Table 9: *H. sapiens* Recon 1 network gaps. Final list of network gaps in Recon 1. Gaps are defined as metabolites that can only be produced or consumed and are compartment-specific. Note that the gap may arise from more than one reaction; only one has been shown here for demonstrative purposes. Each gap was carefully reviewed and classified as either model-scope (i.e., reactions which produce/consume the metabolite are part of pathways which are beyond the scope of this reaction) or knowledge-base (i.e., gap cannot be resolved due to lack of knowledge of how a particular metabolite is produced or consumed).

Reviewer initials
ND: Natalie C. Duarte SAB: Scott A. Becker
NJ: Neema Jamshidi MM: Monica L. Mo
IT: Ines Thiele

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
2mcit	2-Methylcitrate	Produced only	Cytosol	2MCITt	added transport rxn 2MCITt; methycitrate is excreted in urine of patients who suffer from propionic acidaemia (Weidman et al. 1979)	MM
42A3HP24DB	4-(2-Amino-3-hydroxyphenyl)-2,4-dioxobutanoate	Produced only	Cytosol	3HKYNAKGAT	knowledge-base gap	SAB
3hpcoa	3-Hydroxypropionyl-CoA	Consumed only	Cytosol	3HPCOAHYD	model-scope gap	SAB
msa	Malonate semialdehyde	Produced only	Cytosol	3HPPD	knowledge-based gap: this rxn has been described and studied in mammalians, but not in humans; gap could be filled since msa is metabolized in mitochondria, but there is no evidence for msa mitochondrial transport activity	MM
48dhoxquin	4,8-Dihydroxyquinoline	Produced only	Cytosol	3HXKYNOXDA	model-scope gap	SAB
5hoxnfkyn	5-Hydroxy-N-formylkynurenine	Produced only	Cytosol	5HTRPDOX	knowledge-base gap: not enough evidence to include reaction before this in line	SAB
5hxkyn	5-Hydroxykynurenine	Consumed only	Cytosol	5HXKYNDCL	knowledge-base gap: not enough evidence to include reaction before this in line	SAB
46dhoxquin	4,6-Dihydroxyquinoline	Produced only	Cytosol	5HXKYNOXDA	model-scope gap	SAB
thcrm_hs	trihexosyl ceramide (homo sapiens)	Produced only	Cytosol	A4GALTc	pathway complete in Golgi - knowledge gap about extent of cytosolic metabolism of thcrm_hs	NJ
4abut	4-Aminobutanoate	Consumed only	Lysosome	ABUTt2rL	knowledge-base gap	SAB
ppa	Propionate (n-C3:0)	Consumed only	Cytosol	ACCOAL	gap removed; added rxn for extracellular -> cytosolic transport based on ref in thuy's mito model	ND
acgbgbside_hs	beta GalNAc globoside (homo sapiens)	Produced only	Lysosome	ACGBGBSIDEtl	gap removed by single reaction addition: NAGAIby added in analogy to NAGAIy (no real evidence that this occurs in vivo)	NJ
acACP	Acetyl-ACP	Produced only	Cytosol	ACOATA	FA synthesis is lumped, so activation w/ ACP will not be utilized at this point, this may be useful in a future version of the reconstruction if FAS is 'unlumped'	NJ
acorn	N2-Acetyl-L-ornithine	Consumed only	Cytosol	ACODA	knowledge-base gap	SAB
ppa	Propionate (n-C3:0)	Consumed only	Cytosol	ACS2	gap removed; added rxn for extracellular -> cytosolic transport based on ref in thuy's mito model	ND
5moxact	5-Methoxyindoleacetate	Produced only	Cytosol	ACSOMT	model-scope gap: end of the line in KEGG	SAB
ade	Adenine	Consumed only	Lysosome	ADEtl	leave gap; knowledge gap: at least i have no idea of the function of adenine in lysosome but uptake was studied by PMID: 2925670	IT
adpglc	ADPglucose	Consumed only	Cytosol	ADPGLC	leave gap: ADPglucose is an important precursor bacterial glycogen and plant starch synthesis, whereas ADP-mannose has no known physiological function, although the commercially available synthetic compound can replace ADP-heptoses in bacterial outer-membrane lipopolysaccharide synthesis in vitro . ADP-ribose might therefore also be the most important substrate for human in vivo (from discussion of Gasmi et al, 1999)	IT
adpman	ADPmannose	Consumed only	Cytosol	ADPMAN	leave gap: ADPglucose is an important precursor bacterial glycogen and plant starch synthesis, whereas ADP-mannose has no known physiological function, although the commercially available synthetic compound can replace ADP-heptoses in bacterial outer-membrane lipopolysaccharide synthesis in vitro . ADP-ribose might therefore also be the most important substrate for human in vivo (from discussion of Gasmi et al, 1999)	IT
3padsel	3'-Phosphoadenylylselenate	Produced only	Cytosol	ADSELK	knowledge-base gap	SAB
dak2gpe_hs	1-alkenyl 2-acylglycerol 3-phosphoethanolamine plasmalogen (homo sapiens)	Produced only	Cytosol	AGLPED	knowledge gap and model scope limitations - rxns included up to extent of biochem texts (Voet and Voet/Murray's Biochem), further details may be gleanable from lit, will require more time investment	NJ
ahcys	S-Adenosyl-L-homocysteine	Produced only	Endoplasmic Reticulum	AHCYStr	gap filled, added AHCYStr	NJ
ala-L	L-Alanine	Consumed only	Lysosome	ALAt2rL	model-scope gap	SAB
ind3ac	Indole-3-acetate	Produced only	Cytosol	ALDD20x	model-scope gap	SAB
dha	Dihydroxyacetone	Produced only	Cytosol	ALKP	model scope limitations in addition to knowledge gaps: PMID 9370313, 9370314	NJ
12HPET	12-Hydroperoxyeicosa-5,8,10,14-tetraenoate	Produced only	Cytosol	ALOX12	12HPETte, unknown mechanism, needs to get into EC space, inflamm mediator, knowledge gap area (subsequent metabolism, etc)	NJ
12RHPET	12R-Hydroperoxyeicosatetraenoate	Produced only	Cytosol	ALOX12R	12RHPETte, unknown mechanism, needs to get into EC space, inflamm mediator, knowledge gap area (subsequent metabolism, etc)	NJ
15HPET	15-Hydroperoxyeicosatetraenoic acid	Produced only	Cytosol	ALOX15	15HPETte, unknown mechanism, needs to get into EC space, inflamm mediator, knowledge gap area (subsequent metabolism, etc)	NJ
amet	S-Adenosyl-L-methionine	Consumed only	Endoplasmic Reticulum	AMETr	gap filled, added AMETr	NJ
andrstrnglc	androsterone glucuronide	Consumed only	Cytosol	ANDRSTRNGLCte	ANDRSTRNGLCtr, ANDRSTRNGLCte	NJ
ap4a	P1,P4-Bis(5'-adenosyl) tetraphosphate	Consumed only	Cytosol	AP4AH1	leave gap; for explanation read not of reaction	IT

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
m2mn	(alpha-D-mannosyl)2-beta-D-mannosyl-N-acetylglucosamine	Consumed only	Cytosol	A_MANASE	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
