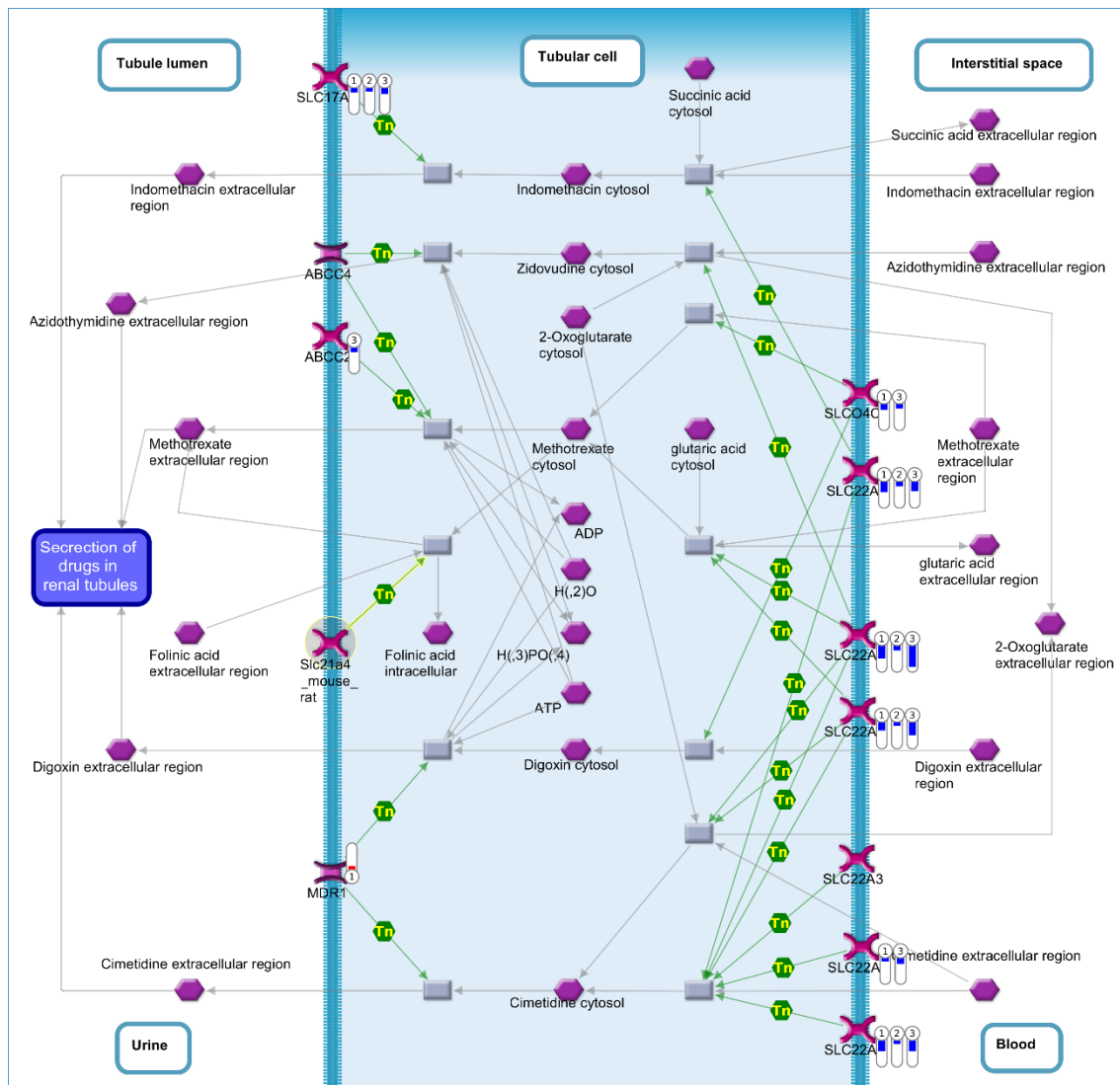
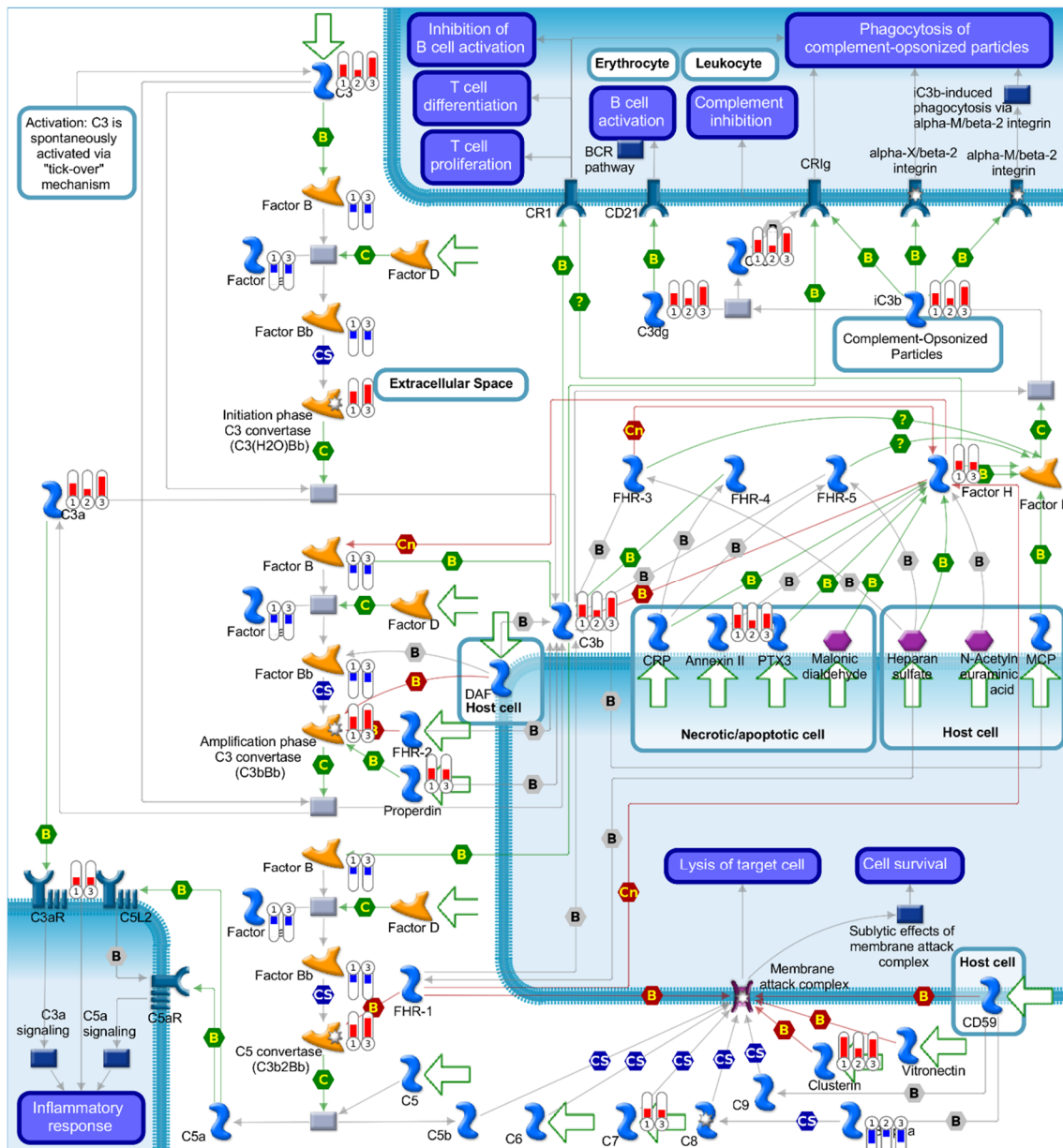


