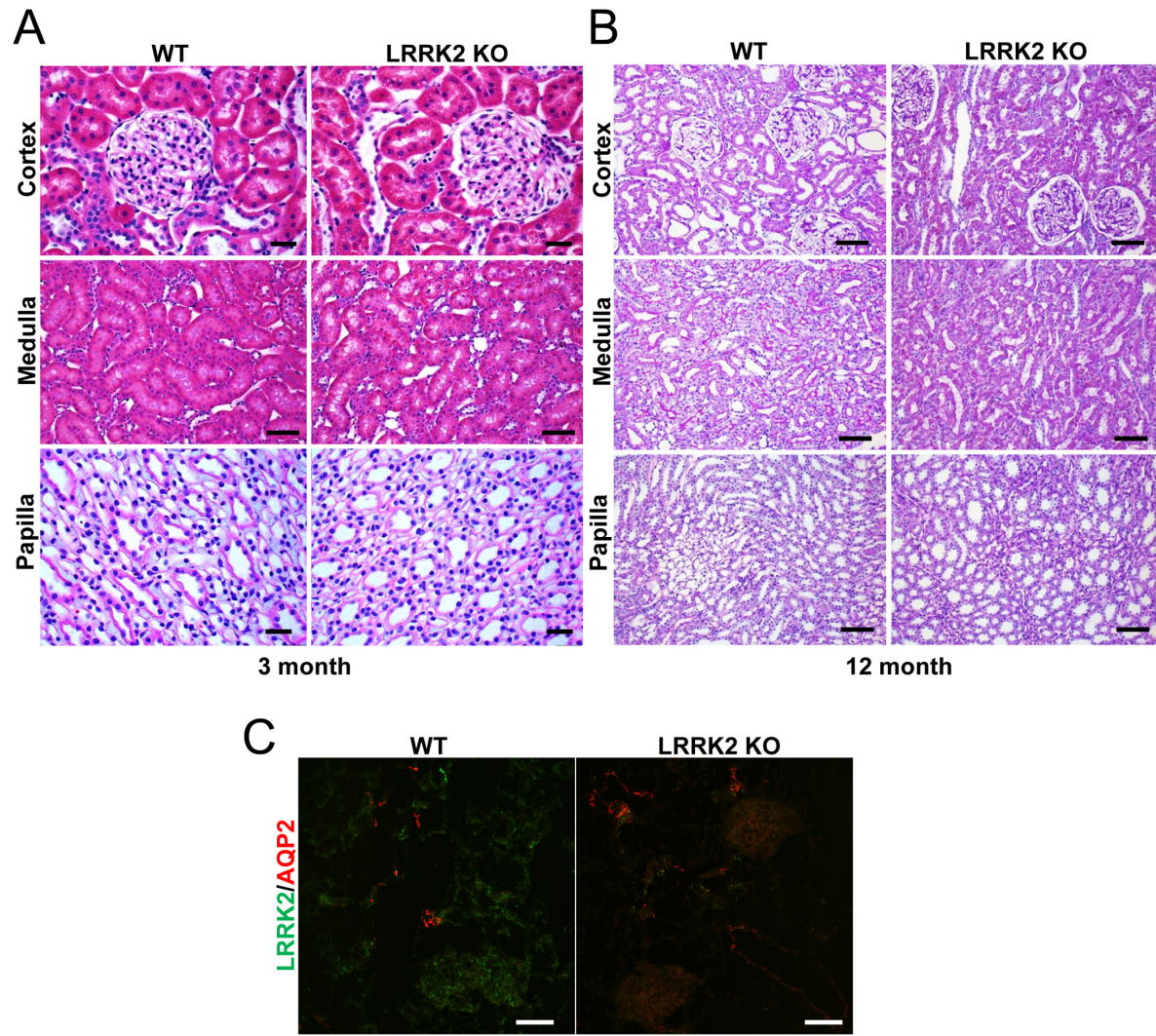