mn	beta-1,4-mannose-N-acetylglucosamine	Produced only	Cytosol	A_MANASE	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
bdg2hc	cis-beta-D-Glucosyl-2-hydroxycinnamate	Consumed only	Cytosol	BDG2HCGHD	model-scope gap: unimportant	SAB
2coum	cis-2-Hydroxy cinnamate	Produced only	Cytosol	BDG2HCGHD	model-scope gap: unimportant	SAB
betald	Betaine aldehyde	Consumed only	Cytosol	BETALDHx	knowledge-based gap	MM
bhb	(R)-3-Hydroxybutanoate	Consumed only	Cytosol	BHBt	gap removed; added extracellular transport rxn	ND
bhb	(R)-3-Hydroxybutanoate	Consumed only	Cytosol	BHBtm	gap removed; added extracellular transport rxn	ND
bz	Benzoate	Consumed only	Cytosol	BZt	gap filled, added BZt	NJ
bz	Benzoate	Consumed only	Cytosol	BZtr	gap filled, added BZt	NJ
cbl2	Cob(II)alamin	Produced only	Mitochondria	CBL2tm	leave for the moment --> unfinished PW	IT
prostg1	(13E)-11alpha-Hydroxy-9,15-dioxoprost-13-enoate	Consumed only	Cytosol	CBR1	principally a knowledge gap problem - further metabolism, etc unknown, since at the 'fringes' partial model scope gap also - see Goodman and Gilman, Murray Biochem for overall pathway	NJ
cca_d3	Calcitroic acid (D3)	Consumed only	Mitochondria	CCA_D3tm	knowledge gap; reactions as well as enzymes for vit D degradation are unknown	IT
chsterol	Cholesterol	Consumed only	Golgi Apparatus	CHSTEROLtg	By IT shows transport between golgi and plasma membrane	NJ
chtn	chitin	Consumed only	Cytosol	CHTNASE	leave gap; function has only been characterized in vitro, no physiologically known function	ND
clpn_hs	cardiolipin (homo sapiens)	Produced only	Cytosol	CLS_hs	cardiolipin is a biomass constituent, should be made part of biomass, in future can also update metabolic interconversions	NJ
co2	CO2	Consumed only	Nucleus	CO2tn	gap is due to transporter rxn in nucleus (not needed now, but ok to leave in)	ND
ntm2amep	N-Trimethyl-2-aminoethylphosphonate	Consumed only	Cytosol	CPCTDTX	knowledge gap - strong evidence for the presence of these metabolites in humans lacking, although the enzyme can carry out this conversion (in addition to others more relevant to human metabolism	NJ
cmpntm2amep	CMP-N-trimethyl-2-aminoethylphosphonate	Produced only	Cytosol	CPCTDTX	knowledge gap - strong evidence for the presence of these metabolites in humans lacking, although the enzyme can carry out this conversion (in addition to others more relevant to human metabolism	NJ
crtn	Creatinine	Produced only	Cytosol	CRTNsyn	model-scope gap: a transporter could be added to get this out of the cell, but relatively unimportant	SAB
crtstrn	Corticosterone	Produced only	Endoplasmic Reticulum	CRTSTRNtr	CRTSTRNtr, CRTSTRNtm	NJ
thcys	Thiocysteine	Produced only	Cytosol	CYSLYSL	knowledge-based gap	MM
ala-D	D-Alanine	Consumed only	Lysosome	DALAt2rL	knowledge-base gap: how does alanine get into the lysosome--good evidence for inclusion regardless of gap	SAB
dmpp	Dimethylallyl diphosphate	Consumed only	Cytosol	DMATT	DMATTx version is complete - w/out gaps - was in original copy of gaps list	NJ
ipdp	Isopentenyl diphosphate	Consumed only	Cytosol	DMATT	GRTTx version is complete - w/out gaps - was not in this list but was in original list as gap	NJ
dmhptcoa	2,6 dimethylheptanoyl-CoA	Consumed only	Cytosol	DMHPTCRNCPT1	DMHPTCRNCPT1 added (although the metabolism of this metabolite has not been well characterized, it should be transportable on the sam carnitine shuttle as other FA)	NJ
lyxnt	L-lyxonate	Produced only	Cytosol	DOGULND1	known gap; could not find any specific info as to how this is metabolized in humans	ND
xylnt	L-Xylonate	Produced only	Cytosol	DOGULND2	known gap; could not find any specific info as to how this is metabolized in humans	ND
thrnt	L-Threonate	Produced only	Cytosol	DOGULNO1	known gap; could not find any specific info as to how this is metabolized in humans	ND
eryth	L-Erythrulose	Produced only	Cytosol	DOGULNO2	known gap; could not find any specific info as to how this is metabolized in humans	ND
e4hglu	L-erythro-4-Hydroxyglutamate	Consumed only	Cytosol	EHGLAT	knowledge-base gap: cytosolic enzyme found for a reaction that is not a gap in the mitochondria	SAB
4h2oglt	4-Hydroxy-2-oxoglutarate	Produced only	Cytosol	EHGLAT	gap OK--cytosolic localized enzyme found for reaction	SAB
s2l2n2m2m	de-Fuc form of PA6 (w/o peptide linkage)	Consumed only	Cytosol	ENGASE	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
n2m2nm	n2m2nmasn (w/o peptide linkage)	Consumed only	Cytosol	ENGASE2	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
n2m2nmn	reducing GlcNAc removed form of n2m2nmasn (w/o peptide)	Produced only	Cytosol	ENGASE2	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
2ameph	(2-Aminoethyl)phosphonate	Consumed only	Cytosol	EPCTX	knowledge gap - strong evidence for the presence of these metabolites in humans lacking, although the enzyme can carry out this conversion (in addition to others more relevant to human metabolism	NJ
cmp2amep	CMP-2-aminoethylphosphonate	Produced only	Cytosol	EPCTX	knowledge gap - strong evidence for the presence of these metabolites in humans lacking, although the enzyme can carry out this conversion (in addition to others more relevant to human metabolism	NJ

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
m2mn	(alpha-D-mannosyl)2-beta-D-mannosyl-N-acetylglucosamine	Consumed only	Cytosol	A_MANASE	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
mn	beta-1,4-mannose-N-acetylglucosamine	Produced only	Cytosol	A_MANASE	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
bdg2hc	cis-beta-D-Glucosyl-2-hydroxycinnamate	Consumed only	Cytosol	BDG2HCGHD	model-scope gap: unimportant	SAB
2coum	cis-2-Hydroxy cinnamate	Produced only	Cytosol	BDG2HCGHD	model-scope gap: unimportant	SAB
betald	Betaine aldehyde	Consumed only	Cytosol	BETALDHx	knowledge-based gap	MM
bhb	(R)-3-Hydroxybutanoate	Consumed only	Cytosol	BHBt	gap removed; added extracellular transport rxn	ND
bhb	(R)-3-Hydroxybutanoate	Consumed only	Cytosol	BHBtm	gap removed; added extracellular transport rxn	ND
