Supplemental Files

Connectivity mapping identifies BI-2536 as a potential drug to treat diabetic kidney disease

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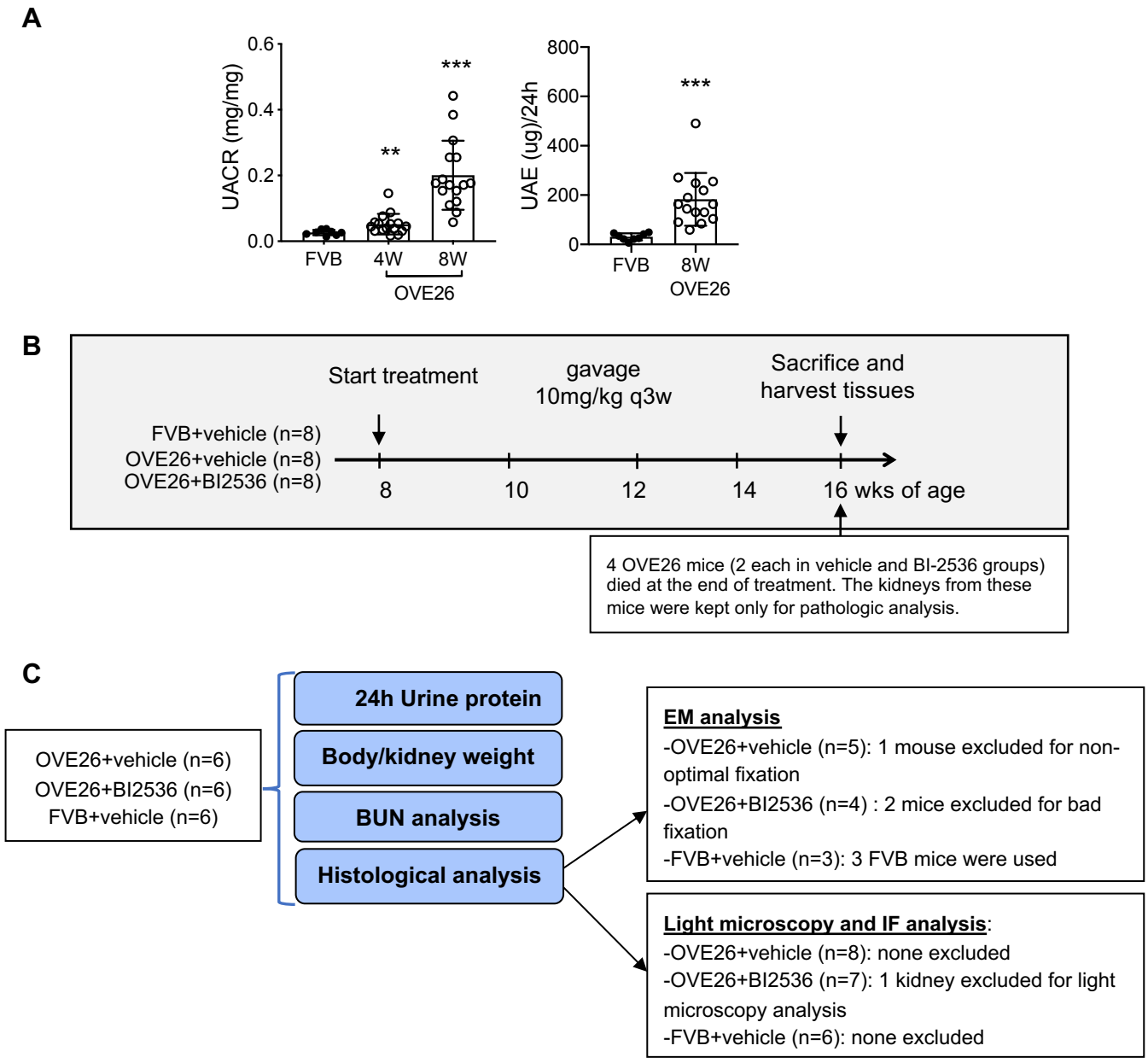
Supplemental Figure 1: Experimental procedures of BI-2536 treatment of OVE26 mice
Supplemental Figure 2: Characteristics of OVE26 mice treated with BI-2536
Supplemental Figure 3: Col IV and F4/80 immunostaining of OVE26 mouse kidneys

