5217f294a455f7406e8f7947a9573f>