

### **Supplementary 1: Comparison of mouse model with yeast and *E. coli* genome-scale models**

The mouse genome-scale model was compared with other unicellular metabolic models such as *E. coli* and yeast. Table S1 shows the comparison of overall network characteristics of the current model with *E. coli*<sup>1</sup> and Yeast.<sup>2</sup> It was clearly evident from Table S1 that *E. coli* has been the well studied organism with high percentage of ORF coverage among the three, which was followed by yeast and mouse. We further examined the conservation of metabolic reactions (Table S2) and metabolites (Fig. S1) across the three organisms to gain insights into their functional characteristics. We included metabolites and reactions only from cytosol in order to avoid the accounting of same reaction from different cellular compartments. The results revealed that 154 reactions (16.2%) were commonly shared among the three, which were predominantly from amino acids, carbohydrate and cofactors and vitamins, while 220 metabolites (18.6%) were commonly shared among them. This indicates that conservation of both metabolites and reactions followed a similar trend. While mouse and yeast shared 221 common reactions, yeast and *E. coli* contained 267 common reactions, thus suggesting that the yeast and *E. coli* may share more common functional pathways than with mouse. A similar result was also observed from the metabolite comparison analysis. These results were highly expected, since these two are unicellular while mouse is a multi-cellular organism.

**Table S1. Comparison of mouse genome-scale network characteristics with yeast and *E. coli* networks**

|                             | Mouse | Yeast | <i>E. coli</i> |
|-----------------------------|-------|-------|----------------|
| ORFs                        | 724   | 904   | 1260           |
| Metabolites                 | 1285  | 1228  | 1668           |
| Cytosol                     | 930   | 634   | 951            |
| Mitochondrial               | 232   | 241   | -              |
| Others                      | -     | 189   | 418            |
| Extracellular               | 123   | 164   | 299            |
| Unique reactions            | 1494  | 1412  | 2077           |
| Cytosol                     | 1085  | 709   | 1187           |
| Mitochondrial               | 161   | 175   | -              |
| Others                      | -     | 133   | 200            |
| Transport                   | 248   | 395   | 690            |
| Knowledge gaps <sup>a</sup> | 367   | N.A   | N.A            |

<sup>a</sup>Knowledge gap refers to number of dead-end metabolites in the network

N.A Not available

**Table S2. Comparison of conserved reactions among the three genome-scale metabolic models**

| Sybsystems              | Common Reactions | Mouse and Yeast | Mouse and <i>E. coli</i> | Yeast and <i>E. coli</i> |
|-------------------------|------------------|-----------------|--------------------------|--------------------------|
| Amino Acids Metabolism  | 28               | 43              | 36                       | 75                       |
| Carbohydrate Metabolism | 38               | 57              | 47                       | 49                       |
| Cofactors and Vitamins  | 30               | 47              | 42                       | 56                       |
| Nucleotides Metabolism  | 25               | 28              | 31                       | 44                       |
| Lipid Metabolism        | 11               | 11              | 17                       | 14                       |
| Energy Metabolism       | 3                | 14              | 5                        | 8                        |
| Others                  | 19               | 21              | 23                       | 21                       |
| Total                   | 154              | 221             | 201                      | 267                      |

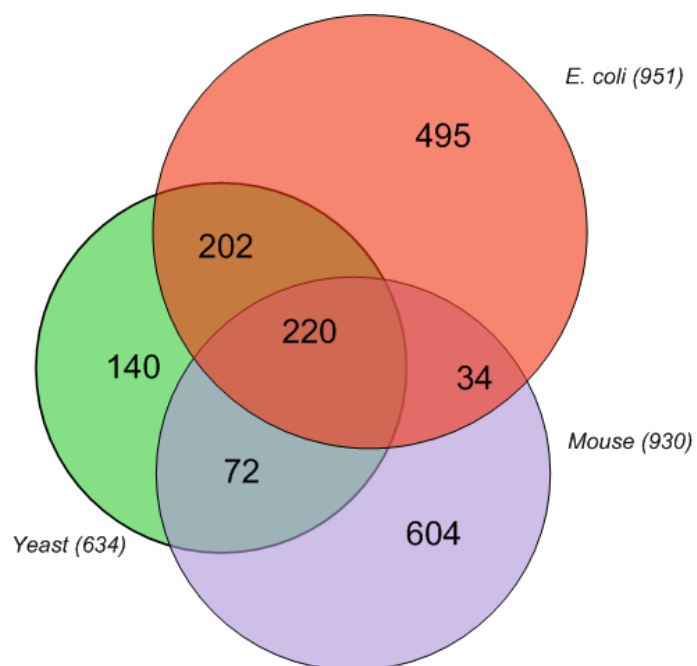


Fig. S1 Comparison of metabolites across mouse, yeast and *E. coli* models. Metabolites from cytosol were only considered for comparison.

## References

1. A. M. Feist and B. Ø. Palsson, *Nat. Biotechnol.*, 2008, 26, 659-667.
2. M. Mo, B. Palsson and M. Herrgard, *BMC Systems Biology*, 2009, 3, 37.