Table S2. List of reactions and the rate equations for the model of tau pathophysiology.

Table S2. List of reactions and the rate equations for t			Vinstia I am	December	Duradurate	D	Unite
Reaction Type Synthesis of 3R tau	Tau synthesis	r(1) =	Kinetic Law k(1);	Reactants -	Tau0	Params k(1)	Units μM-s <sup>-1</sup>
	Phosphorylation of newly synthesized tau	r(2) =	k(2)*x(1)*x(23)/(k(3)+x(1));	Tau0, ATP	TauN, ADP	k(2)	μM <sup>-1</sup> -s <sup>-1</sup>
Phosphorylation & dephosphorylation of free 3R tau	Dephosphorylation of normally phosphorylated tau	r(3) =	k(4)*x(2)/(k(5)+x(2));	TauN	Tau0	k(3) k(4)	<u>µМ</u> s <sup>-1</sup>
	Depriosphorylation of normally phosphorylated tau	1(3) -	K(+) · X(2)/(K(3) · X(2)),	Taury	Tauo	k(5)	s μM
	Phosphorylation of normally phosphorylated tau	r(4) =	k(6)*x(2)*x(23)/(k(7)+x(2));	TauN, ATP	TauH, ADP	k(6)	μM <sup>-1</sup> -s <sup>-1</sup>
	Dephosphorylation of abnormal/misfolded tau	r(5) =	k(8)*x(3)/(k(9)+x(3));	TauH	TauN	k(7) k(8)	<u>иМ</u> s <sup>-1</sup>
						k(9)	uМ
Microtubule binding and release of 3R tau species	Conformation change favoring MT binding Conformational change back to original	r(6) = r(7) =	k(10)*x(1); k(11)*x(7);	Tau0*	Tau0*	k(10) k(11)	s <sup>-1</sup>
	Binding of newly synthesized tau to MT	r(8) =	k(12)*x(7)*x(10);	Tau0*, MT	Tau0*-MT	k(11)	μM <sup>-1</sup> -s <sup>-1</sup>
	Release of newly synthesized tau from MT		k(13)*x(4);	Tau0*-MT	Tau0*, MT	k(13)	s <sup>-1</sup>
	Conformation change favoring MT binding		k(14)*x(2);	TauN	TauN*	k(14)	s <sup>-1</sup>
	Conformational change back to original Binding of normally phosphorylated tau to MT	r(11) = r(12) =	k(15)*x(8); k(16)*x(8)*x(10);	TauN* TauN*, MT	TauN TauN*-MT	k(15) k(16)	s <sup>-1</sup> μM <sup>-1</sup> -s <sup>-1</sup>
	Release of normally phosphorylated tau from MT	r(13) =	k(17)*x(5);	TauN*-MT	TauN*, MT	k(17)	шм -s
	Conformation change favoring MT binding	r(14) =	k(18)*x(3);	TauH	TauH*	k(18)	s <sup>-1</sup>
	Conformational change back to original		k(19)*x(9);	TauH*	TauH	k(19)	s-1
	Binding of misfolded tau to MT Release of misfolded tau from microtubules	r(16) = r(17) =	k(20)*x(9)*x(10); k(21)*x(6);	TauH*, MT TauH*-MT	TauH*-MT TauH*, MT	k(20) k(21)	μM <sup>-1</sup> -s <sup>-1</sup>
Fuce 2D tou degradation by	Degradation of newly synthesized tau		k(22)*x(1)*x(21)*x(23);	Tau0, 20S, ATP	ADP, 20S	k(22)	μM <sup>-2</sup> -s <sup>-1</sup>
Free 3R tau degradation by non-ubiquitin dependent proteasome  Phosphorylation & dephosphorylation of microtubule-bound 3R tau	Degradation of phosphorylated tau		k(23)*x(2)*x(21)*x(23);	TauN, 20S, ATP	ADP, 20S	k(23)	μM <sup>-2</sup> -s <sup>-1</sup>
	Degradation of misfolded tau		k(24)*x(3)*x(21)*x(23);	TauH, 20S, ATP	ADP, 20S	k(24)	uM <sup>-2</sup> -s <sup>-1</sup>
	Phosphorylation of MT-bound newly synthesized tau	r(21) =	k(25)*x(4)*x(23)/(k(26)+x(4));	Tau0*-MT, ATP	TauN*-MT	k(25) k(26)	μM <sup>-1</sup> -s <sup>-1</sup> μM
	Dephosphorylation of MT-bound normally phosphorylated tau	r(22) =	k(27)*x(5)/(k(28)+x(5));	TauN*-MT	Tau0*-MT	k(27)	S <sup>-1</sup>
						k(28)	uМ
	Phosphorylation of MT-bound normally phosphorylated tau	r(23) =	k(29)*x(5)*x(23)/(k(30)+x(5));	TauN*-MT, ATP	TauH-MT	k(29) k(30)	μM <sup>-1</sup> -s <sup>-1</sup> μM
	Dephosphorylation of MT-bound abnormal/misfolded tau	r(24) =	k(31)*x(6)/(k(32)+x(6));	TauH-MT	TauN*-MT	k(31)	s <sup>-1</sup>
	Accordation of micfolded tou with H70	v(25) -	b/(22)#w/(2)#w/(11):	Tout Hen70	TavH Han70	k(32)	uM
R Tau loading by Hsp70	Association of misfolded tau with Hsp70 Hsp70 release		k(33)*x(3)*x(11); k(34)*x(15);	TauH, Hsp70 TauH-Hsp70	TauH-Hsp70 TauH, Hsp70	k(33) k(34)	μM <sup>-1</sup> -s <sup>-1</sup>
	Exchange of Hsp70 for Hsp90		k(35)*x(15)*x(12);	TauH-Hsc70, Hsp90	TauH-Hsp90, Hsc70	k(34)	s μM <sup>-1</sup> -s <sup>-1</sup>
