

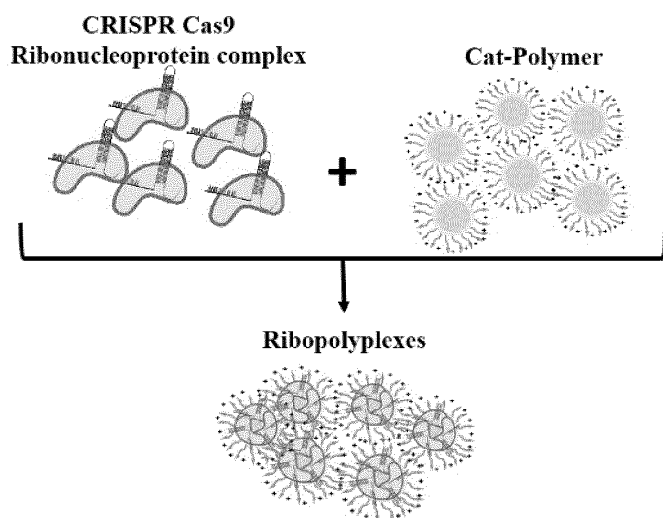


Figure 1

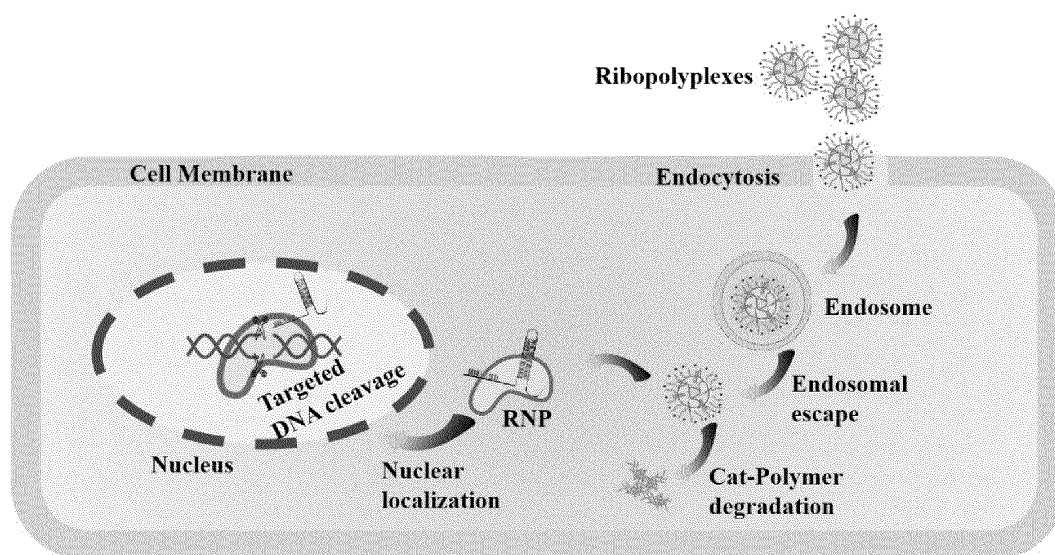