bz	Benzoate	Consumed only	Cytosol	BZt	gap filled, added BZt	NJ
bz	Benzoate	Consumed only	Cytosol	BZtr	gap filled, added BZt	NJ
cbl2	Cob(II)alamin	Produced only	Mitochondria	CBL2tm	leave for the moment --> unfinished PW	IT
prostg1	(13E)-11alpha-Hydroxy-9,15-dioxoprost-13-enoate	Consumed only	Cytosol	CBR1	principally a knowledge gap problem - further metabolism, etc unknown, since at the 'fringes' partial model scope gap also - see Goodman and Gilman, Murray Biochem for overall pathway	NJ
cca_d3	Calcitroic acid (D3)	Consumed only	Mitochondria	CCA_D3tm	knowledge gap; reactions as well as enzymes for vit D degradation are unknown	IT
chsterol	Cholesterol	Consumed only	Golgi Apparatus	CHSTEROLtg	By IT shows transport between golgi and plasma membrane	NJ
chtn	chitin	Consumed only	Cytosol	CHTNASE	leave gap; function has only been characterized in vitro, no physiologically known function	ND
clpn_hs	cardiolipin (homo sapiens)	Produced only	Cytosol	CLS_hs	cardiolipin is a biomass constituent, should be made part of biomass, in future can also update metabolic interconversions	NJ
co2	CO2	Consumed only	Nucleus	CO2tn	gap is due to transporter rxn in nucleus (not needed now, but ok to leave in)	ND
ntm2amep	N-Trimethyl-2-aminoethylphosphonate	Consumed only	Cytosol	CPCTDTX	knowledge gap - strong evidence for the presence of these metabolites in humans lacking, although the enzyme can carry out this conversion (in addition to others more relevant to human metabolism	NJ
cmpntm2amep	CMP-N-trimethyl-2-aminoethylphosphonate	Produced only	Cytosol	CPCTDTX	knowledge gap - strong evidence for the presence of these metabolites in humans lacking, although the enzyme can carry out this conversion (in addition to others more relevant to human metabolism	NJ
crtn	Creatinine	Produced only	Cytosol	CRTNsyn	model-scope gap: a transporter could be added to get this out of the cell, but relatively unimportant	SAB
crtstrn	Corticosterone	Produced only	Endoplasmic Reticulum	CRTSTRNtr	CRTSTRNtr, CRTSTRNtm	NJ
thcys	Thiocysteine	Produced only	Cytosol	CYSLYSL	knowledge-based gap	MM
ala-D	D-Alanine	Consumed only	Lysosome	DALAt2rL	knowledge-base gap: how does alanine get into the lysosome--good evidence for inclusion regardless of gap	SAB
dmpp	Dimethylallyl diphosphate	Consumed only	Cytosol	DMATT	DMATTx version is complete - w/out gaps - was in original copy of gaps list	NJ
ipdp	Isopentenyl diphosphate	Consumed only	Cytosol	DMATT	GRTTx version is complete - w/out gaps - was not in this list but was in original list as gap	NJ
dmhptcoa	2,6 dimethylheptanoyl-CoA	Consumed only	Cytosol	DMHPTCRNCPT1	DMHPTCRNCPT1 added (although the metabolism of this metabolite has not been well characterized, it should be transportable on the sam carnitine shuttle as other FA)	NJ
lyxnt	L-lyxonate	Produced only	Cytosol	DOGULND1	known gap; could not find any specific info as to how this is metabolized in humans	ND
xylnt	L-Xylonate	Produced only	Cytosol	DOGULND2	known gap; could not find any specific info as to how this is metabolized in humans	ND
thrnt	L-Threonate	Produced only	Cytosol	DOGULNO1	known gap; could not find any specific info as to how this is metabolized in humans	ND
eryth	L-Erythrulose	Produced only	Cytosol	DOGULNO2	known gap; could not find any specific info as to how this is metabolized in humans	ND
e4hglu	L-erythro-4-Hydroxyglutamate	Consumed only	Cytosol	EHGLAT	knowledge-base gap: cytosolic enzyme found for a reaction that is not a gap in the mitochondria	SAB
4h2oglt	4-Hydroxy-2-oxoglutarate	Produced only	Cytosol	EHGLAT	gap OK--cytosolic localized enzyme found for reaction	SAB
s2l2n2m2m	de-Fuc form of PA6 (w/o peptide linkage)	Consumed only	Cytosol	ENGASE	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
n2m2nm	n2m2nmasn (w/o peptide linkage)	Consumed only	Cytosol	ENGASE2	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
n2m2nmn	reducing GlcNAc removed form of n2m2nmasn (w/o peptide)	Produced only	Cytosol	ENGASE2	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
2ameph	(2-Aminoethyl)phosphonate	Consumed only	Cytosol	EPCTX	knowledge gap - strong evidence for the presence of these metabolites in humans lacking, although the enzyme can carry out this conversion (in addition to others more relevant to human metabolism	NJ
cmp2amep	CMP-2-aminoethylphosphonate	Produced only	Cytosol	EPCTX	knowledge gap - strong evidence for the presence of these metabolites in humans lacking, although the enzyme can carry out this conversion (in addition to others more relevant to human metabolism	NJ

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
lcts	Lactose	Consumed only	Cytosol	LCTStl	gap removed; have decided to remove this reaction since it probably doesn't exist in the cytosol -- I don't want to associate it with the lysosomal complex until it has been experimentally verified	ND
nformanth	N-Formylanthranilate	Produced only	Cytosol	LFORKYNHYD	reaction based on KEGG--probably OK	SAB
lipoate	Lipoate	Produced only	Cytosol	LIPOti	leave gap for the moment; lipoate gets imported in cell, converted to dihydrolipoate and this compounds is the active form and gets directly exported again - unknown mechanism. Concrete reaction from lipoate to dihydrolipoate is not really clear to me	IT
lanost	Lanosterol	Consumed only	Cytosol	LNS14DM	was stated to occur in cyt and ER -> ER has the completed pathway	NJ
44mctr	4,4-dimethylcholesta-8,14,24-trienol	Produced only	Cytosol	LNS14DM	was stated to occur in cyt and ER -> ER has the completed pathway	NJ
lum3	Lumisterol 3	Produced only	Cytosol	LS3	is not really a gap; conversion takes place when sufficient Vit D has been produced in skin cell - this mechanism avoids toxicity by Vit D - I included this reaction for completeness	IT
2mcit	2-Methylcitrate	Produced only	Cytosol	MCITS	added transport rxn 2MCITt; methycitrate is excreted in urine of patients who suffer from propionic acidaemia (Weidman et al. 1979)	MM
malACP	Malonyl-[acyl-carrier protein]	Produced only	Cytosol	MCOATA	FA synthesis is lumped, so activation w/ ACP will not be utilized at this point, this may be useful in a future version of the reconstruction if FAS is 'unlumped'	NJ
