

1. Supplemental Figures

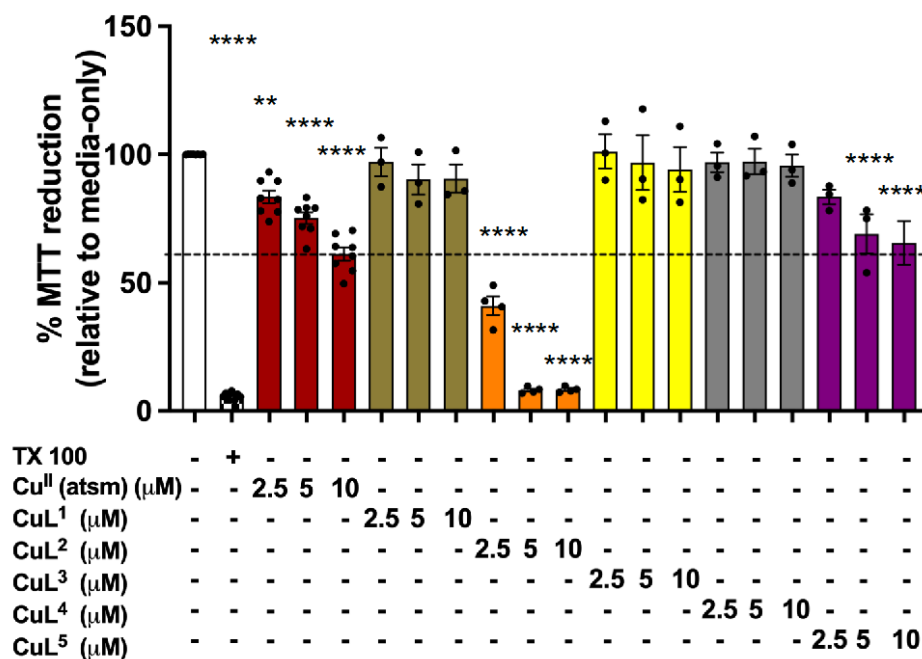


Figure S1. Dose-dependent toxicity assessments by MTT reduction assay exclude CuL² from further study. BE(2)-M17 cultures were incubated for 24h with metal-complexes (2.5–10 μM). Cell viability was assessed by MTT reduction assay. Data are expressed as the percentage of MTT reduction relative to non-treated (media-only) controls and presented as mean ± S.E.M (n ≥ 3). Dotted line across graph represents the average % MTT reduction after treatment of BE(2)-M17 cultures with 10 μM Cu^{II}(atSm) (~60% MTT reduction). Numbers on x-axis represent μM concentration of compound. TX 100= Triton X-100.

