



**Supplementary Figure 1.** The sequence results of double and triple editing with Cas9 protein in PFF cells treated with 2  $\mu$ M M3814 and phosphorothioate-modification ssODN. (A) The gene editing results of RLN3 Exon1 and INS after simultaneously gene editing with Cas9 protein in PFF cells treated with 2  $\mu$ M M3814 and phosphorothioate-modification ssODN. (B) The gene editing results of RLN3 Exon1 and RLN3 Exon2 after simultaneously gene editing with Cas9 protein in PFF cells treated with 2  $\mu$ M M3814 and phosphorothioate-modification ssODN. (C) The gene editing results of RLN3 Exon2 and INS after simultaneously gene editing with Cas9 protein in PFF cells treated with 2  $\mu$ M M3814 and phosphorothioate-modification ssODN. (D) The gene editing results of RLN3 Exon1, RLN3 Exon2 and INS after simultaneously gene editing with Cas9 protein in PFF cells treated with 2  $\mu$ M M3814 and phosphorothioate-modification ssODN.