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Poster Submissions

Poster Title

CRISPR/CAS9 correction of sickle cell anemia mutation in patient-derived iPSCs.

Authors and their Affiliation

F J Molina-Estevez, S Park, C Sommer, A Gianotti-Sommer and G Mostoslavsky
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Please describe the extent of your work in this research

I have participated in the experimental design, perform the experiments, analyzed the results and written this manuscript.

Abstract Submission

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Would you like your abstract to be considered for an oral presentation (students and post docs only)?

Yes

CRISPR/CAS9 correction of sickle cell anemia mutation in patient-derived iPSCs.

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Sickle cell disease (SCD) is a genetic disease with a carrier's frequency as high as 3/1000 births in the Afro-American population. The complex syndrome presents with anemia, intravascular hemolysis, systemic endothelial inflammation and toxic iron overload in the liver. However, the origin of the SCD is a well-characterized point mutation on chromosome 11, affecting the structure of the adult hemoglobin.

The aim of this work is to study the feasibility of the use of SCD patients' cells as the starting point for the generation of disease-free red blood cells.

We took advantage of the two major novel discoveries: cell reprogramming, which allows the generation of induced pluripotent cell lines (iPSC) from adult somatic cells; and the CRISPR/CAS9 system, allowing the generation of engineered nucleases targeting solely the sickle mutation in the *HBB* locus.
We designed and assembled a set guide RNAs directed against de vicinity of the SCD mutation and combined them with ssODNs homologous to the targeted region, except for mutations correcting the SCD mutation and other technical silent mutations either preventing the cleavage of the corrected alleles or facilitating the screened of successfully recombined iPSC colonies.

We present the correction of the sickle cell anemia mutation in patient derived iPSC that retain all their pluripotent features and a normal karyotype after the therapeutic gene editing. The erythropoietic differentiation potential of the corrected iPSCs is being currently investigated as this cells could constitute a real cell therapy alternative to life long medication that this patients need, in a near future.