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Homology Modelling of Neurotransmitter Transporters.

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The dopamine (DAT), serotonin (SERT) and noradrenalin (NET) transporters are molecular targets for different classes of psychotropic drugs. DAT, SERT and NET regulate monoamine concentrations at neuronal synapses by carrying monoamines across neuronal membranes into presynaptic nerve cells, using an inwardly directed sodium gradient as an energy source. Structural information about DAT, SERT and NET transporters and their drug interactions is important for understanding their molecular mechanisms of action, and provide useful tools for new drug discovery. Cocaine and SSRIs share similar molecular mechanisms of action, although cocaine is a highly addictive drug and SSRIs are therapeutic drugs prescribed for the treatment of depression. We have used the crystal structure of Aquifex aeolicus LeuTAa [1] as a template for molecular modelling of DAT, SERT and NET. Psychostimulants and antidepressants have been docked into the DAT, SERT, and NET models to reveal molecular explanations for the various selectivities of these drugs.

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[1] Yamashita A., Singh S. K., Kawate T., Jin Y., Gouaux E.: *Nature* 437 (7056) (2005), 215.