Expression profiling meta-analysis of ACE2 and TMPRSS2, the putative anti-inflammatory receptor and priming protease of SARS-CoV-2 in human cells, and identification of putative modulators

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Supplementary Information

Supplementary Figures

Figure S1. PRISMA flowchart referring to datasets collection from the NCBI and Array Express databases and the pipeline of analyses used for this meta-analysis.

Figure S2. Comparative *ACE2* and *TMPRSS2* genes (mRNA) expression at the shown conditions. Difference of column width, indicate the different number of probes per condition. Data were retrieved from GEO and ArrayExpress. See also Tables S1, S2. *, $P<0.05$; **, $0.1>P>0.05$.

Figure S3. Heatmap of ACE2, TMPRSS2, CTSB and CTSL proteins expression in various somatic tissues, as per the Protein Atlas database. See also Table S4.

Figure S4. KEGG pathways related to ACE2 (A) and TMPRSS2 (B).

Figure S5. KEGG pathways related to CTSB.

Figure S6. KEGG pathways related to CTSL.

Supplementary Tables

Table S1. Levels of differential regulation of the *ACE2* and *TMPRSS2* (when co-isolated) genes in shown experiments. Data were retrieved from GEO and ArrayExpress databases. P values

<0.05 are indicated. Details in relation to GDS (Dataset), GSE (Series), number of probes (PROBES) and probe name (PROBE), experimental conditions (TISSUE/STATE, CONDITION), p-value [adjusted (adj. p-value) or not (p-value)], log fold change (logFC) and fold (FC) change are shown.

Table S2. Levels of differential regulation of the *TMPRSS2* and *ACE2* (when co-isolated) genes in shown experiments. Data were retrieved from GEO and ArrayExpress databases. P values <0.05 are indicated. Shown details are as in Table S1.

Table S3. Differential regulation of *ACE2*, *TMPRSS2*, *CTSB* and *CTSL* genes in shown tissues and cell lines. Data were retrieved from Protein Atlas RNA expression summary and show the consensus RNA-data based on normalized expression (NX) data from three different sources (see, https://www.proteinatlas.org/).

Table S4. Basal levels of ACE2, TMPRSS2, CTSB and CTSL proteins expression in shown tissues and cell lines. Data were retrieved from Protein Atlas. Coloring (as indicated) denotes LOW, MEDIUM and HIGH levels of expression.

Table S5. Differential regulation of *ACE2*, *TMPRSS2*, *CTSB* and *CTSL* genes following treatment of bronchial epithelial cells with IFN1-beta. Data from GEO and ArrayExpress. P values <0.05 are indicated.