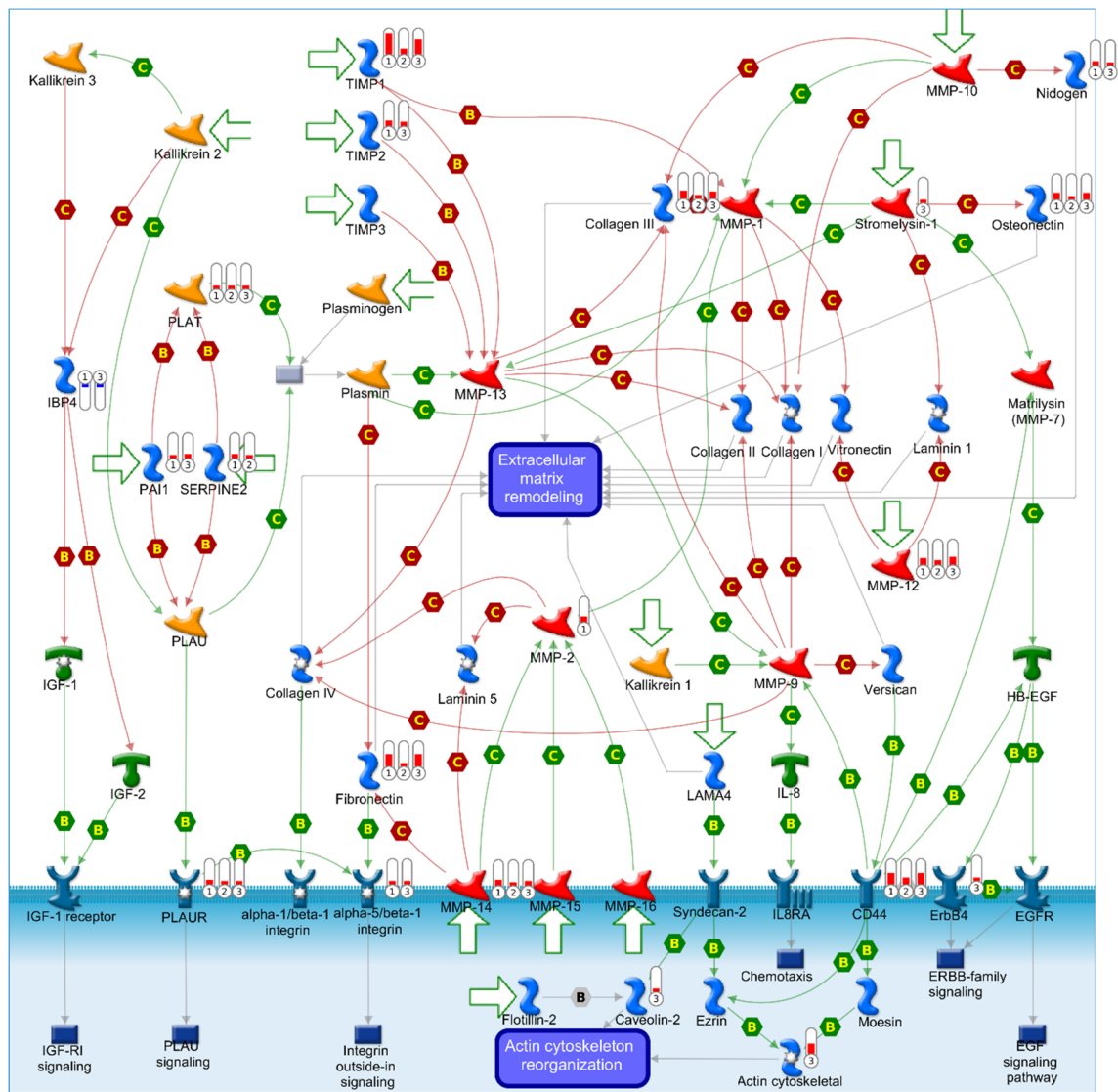
**Figure. S1** The impact of *Trp53* genotype on AAI-induced gene expression *in vivo*. Hierarchical clustering and heat map of significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed (a) *Trp53*(+/+), (b) *Trp53*(+/-) and (c) *Trp53*(-/-) mouse kidneys. The heat map colours are based on gene expression (ordered in a decreasing manner for the AAI group), with red being up-regulated and green being down-regulated. Batches #1 and #2 indicate grouping of samples during cDNA synthesis.



**Figure. S2** Map of renal secretion of drugs in rodents. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (39<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) and down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**.

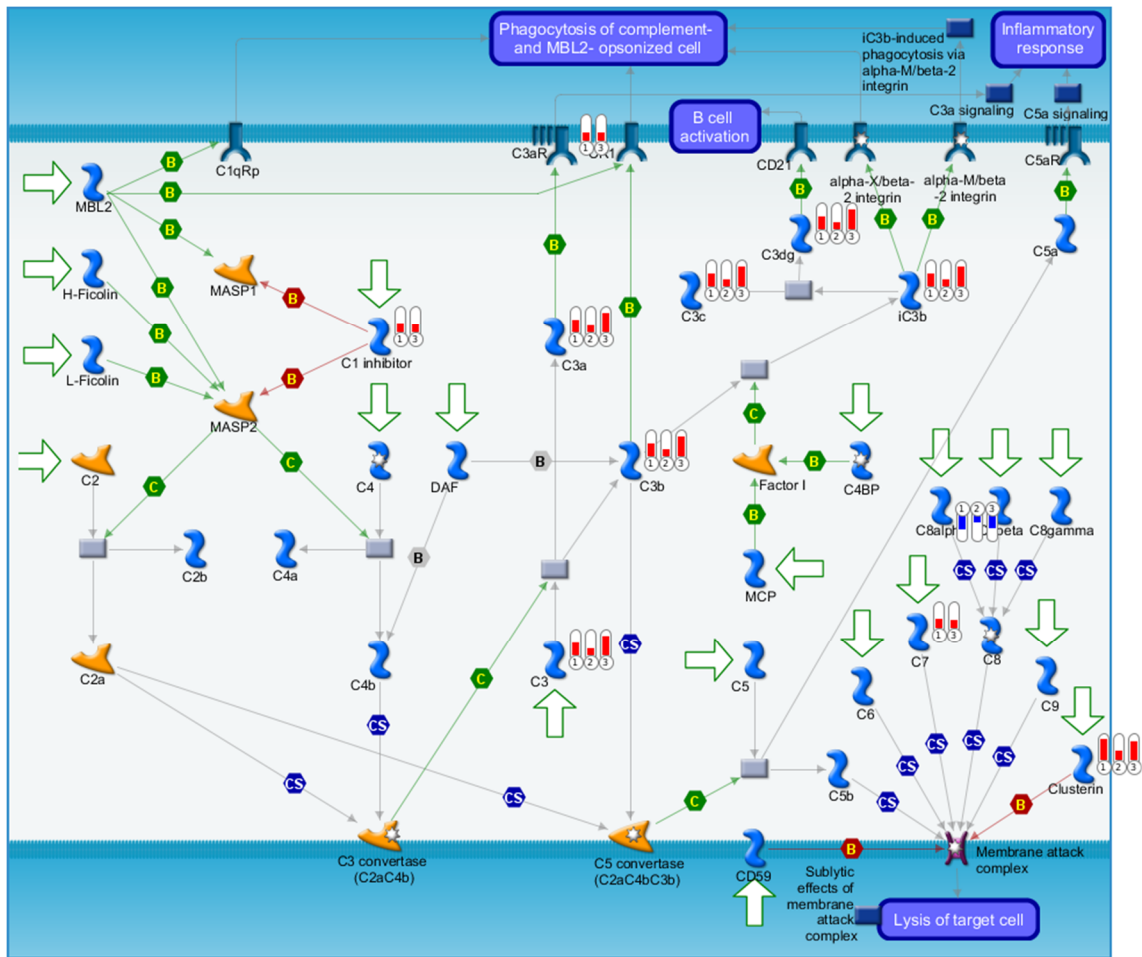


**Figure. S3** Map of alternative complement pathway. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (3<sup>rd</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) and down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**.

