

## Description of Additional Supplementary Files

### Title: Supplementary Data 1.

**Description:** *In vivo* off target analysis of sgFah by GUIDE-tag. **Sheet 1**, UMI number of GUIDE-tag and indel frequency in Fah mice determined by deep sequencing. **Sheet 2**, Statistical analysis of targeted amplicon deep sequencing. p-values were calculated by two-tailed Student's t-test. To adjust for multiple comparisons p-values were adjusted using the Benjamini-Hochberg (BH) method.

### Title: Supplementary Data 2.

**Description:** Potential off-target sites predicted with the Fah sgRNA by CRISPRseek.

### Title: Supplementary Data 3.

**Description:** *In vivo* on target analysis at Actin site by UdiTaS. UMI number of UdiTaS in FVB mice determined by deep sequencing.

### Title: Supplementary Data 4.

**Description:** *In vivo* off target analysis of sgActin by GUIDE-tag. **Sheet 1**, Indel frequency in FVB mice determined by deep sequencing. **Sheet 2**, Statistical analysis of targeted amplicon deep sequencing. p-values were calculated by two-tailed Student's t-test. To adjust for multiple comparisons p-values were adjusted using the Benjamini-Hochberg (BH) method.

### Title: Supplementary Data 5.

**Description:** *In vivo* off target analysis of sgPcsk9 by GUIDE-tag in mouse liver. **Sheet 1**, RAW UMI number of GUIDE-tag in B6 mice determined by deep sequencing. **Sheet 2**, UMI number (Filter 1) of GUIDE-tag in B6 mice determined by deep sequencing. **Sheet 3**, UMI number (Filter 2) of GUIDE-tag in B6 mice determined by deep sequencing. **Sheet 4**, Indel frequency in B6 mice determined by deep sequencing. **Sheet 5**, Statistical analysis of targeted amplicon deep sequencing. p-values were calculated by two-tailed Student's t-test. To adjust for multiple comparisons p-values were adjusted using the Benjamini-Hochberg (BH) method.

### Title: Supplementary Data 6.

**Description:** *In vivo* off target analysis of sgPCSK9 by GUIDE-tag in mouse liver with GUIDE donor or iGUIDE donor. **Sheet 1**, RAW UMI number of GUIDE-tag in B6 mice determined by deep sequencing. **Sheet 2**, UMI number (Filter 1) of GUIDE-tag in B6 mice determined by deep sequencing. **Sheet 3**, Indel frequency in B6 mice determined by deep sequencing.

### Title: Supplementary Data 7.

**Description:** *In vivo* translocation and large deletion analysis by UdiTaS. **Sheet 1**, UMI number of Translocations in Fah, FVB and B6 mice determined by deep sequencing. **Sheet 2**, Statistical analysis of translocations. p-values were calculated by two-tailed Student's t-test. To adjust for multiple comparisons p-values were adjusted using the Benjamini-Hochberg (BH) method.

### Title: Supplementary Data 8.

**Description:** *In vivo* off target analysis of sgPCSK9 by GUIDE-tag in mouse lung. **Sheet 1**, UMI number of GUIDE-tag in Ai9 mice determined by deep sequencing. **Sheet 2**, Indel frequency in Ai9 mice determined by deep sequencing.