3R Tau Refolding	Restoration of TauH to Tau0 via Hsp90		k(8)*x(16)/(k(9)+x(16));	TauH-Hsc90	Tau0-Hsp90	k(8)	s-1
	Release of Tau0 from Hsp90	r(20) -	k(36)*x(17);	Tau0-Her00	Hsp90, Tau0	k(9)	μ <u>Μ</u>
	Exchange of Hsc70 for CHIP		k(37)*x(17); k(37)*x(15)*x(14);	Tau0-Hsp90 TauH-Hsc70, CHIP	TauH-Hsc70-CHIP	k(36) k(37)	s <sup>-1</sup> μM <sup>-1</sup> -s <sup>-1</sup>
Degradation of 3R tau by chaperones	Ubiquitination of tau		k(38)*x(18);	TauH-Hsc70-CHIP	TauHUb, Hsc70, CHIP	k(38)	s-1
	Binding of Bag-2 to the degradation complex		k(39)*x(18)*x(13);	TauH-Hsc70-CHIP, Bag2	TauH-Hsc70-CHIP-Bag2	k(39)	μM <sup>-1</sup> -s <sup>-1</sup>
	Rescue from degradation by Bag2 Degradation of ubiquitinated tau		k(40)*x(19);	TauH-Hsc70-CHIP-Bag2	TauH-Hsc70, CHIP, Bag2 ADP, 26S	k(40) k(41)	s <sup>-1</sup>
vnthesis of 4R tau	Synthesis of 4R tau	r(34) =	k(41)*x(20)*x(22)*x(23); k(42);	TauHUb, 26S, ATP	Tau0	k(41)	μM <sup>-2</sup> -s <sup>-1</sup> μM-s <sup>-1</sup>
vitticsis of 4R (au	Phosphorylation of newly synthesized tau		k(43)*x(25)*x(23)/(k(44)+x(25));	Tau0, ATP	TauN, ADP	k(43)	μM <sup>-1</sup> -s <sup>-1</sup>
Phosphorylation & dephosphorylation of free 4R tau						k(44)	иМ
	Dephosphorylation of normally phosphorylated tau	r(37) =	k(45)*x(26)/(k(46)+x(26));	TauN	Tau0	k(45) k(46)	s-1 uM
	Phosphorylation of normally phosphorylated tau	r(38) =	k(47)*x(26)*x(23)/(k(48)+x(26));	TauN, ATP	TauH, ADP	k(47)	μM <sup>-1</sup> -s <sup>-1</sup>
	Dephosphorylation of abnormal/misfolded tau	r(39) =	k(49)*x(27)/(k(50)+x(27));	TauH	TauN	k(48) k(49)	μ <u>Μ</u>
	Depriospriorylation of abriormal/mistorded tau	1(39) -	K(49) · X(27)/(K(30)+X(27)),	Tauri	Taury	k(50)	s <sup>-1</sup> uM
Microtubule binding and release of 4R tau species	Conformation change favoring MT binding	r(40) =	k(51)*x(25);	Tau0	Tau0*	k(51)	s <sup>-1</sup>
	Conformational change back to original	r(41) =	k(52)*x(31);	Tau0*	Tau0	k(52)	s <sup>-1</sup>
	Binding of newly synthesized tau to MT Release of newly synthesized tau from MT	r(42) = r(43) =	k(53)*x(31)*x(10); k(54)*x(28);	Tau0*, MT Tau0*-MT	Tau0*-MT Tau0*, MT	k(53) k(54)	μM <sup>-1</sup> -s <sup>-1</sup>
	Conformation change favoring MT binding		k(55)*x(26);	TauN	TauN*	k(55)	s <sup>-1</sup>
	Conformational change back to original		k(56)*x(32);	TauN*	TauN	k(56)	s <sup>-1</sup>
	Binding of normally phosphorylated tau to MT	r(46) =	k(57)*x(32)*x(10);	TauN*, MT	TauN*-MT	k(57)	μM <sup>-1</sup> -s <sup>-1</sup>
	Release of normally phosphorylated tau from MT  Conformation change favoring MT binding	r(47) = r(48) =	k(58)*x(29); k(59)*x(27);	TauN*-MT TauH	TauN*, MT TauH*	k(58) k(59)	s <sup>-1</sup>
	Conformational change back to original		k(60)*x(33);	TauH*	TauH	k(60)	s <sup>-1</sup>
	Binding of misfolded tau to MT		k(61)*x(33)*x(10);	TauH*, MT	TauH*-MT	k(61)	μM <sup>-1</sup> -s <sup>-1</sup>
	Release of misfolded tau from microtubules	r(51) =	k(62)*x(30);	TauH*-MT	TauH*, MT	k(62)	s <sup>-1</sup>
Free 4R tau degradation by non-ubiquitin dependent proteasome	Degradation of newly synthesized tau  Degradation of phosphorylated tau		k(63)*x(25)*x(23)*x(21); k(64)*x(26)*x(23)*x(21);	Tau0, 20S, ATP TauN, 20S, ATP	ADP, 20S ADP, 20S	k(63) k(64)	μM <sup>-2</sup> -s <sup>-1</sup> μM <sup>-2</sup> -s <sup>-1</sup>
	Degradation of misfolded tau	r(54) =	k(65)*x(27)*x(23)*x(21);	TauH, 20S, ATP	ADP, 20S	k(65)	μM <sup>-2</sup> -s <sup>-1</sup>
	Phosphorylation of MT-bound newly synthesized tau	r(55) =	k(66)*x(28)*x(23)/(k(67)+x(28));	Tau0*-MT, ATP	TauN*-MT	k(66)	μM <sup>-1</sup> -s <sup>-1</sup>
	Dephosphorylation of MT-bound normally phosphorylated tau	r(56) -	L((9)*-(20)/(L((0))(20)).		Tau0*-MT	k(67)	μM
	prospriory station of Net 1-bound normally phosphory atted tau			TauN*_MT			S.