fna5moxam	Formyl-N-acetyl-5-methoxykynurenamine	Produced only	Cytosol	MELATN23DOX	citation describes reaction but unknown where product goes	SAB
6hoxmelatn	6-Hydroxymelatonin	Produced only	Cytosol	MELATNOX	model-scope gap: end of the line in KEGG	SAB
meoh	Methanol	Consumed only	Lysosome	MEOHtly	gap removed; added transporter for lysosome transport	ND
mi3456p	1D-myo-Inositol 3,4,5,6-tetrakisphosphate	Consumed only	Cytosol	MI3456PK	cannot remove gap; this molecule is currently a dead end	ND
2mcacn	cis-2-Methylaconitate	Consumed only	Cytosol	MICITDr	leave as gap; rxn is low confidence (physiological data from rat), model scope gap for now	ND
micit	methylisocitrate	Produced only	Cytosol	MICITDr	rxn has been removed (since it is incorrect) unfortunately it has been replaced with another (MICITDr) which does NOT remove the gap; this is a knowledge-base gap, not sure if methyl-cis-aconitate or methylisocitrate are physiologically relevant cpds, but	ND
malttr	Maltotriose	Consumed only	Cytosol	MLTG1	leave gap; protein has been functionally verified but could not find any information on its localization	ND
mmcoa-S	(S)-Methylmalonyl-CoA	Consumed only	Cytosol	MMCD	knowledge-based gap	MM
4aabutn	4-Acetamidobutanoate	Produced only	Cytosol	NABTNO	knowledge-base gap: not entirely clear how these metabolites are metabolized	SAB
adprbp	ADPribose 2'-phosphate	Produced only	Cytosol	NADPN	leave gap; exceeds model	IT
na1	Sodium	Produced only	Golgi Apparatus	NAt3_1g	gap is due to transport reaction in Golgi (not needed now, but ok to leave in)	ND
carn	L-Carnosine	Consumed only	Cytosol	NBAHH_ir	model-scope gap: carnosine metabolism not in current model	SAB
nmptrc	N-Methylputrescine	Consumed only	Cytosol	NMPTRCOX	modeling-gap: these compounds are found in mam. cells according to reference, but not in our model	SAB
1mpyr	1-Methylpyrrolinium	Produced only	Cytosol	NMPTRCOX	modeling-gap: these compounds are found in mam. cells according to reference, but not in our model	SAB
no	Nitric oxide	Produced only	Cytosol	NOt	added diffusive transporter	SAB
xtp	XTP	Consumed only	Cytosol	NTPP11	leave gap; knowledge gap	IT
o2s	Superoxide anion	Consumed only	Cytosol	O2St	gap removed; added rxn for diffusion of o2s	ND
o2s	Superoxide anion	Consumed only	Cytosol	O2Stm	gap removed; added rxn for diffusion of o2s	ND
o2s	Superoxide anion	Consumed only	Cytosol	O2Stn	gap removed; added rxn for diffusion of o2s	ND
o2s	Superoxide anion	Consumed only	Nucleus	O2Stn	gap removed; added rxn for diffusion of o2s	ND
o2s	Superoxide anion	Consumed only	Cytosol	O2Stx	gap removed; added rxn for diffusion of o2s	ND
o2s	Superoxide anion	Consumed only	Peroxisome	O2Stx	gap removed; added rxn for diffusion of o2s	ND
hnifedipine	hydroxy nifedipine	Produced only	Cytosol	P4503A4	HNIFEDIPINEte	NJ
pcollglys	Procollagen L-lysine	Consumed only	Cytosol	PCLYSOX	model-scope gap	MM
pcollg5hlys	Procollagen 5-hydroxy-L-lysine	Produced only	Cytosol	PCLYSOX	model-scope gap	MM
pcrn	propionyl-carnitine	Produced only	Mitochondria	PCRNtm	CSNAT3m removed and replaced with CSNAT2m, CSNAT3x made reversible	NJ
pe_hs	phosphatidylethanolamine (homo sapiens)	Produced only	Golgi Apparatus	PE_HStg	pe_hs not used in any Golgi rxns right now	NJ
2pglyc	2-Phosphoglycolate	Consumed only	Cytosol	PGLYCP	appears to be a knowledge base gap (INCOMPLETE!!)	ND
phyQ	Phylloquinone	Produced only	Cytosol	PHYQt	leave gap; knowledge gap	IT
ppa	Propionate (n-C3:0)	Consumed only	Cytosol	PPAt	gap removed; added rxn for extracellular -> cytosolic transport based on ref in thuy's mito model	ND
ppa	Propionate (n-C3:0)	Consumed only	Cytosol	PPAtm	gap removed; added rxn for extracellular -> cytosolic transport based on ref in thuy's mito model	ND
2hyoxplac	2-Hydroxyphenylacetate	Produced only	Cytosol	PPOR	reaction based on KEGG	SAB
pro-D	D-Proline	Consumed only	Lysosome	PRODt2rL	knowledge-base gap: good evidence for inclusion regardless of gap	SAB
pro-L	L-Proline	Consumed only	Lysosome	PROt2rL	knowledge-base gap: good evidence for inclusion regardless of gap	SAB

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
ps_hs	phosphatidylserine (homo sapiens)	Produced only	Endoplasmic Reticulum	PS_HSter	ps_hs not used in any ER reactions currently	NJ
ps_hs	phosphatidylserine (homo sapiens)	Produced only	Golgi Apparatus	PS_HStg	ps_hs not used in any Golgi rxns right now	NJ
pyam5p	Pyridoxamine 5'-phosphate	Produced only	Mitochondria	PYAM5Ptm	leave gap; excedds model	IT
pydx5p	Pyridoxal 5'-phosphate	Produced only	Mitochondria	PYDX5Ptm	leave gap; excedds model	IT
pylald	Perillyl aldehyde	Consumed only	Cytosol	PYLALDOX	knowledge-base gap: unknown where this metabolite goes in humans; low priority subsystem also	SAB
peracd	Perillic acid	Produced only	Cytosol	PYLALDOX	knowledge-base gap: unknown where this metabolite goes in humans; low priority subsystem also	SAB
retn	Retinoate	Produced only	Nucleus	RAtn	leave gap; excedds model	IT
rbl-D	D-Ribulose	Consumed only	Cytosol	RBK_D	gap removed; physiologial evidence that D-ribulose can be taken up by cultured human fibroblasts	ND
rbt	Ribitol	Consumed only	Cytosol	RBTt	gap is due to extracellular transport reaction (not needed now, but ok to leave in)	ND
retncoa	retinoyl CoA	Produced only	Cytosol	RETNCOA	Retinoyl-CoA is used in cell to retinoylate proteins --> I created demand function	IT
dmnoncoa	4,8 dimethylnonanoyl-CoA	Consumed only	Cytosol	SCP22x	Will leave gap at present time, sterol carrier protein can move fatty acid derivatives (usually steroid precursors) into different compartments, details about specific substrates and mechanisms not known	NJ
dtt	Dithiothreitol	Consumed only	Cytosol	SELCYSLY	modeling gap: selenoamino acid metabolism is a low priority	SAB
dttOX	Oxidized dithiothreitol	Produced only	Cytosol	SELCYSLY	modeling gap: selenoamino acid metabolism is a low priority	SAB
selmeth	Selenomethionine	Consumed only	Cytosol	SELMETAT	knowledge-base gap: unknown where selmeth comes from in humans; modeling evidence only, need a source of selenomethionine	SAB