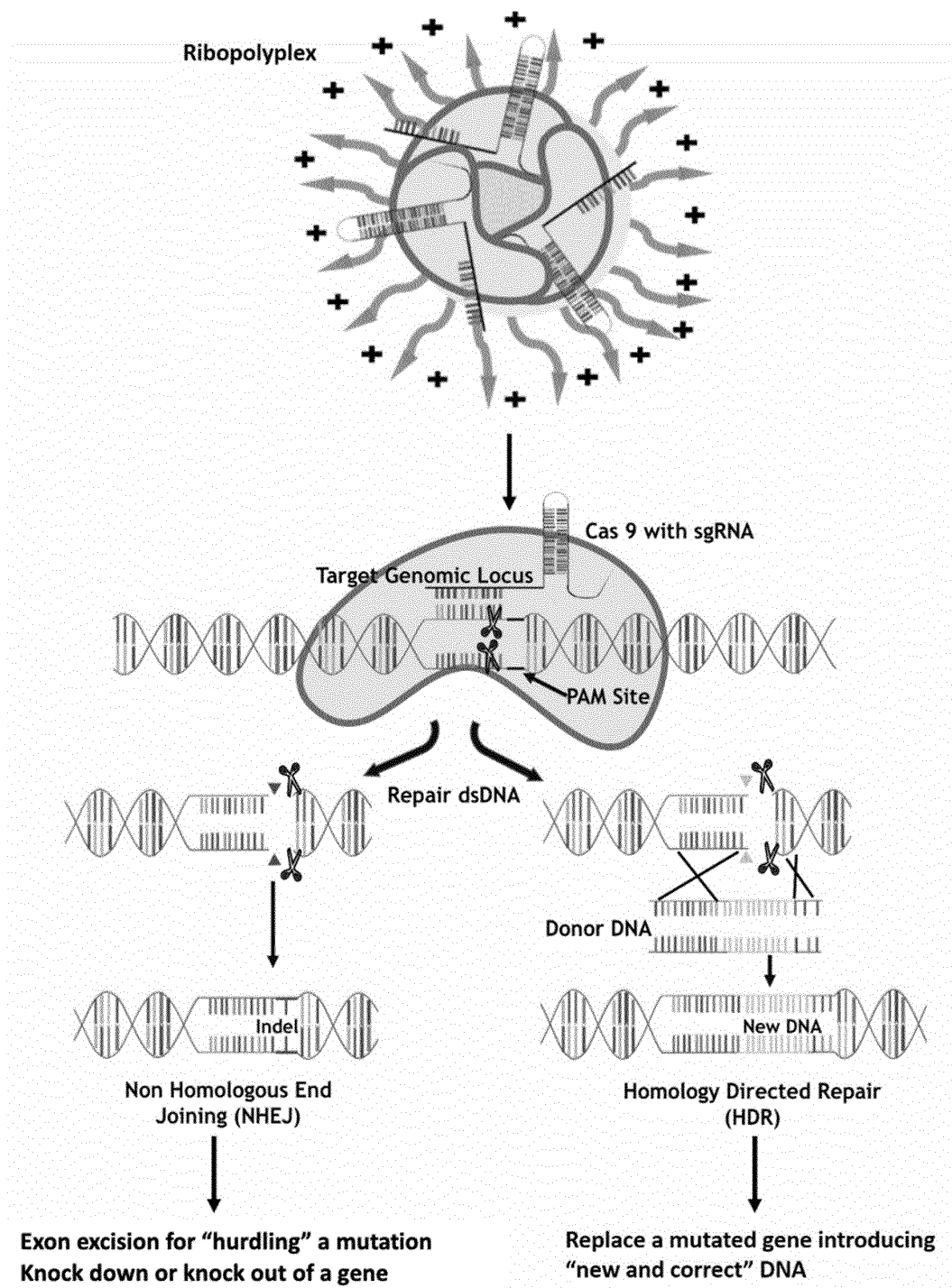
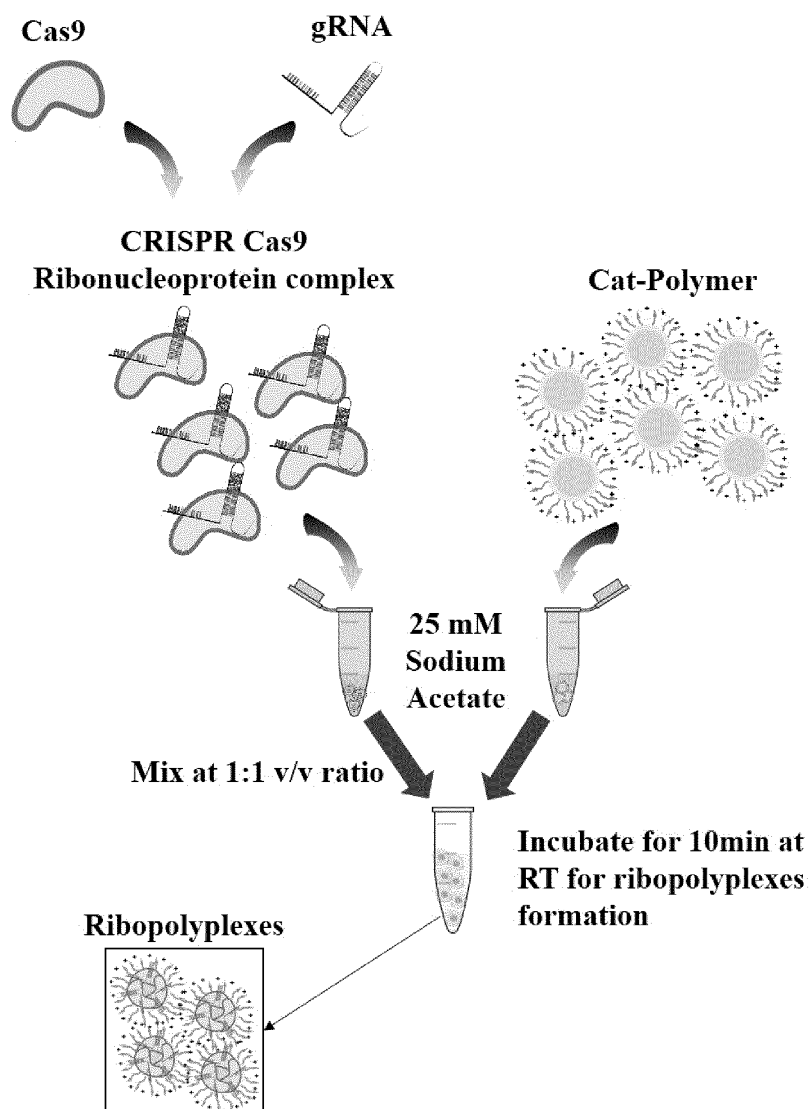