nospnorylation & dephosphorylation of microtubule-			k(68)*x(29)/(k(69)+x(29));	TauN*-MT	1800 -1411	k(68)	μМ
	Phosphorylation of MT-bound normally phosphorylated tau		k(70)*x(29)*x(29)/(k(71)+x(29));	TauN*-MT TauN*-MT, ATP	TauH-MT	k(68) k(69) k(70)	μM μM <sup>-1</sup> -s <sup>-1</sup>
	Phosphorylation of MT-bound normally phosphorylated tau	r(57) =	k(70)*x(29)*x(23)/(k(71)+x(29));	TauN*-MT, ATP	TauH-MT	k(68) k(69) k(70) k(71)	μM <sup>-1</sup> -s <sup>-1</sup> μM
hosphorylation & dephosphorylation of microtubule- ound 4R tau	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau	r(57) = r(58) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30));	TauN*-MT, ATP TauH-MT	TauH-MT TauN*-MT	k(68) k(69) k(70) k(71) k(72) k(73)	µМ <sup>-1</sup> -s <sup>-1</sup> <u>µМ</u> s <sup>-1</sup> иМ
ound 4R tau	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70	r(57) = r(58) = r(59) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11);	TauN*-MT, ATP TauH-MT TauH, Hsp70	TauH-MT TauN*-MT TauH-Hsp70	k(68) k(69) k(70) k(71) k(72) k(73) k(74)	иМ <sup>-1</sup> -s <sup>-1</sup> иМ s <sup>-1</sup> иМ иМ <sup>-1</sup> -s <sup>-1</sup>
ound 4R tau	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release	r(57) = r(58) = r(59) = r(60) =	k(70)*x(29)*x(23)'(k(71)+x(29)); k(72)*x(30)'(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34);	TauN*-MT, ATP  TauH-MT  TauH, Hsp70  TauH-Hsp70	TauH-MT TauN*-MT TauH-Hsp70 TauH, Hsp70	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75)	μM <sup>-1</sup> -s <sup>-1</sup> μM  s <sup>-1</sup> μM  μM <sup>-1</sup> -s <sup>-1</sup>
und 4R tau R Tau loading by Hsp70	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90	r(57) = r(58) = r(59) = r(60) = r(61) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34);	TauN*-MT, ATP TauH-MT TauH, Hsp70 TauH-Hsp70 TauH-Hsc70, Hsp90	TauH-MT TauN*-MT TauH-Hsp70 TauH, Hsp70 TauH-Hsp90, Hsc70	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75)	μM <sup>-1</sup> -s <sup>-1</sup> μM s <sup>-1</sup> μM <sup>-1</sup> -s <sup>-1</sup> s <sup>-1</sup> μM <sup>-1</sup> -s <sup>-1</sup>
und 4R tau R Tau loading by Hsp70	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35));	TauN*-MT, ATP TauH-MT TauH, Hsp70 TauH-Hsp70 TauH-Hsc70, Hsp90 TauH-Hsc90	TauH-MT TauN*-MT TauH-Hsp70 TauH, Hsp70 TauH, Hsp70 TauH-Hsp90, Hsc70 Tau0-Hsp90	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8)	µМ <sup>-1</sup> -s <sup>-1</sup> µМ s <sup>-1</sup> µМ µМ <sup>-1</sup> -s <sup>-1</sup> s <sup>-1</sup> µМ <sup>-1</sup> -s <sup>-1</sup> s <sup>-1</sup>
und 4R tau R Tau loading by Hsp70	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(63) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36);	TauH-MT TauH.Hsp70 TauH-Hsp70 TauH-Hsp70 TauH-Hsc70, Hsp90 TauH-Hsc90 TauH-Hsc90	TauH-HSp70 TauH-HSp70 TauH-HSp70 TauH-HSp90, Hsc70 Tau0-HSp90 HSp90, Tau0	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(9) k(78)	μM <sup>-1</sup> -s <sup>-1</sup> μM  s <sup>-1</sup> μM  μM <sup>-1</sup> -s <sup>-1</sup> μμ <sup>-1</sup> -s <sup>-1</sup> μμ <sup>-1</sup> -s <sup>-1</sup> μM  s <sup>-1</sup> μM  s <sup>-1</sup>
und 4R tau  Tau loading by Hsp70	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(63) = r(64) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36); k(79)*x(34)*x(14);	TauN*-MT, ATP TauH-MT TauH, Hsp70 TauH-Hsp70 TauH-Hsc70, Hsp90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc70, CHIP	TauH-MT TauN*-MT TauH-Hsp70 TauH-Hsp70, TauH-Hsp90, Hsc70 Tau0-Hsp90 Hsp90, Tau0 TauH-Hsc70-CHIP	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(9) k(78)	µМ <sup>-1</sup> -s <sup>-1</sup> µМ  s <sup>-1</sup> µМ  µМ <sup>-1</sup> -s <sup>-1</sup> µМ  µМ <sup>-1</sup> -s <sup>-1</sup> µМ  s <sup>-1</sup> µМ  м <sup>-1</sup> -s <sup>-1</sup> µМ
und 4R tau  Tau loading by Hsp70 Tau Refolding	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(63) = r(64) = r(65) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36);	TauH-MT TauH.Hsp70 TauH-Hsp70 TauH-Hsp70 TauH-Hsc70, Hsp90 TauH-Hsc90 TauH-Hsc90	TauH-HSp70 TauH-HSp70 TauH-HSp70 TauH-HSp90, Hsc70 Tau0-HSp90 HSp90, Tau0	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(9) k(78)	μM <sup>-1</sup> -s <sup>-1</sup> μM  s <sup>-1</sup> μM <sup>-1</sup> -s <sup>-1</sup>