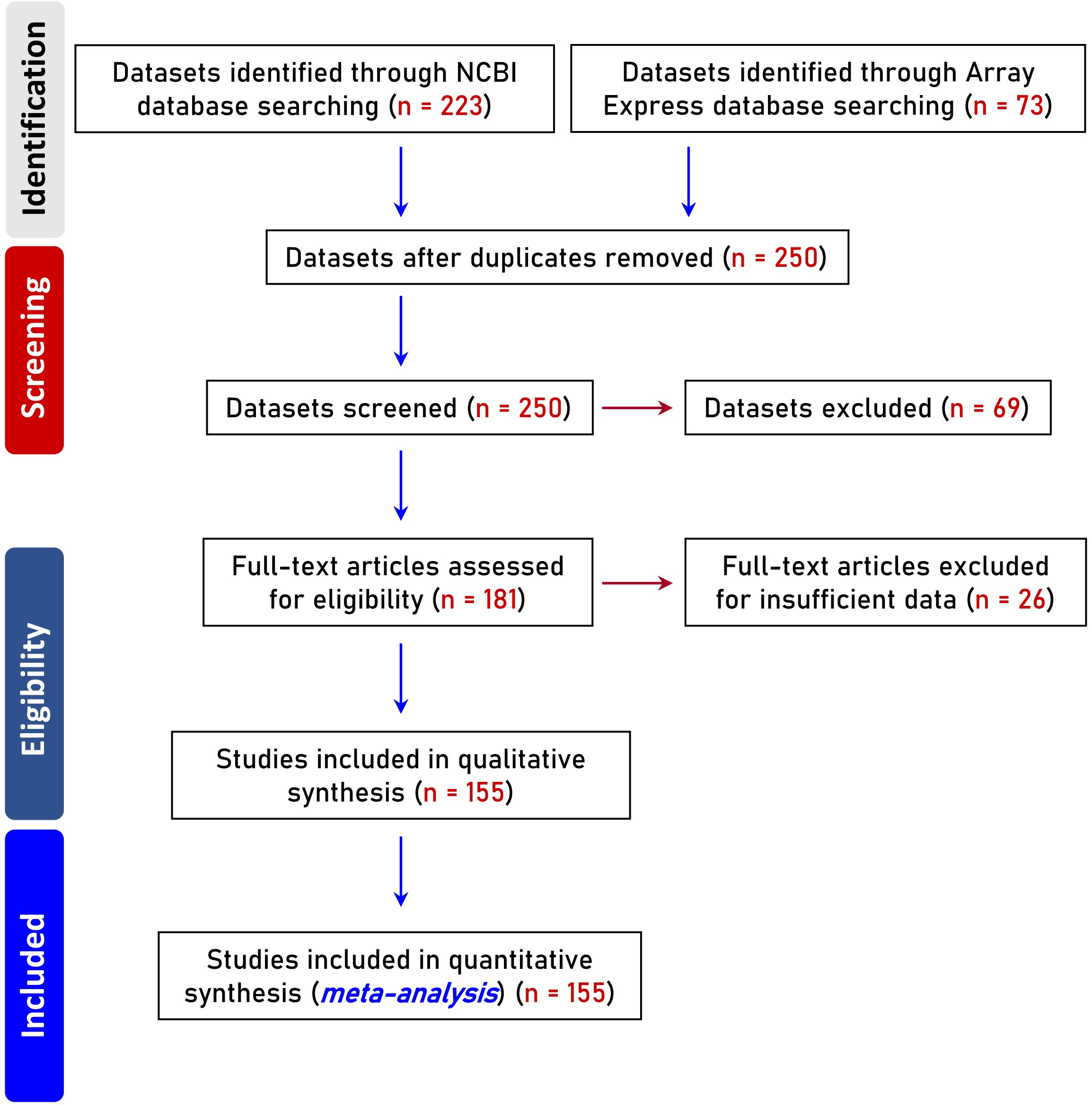
Table S6. Differential regulation of *ACE2*, *TMPRSS2*, *CTSB* and *CTSL* genes following treatment (in shown conditions) with chloroquine. Data from GEO and ArrayExpress. P values <0.05 are indicated.

Table S7. Differential regulation of *ACE2*, *TMPRSS2*, *CTSB* and *CTSL* genes following treatment (in shown conditions) with hydroxychloroquine. Data from GEO and ArrayExpress. P values <0.05 are indicated.

Table S8. KEGG pathways related to ACE2, TMPRSS2, CTSB and CTSL proteins.

Tables S9-S23. Tested drugs (cell assays, animal models, clinical trials, approved) that target components of KEGG pathways related to ACE2, TMPRSS2, CTSB and CTSL. Data were collected from DrugBank.

Table S24-S26. Small molecules or approved drugs with reported activity against clathrin-mediated endocytosis (Table S24); actin- (Table S25) or tubulin- (Table S26) polymerization.



Identification

Datasets identified through NCBI database searching (n = 223)

Datasets identified through Array Express database searching (n = 73)

Datasets after duplicates removed (n = 250)

Screening

Datasets screened (n = 250)

Datasets excluded (n = 69)

Eligibility

Full-text articles assessed for eligibility (n = 181)