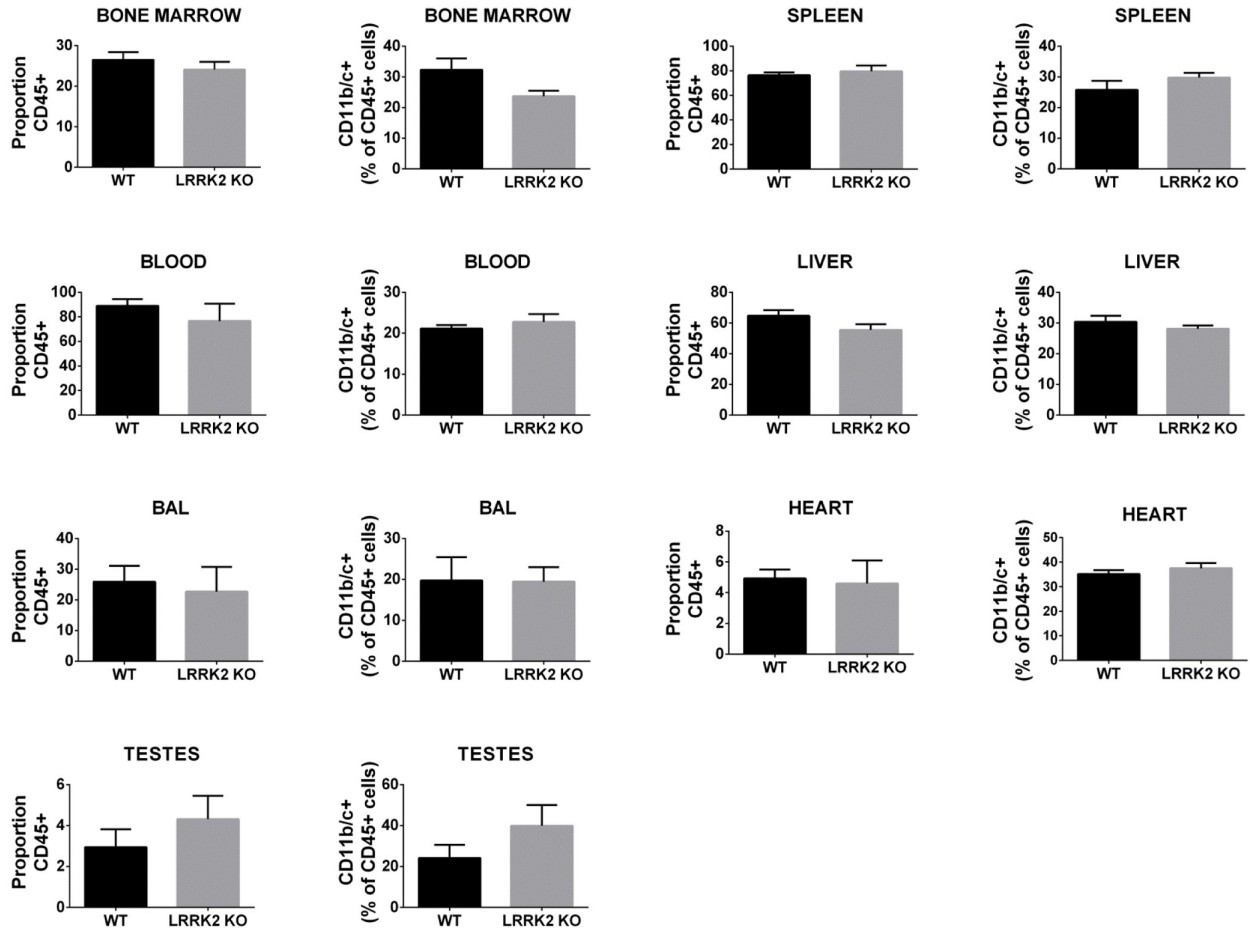