und 4R tau  Tau loading by Hsp70 Tau Refolding	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(64) = r(65) = r(66) = r(67) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36); k(78)*x(34)*x(14); k(80)*x(37); k(81)*x(37)*x(13); k(81)*x(37)*x(13); k(82)*x(38);	TauN*-MT, ATP TauH-HSp70 TauH-Hsp70 TauH-Hsc90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CHIP-Bag2	TauH-MT TauN+-MT TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP-Bag2 TauH-Hsc70, CHIP, Bag2	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(9) k(78) k(79) k(80) k(81) k(82)	им <sup>-1</sup> -s <sup>-1</sup> им  s <sup>-1</sup> им  μм <sup>-1</sup> -s <sup>-1</sup> μμ <sup>-1</sup> -s <sup>-1</sup> μμ <sup>-1</sup> -s <sup>-1</sup> μμ <sup>-1</sup> -s <sup>-1</sup> μμ <sup>-1</sup> -s <sup>-1</sup>
und 4R tau R Tau loading by Hsp70 R Tau Refolding	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70 Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of ubiquitinated tau	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(63) = r(64) = r(65) = r(66) = r(67) = r(68) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36); k(79)*x(34)*x(14); k(80)*x(37); k(81)*x(37)*x(13); k(82)*x(38); k(83)*x(39)*x(22)*x(23);	TauN*-MT, ATP TauH-MT TauH, Hsp70 TauH-Hsc70, Hsp90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CSIP-Bag2 TauH-Hsc70-CSIP-Bag2	TauH-MT TauH-Hsp70 TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Tau0-Hsp90 Hsp90, Tau0 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP-Bag2 TauH-Hsc70, CHIP, Bag2 ADP, 268	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(78) k(78) k(80) k(81) k(82) k(83)	иМ <sup>-1</sup> -s <sup>-1</sup> иМ  иМ <sup>-1</sup> -s <sup>-1</sup> иМ  иМ <sup>-1</sup> -s <sup>-1</sup> иМ  в <sup>-1</sup> иМ <sup>-1</sup> -s <sup>-1</sup> иМ  г <sup>-1</sup> г <sup>-1</sup> иМ  г <sup>-1</sup> г <sup>-1</sup> иМ  г <sup>-1</sup> г <sup>-1</sup>
Tau loading by Hsp70  Tau Refolding  gradation of 4R tau by chaperones	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsr70 for CHIP  Ubiquitination of tau  Binding of Bsg-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of ubiquitinated tau  Generation of ATP	r(57) =  r(58) =  r(59) =  r(60) =  r(61) =  r(62) =  r(63) =  r(64) =  r(65) =  r(66) =  r(66) =  r(67) =  r(68) =  r(68) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36); k(78)*x(34)*x(14); k(80)*x(37); k(80)*x(37); k(81)*x(37)*x(13); k(82)*x(38); k(83)*x(39)*x(22)*x(23); k(83)*x(23);	TauN*-MT, ATP TauH-HISP70 TauH-HISP70 TauH-HISP70 TauH-HISP70, HISP90 TauH-HISP70, CHIP TauH-HISP70, CHIP TauH-HISP70-CHIP, Bag2 TauH-HISP70-CHIP-Bag2 TauH-HISP70-CHIP-Bag2 TauH-USP70-CHIP-Bag2 TauH-USP70-CHIP-Bag2 TauH-	TauH-Hsp70 TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsp90, Tau0 Hsp90, Tau0 Hsp90, Tau0 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP-Bag2 TauH-Hsc70, CHIP, Bag2 ATP	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(78) k(78) k(80) k(81) k(82) k(83)	иМ <sup>1</sup> -s <sup>1</sup> иМ  иМ  иМ <sup>1</sup> -s <sup>1</sup> иМ  иМ <sup>1</sup> -s <sup>1</sup> г <sup>1</sup> иМ  г <sup>1</sup>
	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70 Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of ubiquitinated tau	r(57) =  r(58) =  r(59) =  r(60) =  r(61) =  r(62) =  r(64) =  r(65) =  r(66) =  r(67) =  r(68) =  r(69) =  r(70) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36); k(79)*x(34)*x(14); k(80)*x(37); k(81)*x(37)*x(13); k(82)*x(38); k(83)*x(39)*x(22)*x(23);	TauN*-MT, ATP TauH-MT TauH, Hsp70 TauH-Hsc70, Hsp90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CSIP-Bag2 TauH-Hsc70-CSIP-Bag2	TauH-MT TauH-Hsp70 TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Tau0-Hsp90 Hsp90, Tau0 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP-Bag2 TauH-Hsc70, CHIP, Bag2 ADP, 268	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(78) k(78) k(80) k(81) k(82) k(83)	uM <sup>-1</sup> -s <sup>-1</sup> uM  s <sup>-1</sup> uM  yM <sup>-1</sup> -s <sup>-1</sup> s <sup>-1</sup> µM <sup>-1</sup> -s <sup>-1</sup> y <sup>-1</sup> s <sup>-1</sup> µM <sup>-1</sup> -s <sup>-1</sup> s <sup>-1</sup> µM <sup>-1</sup> -s <sup>-1</sup> s <sup>-1</sup> uM <sup>-1</sup> -s <sup>-1</sup> s <sup>-1</sup> uM <sup>-2</sup> -s <sup>-1</sup> uM <sup>-2</sup> -s <sup>-1</sup> uM <sup>-2</sup> -s <sup>-1</sup> uM <sup>-2</sup> -s <sup>-1</sup> uM <sup>-1</sup> -s <sup>-1</sup>
