SG Global Gene Expression
C57BL/6.NOD-*Aec1Aec2* (disease prone) & **C57BL/6** (asymptomatic controls)
- n=5 per strain per time point (04-, 08-, 12-, 16-weeks)

Ranking Differential Expression
- Collapsing probes to genes
- SAM based ranking of the chronologically closest time-points

GS Resources   *n*=21855
- Gene Ontology (GO)   12467
- NCI (NC)   219
- PFAM (PF)   4147
- KEGG pathways (KE)   225
- Biocarta pathways (BI)   249
- Reactome pathways (RE)   943
- Transcription factor targets (TF) 615
- MicroRNA targets (MI)   793
- Genebands (GB)   393

Data acquisition & resources

GS Enrichment Analysis
- 7871 GS retained (>10 & <1000 genes); 1000 GS permutations

Normalization for Age-related SG Development
- Exclusion of GS showing the same trend in both strains during the same time period (FDRq <0.05; nom. p-value<0.005; TAGS ≥50%)

Leading Edge (LE) Analysis
- Identification of genes contributing to each GS's significance and computation of LE metrics (TAGS, LIST, SIGNAL)
- Flagging LE genes located in *Aec1* and *Aec2*
- Computation of a CONNECTIVITY coefficient matrix representing the overlap between the LE genes of all GSs paired one on one

Data analysis

Requirements for Nodes
For EM-related GS (ancestor either GO_0071944, GO_0031012, GO_0005911):
- (FDRq <0.05)

For EM-associated GS:
- 1st degree neighbor of a EM-related GS (≥8% overlap in the LEs of the EM-related GS and the EM-associated GS)
- FDRq <0.05; nom. p-value <0.005; TAGS ≥50%

Requirements for Edges
- CONNECTIVITY score ≥0.08 (corresponding to ≥8% overlap in the LEs the two GSs)

Network Clustering
- MCL clustering based on -log of CONNECTIVITY

Network building