**Abstract**

Deregulated expression of human lysosomes is a fundamental hallmark of many genetic diseases. Although a number of recent studies have focused on the identification of novel lysosomal genes, few studies have systematically explored the potential role of human lysosomal genes in health and disease. In this study, we performed a genome-wide CRISPR/Cas9 screening of 60 cell lines using a pre-constructed sgRNA library targeting over 55,000 human genes. We identified a list of hundreds of genes, which are likely to be involved in lysosomal biology, and we observed human lysosomal genes with interesting expression patterns. Our results provide a comprehensive list of genes that could potentially be involved in lysosomal biology.

**Pathway Analysis**

In the presented studies, the CRISPR/Cas9 screening platform showed comparable or better performance than RNAi. Conclusions

**Conclusions**

In the presented studies, the CRISPR/Cas9 screening platform showed comparable or better performance than RNAi.

- **Gene knockdown**: The CRISPR/Cas9-mediated gene knockdown rate is comparable to the RNAi knockdown rate.
- **CRISPR assay accuracy**: The CRISPR/Cas9-mediated gene knockdown rate is comparable to the RNAi knockdown rate.
- **CRISPR technology advantage**: CRISPR technology is more efficient and robust than RNAi technology.
- **CRISPR gene editing**: CRISPR technology is more versatile and allows for more precise gene editing.
- **CRISPR technology comparison**: CRISPR technology is more efficient and robust than RNAi technology.