Supplemental Table 1: PL1K study metadata
Supplemental Table 2: Top 50 drugs predicted to reverse 15 input signatures
Supplemental Table 3: DKD consensus genes
Supplemental Table 4: Top 50 drug predicted to reverse DKD consensus signatures

Supplemental File: Full unedited blot for Figures 7 and 8

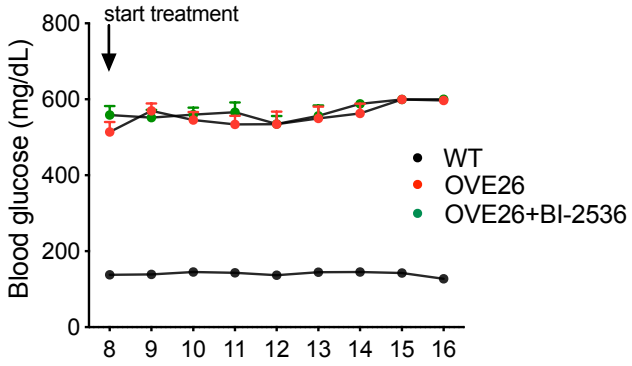
Supp. Figure 1



Supp. Figure 1. Experimental procedures of BI-2536 treatment of OVE26 mice. (A) UACR measurements of OVE26 mice at 4 and 8 weeks of age (left) and total 24-hour UAE at 8 weeks of age (right). **P<0.01 and ***P<0.001 vs. FVB control by 1-way ANOVA with Tukey's multiple comparison test. (B) Schematics of the experimental design, treatment was started in 8-week-old OVE26 mice or wildtype litter mate until 16 weeks of age (n=8 mice per group). (C) Schematics of analysis of mouse samples after 6 weeks of treatment.