R Tau loading by Hsp70 R Tau Refolding	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70 Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of vibiquitinated tau  Generation of ATP  Use of ATP	r(57) =  r(58) =  r(59) =  r(60) =  r(61) =  r(62) =  r(63) =  r(64) =  r(65) =  r(66) =  r(67) =  r(69) =  r(70) =  r(71) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)), k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(76)*x(34)*x(12); k(78)*x(36); k(79)*x(34)*x(14); k(80)*x(37); k(81)*x(37); k(81)*x(37); k(81)*x(37); k(81)*x(37); k(81)*x(37); k(81)*x(37); k(81)*x(37); k(81)*x(37); k(81)*x(37); k(81)*x(37)*x(13); k(82)*x(38); k(83)*x(23);	TauN*-MT, ATP TauH-MT TauH, Hsp70 TauH-Hsc70, Hsp90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc70, CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP-Bag2	TauH-HSP70 TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsp90, Tau0 Hsp90, Tau0 TauH-Hsc70-CHIP TauH-Hsc70-CHIP-Bag2 TauH-Hsc70, CHIP, Bag2 ADP, 26S ATP ADP	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(79) k(78) k(80) k(81) k(82) k(83)	иМ <sup>1</sup> -s <sup>1</sup> иМ  s <sup>1</sup> иМ  μМ <sup>1</sup> -s <sup>1</sup> s <sup>1</sup> μM <sup>1</sup> -s <sup>1</sup> s <sup>1</sup> μM <sup>1</sup> -s <sup>1</sup> s <sup>1</sup> μM <sup>1</sup> -s <sup>1</sup>
t Tau loading by Hsp70 t Tau Refolding	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70 Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of ubiquitinated tau  Generation of ATP  Use of ATP by other processes  Nucleation of Tau3  Dissociation of Tau3  Dissociation of Tau3  Nucleation of Tau4	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(64) = r(66) = r(66) = r(66) = r(67) = r(68) = r(71) = r(71) = r(72) = r(73) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(76)*x(34)*x(12); k(78)*x(35)/(k(9)+x(35)); k(78)*x(36); k(79)*x(34)*x(14); k(80)*x(37); k(81)*x(37)*x(13); k(81)*x(37)*x(13); k(81)*x(37)*x(13); k(83)*x(29)*x(23); k(84)*x(24); k(84)*x(24); k(85)*x(23); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(86)*x(20); k(88)*x(39); k(88)*x(30); k(88)	TauN*-MT, ATP TauH-MT TauH, Hsp70 TauH-Hsc70 TauH-Hsc90 TauH-Hsc90 TauH-Hsc70, CHIP TauH-Hsc70, CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CHIP-Sag2 TauH-Hsc70-C	TauH-MT TauN*-MT TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP-Bag2 TauH-Hsc70, CHIP, Bag2 ADP, 268 ATP ADP Nucleus3 TauH3RUb (2) Nucleus4	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(9) k(78) k(80) k(81) k(82) k(83) k(83)	иМ <sup>3</sup> -s <sup>3</sup> иМ м им <sup>3</sup> -s <sup>3</sup> иМ м м м м м м м м м м м м м м м м м м
R Tau loading by Hsp70 R Tau Refolding ggradation of 4R tau by chaperones	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Restoration of TauH to Tau0 via Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of ubiquitinated tau  Generation of ATP  Use of ATP by other processes  Nucleation of Tau3  Dissociation of Tau3  Dissociation of Tau4  Dissociation of Tau4 Nucleus	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(63) = r(64) = r(65) = r(66) = r(67) = r(69) = r(70) = r(71) = r(72) = r(73) = r(74) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36); k(79)*x(34)*x(14); k(80)*x(37); k(81)*x(37)*x(13); k(82)*x(38); k(82)*x(38); k(83)*x(39)*x(22)*x(23); k(84)*x(24); k(85)*x(23); k(86)*x(23); k(86)*x(24); k(86)*x(24); k(86)*x(24); k(86)*x(24); k(86)*x(23);	TauN*-MT, ATP  TauH-MT  TauH-Hsp70  TauH-Hsp70  TauH-Hsc70, Hsp90  TauH-Hsc70, CHIP  TauH-Hsc70-CHIP  TauH-Hsc70-CHIP  TauH-Hsc70-CHIP  TauH-Hsc70-CHIP, Bag2  TauH-Hsc70-CHIP, Bag2  TauH-Hsc70-CHIP, Bag2  TauH-Hsc70-CHIP, Bag3  TauH-Hsc70-CHIP-Bag3  TauH-Hsc70-CHI	TauH-MT TauN*-MT TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 ADP, 268 ATP ADP, and	k(68) k(69) k(70) k(71) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(9) k(78) k(9) k(81) k(84) k(83) k(84) k(85)	иМ <sup>3</sup> -s <sup>-1</sup> иМ  s <sup>-1</sup> иМ  y <sup>-1</sup> s <sup>-1</sup> иМ <sup>3</sup> иМ <sup>3</sup> -s <sup>-1</sup> иМ <sup>3</sup> -s <sup>-1</sup> иМ  s <sup>-1</sup> г <sup>-1</sup> иМ  s <sup>-1</sup> г <sup>-1</sup>
R Tau loading by Hsp70 R Tau Refolding	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Restoration of Tau1 to Tau0 via Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of AIP  Use of ATP by other processes  Nucleation of Tau3  Dissociation of Tau4  Dissociati	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(63) = r(64) = r(65) = r(66) = r(66) = r(67) = r(68) = r(70) = r(72) = r(72) = r(72) = r(74) = r(74) = r(75) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(35)/(k(9)+x(35)); k(78)*x(36); k(78)*x(37); k(80)*x(37); k(81)*x(37)*x(13); k(82)*x(38); k(83)*x(37)*x(12); k(83)*x(29)*x(22); k(84)*x(24); k(85)*x(23); k(86)*x(20)·2; k(86)*x(20)·2; k(86)*x(20)·2; k(86)*x(40); k(88)*x(40); k(88)*x(40); k(88)*x(40); k(89)*x(40);	TauN*-MT, ATP TauH-Hsp70 TauH-Hsp70 TauH-Hsc90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc70, CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CH	TauH-MT TauN*-MT TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70, CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 ADP, 26S ATP ADP Nucleus3 TauH-Hsc70, MIP, Bag2 Nucleus4 TauH-HgUb (2) Nucleus4 TauH-HgUb (2)	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(77) = k(8) k(79) k(80) k(81) k(82) k(83) k(84) k(85) k(88) k(88)	иМ <sup>2</sup> -s <sup>2</sup> иМ  s <sup>3</sup> иМ  μМ <sup>2</sup> -s <sup>3</sup> s <sup>4</sup> иМ  s <sup>7</sup> иМ  s <sup>7</sup> иМ  s <sup>3</sup> иМ  s <sup>3</sup> иМ  s <sup>4</sup> иМ  в <sup>4</sup> иМ  s <sup>4</sup> иМ  в <sup>4</sup> и