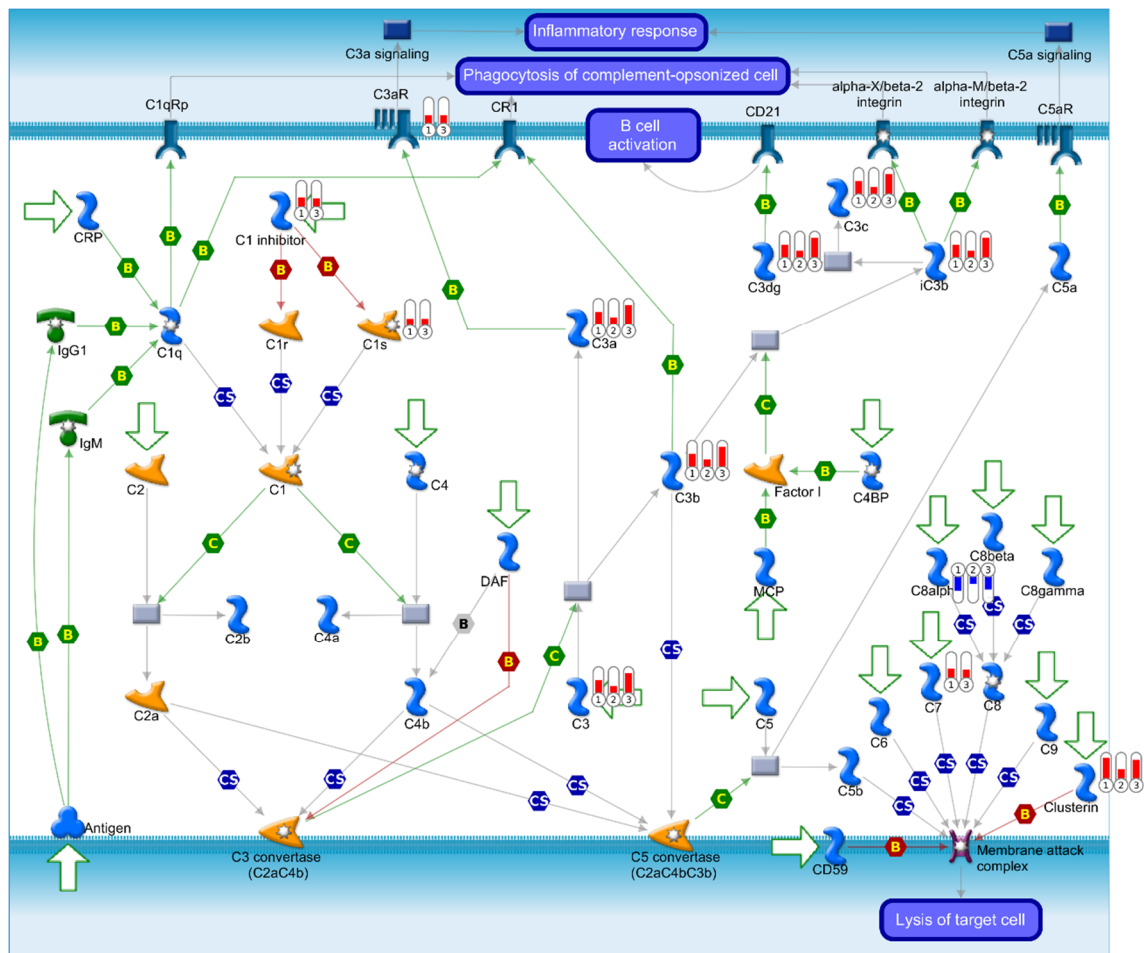


**Figure. S4** Map of extracellular matrix remodelling. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (4<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) and down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**.

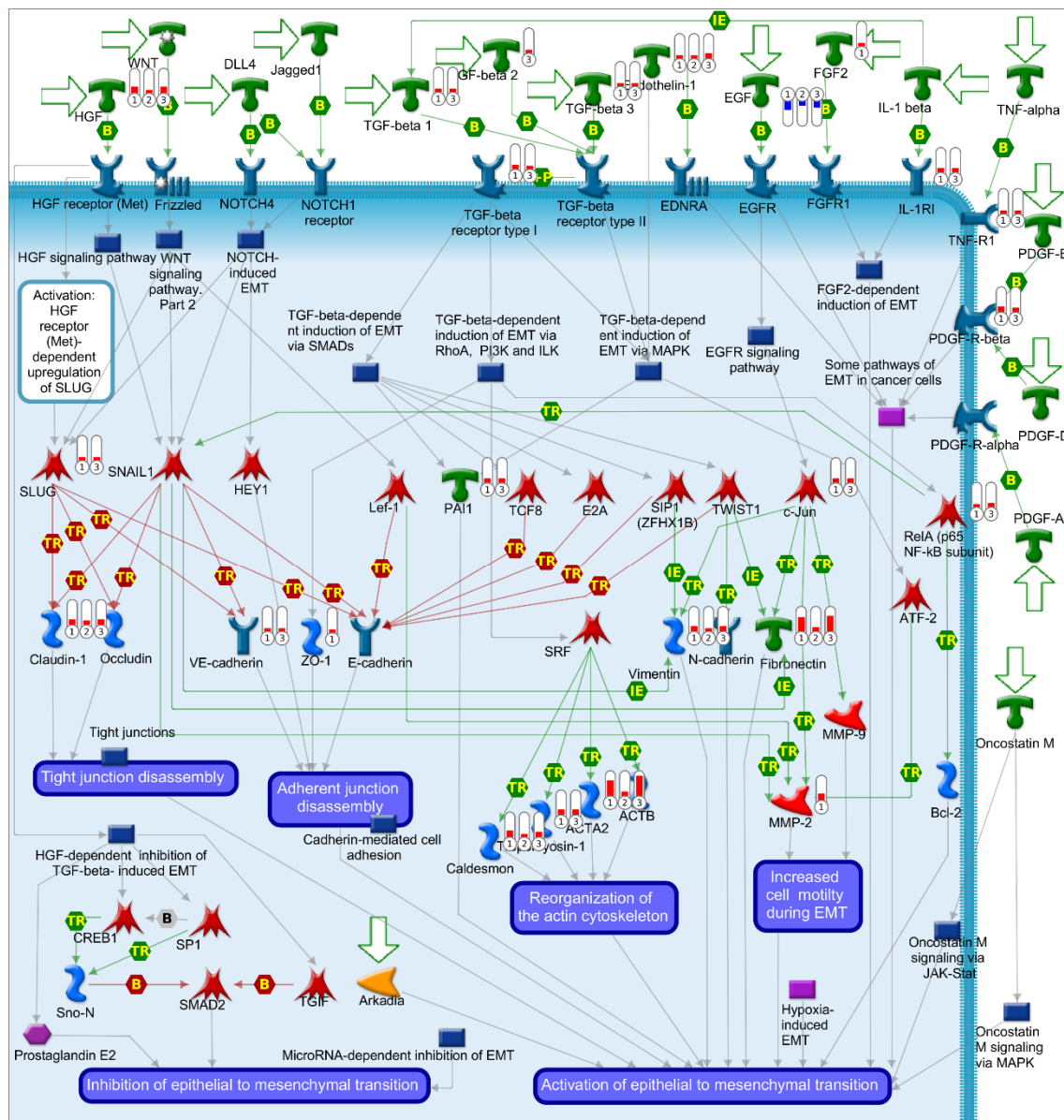




**Figure. S5** Map of lectin-induced complement pathway. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (6<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**.

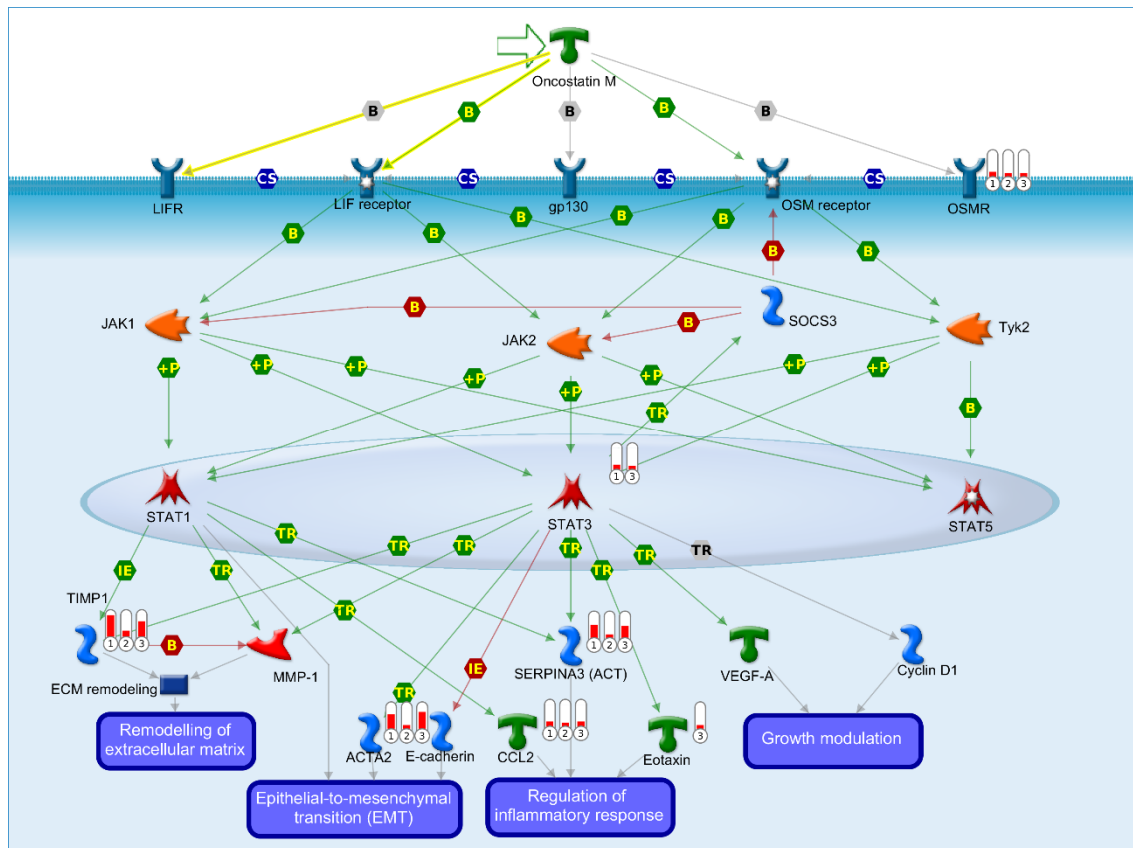


**Figure. S6** Map of classical complement pathway. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (8<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) and down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**.