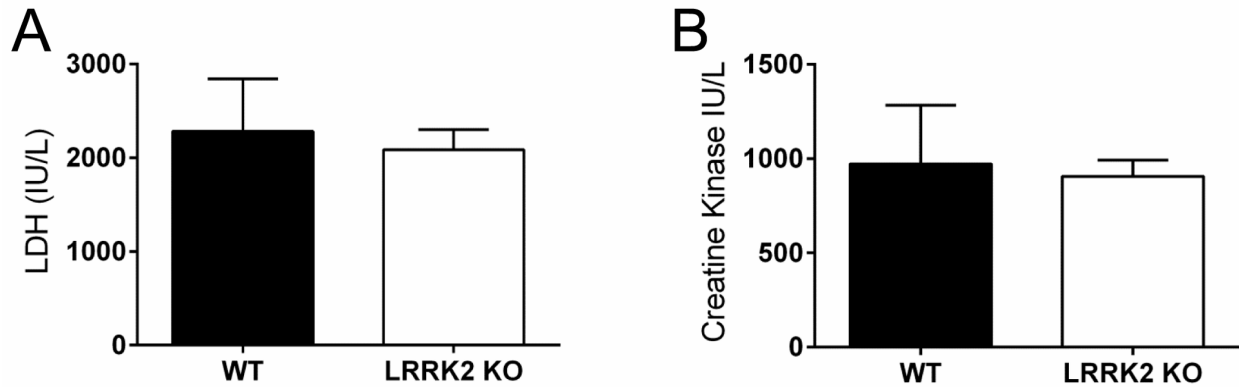
Supplementary Material



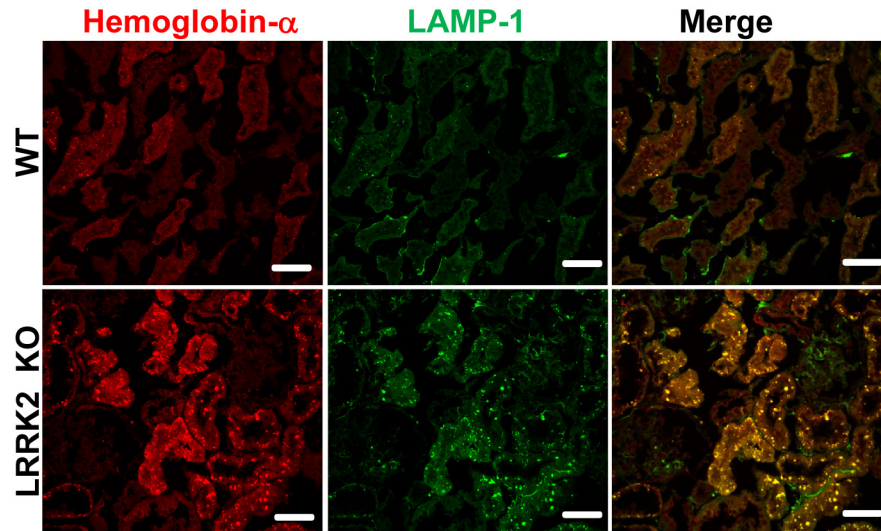
Supplementary Figure S1. Normal kidney anatomy in *LRRK2* KO rats. A) Hematoxylin and eosin (H&E) staining of 3 month WT and *LRRK2* KO kidneys sections are shown. No morphological abnormalities or other evidence of kidney disease is apparent. Scale bar represents 20 μm for the top and bottom panels and 50 μm for the middle panels. B) Representative images of periodic acid-Schiff (PAS) staining of 12 month WT and *LRRK2* KO kidneys sections are shown. While it was not quantified, it is noteworthy that the PAS stain in the *LRRK2* KO renal tubules of the cortex and medulla is of greater intensity than in the WT kidneys, which may reflect the PAS detection of glycoproteins and glycolipids. Scale bar represents 50 μm . C) Confocal images of immunofluorescence staining of LRRK2 (green color) and Aquaporin-2, AQP2 (red color), from 5 μm thick cryosections of cortex from 3-month old WT rat kidneys are shown. Scale bar represents 50 μm .