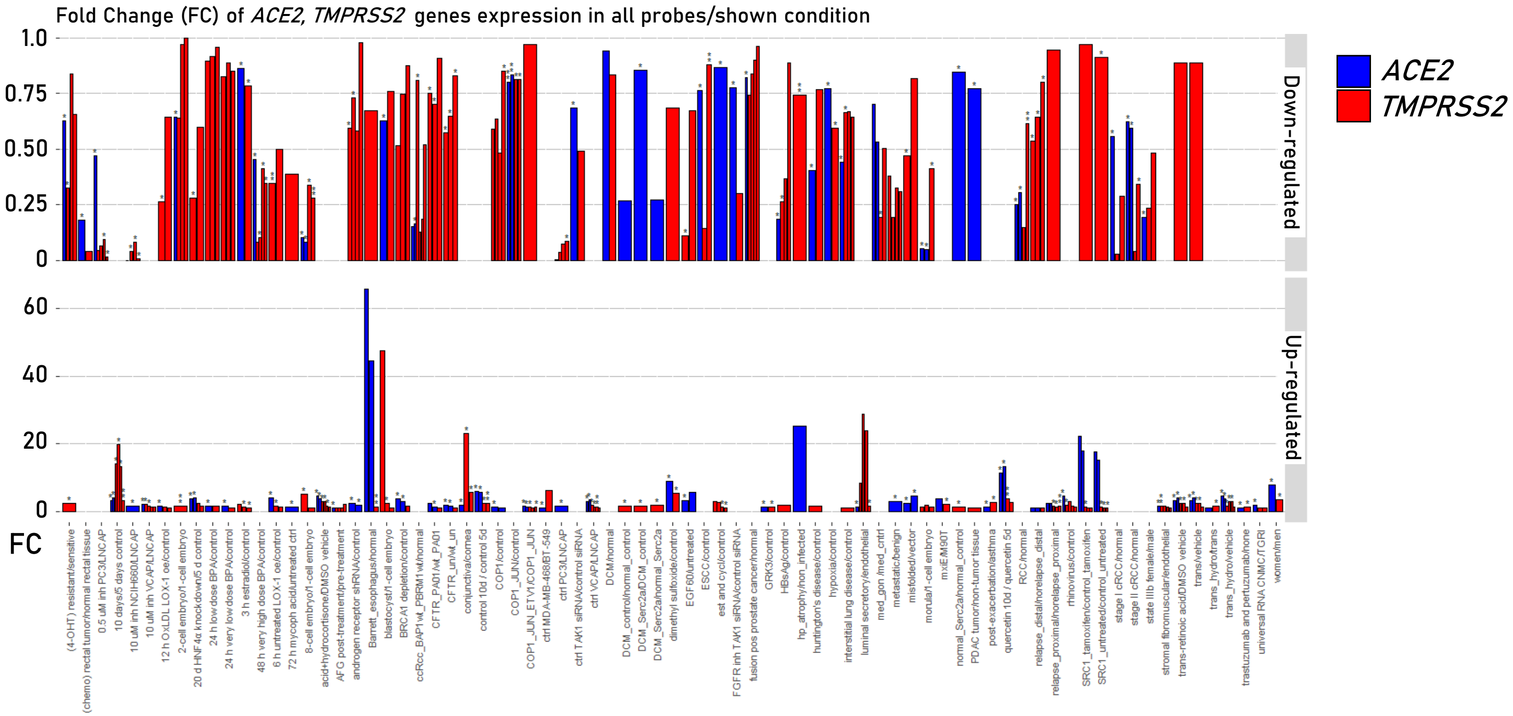
Full-text articles excluded for insufficient data (n = 26)

Studies included in qualitative synthesis (n = 155)