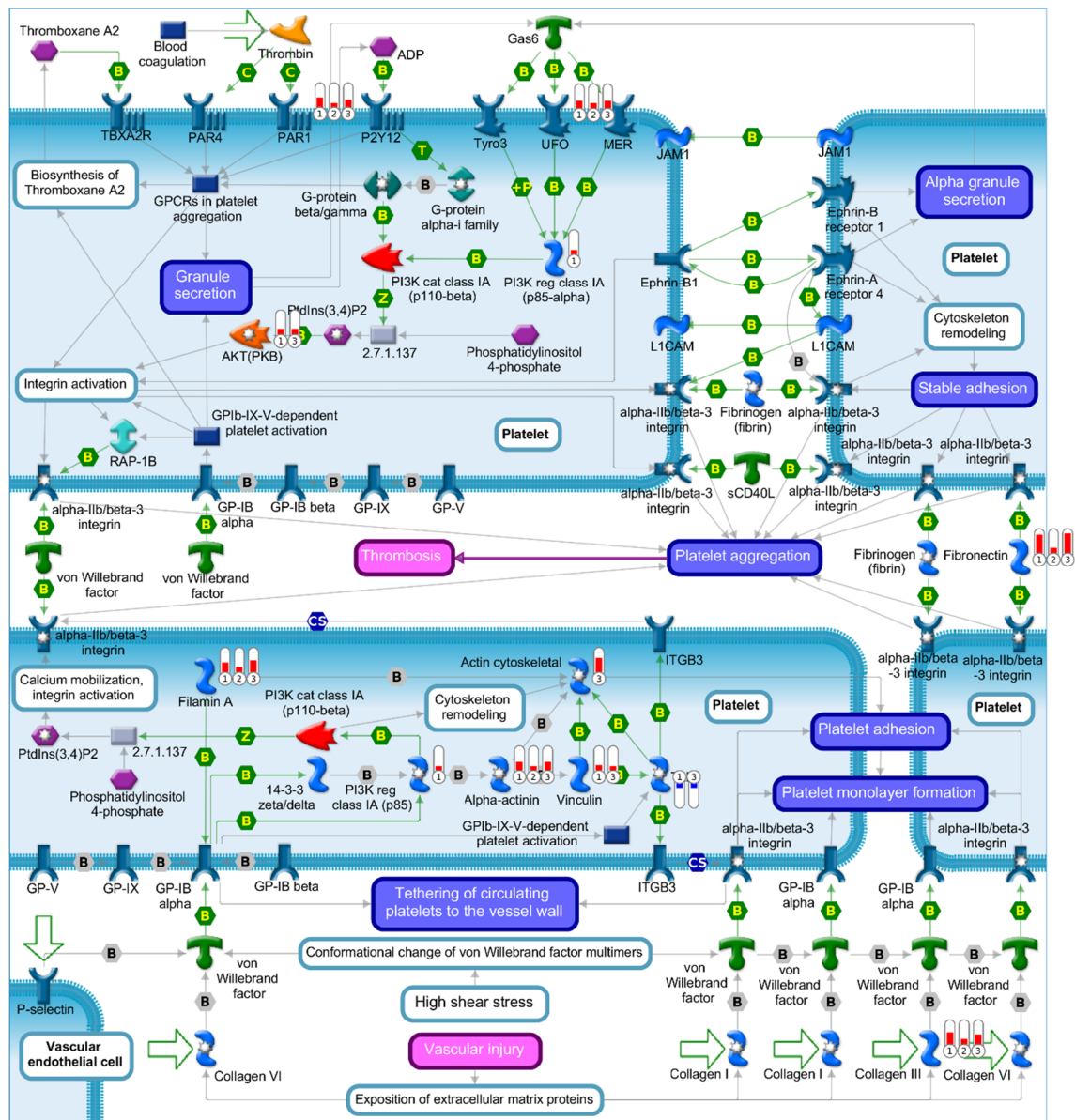
**Figure. S7** Map of regulation of EMT. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (11<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) and down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**. Abbreviation: epithelial-to-mesenchymal transition (EMT).





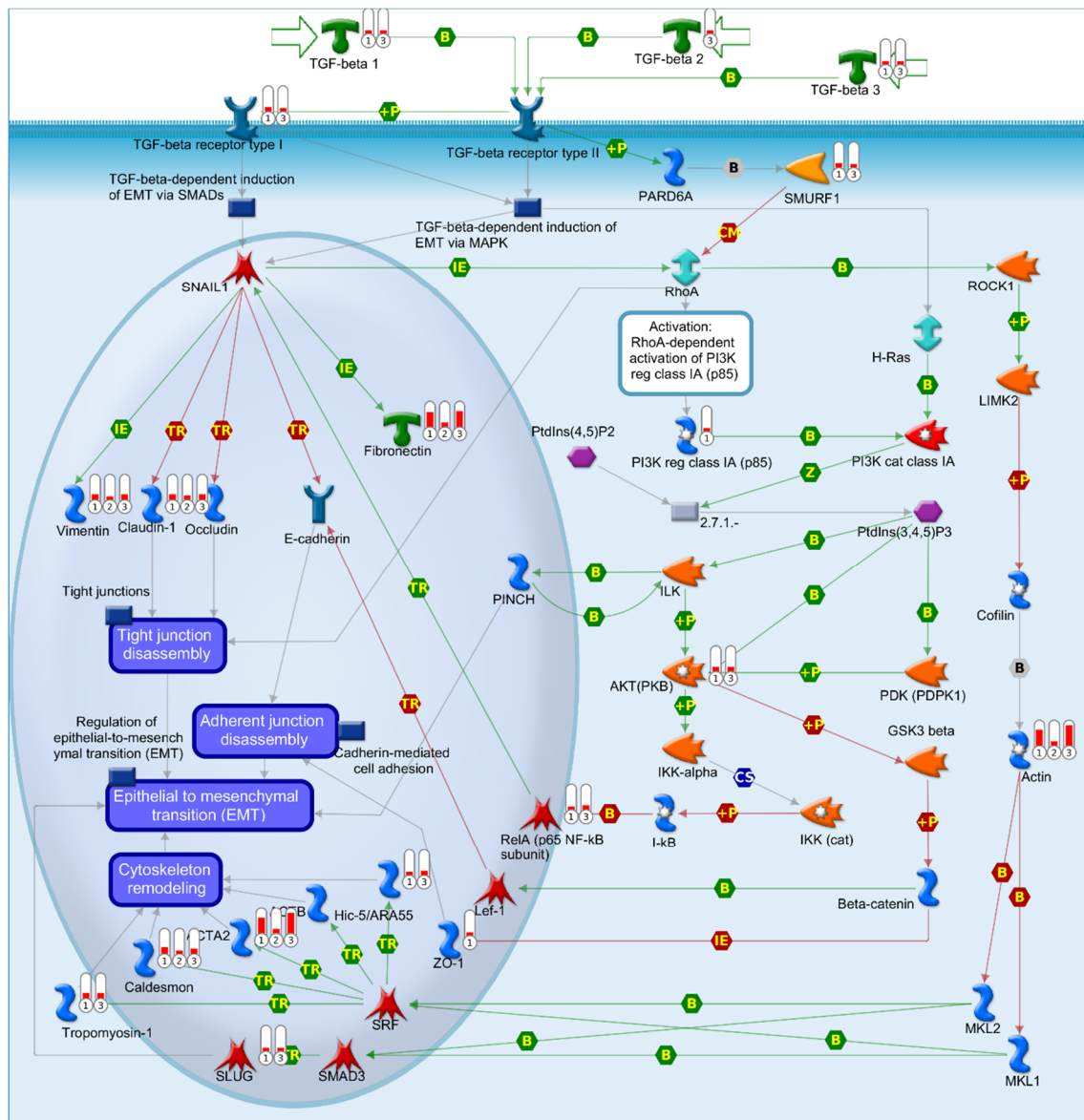
**Figure. S9** Map of oncostatin M signalling via JAK-STAT. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (14<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**. Abbreviations: Janus kinase (JAK); signal transducer and activator of transcription (STAT).