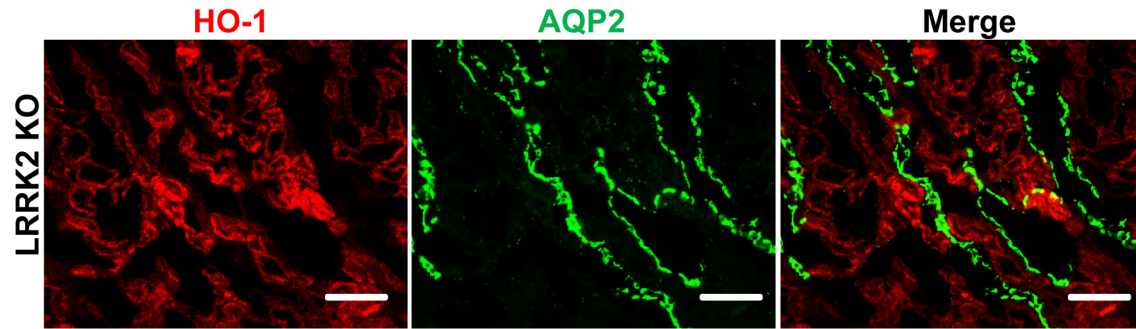
Supplementary Figure S2. Comparison of CD45⁺ CD11b/c⁺ cells in the indicated organs or tissues of WT and *LRRK2* KO rats. Bar graphs depict results of flow cytometry experiments wherein single cell suspensions from the indicated organ or tissue were stained with CD45 and CD11b/c to quantify intra-organ macrophages (CD45⁺ CD11b/c⁺). Cells were obtained from the organs of 4 WT and 5 *LRRK2* KO rats. % of CD45⁺ cells denotes overall proportions of 7-AAD negative/CD45⁺ cells, % of CD11b/c⁺ cells denotes the proportion of CD45⁺ cells that express CD11b/c. BAL- Broncho-alveolar lavage.



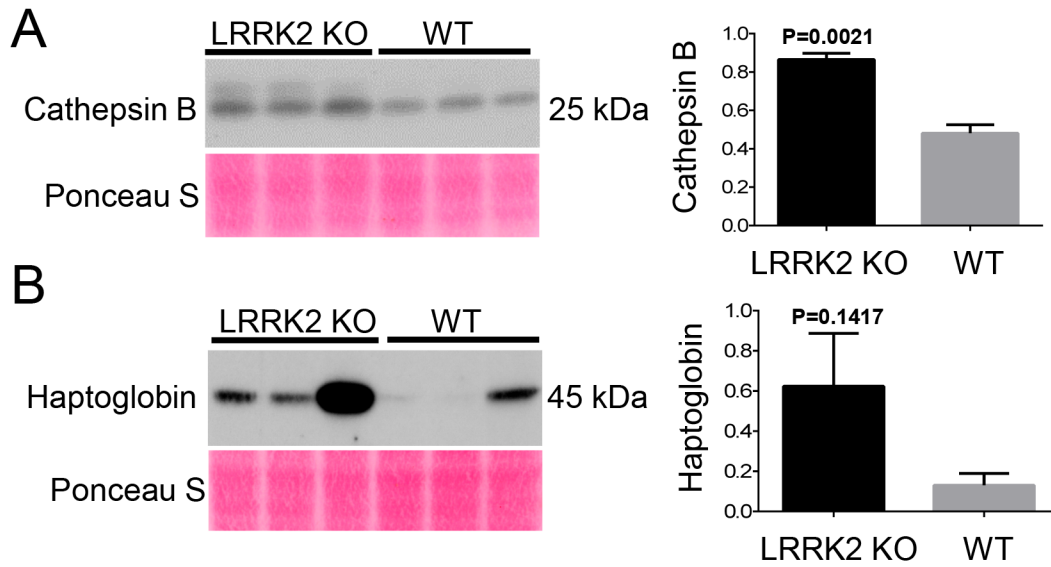
Supplementary Figure S3. Measures of muscle injury 24 hours after glycerol injection. A) Levels of serum lactate dehydrogenase (IU/L- international units/liter) at 24 hours after glycerol injection in WT and LRRK2 KO animals, indicating the same degree of muscle injury in both groups. B) Levels of creatine kinase (IU/L) at 24 hours after glycerol injection in WT and LRRK2 KO animals, indicating the same degree of muscle injury in both groups. Levels are represented as mean \pm S.E.M from N=3 WT rats and N=5 LRRK2 KO rats.