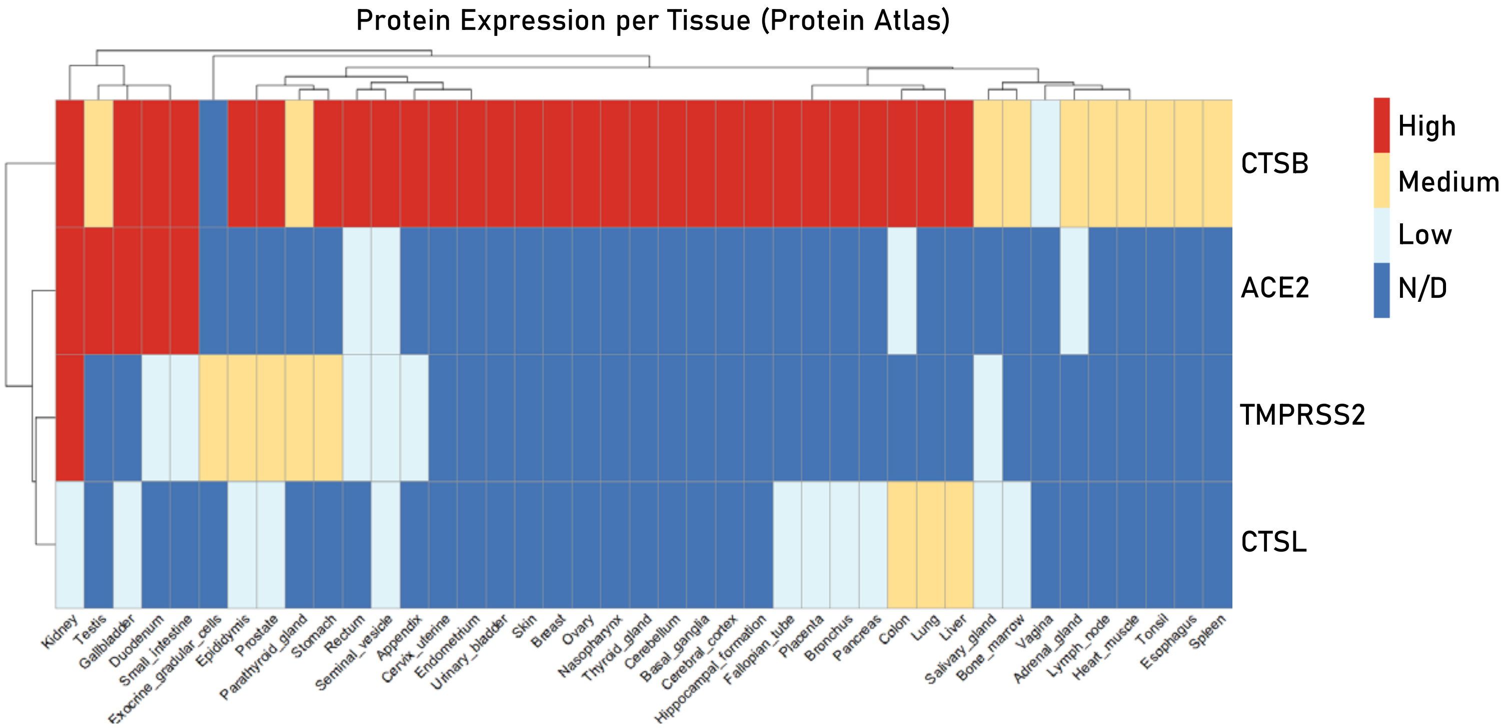
Included

Studies included in quantitative synthesis (***meta-analysis***) (n = 155)

