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**Supplemental Information**

**Targeting Adeno-Associated Virus Vectors  
for Local Delivery to Fractures  
and Systemic Delivery to the Skeleton**

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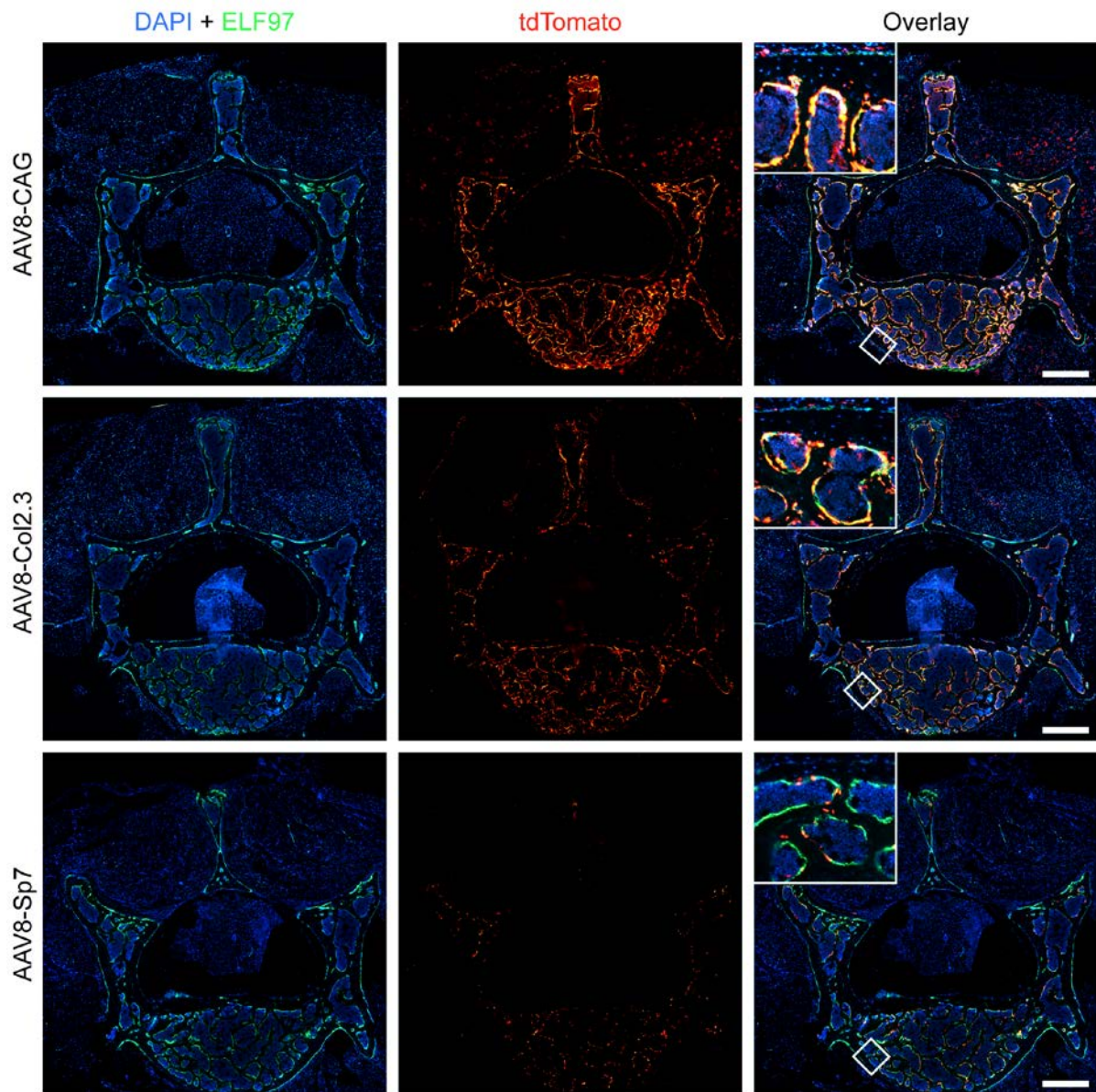
## Supplementary Data

**Supplementary Table 1: AAV variants tested in tibial fracture model** with amount of viral genomes (vg) injected into each tibial fracture and visual grading of tdTomato expression within muscle, callus, and osteoblasts of tissue sections