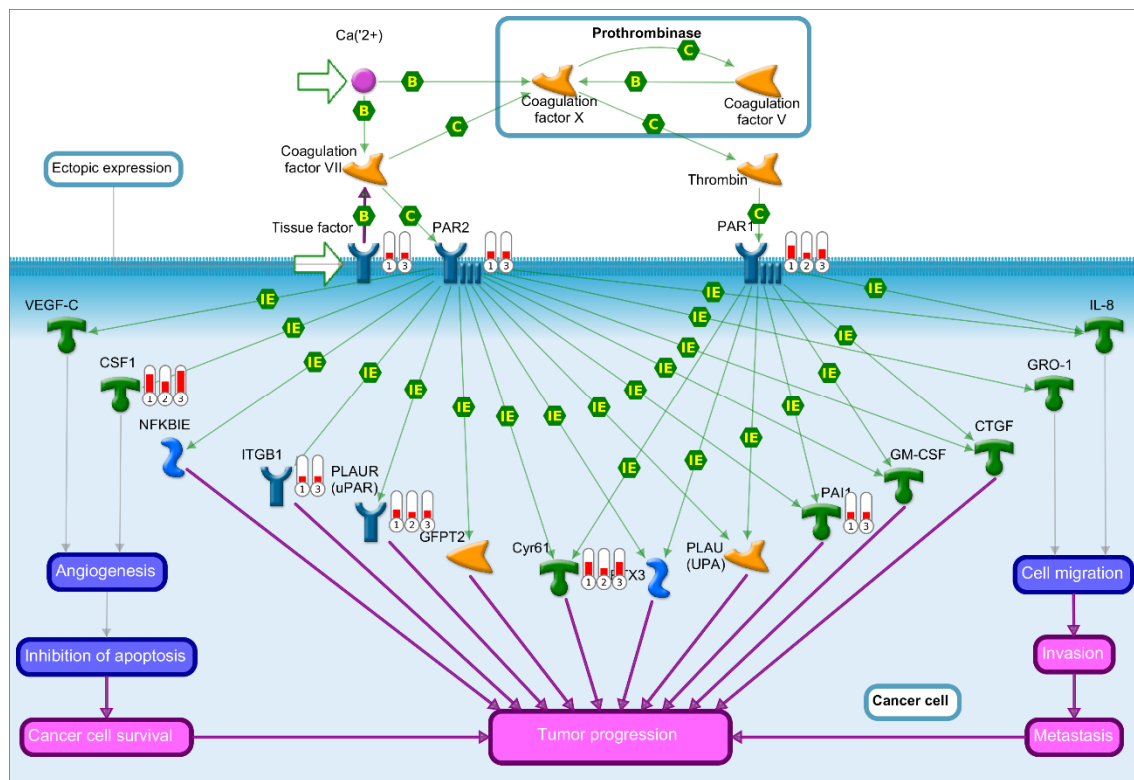


**Figure. S10** Map of high shear stress-induced platelet activation. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (18<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) and down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**.



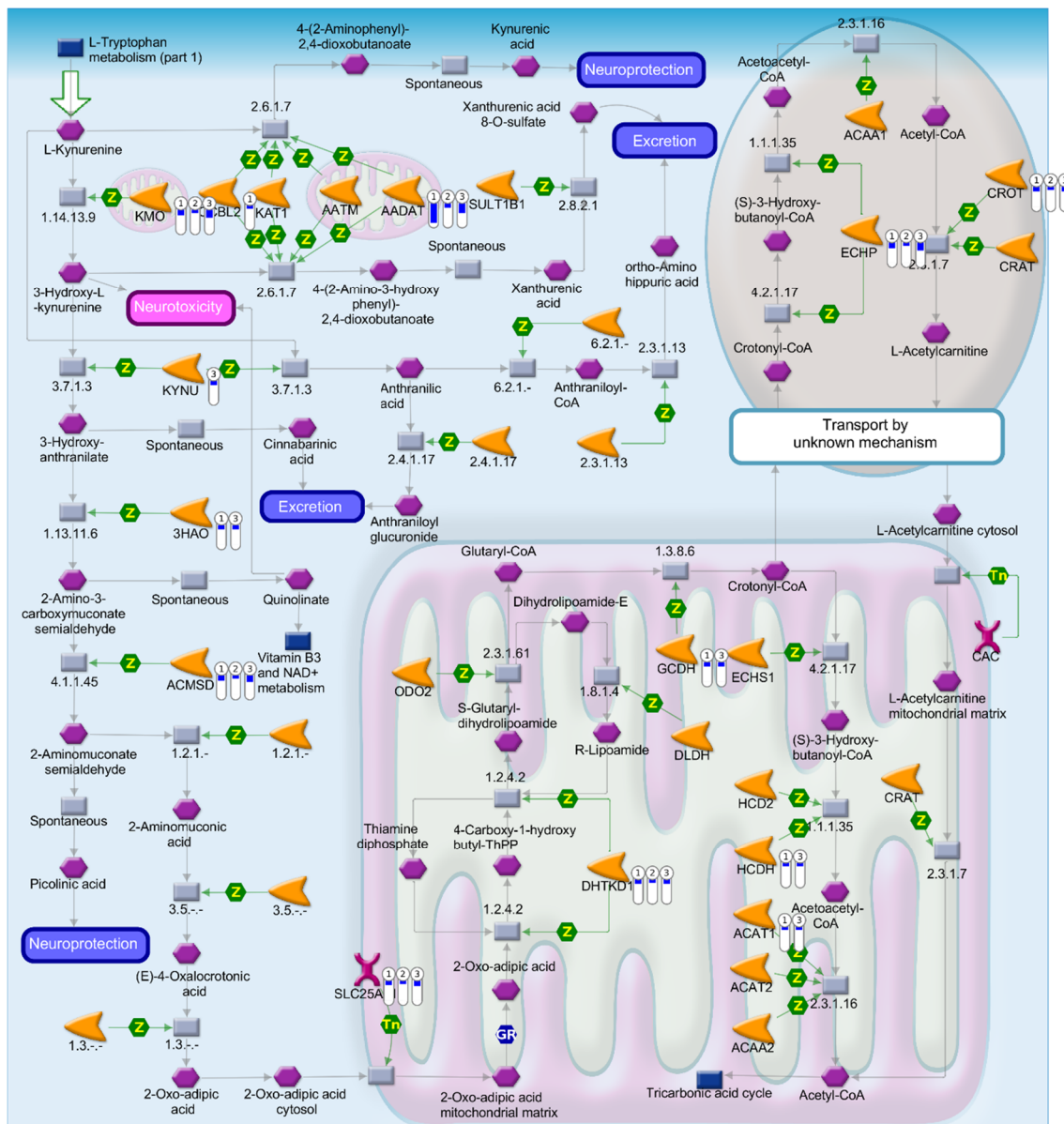


**Figure. S11** Map of TGF- $\beta$ -dependent induction of EMT via RhoA, PI3K and ILK. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (19<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**. Abbreviations: epithelial-to-mesenchymal transition (EMT); integrin-linked protein kinase (ILK); phosphoinositide 3-kinase (PI3K); RAS homolog gene family, member A (RhoA); transforming growth factor  $\beta$  (TGF- $\beta$ ).