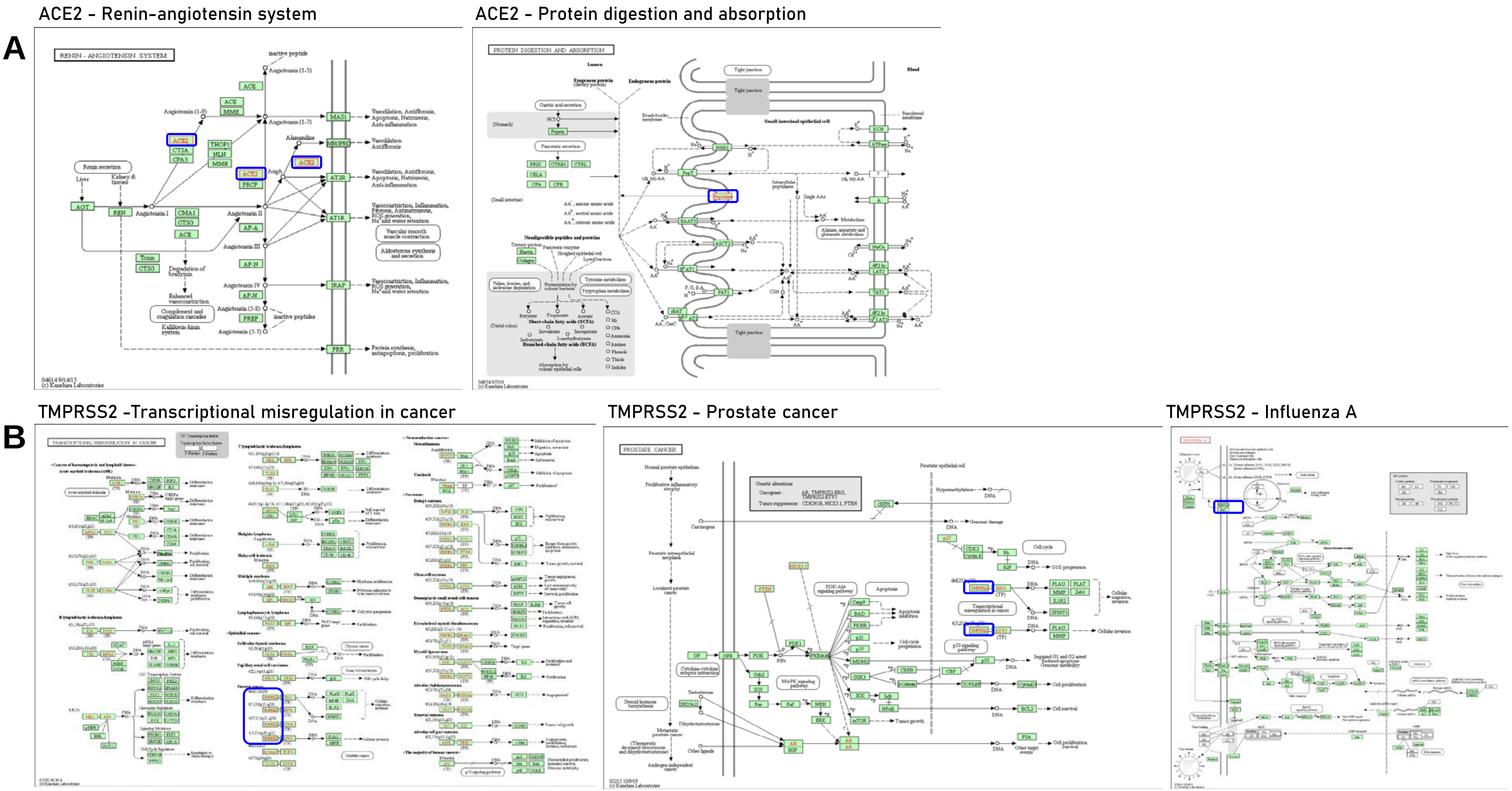
Gkogkou et al. Fig. S1



Gkogkou et al. Fig. S2

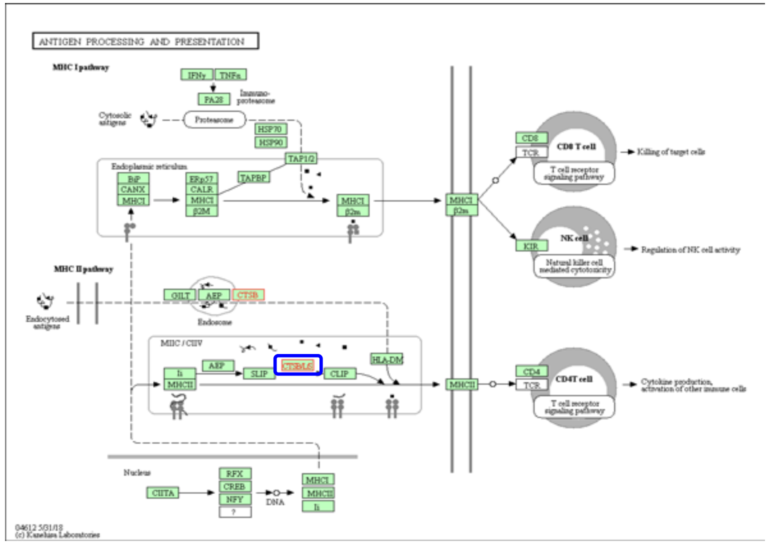

Protein Expression per Tissue (Protein Atlas)

