

## Supplement 1. Disease Modelling – Background and Rationale

To mimic early-stage CKD, renal function was artificially reduced by performing a unilateral nephrectomy. Briefly, a small lumbar incision was made and the left kidney was removed from each rat. Unilateral nephrectomies are an appropriate model of early-stage CKD in rats, as opposed to the commonly used 5/6 nephrectomy which more closely models end-stage renal disease. Unilateral nephrectomies result in compensatory enlargement of the remnant kidney [61-65], increased serum creatinine concentrations [63, 66, 67], increased focal glomerulosclerosis [68, 69], increased mesangial sclerosis [68], increased interstitial fibrosis [68], increased proteinuria [66, 68, 70], and increased urinary albumin excretion [69]. In addition to nephrectomising the rats, SHR<sub>s</sub> were used to mimic the elevated blood pressure that is common in CKD. In male SHR<sub>s</sub>, that have not undergone a nephrectomy, systolic blood pressure consistently increases at a rate of approximately 3.5 mmHg per week beginning at approximately 8 weeks of age, the initiation of intervention in the present study, plateauing at roughly 16 weeks of age, the termination of intervention in the present study [71, 72]. In addition, SHR<sub>s</sub> have fewer glomeruli than other strains [73], resulting in a reduced glomerular volume which is thought to influence blood pressure, making SHR<sub>s</sub> an appropriate model for hypertension- and CKD-related research.

## References

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