Figure 2

**Figure 3**

**Figure 4**

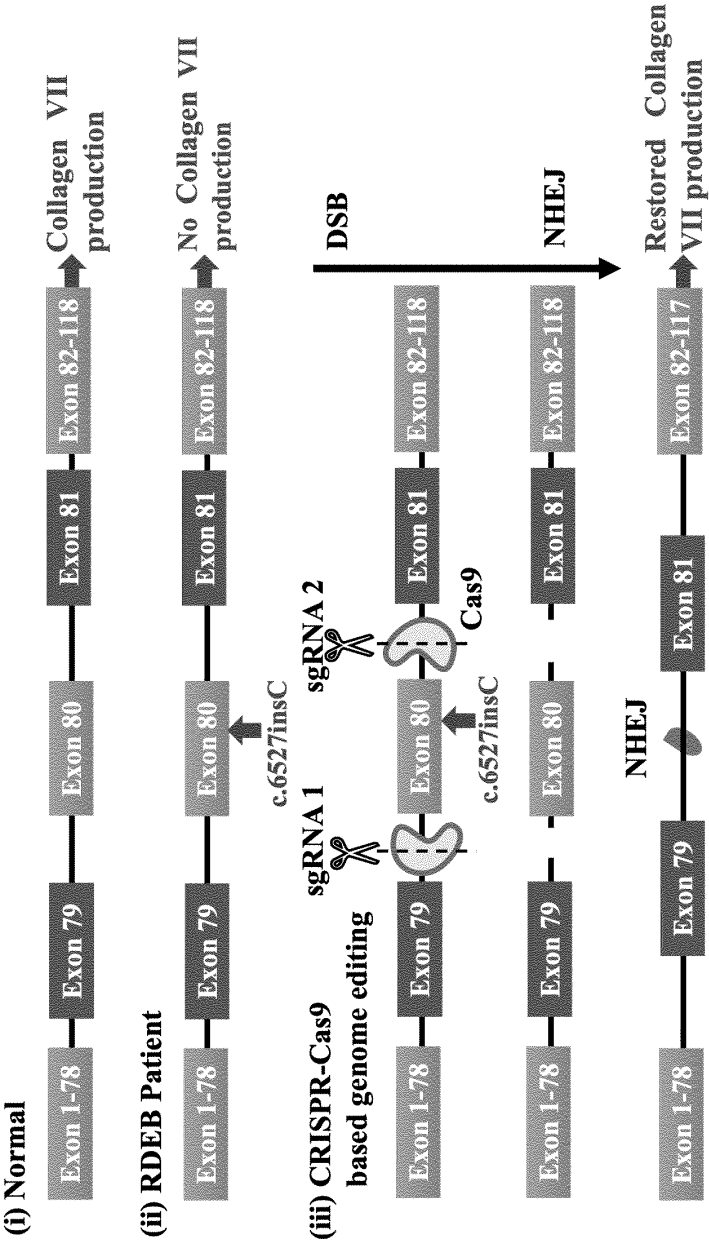


Figure 5