Gkogkou et al. Fig. S3

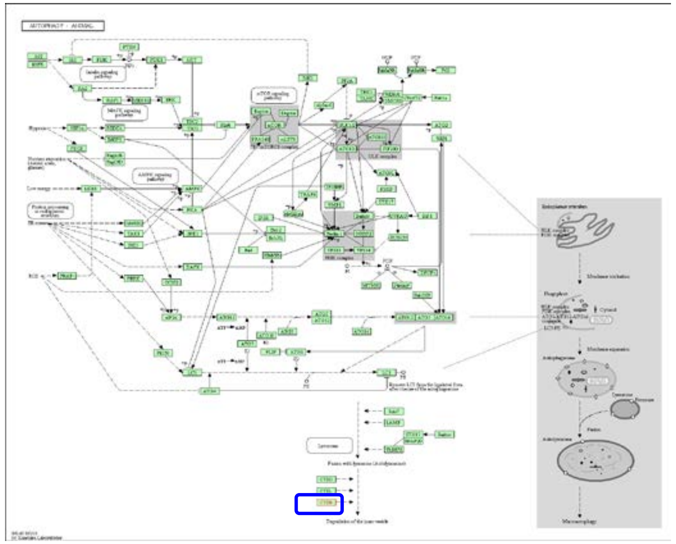


Gkgkou et al. Fig. S4

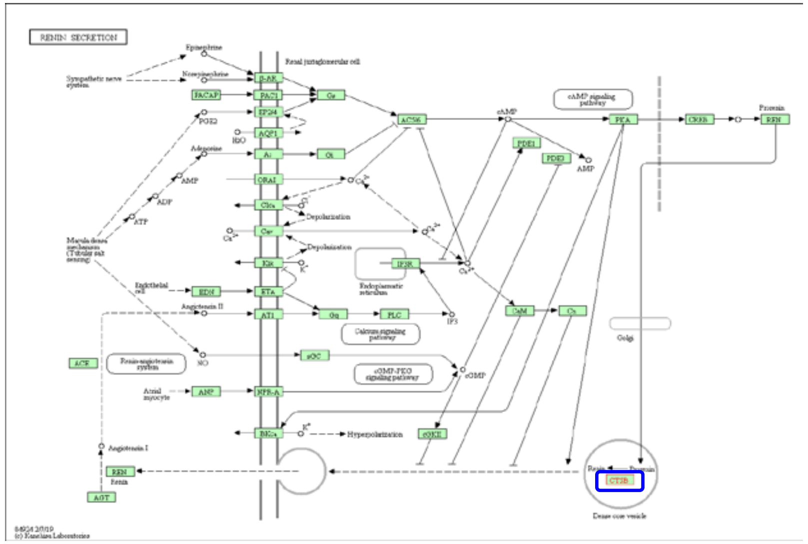
CTSB – Antigen processing and presentation