selnp	Selenophosphate	Produced only	Cytosol	SELNPS	model-scope gap: although there is not a great deal of information about selenoamino acid metabolism, this area is not particularly important to the initial model	SAB
l2n2m2mn	de-Fuc, reducing GlcNAc removed, de-Sia form of PA6 (w/o peptide linkage)	Produced only	Cytosol	SIAASE	leave reaction even though it causes gap; it's a redundant reaction since the primary rxn is in lysosome, but there's evidence it might be in cytosol	ND
spc_hs	sphingosylphosphorylcholine (homo sapiens)	Produced only	Cytosol	SMPD4	filled with SMPD4 and SPC_HSt - note that each one individually could have resolved the gap, however the evidence for both reactions was approximately the same	NJ
spc_hs	sphingosylphosphorylcholine (homo sapiens)	Produced only	Cytosol	SPC_HSt	filled with SMPD4 and SPC_HSt - note that each one individually could have resolved the gap, however the evidence for both reactions was approximately the same	NJ
spc_hs	sphingosylphosphorylcholine (homo sapiens)	Produced only	Cytosol	SPHMDAc	filled with SMPD4 and SPC_HSt - note that each one individually could have resolved the gap, however the evidence for both reactions was approximately the same	NJ
f5hoxkyn	Formyl-5-hydroxykynurenamine	Produced only	Cytosol	SRTN23OX	model-scope gap	SAB
nmthsrtn	N-Methylserotonin	Produced only	Cytosol	SRTNMTX	knowledge-base gap: KEGG is the only evidence for this reaction	SAB
dtdprmn	dTDP-L-rhamnose	Produced only	Cytosol	TDPDRR	leave gap; according to Devlin, dTDP leads to UDP-GalNAc biosynthesis in mammals, but I can't find any evidence how this might occur	ND
thm	Thiamin	Produced only	Mitochondria	THMt2m	leave gap; knowledge based: It is thought that this SLC19A2 is also reponsible for the mitochondrial transport since cells of TRMA patients (thiamine-responive megaloblastic anemia) in this gene show no mitochondrial transport of thiamine. Role of thiamine in mitochondria is not clear (therefore will be a gap) since there is no mitochondrial thiamine diphosphokinase)	IT
phom	O-Phospho-L-homoserine	Consumed only	Cytosol	THRS	knowledge-based gap	MM
q10	Ubiquinone-10	Consumed only	Cytosol	TRDR2	leave gap knowledge gap: q10h2 Ubiquinol-10 Produced only Cytosol TRDR2 Miscellaneous [c]:h+nadph+q10--->nadp+q10h2 IT leave gap; knowledge gap:	IT
q10	Ubiquinone-10	Consumed only	Cytosol	TRDR3	leave gap knowledge gap: q10h2 Ubiquinol-10 Produced only Cytosol TRDR3 Miscellaneous [c]:h+nadh+q10--->nad+q10h2 IT leave gap; knowledge gap:	IT
tre	Trehalose	Consumed only	Cytosol	TREH	leave gap; rxn only based on sequence annotation	ND
ts3	Tachysterol 3	Produced only	Cytosol	TS3	is not really a gap; conversion takes place when sufficient Vit D has been produced in skin cell - this mechanism avoids toxicity by Vit D - I included this reaction for completeness	IT
txa2	Thromboxane A2	Consumed only	Cytosol	TXA2te	removed gap, replaced TXA2te	NJ
txa2	Thromboxane A2	Consumed only	Cytosol	TXA2tr	removed gap, replaced TXA2te	NJ
udpg	UDPglucose	Produced only	Golgi Apparatus	UDPGLCtg	gap is due to transporter rxn in Golgi (not needed now, but ok to leave in)	ND
udpacgal	UDP-N-acetyl-D-galactosamine	Produced only	Endoplasmic Reticulum	UGALNACter	udpacgal is not used in any ER reactions currently	NJ
whtststerone	w hydroxy testosterone	Consumed only	Cytosol	WHTSTSTERONEte	WHTSTSTERONEte - unkown transporter and metabolism	NJ

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
xol7ah2	3alpha,7alpha-Dihydroxy-5beta-cholestane	Produced only	Endoplasmic Reticulum	XOL7AH2tr	no xol7ah2 reactions in ER right now	NJ
xolest2_hs	cholesterol ester (from FULLR2)	Produced only	Cytosol	XOLEST2te	xolest2_hs produced extracellularly, currently no intracellular reaction in model w/ xol from R2	NJ
xoltriol	3alpha,7alpha,12alpha-Trihydroxy-5beta-cholestane	Produced only	Endoplasmic Reticulum	XOLTRIOLtr	no xoltriol reactions in ER right now	NJ
2mcit	2-Methylcitrate	Produced only	Cytosol	2MCITt	added transport rxn 2MCITt; methycitrate is excreted in urine of patients who suffer from propionic acidaemia (Weidman et al. 1979)	MM
andrstrnglc	androsterone glucuronide	Consumed only	Cytosol	ANDRSTRNGLCte	ANDRSTRNGLCtr, ANDRSTRNGLCte	NJ
bhb	(R)-3-Hydroxybutanoate	Consumed only	Cytosol	BHBt	gap removed; added extracellular transport rxn	ND
bz	Benzoate	Consumed only	Cytosol	BZt	gap filled, added BZt	NJ
hom-L	L-Homoserine	Produced only	Cytosol	HOMt4	knowledge-based gap; insufficient evidence to show that homoserine i an intermediate of the cystathione g-lyase rxn, which would have removed gap	MM
lipoate	Lipoate	Produced only	Cytosol	LIPOti	leave gap for the moment; lipoate gets imported in cell, converted to dihydrolipoate and this compounds is the active form and gets directly exported again - unknown mechanism. Concrete reaction from lipoate to dihydrolipoate is not really clear to me	IT
no	Nitric oxide	Produced only	Cytosol	NOt	added diffusive transporter	SAB
o2s	Superoxide anion	Consumed only	Cytosol	O2St	gap removed; added rxn for diffusion of o2s	ND
phyQ	Phylloquinone	Produced only	Cytosol	PHYQt	leave gap; knowledge gap	IT
ppa	Propionate (n-C3:0)	Consumed only	Cytosol	PPAt	gap removed; added rxn for extracellular -> cytosolic transport based on ref in thuy's mito model	ND
rbt	Ribitol	Consumed only	Cytosol	RBTt	gap is due to extracellular transport reaction (not needed now, but ok to leave in)	ND
spc_hs	sphingosylphosphorylcholine (homo sapiens)	Produced only	Cytosol	SPC_HSt	filled with SMPD4 and SPC_HSt - note that each one individually could have resolved the gap, however the evidence for both reactions was approximately the same	NJ
txa2	Thromboxane A2	Consumed only	Cytosol	TXA2te	removed gap, replaced TXA2te	NJ
whtststerone	w hydroxy testosterone	Consumed only	Cytosol	WHTSTSTERONEte	WHTSTSTERONEte - unkown transporter and metabolism	NJ
xolest2_hs	cholesterol ester (from FULLR2)	Produced only	Cytosol	XOLEST2te	xolest2_hs produced extracellularly, currently no intracellular reaction in model w/ xol from R2	NJ