R Tau loading by Hsp70  R Tau Refolding  egradation of 4R tau by chaperones  IP generation and use by other processes	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Restoration of TauH to Tau0 via Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of ubiquitinated tau  Generation of ATP  Use of ATP by other processes  Nucleation of Tau3  Dissociation of Tau3  Dissociation of Tau4  Dissociation of Tau4 Nucleus	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(64) = r(65) = r(66) = r(66) = r(67) = r(68) = r(70) = r(71) = r(72) = r(73) = r(75) = r(75) = r(75) =	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36); k(79)*x(34)*x(14); k(80)*x(37); k(81)*x(37)*x(13); k(82)*x(38); k(82)*x(38); k(83)*x(39)*x(22)*x(23); k(84)*x(24); k(85)*x(23); k(86)*x(23); k(86)*x(24); k(86)*x(24); k(86)*x(24); k(86)*x(24); k(86)*x(23);	TauN*-MT, ATP  TauH-MT  TauH-Hsp70  TauH-Hsp70  TauH-Hsc70, Hsp90  TauH-Hsc70, CHIP  TauH-Hsc70-CHIP  TauH-Hsc70-CHIP  TauH-Hsc70-CHIP  TauH-Hsc70-CHIP, Bag2  TauH-Hsc70-CHIP, Bag2  TauH-Hsc70-CHIP, Bag2  TauH-Hsc70-CHIP, Bag3  TauH-Hsc70-CHIP-Bag3  TauH-Hsc70-CHI	TauH-MT TauN*-MT TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 ADP, 268 ATP ADP, and	k(68) k(69) k(70) k(71) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(9) k(78) k(9) k(81) k(84) k(83) k(84) k(85)	иМ <sup>1</sup> -s <sup>1</sup> иМ  s <sup>1</sup> иМ  s <sup>1</sup> иМ  s <sup>1</sup> иМ <sup>1</sup> -s <sup>1</sup> иМ  s <sup>1</sup> г  г  г  г  г  г  г  г  г  г  г  г  г
R Tau loading by Hsp70  R Tau Refolding  egradation of 4R tau by chaperones  IP generation and use by other processes	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70 Hsp70 release  Exchange of Hsp70 for Hsp90 Restoration of TauH to Taud via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of vibiquitinated tau  Generation of ATP  Use of ATP by other processes  Nucleation of Tau3  Dissociation of Tau3  Dissociation of Tau4  Dissociation of Tau4  Dissociation of Tau3  Dissociation of Tau4  Dissociation of Tau3  Dissociation of Tau3 length 3  Dissociation  Formation of Tau3, 1> 3 from Tau3 aggregates of length 3  Formation of agg of 1> 3 from Tau3 aggregates of 1> 3	r(57) = r(58) = r(59) = r(60) = r(61) = r(62) = r(64) = r(65) = r(66) = r(66) = r(67) = r(70) = r(71) = r(72) = r(73) = r(74) = r(75) = r(77) = r(78) = r(88)	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)), k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(76)*x(34)*x(12); k(78)*x(36); k(78)*x(36); k(78)*x(36); k(78)*x(36); k(81)*x(37)*x(13); k(81)*x(37)*x(13); k(81)*x(37)*x(13); k(81)*x(21); k(81)*x(21); k(81)*x(22)*x(23); k(84)*x(24); k(85)*x(23); k(84)*x(24); k(85)*x(23); k(86)*x(20)*2; k(86)*x(20)*2; k(88)*x(39)*2; k(88)*x(39)*2; k(89)*x(20)*x(40); k(88)*x(39)*2; k(89)*x(41); k(89)*x(41); k(90)*x(20)*x(40); k(91)*x(42); k(90)*x(20)*x(42); k(90)*x(20)*x(42); k(90)*x(20)*x(43);	TauN*-MT, ATP TauH-MT TauH, Hsp70 TauH-Hsc70 TauH-Hsc90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CHIP-Ba	TauH-HSP70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsc70-CHIP TauH-Hsc70-CHIP-Bag2 TauH-Hsc70, CHIP, Bag2 ADP, 26S ATP ADP Nucleus3 TauH-Hsc70, HIP, Bag2 TauH-Hsc70, HIP, Bag2 ADP, 26S ATP ADP Nucleus3 TauH-HsC70, HIP, Bag2 ADP, 26S ATP ADP Nucleus3 TauH-HsC70, HIP, Bag2 ADP, ADP Nucleus3 TauH-HsC70, HIP, Bag2 ADP Nucleus3 TauH-HSU0 (2) Agg33 Nucleus4 TauH-HSU0 (2) Agg33 Nucleus3, TauH-JRUB Ap	k(68) k(69) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(77) = k(8) k(79) k(80) k(81) k(82) k(83) k(84) k(85) k(88) k(89) k(90) k(91)	иМ <sup>1</sup> -s <sup>1</sup> иМ  s <sup>1</sup> иМ  s <sup>1</sup> иМ <sup>3</sup> -s <sup>1</sup> иМ  s <sup>1</sup> иМ  в <sup>1</sup> иМ  s <sup>1</sup> иМ  в <sup>1</sup> иМ  н  н  н  н  н  н  н  н  н  н  н  н  н