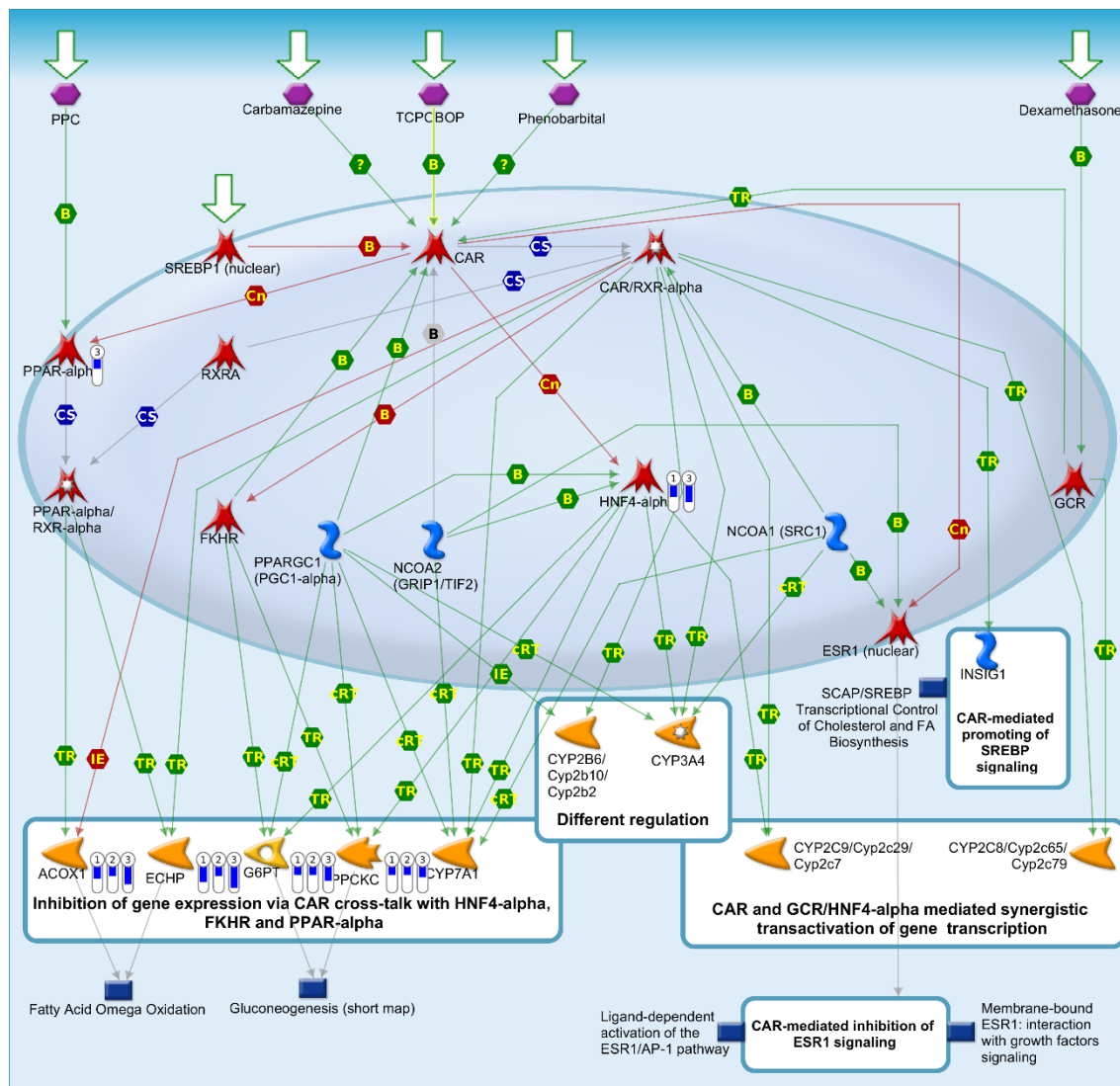


**Figure. S12** Map of tissue factor signalling in cancer. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (26<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**.



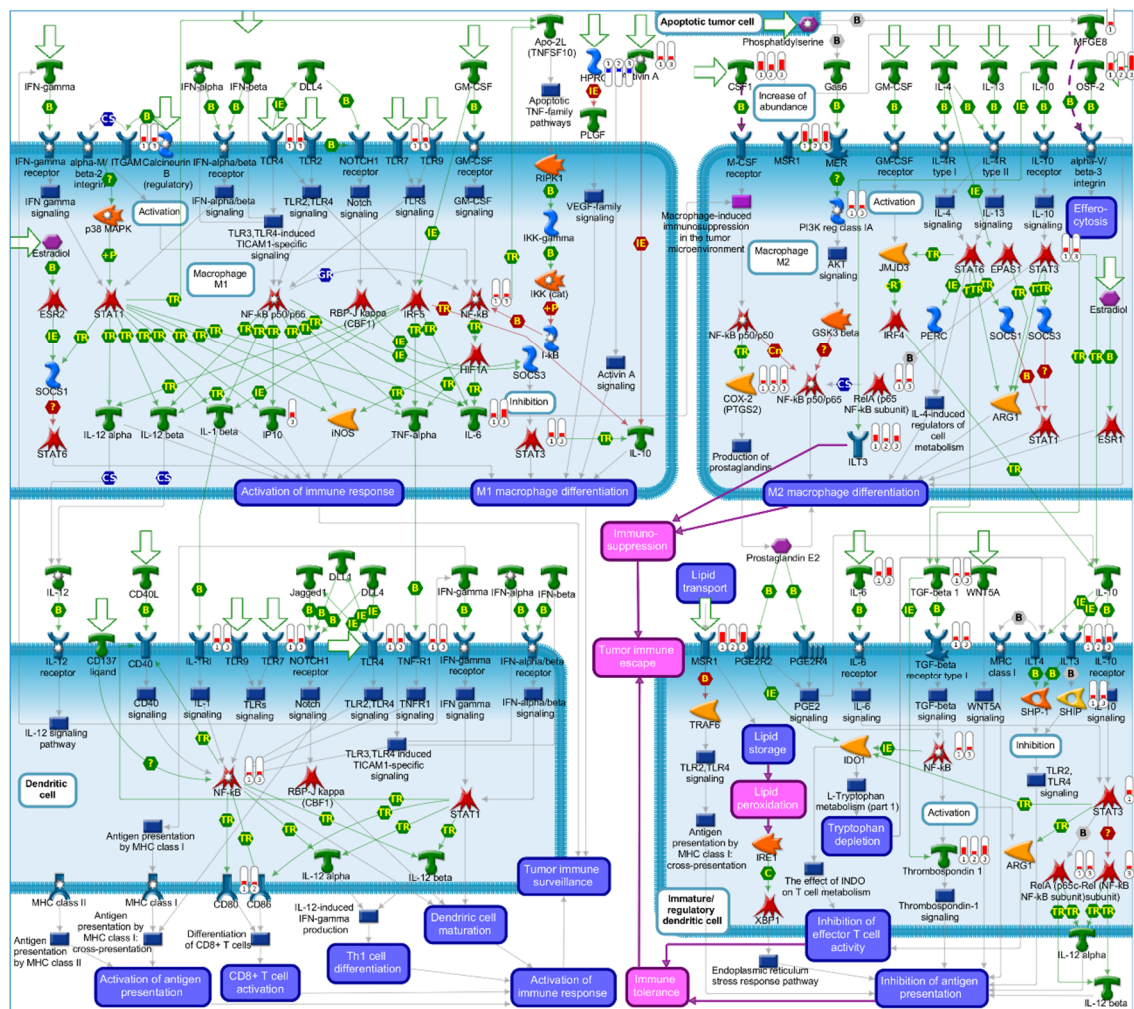


**Figure. S14** Map of L-Tryptophan metabolism. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53(+/+)*, *Trp53(+/-)* and *Trp53(-/-)* mouse kidneys were compared in MetaCore™. The enriched pathway (37<sup>th</sup> out of top 50;  $p < 0.05$ ) shows down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53(+/+)*, 2) *Trp53(+/-)* and 3) *Trp53(-/-)*. For detailed legend see **Figure. S22**.



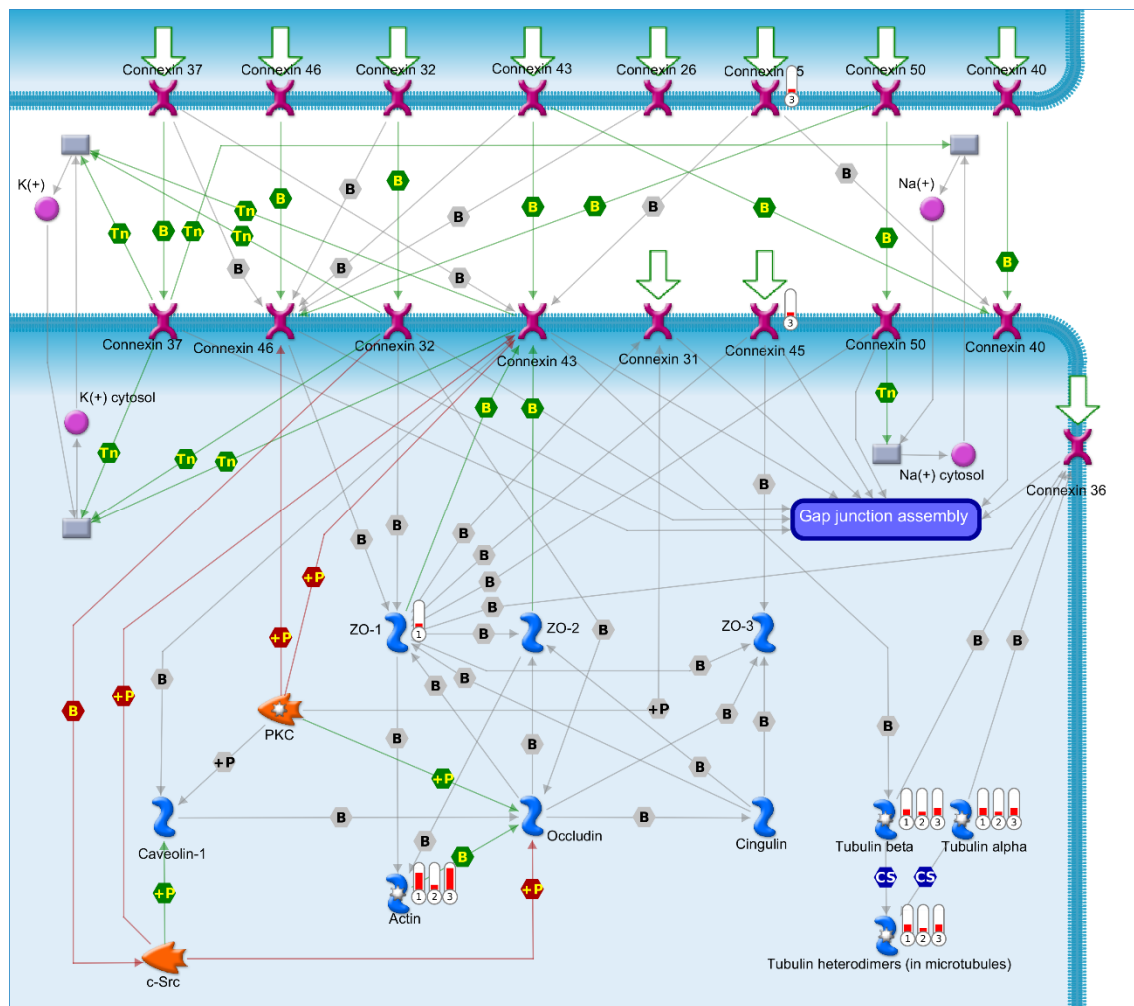
**Figure. S15** Map of CAR signalling via cross-talk in rodents. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (38<sup>th</sup> out of top 50;  $p < 0.05$ ) shows down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**. Abbreviation: constitutive androstane receptor (CAR).