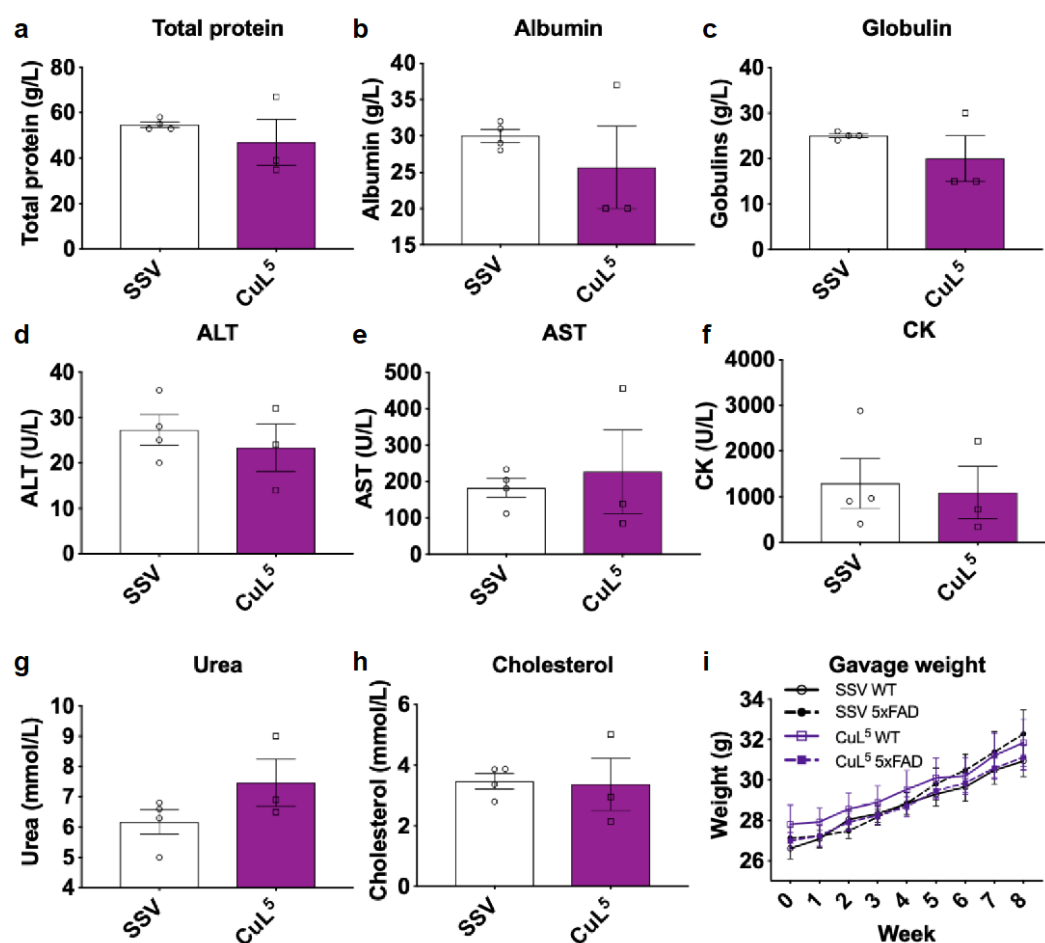


Figure S2. Treatment with CuL⁵ did not induce significant toxicity *in vivo*. For 1 week, non-transgenic WT mice were gavaged once daily with SSV or escalating doses (3–30mg/kg) of CuL⁵. At experimental end-point, blood samples were collected and analyses for the concentrations of a panel biomarkers, including (a) total protein, (b) albumin, (c) globulin, (d) ALT, (e) AST, (f) CK, (g) Urea and (h) cholesterol. These biomarkers were used as a proxy measure of the function and health of organs involved in drug metabolism, including the kidney and liver. The data for individual biomarkers are presented as the mean ± S.E.M from n=3–4 per treatment group and analysed for statistical significance using two-tailed Student's t-test. (i) SSV or CuL⁵ (30mg/kg) were delivered to WT or 5xFAD mice by oral gavage, once daily, for a period of 8 weeks. Individual mice were weighed once at the start of the trial (week 0) and also once a week throughout the treatment period. Across 9 time-points (weeks 0–8), the weights of animals in each treatment group are presented as mean ± S.E.M from n=5–8 per treatment group. The differences in the weights of the animals between treatment groups at each time-point were analysed for statistical significance using one-way ANOVA.

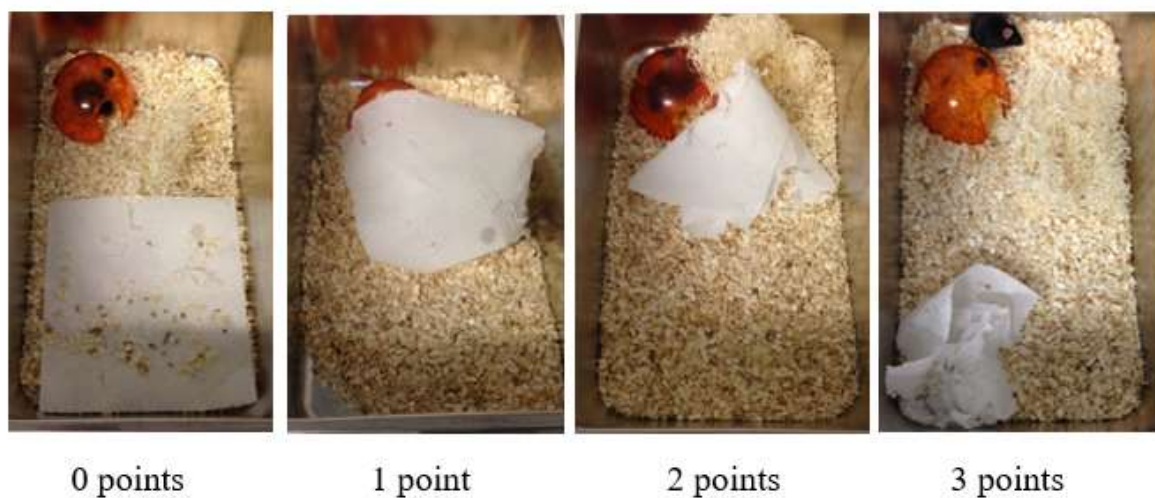


Figure S3. Images of exemplary nests and the nest-building rating scale used in the current study.

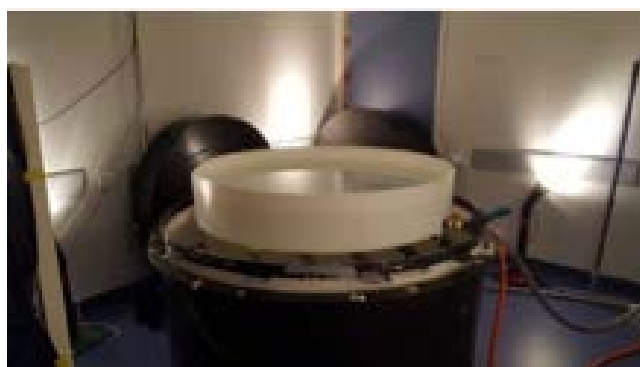


Figure S4. The pool and test conditions in Morris water maze (MWM).

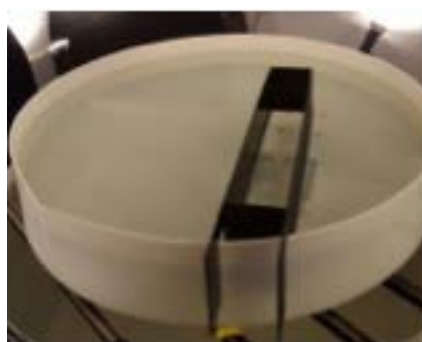


Figure S5. MWM practice trough.