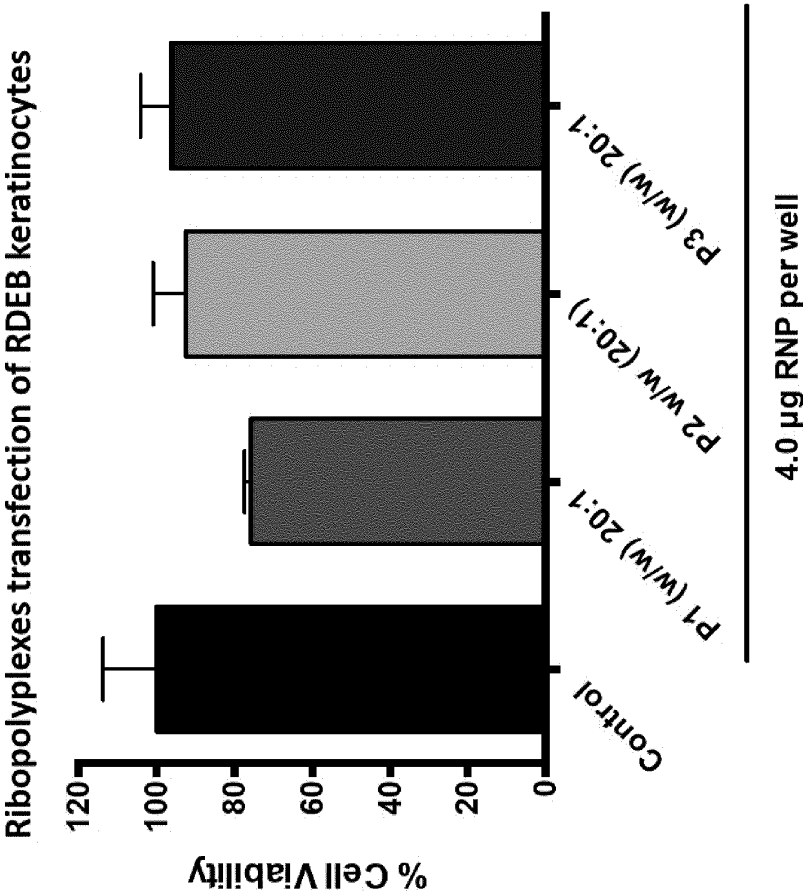


Figure 6

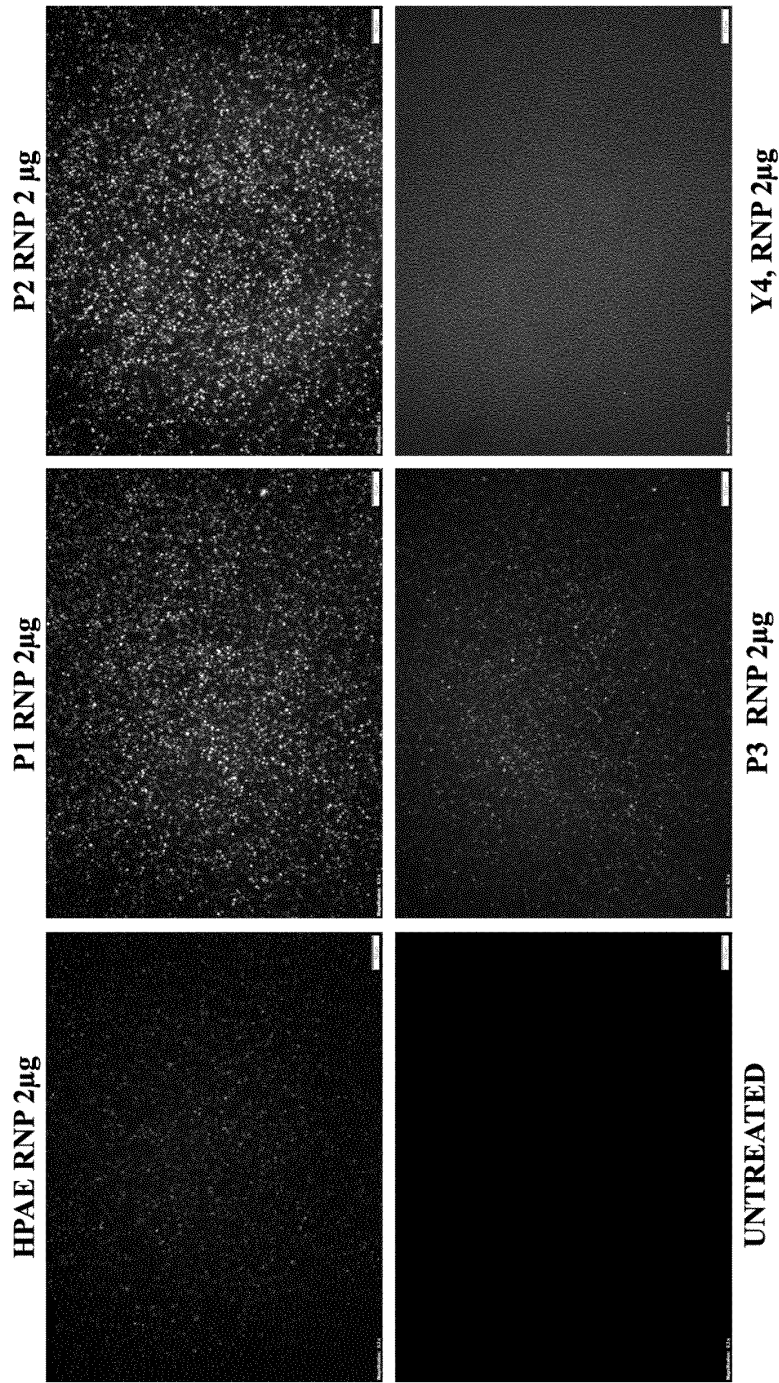


Figure 7

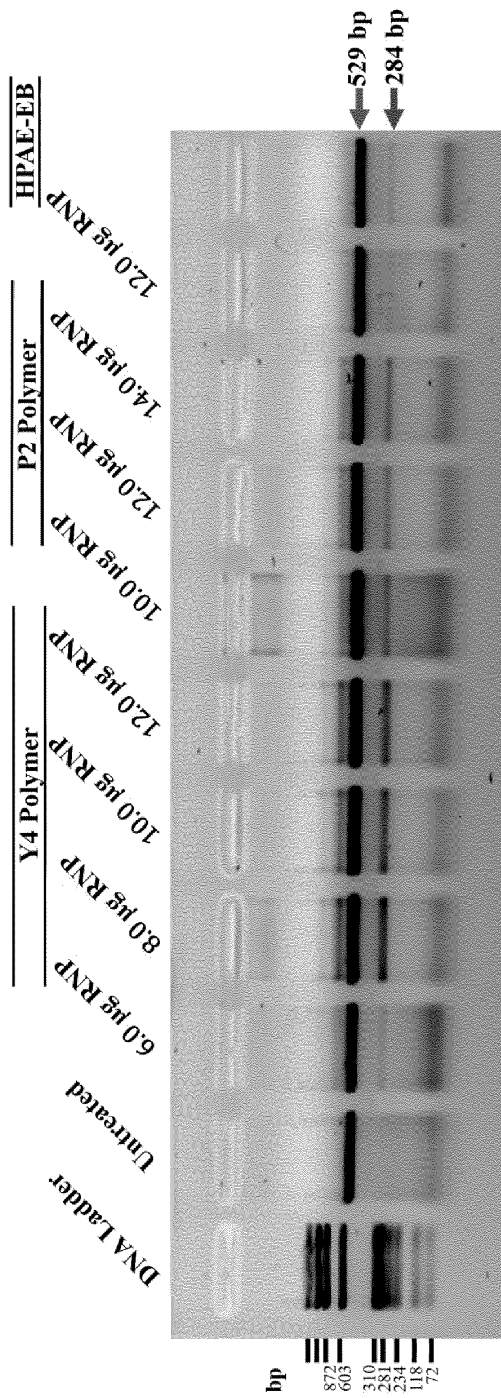