gncore1	GlcNAc-alpha-1,4-Core 1	Produced only	Golgi Apparatus	A4GNT1g	gap ok; this is a core structure can undergo tissue-specific, developmentally regulated, or protein-specific modifications (which are not included in this model)	ND
gncore2	GlcNAc-alpha-1,4-Core 2	Produced only	Golgi Apparatus	A4GNT2g	gap ok; this is a core structure can undergo tissue-specific, developmentally regulated, or protein-specific modifications (which are not included in this model)	ND
chsterol	Cholesterol	Consumed only	Golgi Apparatus	CHSTEROLtg	By IT shows transport between golgi and plasma membrane	NJ
core5	Core 5	Produced only	Golgi Apparatus	CORE5GTg	gap ok; this is a core structure can undergo tissue-specific, developmentally regulated, or protein-specific modifications (which are not included in this model)	ND
core7	Core 7	Produced only	Golgi Apparatus	CORE7GTg	gap ok; this is a core structure can undergo tissue-specific, developmentally regulated, or protein-specific modifications (which are not included in this model)	ND
core8	Core 8	Produced only	Golgi Apparatus	CORE8GTg	gap ok; this is a core structure can undergo tissue-specific, developmentally regulated, or protein-specific modifications (which are not included in this model)	ND
glc1man	glucose-1,3-mannose oligosaccharide	Produced only	Golgi Apparatus	ENMAN1g	gap OK; as far as I understand, these are markers for mannosidase activity in Golgi so presumably remain there	ND
glc2man	(2)[glucose-1,3]-mannose oligosaccharide	Produced only	Golgi Apparatus	ENMAN2g	gap OK; as far as I understand, these are markers for mannosidase activity in Golgi so presumably remain there	ND
glc3man	glucose-1,2-(2)[glucose-1,3]-mannose oligosaccharide	Produced only	Golgi Apparatus	ENMAN3g	gap OK; as far as I understand, these are markers for mannosidase activity in Golgi so presumably remain there	ND
glc1man	glucose-1,3-mannose oligosaccharide	Produced only	Golgi Apparatus	ENMAN4g	gap OK; as far as I understand, these are markers for mannosidase activity in Golgi so presumably remain there	ND
glc1man	glucose-1,3-mannose oligosaccharide	Produced only	Golgi Apparatus	ENMAN5g	gap OK; as far as I understand, these are markers for mannosidase activity in Golgi so presumably remain there	ND
glc1man	glucose-1,3-mannose oligosaccharide	Produced only	Golgi Apparatus	ENMAN6g	gap OK; as far as I understand, these are markers for mannosidase activity in Golgi so presumably remain there	ND
Ser/Thr	protein-linked serine or threonine residue (O-glycosylation site)	Consumed only	Golgi Apparatus	GALNTg	gap ok; represents peptide binding site for O-glycans	ND
galside_hs	galactocerebroside (homo sapiens)	Consumed only	Cytosol	GALSIDEtg	gap resolved added GALSIDEtl	NJ
coa	Coenzyme A	Produced only	Golgi Apparatus	GAO1g	CHAT is complete (in cytosol)	NJ
coa	Coenzyme A	Produced only	Golgi Apparatus	GAO2g	CHAT is complete (in cytosol)	NJ
k	potassium	Produced only	Golgi Apparatus	Kt3g	gap is due to transporter rxn in Golgi (not needed now, but ok to leave in)	ND

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
n5m2masn	((N-acetyl-D-glucosaminyl)5-(alpha-D-mannosyl)2-beta-D-mannosyl-diacetylchitobiosyl)-L-asparagine (protein)	Produced only	Golgi Apparatus	M16N4Tg	gap OK; leave as dead-end of N-glycan synthesis since its degradation is not included in model	ND
f1a	F1alpha	Produced only	Golgi Apparatus	N4Tg	gap ok; this is a core structure can undergo tissue-specific, developmentally regulated, or protein-specific modifications (which are not included in this model)	ND
na1	Sodium	Produced only	Golgi Apparatus	NAt3_1g	gap is due to transport reaction in Golgi (not needed now, but ok to leave in)	ND
camp	cAMP	Consumed only	Golgi Apparatus	PDE1g	exceeds model; leave gap	IT
amp	AMP	Produced only	Golgi Apparatus	PDE1g	exceeds model; leave gap since cAMP is gap too	IT
35cgmp	3',5'-Cyclic GMP	Consumed only	Golgi Apparatus	PDE4g	exceeds model; leave gap	IT
pe_hs	phosphatidylethanolamine (homo sapiens)	Produced only	Golgi Apparatus	PE_HStg	pe_hs not used in any Golgi rxns right now	NJ
ps_hs	phosphatidylserine (homo sapiens)	Produced only	Golgi Apparatus	PS_HStg	ps_hs not used in any Golgi rxns right now	NJ
udpg	UDPglucose	Produced only	Golgi Apparatus	UDPGLCtg	gap is due to transporter rxn in Golgi (not needed now, but ok to leave in)	ND
3amp	3'-AMP	Consumed only	Lysosome	3NTD7l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
pi	Phosphate	Produced only	Lysosome	3NTD7l	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT
4abut	4-Aminobutanoate	Consumed only	Lysosome	ABUTt2rL	knowledge-base gap	SAB
acgbgbside_hs	beta GalNAc globoside (homo sapiens)	Produced only	Lysosome	ACGBGBSIDEtl	gap removed by single reaction addition: NAGAIby added in analogy to NAGAIy (no real evidence that this occurs in vivo)	NJ
ade	Adenine	Consumed only	Lysosome	ADEtl	leave gap; knowledge gap: at least i have no idea of the function of adenine in lysosome but uptake was studied by PMID: 2925670	IT
ala-L	L-Alanine	Consumed only	Lysosome	ALAt2rL	model-scope gap	SAB
chsterol	Cholesterol	Consumed only	Lysosome	CHSTEROLt1	Assumed flip-flop mechanism - if not used in lysosome currently it's okay	NJ
ala-D	D-Alanine	Consumed only	Lysosome	DALAt2rL	knowledge-base gap: how does alanine get into the lysosome--good evidence for inclusion regardless of gap	SAB
fald	Formaldehyde	Produced only	Lysosome	FALDtly	gap removed; added transporter for lysosomal transport	ND
galside_hs	galactocerebroside (homo sapiens)	Consumed only	Cytosol	GALSIDEtl	gap resolved added GALSIDEtl	NJ
gly	Glycine	Consumed only	Lysosome	GLYt2rL	knowledge-base gap: how does glycine get into the lysosome--good evidence for inclusion regardless of gap	SAB
h2o2	Hydrogen peroxide	Consumed only	Lysosome	H2O2tly	gap removed; found physiological evidence that can diffuse across compartments	ND
hxan	Hypoxanthine	Consumed only	Lysosome	HXANtl	Gene associated--IT's addition	SAB
idour	L-Iduronate	Consumed only	Cytosol	IDOURtly	knowledge gap; makes sense that idour is transported to cytosol (to maintain osmotic balance in lysosome) but I can't find any specific rxn which consume it there	ND
