

Figure S1: Number of connected components per year.

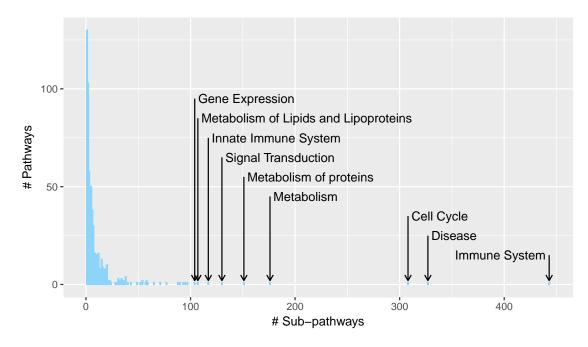


Figure S2: Distribution of the number of sub-pathways for all pathways. There are 2051 pathways annotated in total. Most pathways (1397) do not contain any sub-pathways. Of the remaining 650, most contain few sub-pathways. The nine pathways with more than 100 sub-pathways are annotated in the plot. Innate Immune System is a sub-pathway of Immune System, Metabolism of Lipids and Lipoproteins is a sub-pathway of Metabolism, the other pathways are all top-level pathways.

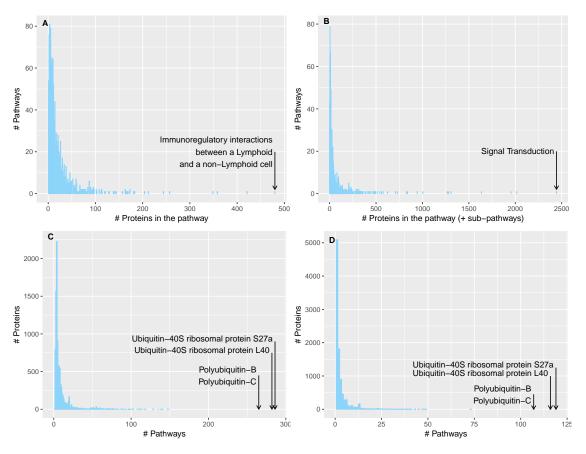


Figure S3: Number of proteins per pathway and vice versa. A) Number of proteins directly occurring in each pathway. B) Number of proteins occurring in each pathway, including the proteins occurring in sub-pathways. C) Number of pathways a protein occurs in, including the pathways where the protein occurs in a sub-pathway. D) Number of pathways a protein directly occurs in.

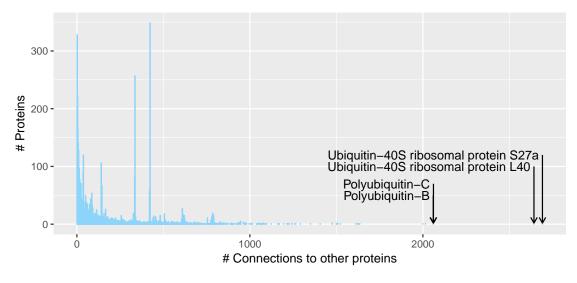


Figure S4: Distribution of the number of connections for each protein. The two big spikes around 400 connections are mainly olfactory receptors and zinc fingers.

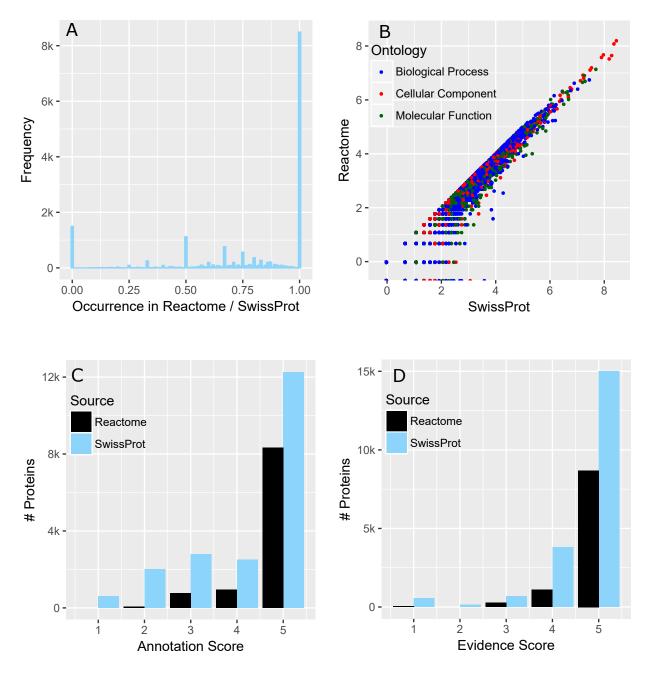


Figure S5: Potential biases in the curation process. Relative occurrence of GO terms (A and B) or protein annotations (C and D) in Reactome vs. SwissProt. A) The number of GO terms that occur with the relative amount indicated on the x-axis (bins of 0.01). B) Each point indicates one GO term. The axes are log-scale, and terms not included in Reactome are plotted at the bottom of the plot. Red: Cellular Component; green: Molecular Function; blue: Biological Process. C) Distributions of annotation and D) evidence scores of proteins in SwissProt and Reactome. Higher scores indicate more annotation and better evidence. Reactome contains only about half of the proteins in SwissProt, hence the much lower bars in general for Reactome.

Table S1: The number of pathways a sub-pathway directly participates in. Only those sub-pathways that are directly part of more than two pathways are shown.

Pathway Name	Parents
RAF/MAP kinase cascade	20
PIP3 activates AKT signaling	9
DAG and IP3 signaling	5
TAK1 activates NFkB by phosphorylation and activation of IKKs complex	4
MAP kinase activation in TLR cascade	4
Spry regulation of FGF signaling	4
MyD88:Mal cascade initiated on plasma membrane	3