Figure 8

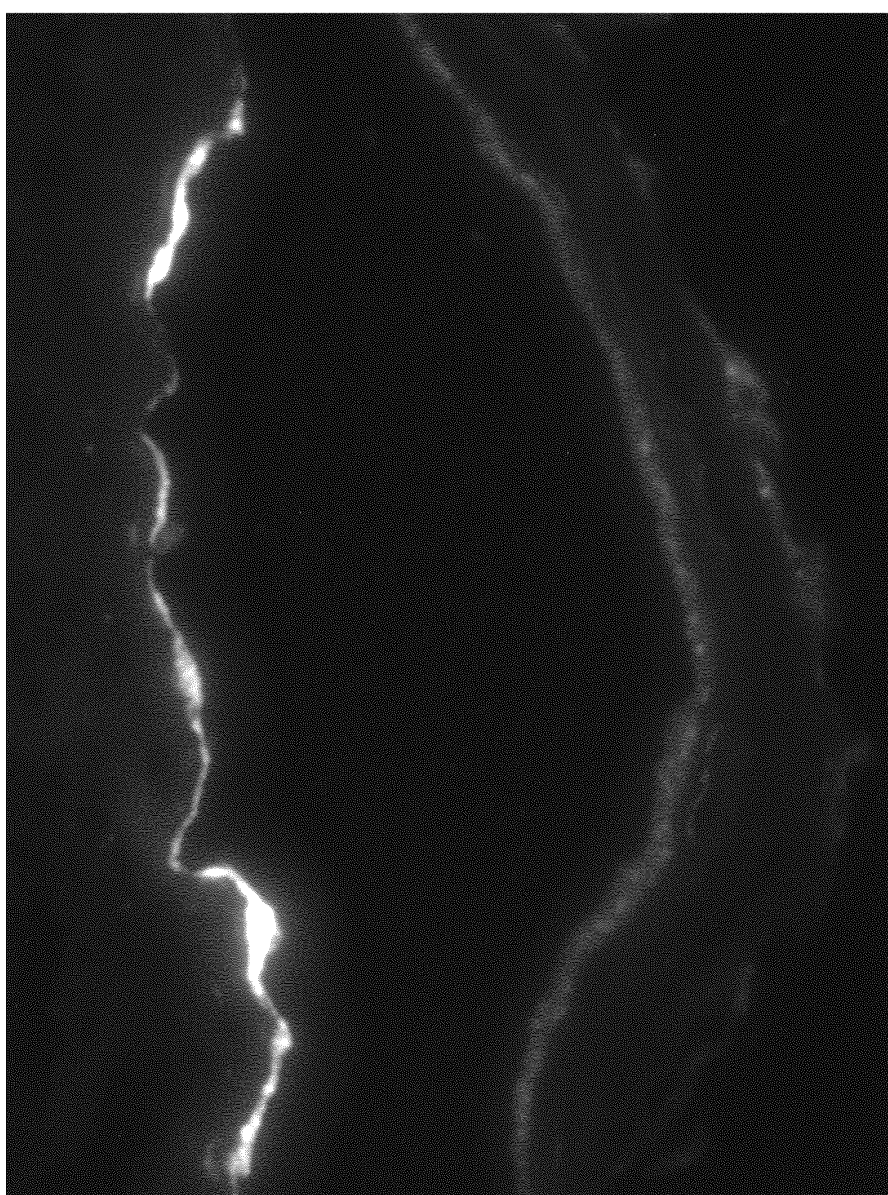
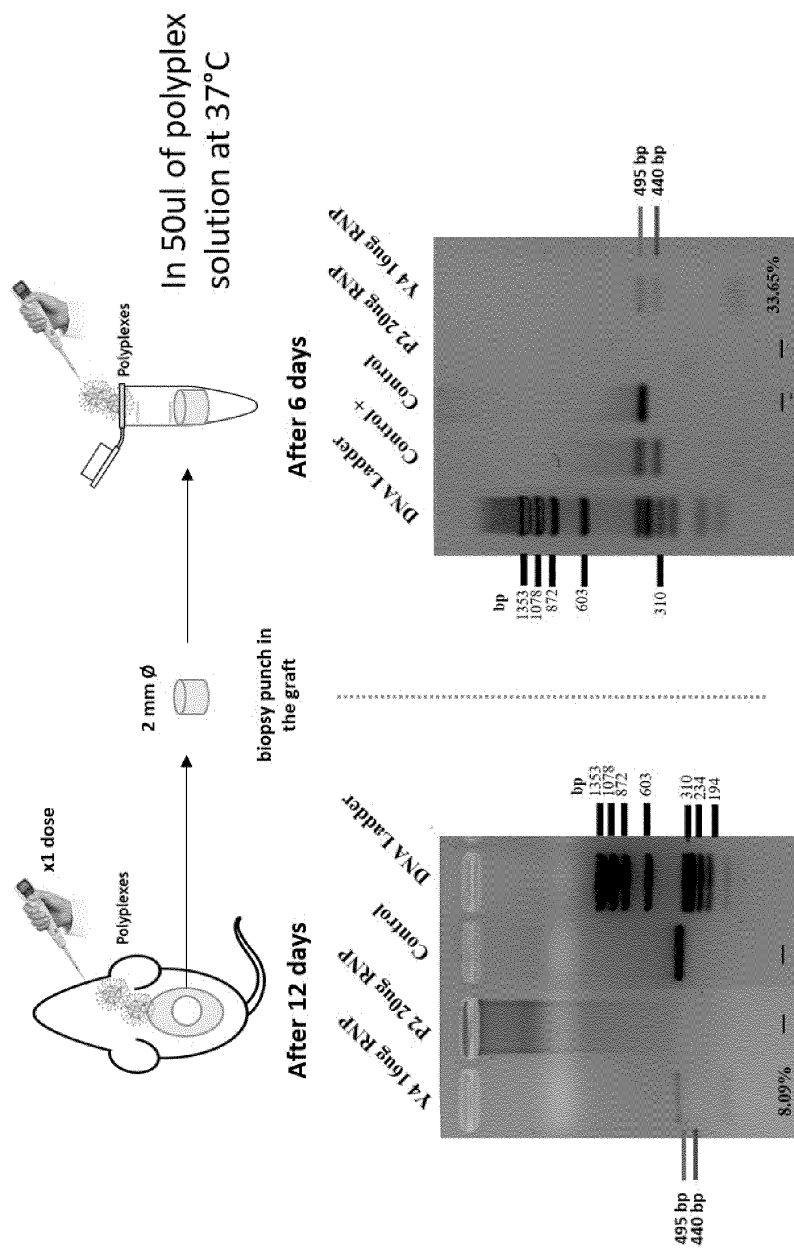


