



### Supplemental Figure 3.

**A** and **B**, Mendelian Randomization analysis using GWAS summary statistics was performed and the effect of circulating metabolites on RCC odds was assessed revealing a significant association between HDL particles and RCC risk. Estimates reflect the OR (95% CI) for RCC per SD increase in circulating metabolite concentration. (Red = significant). **C**, Body weight average of nude mice subcutaneously implanted with A498 cells and fed a no cholesterol (0%) or a high cholesterol (2%) diet for 70 days. **D**, Analysis of serum total cholesterol from nude mice subcutaneously implanted with A498 cells and fed a no cholesterol (0%) or a high cholesterol (2%) diet for 70 days. (All experiments were performed in at least triplicates and statistical analysis was applied with \*= $P < 0.05$ , \*\*= $P < 0.01$ , \*\*\*= $P < 0.001$ , n.s=non-significant).