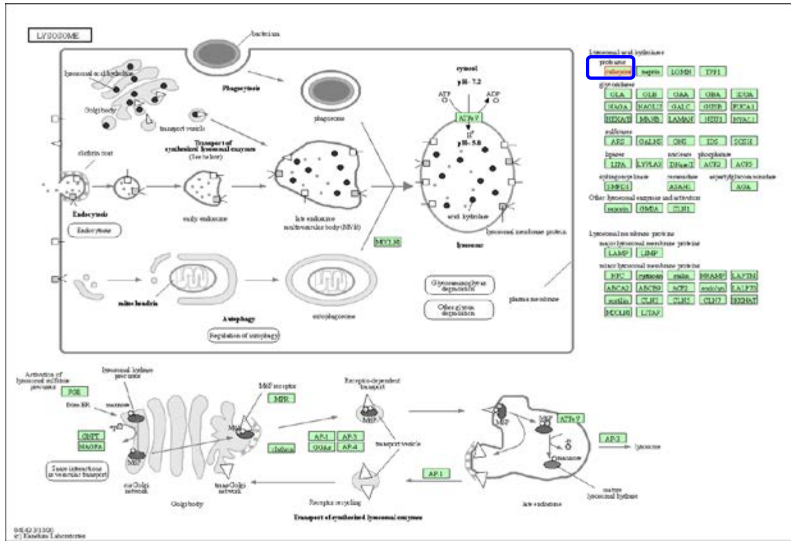
CTSB- Autophagy – animal



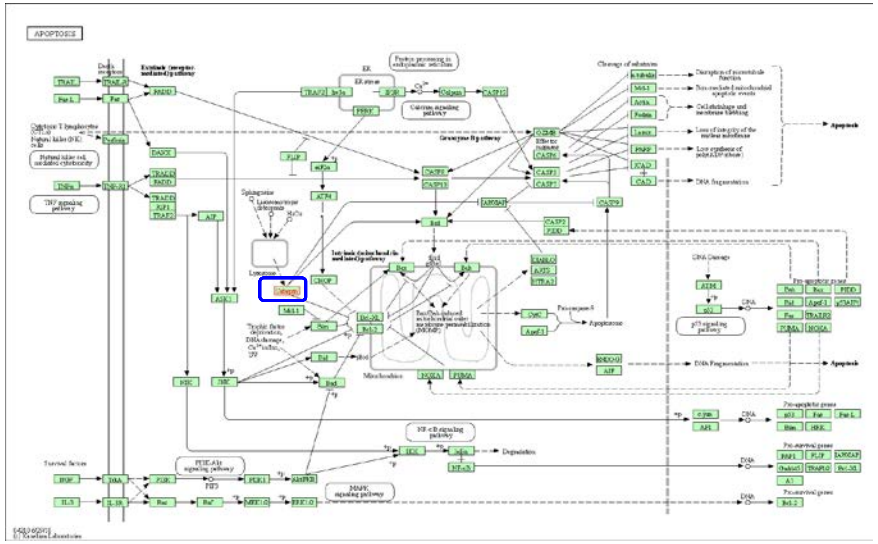
CTSB – Renin secretion



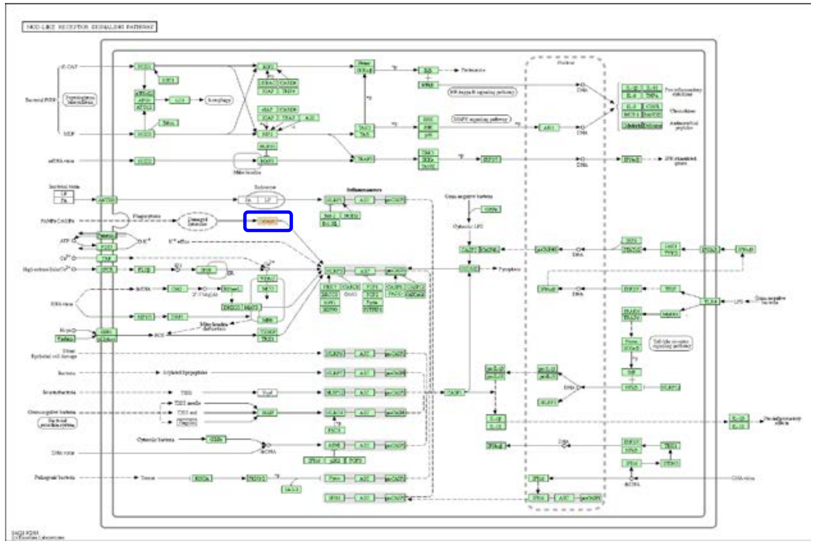
CTSB – Lysosome



CTSB – Apoptosis

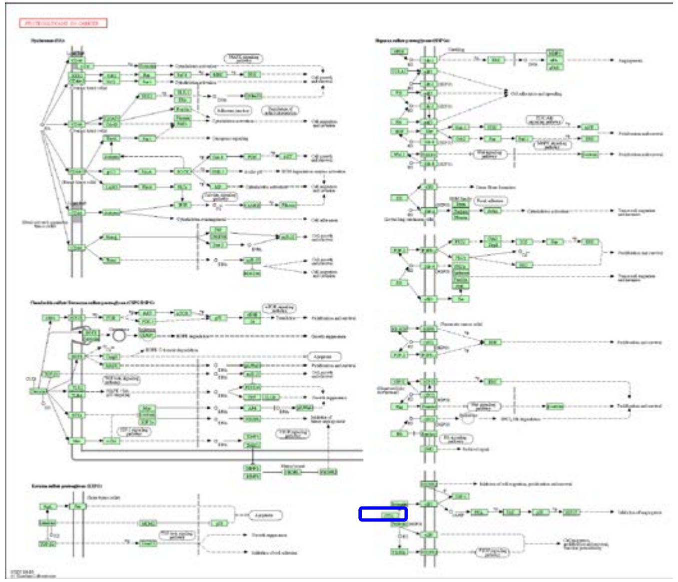


CTSB – NOD-like receptor signaling pathway