Figure 9



Bands – deletion: Full COL7A1 amplicon 495bp; exon 80 excision
COL7A1 amplicon 440bp – deletion of 55bp
Conclusions: Y4 16ugRNP correction *in vivo* and *ex vivo*

Figure 10

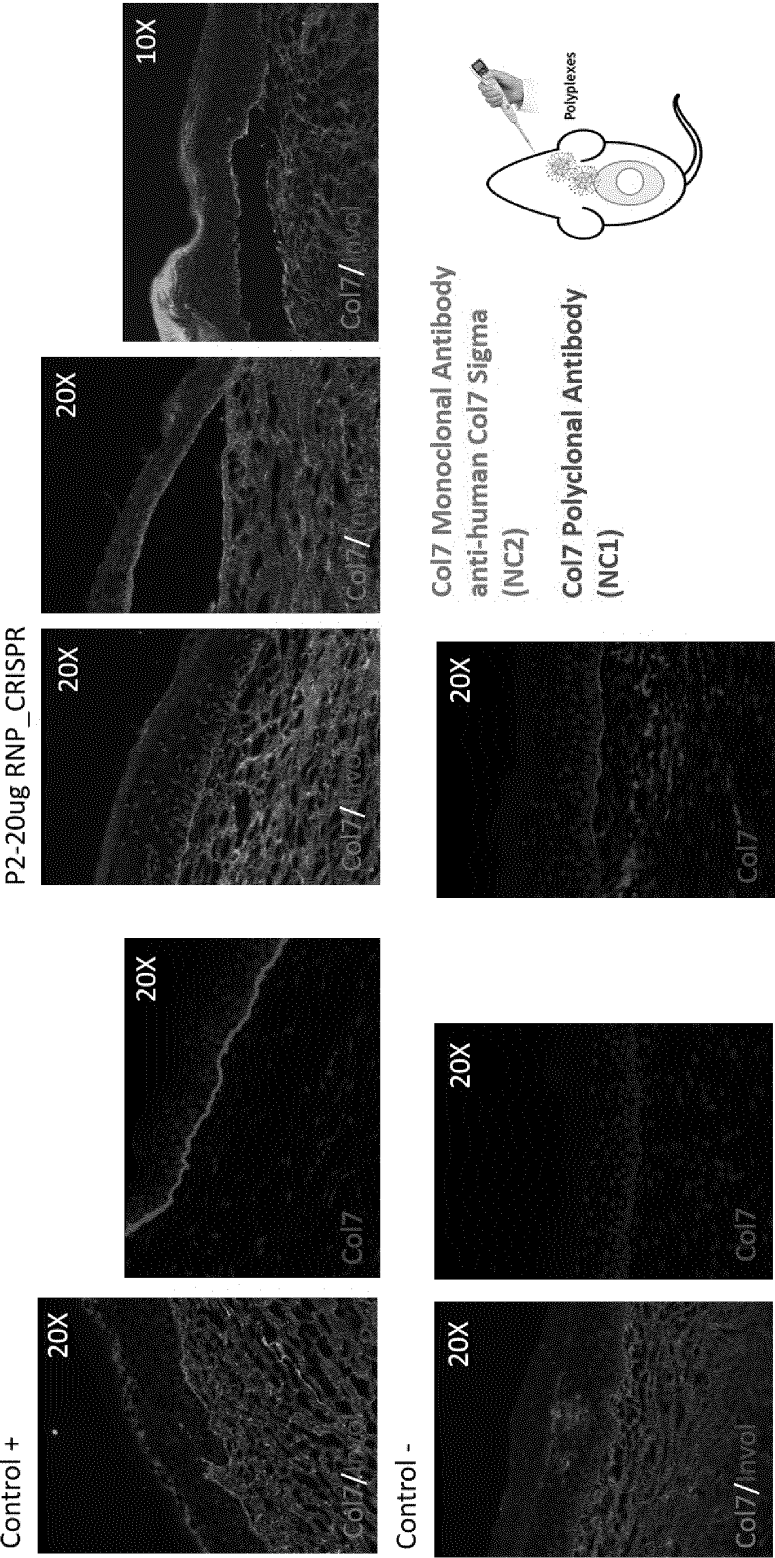
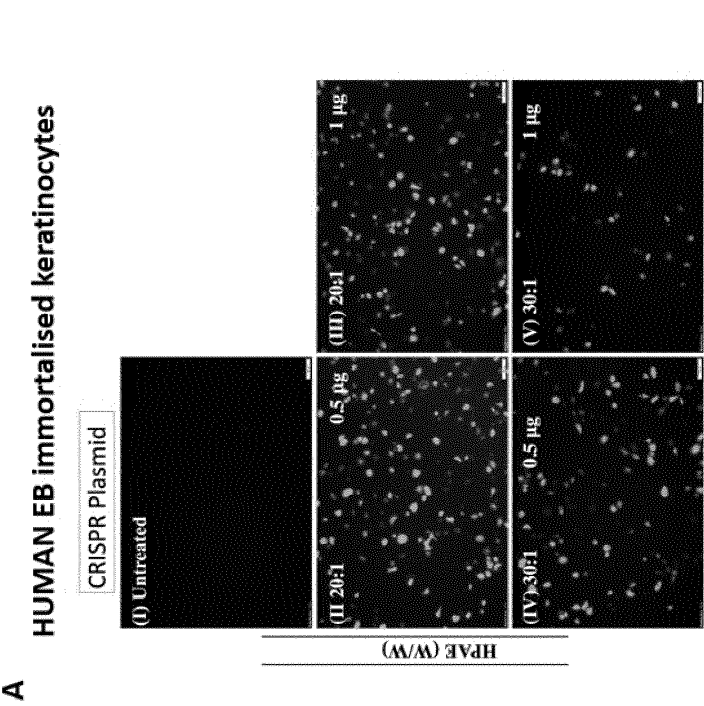
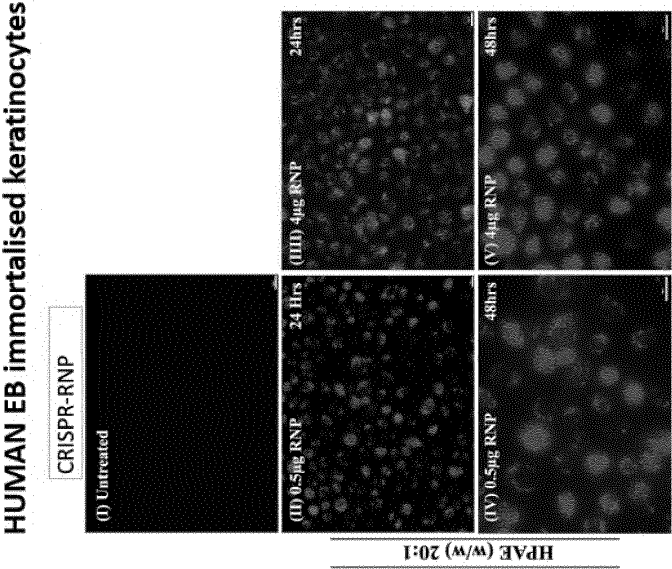


Figure 11