ins	Inosine	Consumed only	Lysosome	INStl	Gene associated--IT's addition	SAB
pi	Phosphate	Produced only	Lysosome	LAPCOAl	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT
lcts	Lactose	Consumed only	Cytosol	LCTStl	gap removed; have decided to remove this reaction since it probably doesn't exist in the cytosol -- I don't want to associate it with the lysosomal complex until it has been experimentally verified	ND
meoh	Methanol	Consumed only	Lysosome	MEOHtly	gap removed; added transporter for lysosome transport	ND
malttr	Maltotriose	Consumed only	Lysosome	MLTG1ly	leave gap; this rxn is valid in vivo, malttr usually arises from glycogen deg, but does not appear in our network for modeling reasons (only made representative structure for glycogen and malttr doesn't happen to be one of its degradation products)	ND
acgbgbside_hs	beta GalNAc globoside (homo sapiens)	Produced only	Lysosome	NAGAlby	gap removed by single reaction addition: NAGAIby added in analogy to NAGAIy (no real evidence that this occurs in vivo)	NJ
ump	UMP	Consumed only	Lysosome	NTD2l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
pi	Phosphate	Produced only	Lysosome	NTD2l	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
dcmp	dCMP	Consumed only	Lysosome	NTD3l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
dcyt	Deoxycytidine	Produced only	Lysosome	NTD3l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
pi	Phosphate	Produced only	Lysosome	NTD3l	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT
cmp	CMP	Consumed only	Lysosome	NTD4l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
pi	Phosphate	Produced only	Lysosome	NTD4l	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT
dtmp	dTMP	Consumed only	Lysosome	NTD5l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
pi	Phosphate	Produced only	Lysosome	NTD5l	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT
damp	dAMP	Consumed only	Lysosome	NTD6l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
dad-2	Deoxyadenosine	Produced only	Lysosome	NTD6l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
pi	Phosphate	Produced only	Lysosome	NTD6l	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT
amp	AMP	Consumed only	Lysosome	NTD7l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
pi	Phosphate	Produced only	Lysosome	NTD7l	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT
dgmp	dGMP	Consumed only	Lysosome	NTD8l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
dgsn	Deoxyguanosine	Produced only	Lysosome	NTD8l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
pi	Phosphate	Produced only	Lysosome	NTD8l	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT
gmp	GMP	Consumed only	Lysosome	NTD9l	nucleotide monophosphates come from DNA and RNA degradation in lysosome (by acid exonucleoase and acid ribonuclease). Will be dead-end in model as well as their efflux transport systems.	IT
pi	Phosphate	Produced only	Lysosome	NTD9l	DNA and RNA degradation takes place in the Lysosome. The associated reactions are dead-ends in the model since we do not model DNA, RNA. Thus, pi coming from these dead-end reaction can easily stay a gap for the moment since it will not effect the model capacities but a pi-transport system from/to Lysosome is not known to me.	IT
h2o2	Hydrogen peroxide	Consumed only	Lysosome	PRDX1l	gap removed; found physiological evidence that can diffuse across compartments	ND
meoh	Methanol	Consumed only	Lysosome	PRDX1l	gap removed; added transporter for lysosome transport	ND
fald	Formaldehyde	Produced only	Lysosome	PRDX1l	gap removed; added transporter for lysosomal transport	ND

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
pro-D	D-Proline	Consumed only	Lysosome	PRODt2rL	knowledge-base gap: good evidence for inclusion regardless of gap	SAB
pro-L	L-Proline	Consumed only	Lysosome	PROt2rL	knowledge-base gap: good evidence for inclusion regardless of gap	SAB
1a2425thvitd2	1-alpha,24R,25-Trihydroxyvitamin D2	Produced only	Mitochondria	1a,24,25VITD2Hm	resolved gap; included ER import	IT
1a2425thvitd3	1-alpha,24R,25-Trihydroxyvitamin D3	Produced only	Mitochondria	1a,24,25VITD3Hm	resolved gap; included ER and cytosolic export	IT
1a2425thvitd2	1-alpha,24R,25-Trihydroxyvitamin D2	Produced only	Mitochondria	1a,25VITD2Hm	resolved gap; included ER import	IT
1a2425thvitd3	1-alpha,24R,25-Trihydroxyvitamin D3	Produced only	Mitochondria	1a,25VITD3Hm	resolved gap; included ER and cytosolic export	IT
3hbcoa-R	(R)-3-Hydroxybutanoyl-CoA	Produced only	Mitochondria	3HBCDm	Reactions not currently used since lumped FA ox rxns used, in future updates if FA ox is broken up they will be used	NJ
5hoxindact	5-Hydroxyindoleacetaldehyde	Consumed only	Mitochondria	5HOXINDACTOXm	knoweldge-base gap: unknown if/how molecules are transported	SAB
5hoxindoa	5-Hydroxyindoleacetate	Produced only	Mitochondria	5HOXINDACTOXm	knoweldge-base gap: unknown if/how molecules are transported	SAB
acglu	N-Acetyl-L-glutamate	Produced only	Mitochondria	ACGSm	knowledge-base gap	SAB
adprib	ADPribose	Consumed only	Mitochondria	ADPRDPm	leave gap; exceeds model	IT
r5p	alpha-D-Ribose 5-phosphate	Produced only	Mitochondria	ADPRDPm	leave gap; r5p is normally metabolized by pentose-phosphate pathway in cytosol. Since adprib, the substrate of the reaction, is also a gap, I will not include a mitochondrial transport reaction just for model purpose	IT
ptrc	Putrescine	Produced only	Mitochondria	AGMTm	Localization data for reactions causes this gap--OK	SAB
acg5p	N-Acetyl-L-glutamyl 5-phosphate	Consumed only	Mitochondria	AGPRim	knowledge-base gap: also reaction isn't so certain	SAB
acg5sa	N-Acetyl-L-glutamate 5-semialdehyde	Produced only	Mitochondria	AGPRim	knowledge-base gap: also reaction isn't so certain	SAB
id3acald	Indole-3-acetaldehyde	Consumed only	Mitochondria	ALDD20xm	model-scope gap	SAB
ind3ac	Indole-3-acetate	Produced only	Mitochondria	ALDD20xm	model-scope gap	SAB
