**Supplementary Data 1** - 1716 up-regulated genes in IRI samples on day 2 (n=4) compared to SHAM (n=4) with false discovery rate (FDR) < 5% and fold change +/- 2. RNA-seq differential gene expression was done using DESeq2<sup>1</sup>. The function of the R package DESeq2 (Differential expression analysis based on Negative Binomial distribution) is to perform three steps: (i) estimation of size factors; (ii) estimation of dispersion; (iii) Negative Binomial GLM fitting and Wald statistics<sup>1</sup>.

**Supplementary Data 2** - 919 down-regulated genes in IRI samples on day 2 (n=4) compared to SHAM (n=4). RNA-seq differential gene expression was determined using DESeq2<sup>1</sup>. The function of the R package DESeq2 (Differential expression analysis based on Negative Binomial distribution) is to perform three steps: (i) estimation of size factors; (ii) estimation of dispersion; (iii) Negative Binomial GLM fitting and Wald statistics<sup>1</sup>.

**Supplementary Data 3** – SHARED enhancer - gene assignment. Enhancers were assigned to the 'nearest' gene (within 100kb) using GREAT<sup>2</sup>.

**Supplementary Data 4** – IRI decreased enhancer - gene assignment. Enhancers were assigned to the 'nearest' gene (within 100kb to the TTS) using  $GREAT^2$ .

**Supplementary Data 5** – IRI increased enhancer - gene assignment. Enhancers were assigned to the 'nearest' gene (within 100kb to the TSS) using GREAT<sup>2</sup>.

**Supplementary Data 6** – IRI decreased super-enhancer - gene assignment. Super-enhancers were assigned to the 'nearest' gene (within 100kb to the TTS) using GREAT<sup>2</sup>.

**Supplementary Data 7** – IRI increased super-enhancer - gene assignment. Super-enhancers were assigned to the 'nearest' gene (within 100kb to the TTS) using GREAT<sup>2</sup>.

**Supplementary Data 8** – SHARED super-enhancer - gene assignment. Super-enhancers were assigned to the 'nearest' gene (within 100kb to the TTS) using GREAT<sup>2</sup>.

**Supplementary Data 9** - All identified transcription factor motifs in each of the three categories, SHARED, IRI-decreased, IRI-increased ranked by p-value. HOMER<sup>3</sup> was used for motif analysis using the default settings.

**Supplementary Data 10** - 676 up-regulated genes in the IRI JQ1 day 2 kidneys (n=4) compared to IRI day 2 kidneys (n=4) with false discovery rate (FDR) < 5% and fold change +/- 2. RNA-seq differential gene expression was done using DESeq2<sup>1</sup>. The function of the R package DESeq2 (Differential expression analysis based on Negative Binomial distribution) is to perform three steps: (i) estimation of size factors; (ii) estimation of dispersion; (iii) Negative Binomial GLM fitting and Wald statistics<sup>1</sup>.

**Supplementary Data 11** - 2378 down-regulated genes in IRI JQ1 day 2 kidneys (n=4) compared to IRI day 2 kidneys (n=4) with false discovery rate (FDR) < 5% and fold change +/- 2. RNA-seq differential gene expression was done using DESeq2<sup>1</sup>. The function of the R package DESeq2 (Differential expression analysis based on Negative Binomial distribution) is to perform three steps: (i) estimation of size factors; (ii) estimation of dispersion; (iii) Negative Binomial GLM fitting and Wald statistics<sup>1</sup>.

**Supplementary Data 12** - 774 up-regulated genes in SHAM JQ1 day 2 kidneys (n=3) compared to SHAM vehicle day 2 kidneys (n=4) with false discovery rate (FDR) < 5% and fold change +/-2. RNA-seq differential gene expression was done using DESeq2<sup>1</sup>. The function of the R package DESeq2 (Differential expression analysis based on Negative Binomial distribution) is to perform three steps: (i) estimation of size factors; (ii) estimation of dispersion; (iii) Negative Binomial GLM fitting and Wald statistics<sup>1</sup>.

**Supplementary Data 13** - 1667 down-regulated genes in SHAM JQ1 day 2 kidneys (n=3) compared to SHAM vehicle day 2 kidneys (n=4) with false discovery rate (FDR) < 5% and fold change +/- 2. RNA-seq differential gene expression was done using DESeq2<sup>1</sup>. The function of the R package DESeq2 (Differential expression analysis based on Negative Binomial distribution) is to perform three steps: (i) estimation of size factors; (ii) estimation of dispersion; (iii) Negative Binomial GLM fitting and Wald statistics<sup>1</sup>.

**Supplementary Data 14** - Gene Ontology (GO) term: molecular function significantly enriched by down-regulated genes (1667 genes) after two days of JQ1 treatment in SHAM kidneys.

**Supplementary Data 15** – List of genes elevated in kidney tissue based on RNA-seq analysis comparing human tissues <sup>4</sup>. Marked in light blue: genes also down-regulated under JQ1 treatment in SHAM kidneys