Supplementary Figure S4. Accumulation of hemoglobin- α in the cortex of *LRRK2* KO rat kidneys. *LRRK2* KO kidneys have increased hemoglobin- α staining specifically in the renal tubules that colocalize with lysosome associated membrane protein 1 (LAMP-1) stained structures. Confocal images of immunofluorescence staining of hemoglobin- α (red) and LAMP-1 (LAMP-1; green) in cortex from 3-month WT and *LRRK2* KO rat kidneys are shown. Scale bar is 50 μ m.



Supplementary Figure S5. HO-1 staining does not colocalize with the AQP2 staining. Representative images of immunofluorescence staining of HO-1 (red) and aquaporin-2 (AQP2, green) from 5 μ m thick cryosections of outer medulla from 3 month WT and *LRKR2* KO rats. The HO-1 staining did not colocalize with the AQP2 staining thus excluding the colocalization with the collecting ducts. Scale bar indicates 200 μ m.



Supplementary Figure S6. Confirmation of upregulated proteins in *LRRK2* KO kidneys. Western blots and corresponding densitometry analyses (normalized to Ponceau S) of total kidney protein lysates from 12 month old WT and *LRRK2* KO kidneys using A) anti-Cathepsin-B and B) anti-Haptoglobin antibodies are shown. Ponceau S is shown for loading. Graphs are represented as mean \pm S.E.M from N=3 WT rats and N=3 *LRRK2* KO rats.

Supplementary Table S1. Intensities of identified peaks (m/z) from LRRK2 KO lipid extract.

| LRRK2 KO Lipid extract | | | |
|------------------------|------------------|------------|------------------|
| <u>m/z</u> | <u>Intensity</u> | <u>m/z</u> | <u>Intensity</u> |
| 1278.0 | 298.01 | 1564.2 | 1480.72 |
| 1302.0 | 209.99 | 1567.2 | 1180.4 |
| 1304.0 | 238.65 | 1569.3 | 1502.03 |
| 1306.0 | 216.16 | 1571.2 | 1046.7 |
| 1326.0 | 342.33 | 1572.3 | 456.31 |
| 1354.0 | 244.06 | 1575.3 | 338.83 |
| 1463.2 | 194 | 1589.3 | 630.15 |
| 1485.2 | 348.21 | 1592.3 | 2066.09 |
| 1492.2 | 369.32 | 1594.3 | 722.66 |
| 1494.2 | 450.2 | 1596.3 | 757.25 |
| 1513.2 | 429.2 | 1598.3 | 608.42 |
| 1516.2 | 1209.58 | 1617.3 | 436.03 |
| 1518.3 | 654.01 | 1620.3 | 764.83 |
| 1519.3 | 362.06 | 1623.4 | 295.02 |
| 1521.3 | 430.98 | 1625.4 | 298.63 |
| 1540.2 | 1050.48 | 1724.3 | 253.22 |
| 1542.2 | 1619.22 | 1751.2 | 269.17 |
| 1544.3 | 1307.73 | 1772.3 | 307.19 |
| 1547.3 | 467.09 | 1800.3 | 340.46 |
| 1549.3 | 317.14 | | |