Monoamine

Overview: Plasma membrane located monoamine transporters (provisional nomenclature) transport the hormone/transmitters adrenaline, noradrenaline, dopamine and 5-hydroxytryptamine, and are members of the solute carrier family 6 (SLC6) of sodium- and chloride-dependent neurotransmitter transporters that includes the GABA and glycine transporters (Chen *et al*., 2004). The members of this superfamily share a structural motif of 12 putative transmembrane segments (Palacín *et al*., 1998). A high-resolution structure of a bacterial homologue of these transporters has been reported recently (Yamashita *et al*., 2005).

Nomenclature	DAT	NET	SERT
Systematic name	SLC6A3	SLC6A2	SLC6A4
Other names	DAT1	NAT1	5-HTT, SERT1
Ensembl ID	ENSG00000142319	ENSG00000103546	ENSG00000108576
Endogenous substrates	Dopamine, adrenaline, noradrenaline	Noradrenaline, adrenaline, dopamine	5-HT
Synthetic substrates	Amphetamine, methamphetamine, MPP^+	Amphetamine, methamphetamine, MPP^+	*p*-Chloroamphetamine, MDMA
Selective inhibitors	Mazindol (8.0), WIN35428 (7.9), GBR12935 (7.6)	Mazindol (8.9), nisoxetine (8.4), nomifensine (8.1)	Paroxetine (9.6, Tatsumi *et al.,* 1997), sertraline (9.1), fluoxetine (8.5, Tatsumi *et al.,* 1997)
Probes	[^{3}H]-GBR12935 (3 nM, Pristupa *et al.,* 1994), [^{3}H]-WIN35428 (10 nM, Pristupa *et al.,* 1994)	[^{3}H]-Mazindol (0.5 nM), [^{3}H]-nisoxetine (4 nM)	[^{3}H]-Paroxetine (0.2 nM), [^{3}H]-citalopram (5 nM)
Predicted stoichiometry	1 Dopamine:1–2 Na^+:1 Cl^- (Gu *et al.,* 1994)	1 Noradrenaline: 1 Na^+:1 Cl^- (Gu *et al.,* 1996)	1 5-HT:1 Na^+:1 Cl^- (in), +1 K^+ (out) (Talvenheimo *et al.,* 1983)

[^{125}I]-RTI55 labels all three transporters with affinities between 0.5 and 5 nM. Cocaine is an inhibitor of all three transporters with pK_i values between 6.5 and 7.2. Potential alternative splicing sites in non-coding regions of SERT and NET have been identified. A bacterial homologue of SERT shows allosteric modulation by selected anti-depressants (Singh *et al*., 2007).

Abbreviations: GBR12935, 1-(2-[diphenylmethoxy]ethyl)-4-(3-phenylpropyl)piperazine; **MDMA**, 3,4-methylenedioxymethamphetamine; **MPP^+**, 1-methyl-4-phenylpyridinium; **RTI55**, 2β-carbomethoxy-3β-(4-iodophenyl) tropane (also known as β-CIT); **WIN35428**, 2β-carboxymethy-3β-(4-fluorophenyl)tropane (also known as β-CFT)

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