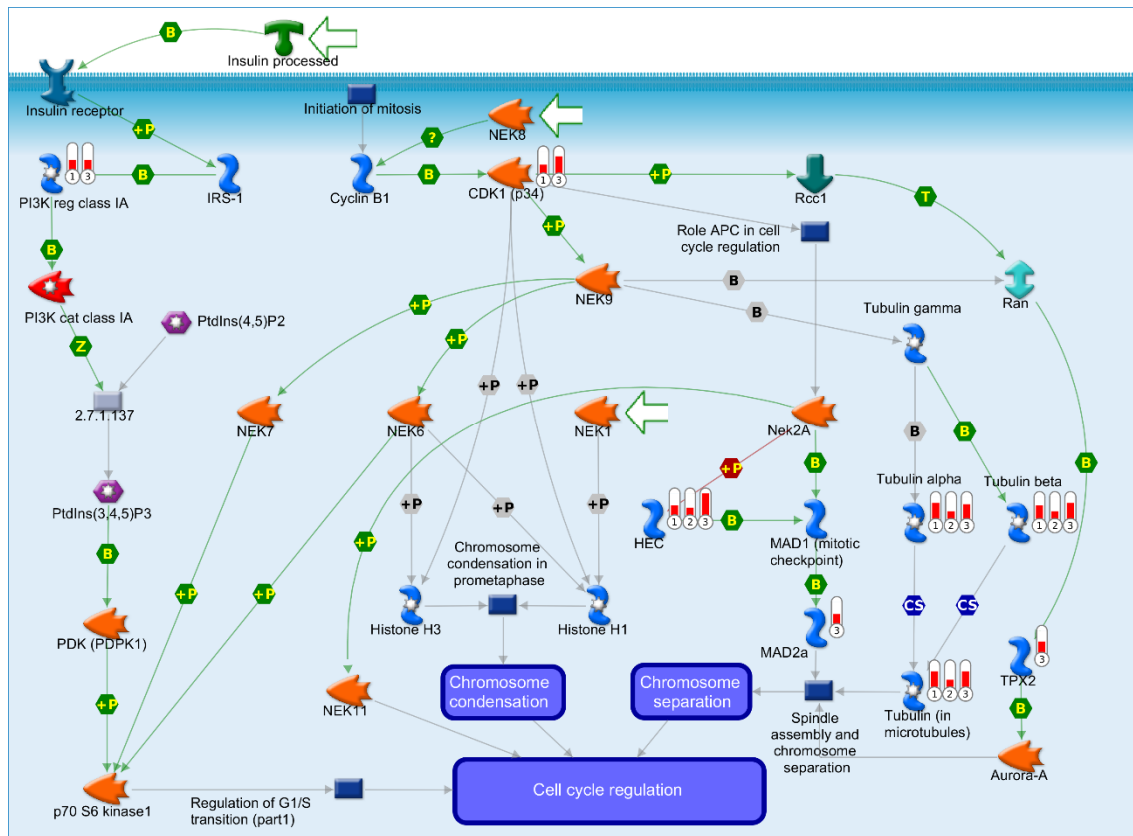


**Figure. S16** Map of macrophage and dendritic cell phenotype shift in cancer. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (41<sup>st</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) and down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**.