Vector	Amount injected (vg)	tdTomato expression (muscle)	tdTomato expression (callus)	tdTomato expression (osteoblasts)
AAV1	2.46×10 <sup>11</sup>	+++	+	+
AAV2	9.50×10 <sup>10</sup>	+++	+++	++
AAV3	1.46×10 <sup>11</sup>	+++	+	+
AAV4	5.32×10 <sup>11</sup>	+	+	+
AAV5	2.18×10 <sup>11</sup>	+	+	-
AAV6	1.19×10 <sup>10</sup>	+	+	-
AAV8	5.94×10 <sup>11</sup>	+++	+++	+++
AAV9	3.24×10 <sup>11</sup>	+++	+++	+++
AAVrh10	1.87×10 <sup>11</sup>	+	+	+
AAV-DJ	1.81×10 <sup>11</sup>	+++	+++	+++
AAV-DJ8	2.48×10 <sup>11</sup>	+++	+++	++
AAV-2i8	9.40×10 <sup>10</sup>	+++	+	+
AAV-7m8	1.03×10 <sup>11</sup>	+	-	-
AAV-LK01	3.84×10 <sup>10</sup>	+	-	-
AAV-LK02	2.20×10 <sup>11</sup>	+	+	-
AAV-LK03	2.05×10 <sup>11</sup>	+++	+	-
AAV-LK19	1.89×10 <sup>11</sup>	+	-	-
AAV-Anc80	8.88×10 <sup>9</sup>	+++	+	+

	AAV1	AAV2	AAV3	AAV4	AAV5	AAV6	AAV8	AAV9	AAVrh10	AAV-DJ	AAV-DJ8	AAV-2i8	AAV-7m8	AAV-LK01	AAV-LK02	AAV-LK03	AAV-LK19	AAV-Anc80
MOI 1	$8 \times 10^5$	$3 \times 10^5$	$5 \times 10^5$	$9 \times 10^5$	$7 \times 10^5$	$8 \times 10^4$	$1 \times 10^6$	$6 \times 10^5$	$5 \times 10^5$	$6 \times 10^5$	$4 \times 10^5$	$3 \times 10^5$	$3 \times 10^5$	$1 \times 10^5$	$4 \times 10^5$	$3 \times 10^5$	$3 \times 10^5$	$6 \times 10^4$
MOI 2	$4 \times 10^5$	$2 \times 10^5$	$2 \times 10^5$	$5 \times 10^5$	$4 \times 10^5$	$4 \times 10^4$	$6 \times 10^5$	$3 \times 10^5$	$3 \times 10^5$	$3 \times 10^5$	$2 \times 10^5$	$2 \times 10^5$	$2 \times 10^5$	$6 \times 10^4$	$2 \times 10^5$	$2 \times 10^5$	$2 \times 10^5$	$3 \times 10^4$
MOI 3	$2 \times 10^5$	$6 \times 10^4$	$1 \times 10^5$	$4 \times 10^5$	$1 \times 10^5$	$2 \times 10^4$	$4 \times 10^5$	$1 \times 10^5$	$2 \times 10^5$	$1 \times 10^5$	$2 \times 10^5$	$6 \times 10^4$	$7 \times 10^4$	$3 \times 10^4$	$1 \times 10^5$	$1 \times 10^5$	$1 \times 10^5$	$1 \times 10^4$
MOI 4	$8 \times 10^4$	$3 \times 10^4$	$5 \times 10^4$	$2 \times 10^5$	$7 \times 10^4$	$8 \times 10^3$	$2 \times 10^5$	$6 \times 10^4$	$1 \times 10^5$	$6 \times 10^4$	$8 \times 10^4$	$3 \times 10^4$	$3 \times 10^4$	$1 \times 10^4$	$7 \times 10^4$	$7 \times 10^4$	$6 \times 10^4$	$6 \times 10^3$

**Supplementary Figure 1: MOIs used for transduction of hFOB1.19 cells in Figure 4, expressed in vector genomes (vg) per cell**



**Supplementary Figure 2: Representative cryosections of L3 vertebrae from Ai9 mice receiving  $5 \times 10^{11}$  vg of AAV constructs, stained with ELF 97 for alkaline phosphatase.** Similar to the results for tibiae, high expression of tdTomato throughout the bone and muscle of the vertebral sections were detected in CAG samples. Col2.3 and Sp7 samples showed expression restricted to bone cells staining with ELF 97 and ELF 97 negative cells present within the bone matrix which appear to be osteocytes. Scale bars represent 500  $\mu\text{m}$ .