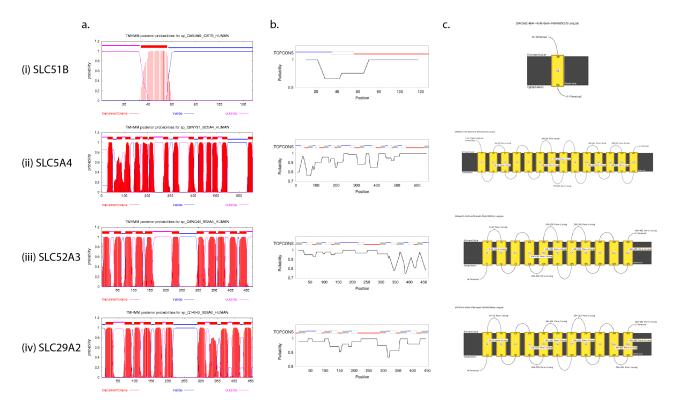
## **Supplementary Figures**



Supplementary Figure 1. Transmembrane helix prediction for selected SLC members. Transmembrane helices were predicted using (a) TMHMM (v. 2.0)<sup>13</sup>, (b) MEMSAT-SVM<sup>14</sup>, and (c) TOPCONS<sup>15</sup> for the (i) organic solute transporter subunit  $\beta$  (SLC51B), (ii) low affinity Na<sup>+</sup>-glucose co-transporter SLC5A4, (iii) riboflavin transporter 2 (SLC52A3), and (iv) equilibrative nucleoside transporter 2 (SLC29A2). The predicted transmembrane helices are indicated by red bars (TMHMM), white/gray rectangles (MEMSAT-SVM), and yellow bars (TOPCONS). SLC51B, SLC5A4, SLC52A3, and SLC29A2 are predicted to have 1, 14, 11, and 11 transmembrane helices, respectively, by the three predictors.

## **Supplementary Tables**

Family <sup>a</sup>	Function <sup>b</sup>	Template Structure <sup>c</sup>	Percent Sequence Identity <sup>d</sup>	Representative Ligands <sup>e</sup>
SLC1 (7)	High-affinity glutamate and neutral amino acid transporter family	Glt(Ph) <sup>16</sup>	34 (3.6 × 10 <sup>-90</sup> )	Glutamate <sup>3</sup> , glutamine <sup>3</sup>
SLC2 (14)	Facilitative glucose transporters	XyIE <sup>*17</sup>	31 (2.8 × 10 <sup>-54</sup> )	Glucose <sup>3</sup> , uric acid <sup>3</sup>
SLC5 (12)	Na⁺- glucose co- transporters	vSGLT <sup>#18</sup>	32 (1.1 × 10 <sup>-69</sup> )	Dapagliflozin <sup>2</sup> , canagliflozin <sup>2</sup> , ipragliflozin <sup>2</sup>
SLC6 (21)	Na <sup>+</sup> - and Cl <sup>-</sup> - dependent neurotransmitter transporters	LeuT <sup>#19</sup>	26 (6 × 10 <sup>-109</sup> )	Fluoxetine <sup>1</sup> , fluvoxamine <sup>1</sup> , citalopram <sup>1</sup> , venlafaxine <sup>1</sup> , paroxetine <sup>1</sup> , radioiodinated metaiodobenzylguanidine <sup>2</sup> ( <sup>131</sup> I-MIBG), serotonin <sup>3</sup> , norepinephrine <sup>3</sup> , dopamine <sup>3</sup> , GABA <sup>3</sup> , amino acids <sup>3</sup>
SLC13 (5)	Na⁺- sulfate/carboxylate co-transporters	VcINDY <sup>20</sup>	32 (1.7 × 10 <sup>-47</sup> )	Succinate <sup>3</sup> , citrate <sup>3</sup> , alpha-ketoglutarate <sup>3</sup>
SLC25 (46)	Mitochondrial carriers	UCP2 <sup>21</sup>	96 (1.4 × 10 <sup>-62</sup> )	Citrate <sup>3</sup> , ornithine <sup>3</sup> , adenosine triphosphate <sup>3</sup> , aspartate <sup>3</sup> , thiamine pyrophosphate <sup>3</sup>



## Supplementary Table 1: Selected SLC families (which contain drug targets) that can be modeled based on a template structures.

- Family marks the human SLC family, as annotated by the Bioparadigms database<sup>23</sup>. The а number of human protein sequences in the family is provided in parenthesis.
- b *Function* gives the function of the human family, as described in the Bioparadigms database
- Template Structure describes the most related atomic structure to the family. Structures with С the MFS and NSS folds are marked with '\*' and '#', respectively.
- d Percent Sequence Identity provides the percent sequence identity of the best scoring hit from each family; E-value is given in parenthesis.
- Representative Ligands gives examples of small molecules that interacts with the е transporter. A small molecule ligand can be one of the following:

<sup>1</sup>Clinical drug that is an inhibitor of the transporter.

<sup>2</sup>Clinical drug that is a substrate of the transporter.

<sup>3</sup>Endogenous compound that is substrate of the transporter.