Green fluorescence confirms successful transfection of patient derived immortalized RDEB keratinocytes with CRISPR plasmid.

Conclusion: Transfection achieved in some cells; overall efficiency is low.



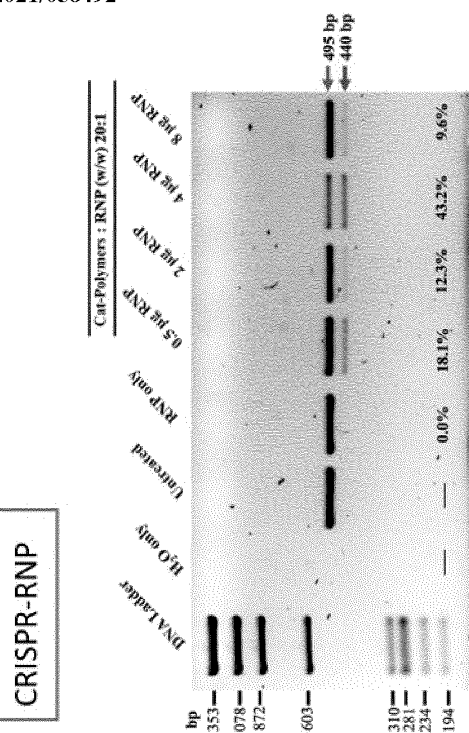
Red fluorescence confirms successful transfection of patient derived immortalized RDEB keratinocytes with CRISPR-RNP.