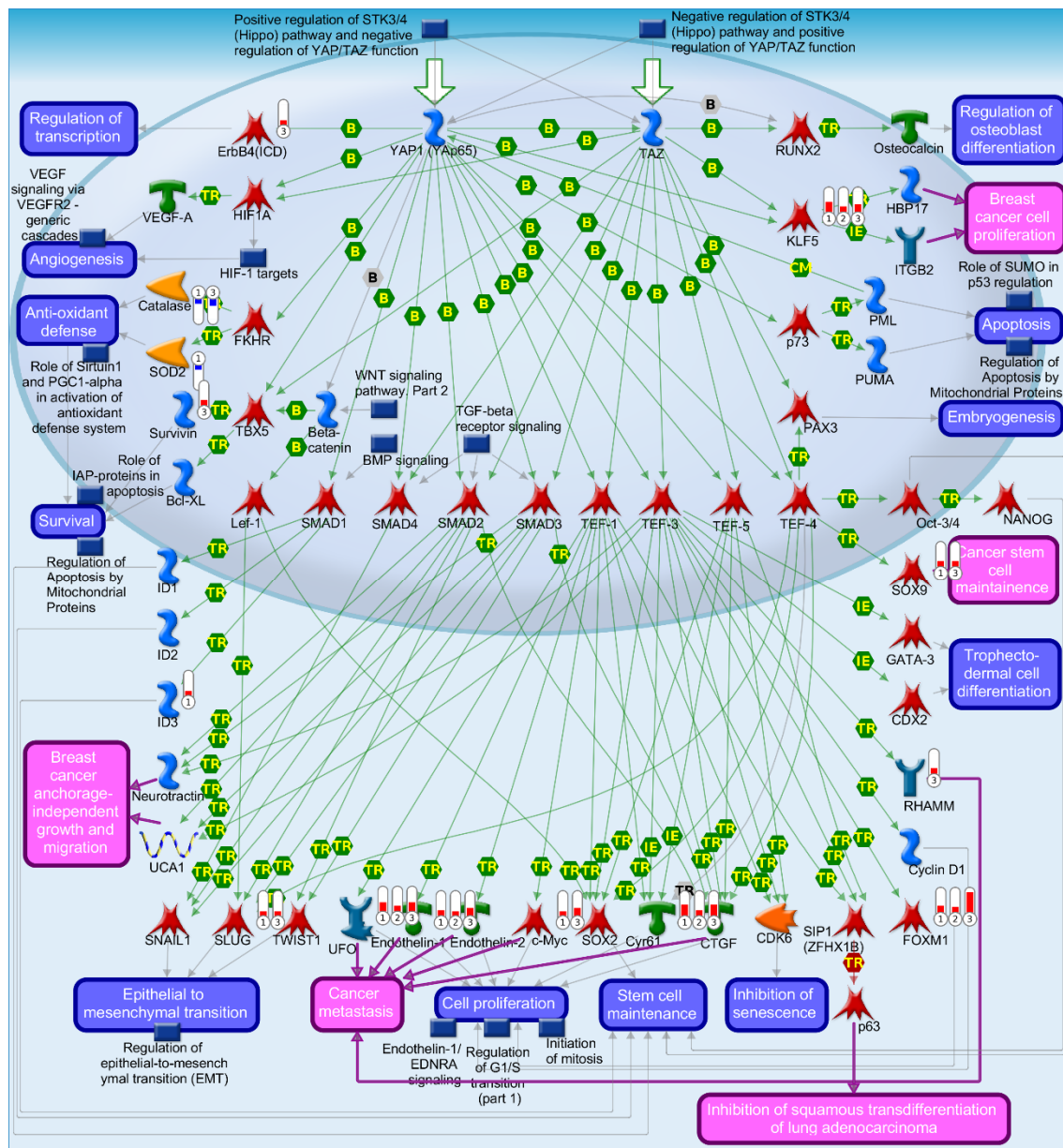




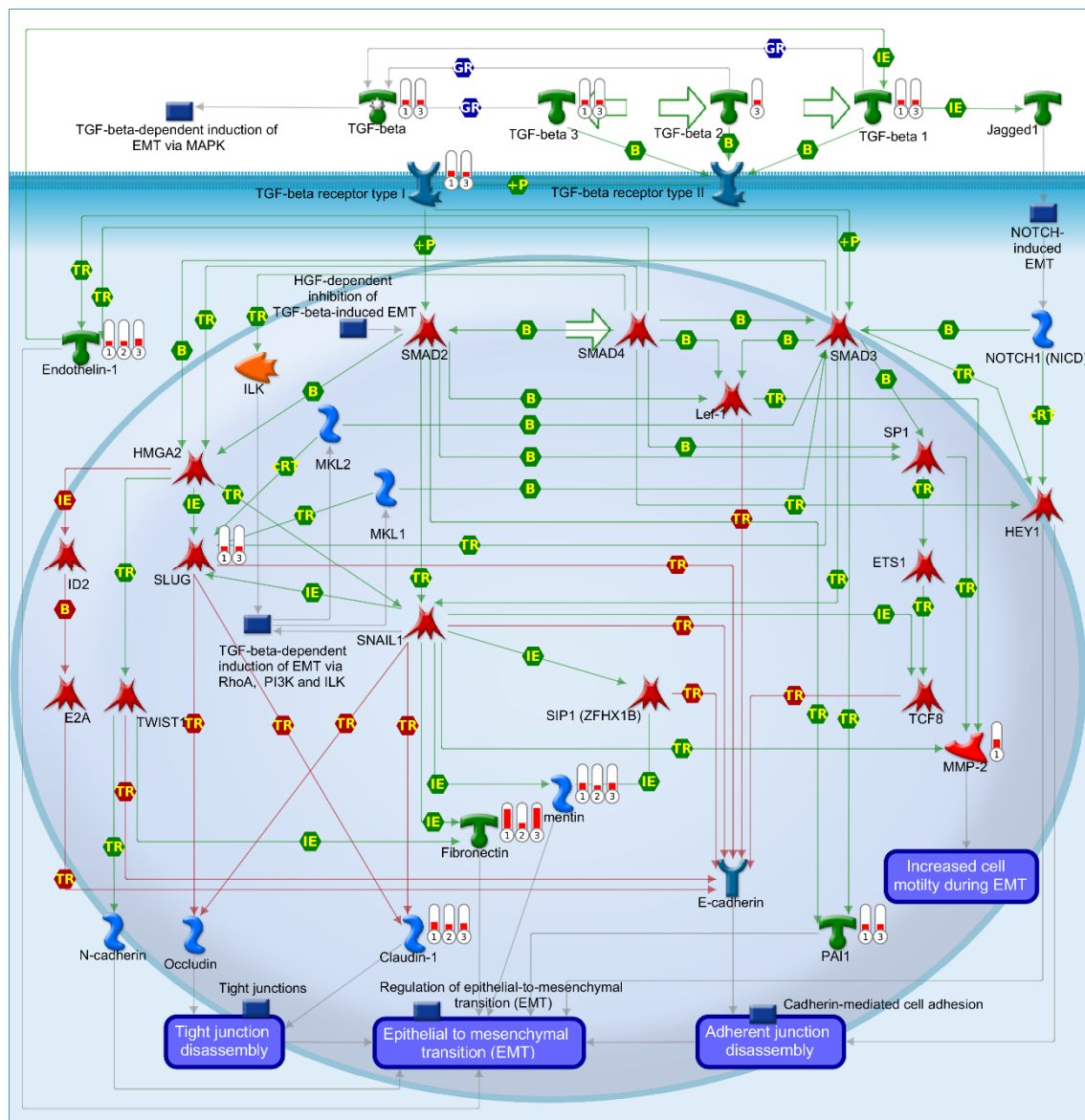
**Figure. S17** Map of gap junctions. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (44<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**.



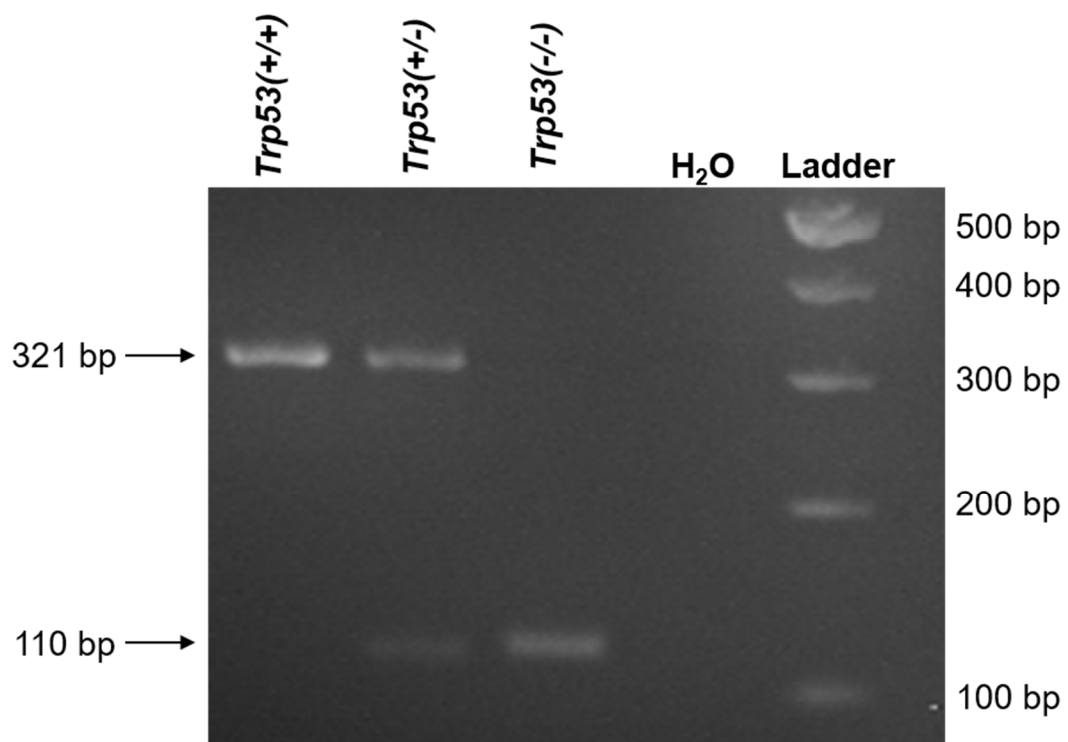
**Figure. S18** Map of role of NEK in cell cycle regulation. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (47<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**. Abbreviation: never in mitosis, gene A-related kinase (NEK).



**Figure. S19** Map of YAP/TAZ-mediated co-regulation of transcription. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (49<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) and down-regulated (thermometer-like symbols in blue) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**. Abbreviations: Tafazzin (TAZ); yes-associated protein (YAP).



**Figure. S20** Map of TGF- $\beta$ -dependent induction of EMT via SMADs. Significantly altered ( $p < 0.05$ ; fold change  $\pm 2$ ) genes for AAI-exposed *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse kidneys were compared in MetaCore™. The enriched pathway (50<sup>th</sup> out of top 50;  $p < 0.05$ ) shows up-regulated (thermometer-like symbols in red) genes. Numbers indicate genotype: 1) *Trp53*(+/+), 2) *Trp53*(+/-) and 3) *Trp53*(-/-). For detailed legend see **Figure. S22**. Abbreviations: epithelial-to-mesenchymal transition (EMT); *Sma* mothers against DPP homology (SMAD); transforming growth factor  $\beta$  (TGF- $\beta$ ).













**Figure. S21** Example of a *Trp53*(+/+), *Trp53*(+/-) and *Trp53*(-/-) mouse genotyping PCR. H<sub>2</sub>O indicates the negative control. bp, base pairs.

































MetaCore

# Quick reference guide

User Data

NETWORKS	MAPS
 Up-regulated (+) Object has user data with positive value	
 Down-regulated (-) Object has user data with negative value	
 Mixed-signal (+/-) Object has user data with both positive and negative values	
 Gene variants Object has user data with gene variants	
 Mixed data Object has user data with both expression values and gene variants	

Network Objects

ENZYMES		GENERIC CLASSES	
 Generic enzyme		 Receptor ligand	
<b>KINASE</b>	<b>PHOSPHATASE</b>	 Transcription factor	
 Generic kinase	 Generic phosphatase	 Protein	
 Protein kinase	 Protein phosphatase	 Compound	
 Lipid kinase	 Lipid phosphatase	 Predicted metabolite or user's structure	
<b>PHOSPHOLIPASE</b>		 Inorganic ion	
 Generic phospholipase		 Reaction	
<b>PROTEASE</b>	<b>GTPASE</b>	 DNA	
 Generic protease	 G-alpha	 RNA	
 Metalloprotease	 RAS - superfamily	 Generic binding protein	
		 Cell membrane glycoprotein	
<b>CHANNELS/TRANSPORTERS</b>		<b>G PROTEIN ADAPTOR/REGULATORS</b>	
 Generic channel		 G beta/gamma	
 Ligand-gated ion channel		 Regulators (GDI, GAP, GET, etc.)	
 Voltage-gated ion channel			
 Transporter			
<b>GROUPS OF OBJECTS</b>			
 A complex or a group Proteins physically connected into a complex or related as a family			
 Logical association Proteins linked by logical relations or physical interactions			
 Custom association Group of collapsed objects chosen by user			

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Figure. S22 MetaCore™ “Quick reference guide” (Part 1).



## Interactions between objects



## Objects on maps

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**Figure. S22** MetaCore™ “Quick reference guide” (Part 2).