Supp. Figure 2

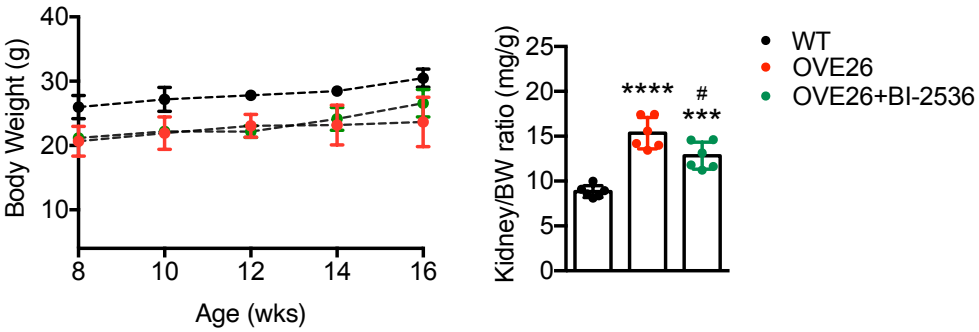
A



B

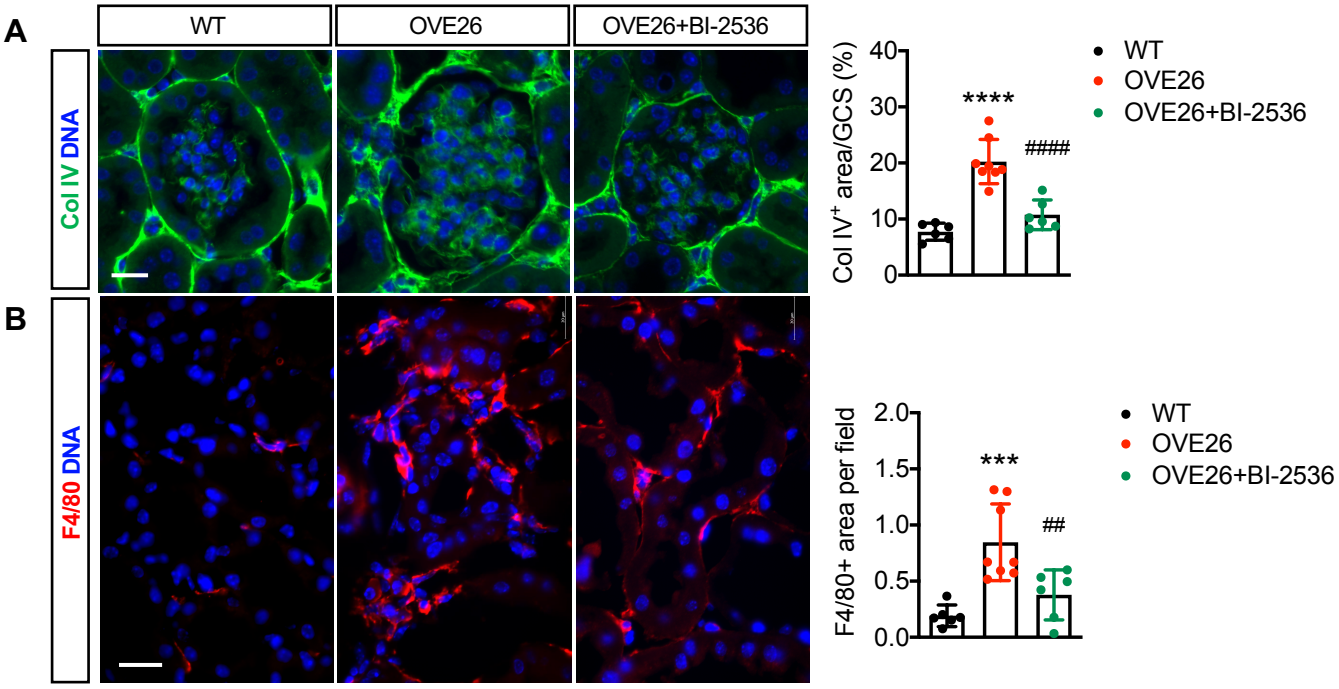
	systolic BP (mm Hg)	diastolic BP (mm Hg)
WT + vehicle	92.27±44.17	63.033±44.73
OVE26 + vehicle	110.43±40.80	72.43±21.40
OVE26 + BI2536	99.33±44.72	64.33±22.92

C



Supp. Figure 2. Characteristics of OVE26 mice treated with BI-2536. (A) Average blood glucose measurements of control and diabetic mice. (B) Blood pressure assessment with tail cuff telemetry at 16 weeks post-treatment (n=6 mouse per group). The differences between WT and OVE26 mice were not statistically significant. (C) Body weight of wildtype (WT), OVE26, and OVE26 treated with BI-2536 (OVE26+BI-2536) from 8 weeks to 16 weeks of age and kidney to body weight (BW) ratio at 16 weeks of age. ***p<0.001, and ****<0.0001 vs. WT; #p<0.05, vs. OVE26 by 1-way ANOVA with Tukey's multiple comparison test.

Supp. Figure 3



Supp. Figure 3. Col IV and F4/80 immunostaining of OVE26 mouse kidneys. Representative immunofluorescent images and quantification of COL IV and (B) F4/80. Scale bars, 20μm. Quantification is shown for percentage of Col IV+ area per glomerular cross section (GCS, n=6-8 mice per group, at least 30 glomeruli analyzed per mouse) and fraction of F4/80 area per field (n=6-8 mice per group, at least 20 fields scored per mouse). ***p<0.001, and ****<0.0001 vs. WT; ##p<0.01, and ####p<0.0001 vs. OVE26 by 1-way ANOVA with Tukey's multiple comparison test.