Conclusion: High transfection efficiency achieved in with the RNP system in comparison to plasmid approach.

Figure 12

HUMAN EB immortalised keratinocytes

HUMAN EB immortalised keratinocytes



Bands – deletion: Full COL7A1 amplicon 320bp;
exon 80 excision COL7A1 amplicon 265bp – deletion
of 45bp

Conclusion: correction achieved with 20:1 and 30:1 ratios but efficiency very low only suitable for ex vivo application.

Bands – deletion: Full COL7A1 amplicon 495bp; exon
80 excision COL7A1 amplicon 440bp – deletion of
55bp

Conclusion: higher correction efficiency achieved with the RNP system, in some cases around 40%.

Figure 13

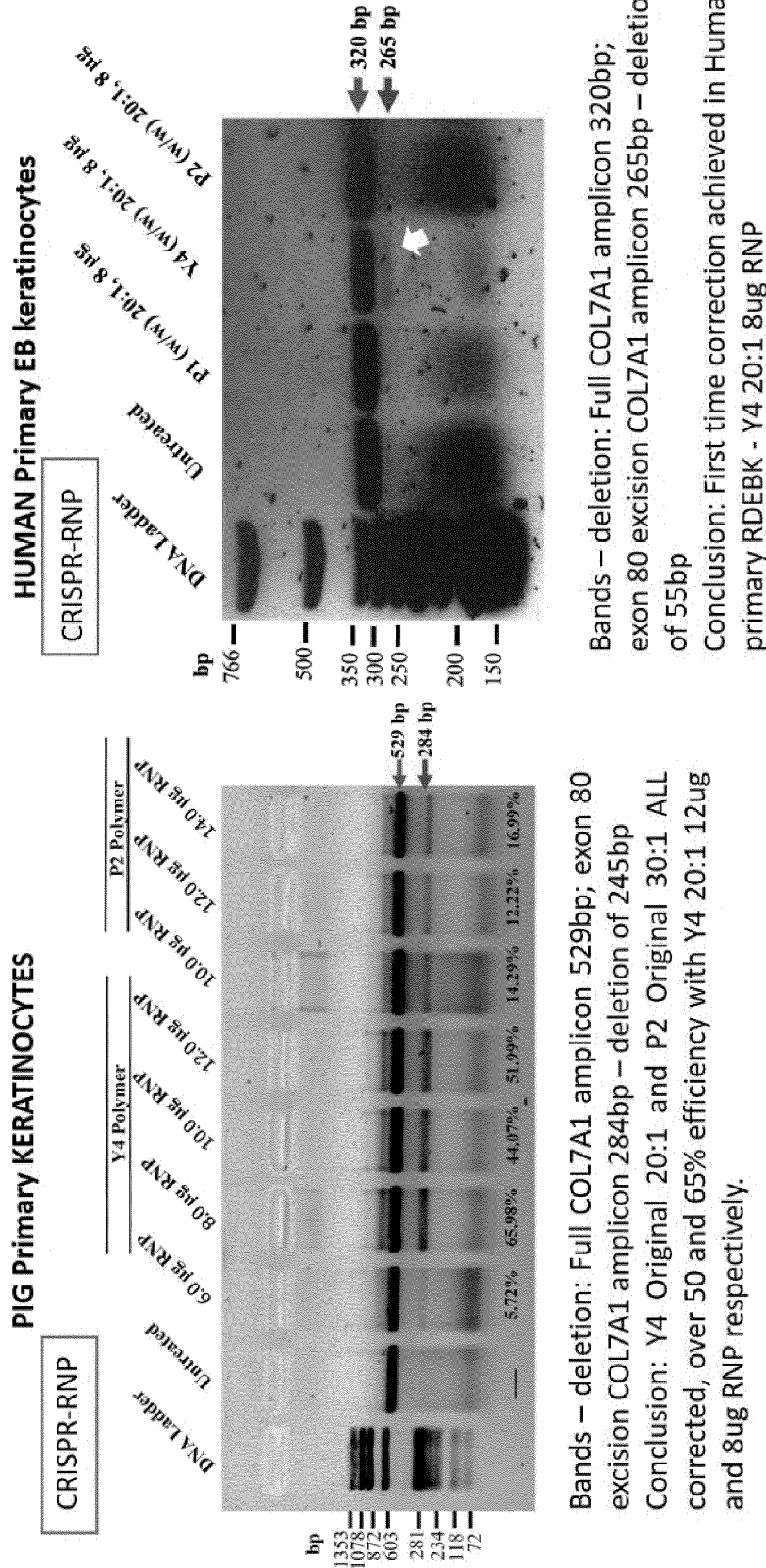


Figure 14