R Tau loading by Hsp70  R Tau Refolding  egradation of 4R tau by chaperones  IP generation and use by other processes	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70 Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of ubiquitinated tau  Generation of ATP  Use of ATP by other processes  Nucleation of Tau3  Dissociation of Tau4  Dissociation of Tau4 Nucleus  Nucleation of Tau4  Dissociation of Tau3, length 3  Dissociation of Tau3, aggregate of length 3  Formation of aggregates 1-3  Dissociation of aggregates 1-3  Dissociation of aggregates 1-3  Dissociation of aggregates 1-3	r(57) =  r(58) =  r(59) =  r(60) =  r(61) =  r(62) =  r(63) =  r(64) =  r(66) =  r(66) =  r(67) =  r(71) =  r(72) =  r(73) =  r(74) =  r(75) =  r(77) =  r(77) =  r(77) =  r(77) =  r(77) =  r(77) =  r(78) =  r(78) =  r(78) =  r(79)	k(70)*x(29)*x(23)(k(71)+x(29)); k(72)*x(30)(k(73)+x(30)); k(74)*x(27)*x(11); k(73)*x(34); k(76)*x(34); k(76)*x(34); k(76)*x(34); k(78)*x(35)(k(9)+x(35)); k(78)*x(36); k(79)*x(34)*x(14); k(80)*x(37); k(81)*x(37)*x(13); k(81)*x(37)*x(13); k(82)*x(38); k(82)*x(38); k(83)*x(29)*x(23); k(84)*x(24); k(83)*x(39)*x(22)*x(23); k(84)*x(24); k(83)*x(39)*x(22)*x(23); k(84)*x(24); k(83)*x(39)*x(22)*x(23); k(84)*x(24); k(83)*x(39); k(86)*x(20)*x(21); k(89)*x(40); k(89)*x(40); k(89)*x(40); k(90)*x(40); k(90)*x(20)*x(40); k(90)*x(20)*x(40); k(90)*x(20)*x(40); k(90)*x(20)*x(42); k(90)*x(20)*x(42); k(90)*x(20)*x(43); k(90)*x(20)*x(43); k(90)*x(20)*x(43); k(90)*x(20)*x(43);	TauN*-MT, ATP TauH-Hsp70 TauH-Hsp70 TauH-Hsp70 TauH-Hsc70, Hsp90 TauH-Hsc70, CHIP, TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP, Bag2 TauH-Usc70-CHIP, Bag2 TauH-	TauH-MT TauH-Hsp70 TauH-Hsp90 TauH-Hsp90 Hsp90 Hsp90, Tau0 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 ADP, 26S ATP ADP Nucleus3 TauH3RUb (2) Nucleus4 TauH4RUb (2) Agg33 AugustauH3RUB Ap Ap Ap TauH3RUB, Ap	k(68)   k(69)   k(70)   k(70)   k(70)   k(71)   k(72)   k(73)   k(74)   k(75)   k(76)   k(77) = k(8)   k(79)   k(81)   k(81)   k(82)   k(84)   k(85)   k(86)   k(87)   k(88)   k(87)   k(88)   k(89)   k(90)   k(91)   k(90)   k(91)   k(90)   k(91)   k(90)   k(91)   k(90)   k(91)   k(90)   k(91)   k(91)	uM'-s-1  uM  uM  uM'-s-1  s-1  uM'-s-1  s-1  uM'-s-1
R Tau loading by Hsp70  R Tau Refolding  egradation of 4R tau by chaperones	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70  Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Restoration of Tau1 to Tau0 via Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of via via training to the degradation of ATP  Use of ATP by other processes  Nucleation of Tau3  Dissociation of Tau3 Nucleus  Nucleation of Tau4 Nucleus  Formation of Tau4 Nucleus  Formation of Tau4 Nucleus  Formation of Tau4 Nucleus  Formation of Tau3 Js from Tau3 aggregate of length 3  Formation of Tau3, 1> 3 from Tau3 aggregate of length 3  Formation of Tau4, length 3  Dissociation formation of Tau4, length 3  Formation of Tau4, length 3	r(57) = r(58) = r(59) = r(60) = r(63) = r(63) = r(63) = r(63) = r(63) = r(64) = r(65) = r(66) = r(66) = r(70) = r(71) = r(73) = r(73) = r(74) = r(75) = r(76) = r(77) = r(78) = r(77) = r(78) = r(78) = r(79) = r(78) = r(88)	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(75)*x(34); k(76)*x(34)*x(12); k(77)*x(35)/(k(9)+x(35)); k(78)*x(36); k(78)*x(36); k(78)*x(37); k(80)*x(37); k(81)*x(37)*x(13); k(82)*x(38); k(83)*x(37)*x(22)*x(23); k(84)*x(24); k(85)*x(23); k(85)*x(23); k(86)*x(20)·2; k(86)*x(20)·2; k(86)*x(20)·2; k(86)*x(20)·2; k(88)*x(39)*x(20)*x(40); k(88)*x(39)*x(20)*x(40); k(88)*x(39)*x(20)*x(40); k(88)*x(39)*x(20)*x(40); k(88)*x(39)*x(20)*x(40); k(89)*x(20)*x(40); k(90)*x(20)*x(40); k(90)*x(20)*x(41); k(90)*x(20)*x(41);	TauN*-MT, ATP TauH-Hsp70 TauH-Hsp70 TauH-Hsc90 TauH-Hsc90 TauH-Hsc90 TauH-Hsc70, CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 TauH-Hsc	TauH-MT TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70, CHIP, Bag2 TauH-Hsc70, CHIP, Bag2 ADP, 26S ATP ADP Nucleus TauH-HscW, CHIP-Bag2 TauH-HscW, CHIP, Bag2 ADP, 26S ATP ADP Nucleus TauH-HscW, CHIP, Bag2 ADP, 26S ATP ADP Nucleus TauH-HscW, CHIP, Bag2 ADP Nucleus TauH-HscW, CHIP, Bag2 ADP TauH-HscW, CHIP, Bag2 ADP TauH-HscW, CHIP, Bag2 ADP TauH-HscW, CHIP ADP ADP TauH-HscW, ABP ADP TauH-HscW, ABP ABP TauH-HscW, ABP Agg43	k(68) k(70) k(70) k(71) k(72) k(73) k(74) k(75) k(76) k(77) = k(8) k(79) k(80) k(81) k(81) k(82) k(83) k(84) k(85) k(86) k(87) k(88) k(89) k(90) k(90) k(90)	uM'-s-1 uM yM'-s-1 s'- uM'-s-1 s'- uM'-s-1 s'- uM'-s-1 s'- uM'-s-1 s'- uM'-s-1 s'- uM'-s-1 uM'-s-1 s'- uM'-s-1 uM'-s-1 s'- uM'-s-1 uM'-s-1 uM'-s-1 uM'-s-1