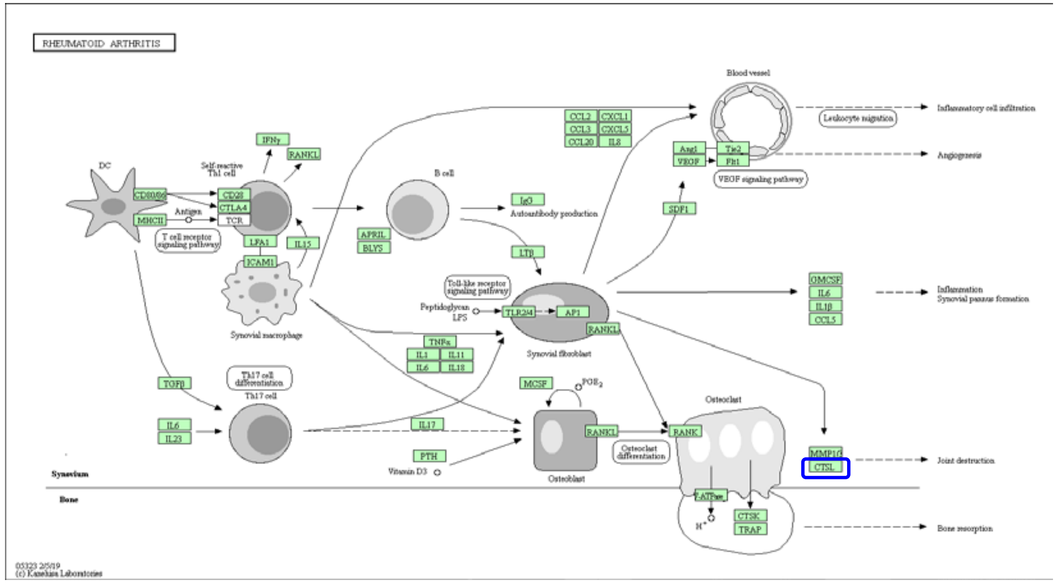


Gkogkou et al. Fig. S5

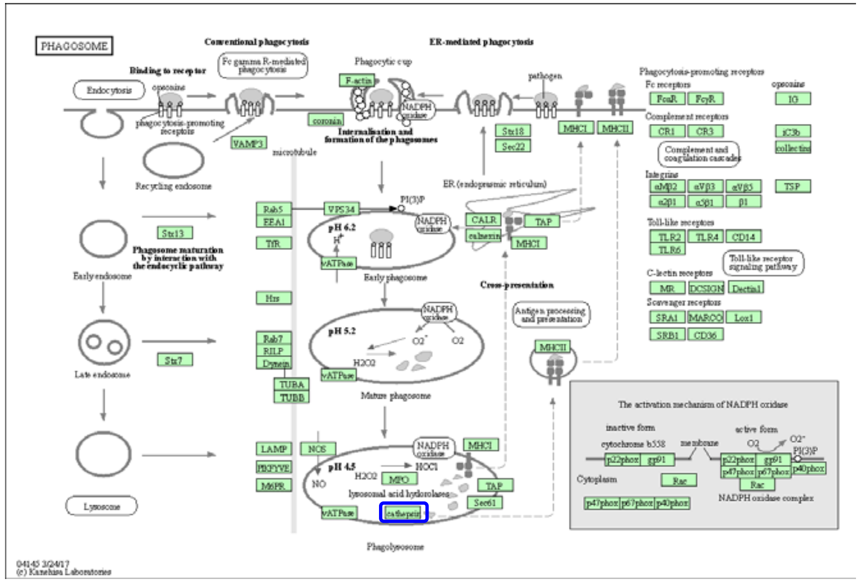
CTSL - Proteoglycans in cancer



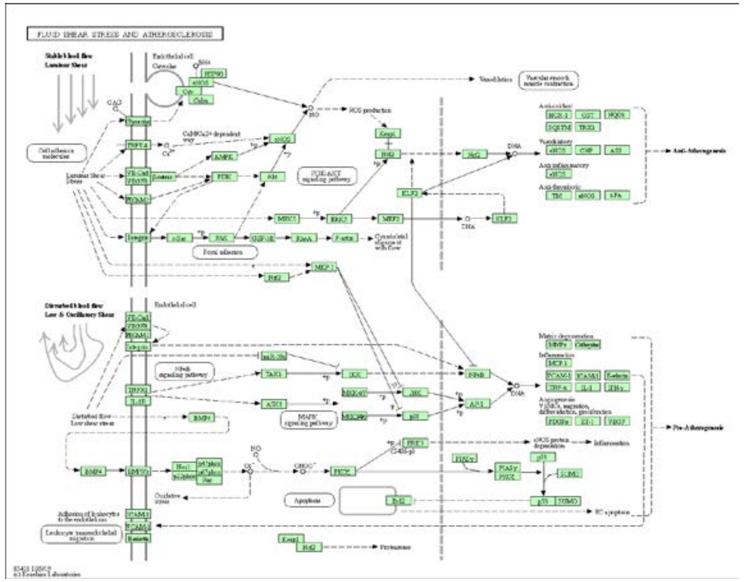
CTSL - Rheumatoid arthritis



CTSL - Phagosome



CTSL -Fluid shear stress and atherosclerosis



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