R Tau loading by Hsp70  R Tau Refolding  egradation of 4R tau by chaperones  IP generation and use by other processes	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70 Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Tau0 via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of ubiquitinated tau  Generation of ATP  Use of ATP by other processes  Nucleation of Tau3  Dissociation of Tau4  Dissociation of Tau4 Nucleus  Nucleation of Tau4  Dissociation of Tau3, length 3  Dissociation of Tau3, aggregate of length 3  Formation of aggregates 1-3  Dissociation of aggregates 1-3  Dissociation of aggregates 1-3  Dissociation of aggregates 1-3	r(57) = r(58) = r(58) = r(59) = r(60) = r(61) = r(62) = r(63) = r(64) = r(65) = r(67) = r(70) = r(71) = r(73) = r(74) = r(75) = r(75) = r(76) = r(77) = r(77) = r(78) = r(78) = r(80)	k(70)*x(29)*x(23)(k(71)+x(29)); k(72)*x(30)(k(73)+x(30)); k(74)*x(27)*x(11); k(73)*x(34); k(76)*x(34); k(76)*x(34); k(76)*x(34); k(78)*x(35)(k(9)+x(35)); k(78)*x(36); k(79)*x(34)*x(14); k(80)*x(37); k(81)*x(37)*x(13); k(81)*x(37)*x(13); k(82)*x(38); k(82)*x(38); k(83)*x(29)*x(23); k(84)*x(24); k(83)*x(39)*x(22)*x(23); k(84)*x(24); k(83)*x(39)*x(22)*x(23); k(84)*x(24); k(83)*x(39)*x(22)*x(23); k(84)*x(24); k(83)*x(39); k(86)*x(20)*x(21); k(89)*x(40); k(89)*x(40); k(89)*x(40); k(90)*x(40); k(90)*x(20)*x(40); k(90)*x(20)*x(40); k(90)*x(20)*x(40); k(90)*x(20)*x(42); k(90)*x(20)*x(42); k(90)*x(20)*x(43); k(90)*x(20)*x(43); k(90)*x(20)*x(43); k(90)*x(20)*x(43);	TauN*-MT, ATP TauH-Hsp70 TauH-Hsp70 TauH-Hsp70 TauH-Hsc70, Hsp90 TauH-Hsc70, CHIP, TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP, Bag2 TauH-Hsc70-CHIP, Bag2 TauH-Usc70-CHIP, Bag2 TauH-	TauH-MT TauH-Hsp70 TauH-Hsp90 TauH-Hsp90 Hsp90 Hsp90, Tau0 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP, Bag2 ADP, 26S ATP ADP Nucleus3 TauH3RUb (2) Nucleus4 TauH4RUb (2) Agg33 AugustauH3RUB Ap Ap Ap TauH3RUB, Ap	k(68)   k(69)   k(70)   k(70)   k(70)   k(71)   k(72)   k(73)   k(74)   k(75)   k(76)   k(77) = k(8)   k(79)   k(81)   k(81)   k(82)   k(84)   k(85)   k(86)   k(87)   k(88)   k(87)   k(88)   k(89)   k(90)   k(91)   k(90)   k(91)   k(90)   k(91)   k(90)   k(91)   k(90)   k(91)   k(90)   k(91)   k(91)	LM 1-s 1
Tau loading by Hsp70  Tau Refolding  gradation of 4R tau by chaperones	Phosphorylation of MT-bound normally phosphorylated tau  Dephosphorylation of MT-bound abnormal/misfolded tau  Association of misfolded tau with Hsp70 Hsp70 release  Exchange of Hsp70 for Hsp90  Restoration of TauH to Taud via Hsp90  Release of Tau0 from Hsp90  Exchange of Hsc70 for CHIP  Ubiquitination of tau  Binding of Bag-2 to the degradation complex  Rescue from degradation by Bag2  Degradation of ubiquitinated tau  Generation of ATP  Use of ATP by other processes  Nucleation of Tau3  Dissociation of Tau3 Nucleus  Nucleation of Tau4  Dissociation of Tau4  Dissociation  Formation of Tau3, length 3  Dissociation  Formation of Tau3, 1> 3 from Tau3 aggregate of length 3  Formation of Tau4, length 3  Dissociation of Dissocia	r(57) = r(58) = r(59) = r(59) = r(60) = r(63) = r(63) = r(64) = r(65) = r(67) = r(67) = r(67) = r(70) = r(71) = r(72) = r(73) = r(74) = r(77) = r(78) = r(81) = r(81) = r(82)	k(70)*x(29)*x(23)/(k(71)+x(29)); k(72)*x(30)/(k(73)+x(30)); k(74)*x(27)*x(11); k(75)*x(34); k(76)*x(34)*x(12); k(76)*x(34)*x(12); k(78)*x(35)/(k(9)+x(35)); k(78)*x(36); k(79)*x(34)*x(14); k(80)*x(37); k(81)*x(37)*x(13); k(81)*x(37)*x(13); k(83)*x(23); k(84)*x(24); k(83)*x(23); k(84)*x(24); k(83)*x(23); k(84)*x(24); k(85)*x(23); k(86)*x(20).72; k(87)*x(40); k(88)*x(39)*x(22)*x(23); k(88)*x(20).72; k(87)*x(40); k(89)*x(20).72; k(89)*x(20).74(2); k(90)*x(20)*x(40); k(90)*x(40); k(9	TauN*-MT, ATP  TauH-MT  TauH-Hsp70  TauH-Hsc70, Hsp90  TauH-Hsc70, CHIP, TauH-Hsc70-CHIP, Bag2  TauH-Hsc70-CHIP, B	TauH-MT TauN+-MT TauN+-MF TauH-Hsp70 TauH-Hsp90, Hsc70 TauH-Hsp90, Hsc70 TauH-Hsc70-CHIP TauH-Hsc70-CHIP TauH-Hsc70-CHIP-Bag2 TauH-Hsc70-CHIP-Bag2 ADP, 268 ATP ADP Nucleus3 TauH3RUB (2) Nucleus4 TauH4RUb (2) Agg33 Nucleus3, TauH3RUB Ap Ap TauH3RUB, Ap Ap TauH3RUB, Ap Agg43 Nucleus4, TauH4RUB	k(68)   k(70)   k(71)   k(72)   k(73)   k(74)   k(75)   k(76)   k(77) = k(8)   k(79)   k(80)   k(81)   k(81)   k(83)   k(84)   k(85)   k(86)   k(87)   k(88)   k(89)   k(91)   k(90)   k(91)   k(90)   k(91)   k(90)   k(91)   k(92)   k(93)   k(93)   k(93)   k(93)   k(93)   k(93)   k(94)   k(94)	uM <sup>1</sup> -s <sup>-1</sup> uM y <sup>1</sup> -s <sup>-1</sup> y <sup>1</sup> y <sup>1</sup> -s <sup>-1</sup> s <sup>-1</sup> y <sup>1</sup> -s <sup>-1</sup> s <sup>-1</sup> y <sup>1</sup> -s <sup>-1</sup> y <sup>1</sup> y <sup>1</sup> -s <sup>1</sup> y <sup>2</sup> -s <sup>2</sup> y <sup>2</sup> -s <sup></sup>