bamppald	beta-Aminopropion aldehyde	Consumed only	Mitochondria	BAMPPALDOXm	knowledge-base gap: not known how/if metabolites get into and out o mitochondria	SAB
bhb	(R)-3-Hydroxybutanoate	Consumed only	Cytosol	BHBtm	gap removed; added extracellular transport rxn	ND
c2m26dcoa	cis-2-Methyl-5-isopropylhexa-2,5-dienoyl-CoA	Consumed only	Mitochondria	C2M26DCOAHLm	model-scope gap: unimportant	SAB
cbl2	Cob(II)alamin	Produced only	Mitochondria	CBL2tm	leave for the moment --> unfinished PW	IT
cbl1	Cob(I)alamin	Consumed only	Mitochondria	CBLATm	leave for the moment --> unfinished PW	IT
adocbl	Adenosylcobalamin	Produced only	Mitochondria	CBLATm	leave for the moment --> unfinished PW	IT
cca_d3	Calcitroic acid (D3)	Consumed only	Mitochondria	CCA_D3tm	knowledge gap; reactions as well as enzymes for vit D degradation are unknown	IT
chsterol	Cholesterol	Consumed only	Lysosome	CHSTEROLt1	Assumed flip-flop mechanism - if not used in lysosome currently it's okay	NJ
clpndcoa	clupanodonyl CoA	Produced only	Mitochondria	CLPNDCPT2	was not removed - technically/physiologically the reaction CAN occur, however long chain fatty acids (>C22) won't be oxidized in the mitochondria so it is unlikely to be used	NJ
pcrn	propionyl-carnitine	Produced only	Mitochondria	CSNAT2m	CSNAT3m removed and replaced with CSNAT2m, CSNAT3x made reversible	NJ
cys-L	L-Cysteine	Consumed only	Mitochondria	CYSTAm	knowledge-based gap	MM
mercppyr	Mercaptopyruvate	Produced only	Mitochondria	CYSTAm	knowledge-based gap	MM
3aib-D	D-3-Amino-isobutanoate	Consumed only	Mitochondria	D3AIBTm	gap eliminated; MM added mitochondrial transport reaction (3AIBtm)	IT
dd2coa	trans-Dodec-2-enoyl-CoA	Consumed only	Mitochondria	DCIm	Reactions not currently used since lumped FA ox rxns used, in future updates if FA ox is broken up they will be used	NJ
dd3coa	3-dodecenoyl CoA	Produced only	Mitochondria	DCIm	Reactions not currently used since lumped FA ox rxns used, in future updates if FA ox is broken up they will be used	NJ
dcyt	Deoxycytidine	Consumed only	Mitochondria	DCK1m	leave gap for the moment; i discovered the reaction (DCK1m) during the gap filling process but i could not find any other evidence how dcyt comes into the mitochondria. Dcmp will certainly originate from mtDNA. The reaction is right now reversible but i think that the most probable direction is towards the dcmp production which leaves the question where dcyt is coming from.	IT
dcmp	dCMP	Produced only	Mitochondria	DCK1m	leave gap for the moment; i discovered the reaction (DCK1m) during the gap filling process but i could not find any other evidence how dcyt comes into the mitochondria. Dcmp will certainly originate from mtDNA. The reaction is right now reversible but i think that the most probable direction is towards the dcmp production which leaves the question where dcyt is coming from.	IT
tdcoa	Tetradecanoyl-CoA (n-C14:0CoA)	Produced only	Mitochondria	FAOXC140	FAOXC140 added	NJ
glyclt	Glycolate	Produced only	Mitochondria	GCALDDm	leave gap; can't find any refs as to what happens to mitochondrial glyc -- could be transported to cytosol, but no evidence for this nor need for its transport in model	ND
ser-L	L-Serine	Consumed only	Mitochondria	GHMT2rm	knowledge-based gap	MM
3htmelys	3-Hydroxy-N6,N6,N6-trimethyl-L-lysine	Consumed only	Mitochondria	GHMT3m	knowledge-based gap	MM

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
4tmeabut	4-Trimethylammoniobutanal	Produced only	Mitochondria	GHMT3m	knowledge-based gap	MM
glac	D-glucurono-6,3-lactone	Consumed only	Mitochondria	GLACOm	leave gap; this reaction was added based on only modeling evidence	ND
glcr	D-Glucarate	Produced only	Mitochondria	GLACOm	ok; glucaric acid seems to be a dead end metabolite [Marsh, Carb Res 1986]	ND
glyclt	Glycolate	Produced only	Mitochondria	GLYCLTDym	leave gap; can't find any refs as to what happens to mitochondrial glyc -- could be transported to cytosol, but no evidence for this nor need for its transport in model	ND
lgt-S	(R)-S-Lactoylglutathione	Consumed only	Mitochondria	GLYOXm	gap ok; function of the mitochondrial pool of glyoxalase II activity is unknown	ND
alpa_hs	lysophosphatidic acid (homo sapiens)	Produced only	Mitochondria	GPAMm_hs	knowledge gap, pathway complete in cytosol - see PMID: 10514455, suggests that pa_hs crosses mit membrane (rat)	NJ
h2co3	carbonic acid	Produced only	Mitochondria	H2CO3D2m	genes and good evidence, passed to NCD	SAB
h2co3	carbonic acid	Produced only	Mitochondria	H2CO3Dm	genes and good evidence, passed to NCD	SAB
hexccoa	Hexacosanoyl-CoA (n-C26:0CoA)	Produced only	Mitochondria	HEXCCPT2	was not removed - technically/physiologically the reaction CAN occur, however long chain fatty acids (>C22) won't be oxidized in the mitochondria so it is unlikely to be used	NJ
4hpro-LT	trans-4-Hydroxy-L-proline	Consumed only	Mitochondria	HPROxm	model-scope gap: no collagen in model currently	SAB
hpyr	Hydroxypyruvate	Consumed only	Mitochondria	HPYRDCm	true knowledge gap; there are very few reports describing the properties of this enzyme, none in human tissues	ND
im4act	Imidazole-4-acetaldehyde	Consumed only	Mitochondria	IMACTD_m	knowledge-base gap: not known how this gets to mitochondria	SAB
im4ac	Imidazole-4-acetate	Produced only	Mitochondria	IMACTD_m	model-scope gap: potential end-product	SAB
imp	IMP	Produced only	Mitochondria	INSKm	what the hell is happening with this??? No evidence for biosynthetic pathway of atp/gtp from imp in mito	IT
lald-D	D-Lactaldehyde	Consumed only	Mitochondria	LCADi_Dm	knowledge gap; this step is not wel characterized in humans	ND
lald-L	L-Lactaldehyde	Consumed only	Mitochondria	LCADim	knowledge gap; this step is not wel characterized in humans	ND
Lcyst	L-Cysteate	Consumed only	Mitochondria	LCYSTATm	knowledge-based gap	MM
lgnccoa	lignocericyl coenzyme A	Produced only	Mitochondria	LGNCCPT2	was not removed - technically/physiologically the reaction CAN occur, however long chain fatty acids (>C22) won't be oxidized in the mitochondria so it is unlikely to be used	NJ
ACP	acyl carrier protein	Consumed only	Mitochondria	MCOATAm	FA synthesis is lumped, so activation w/ ACP will not be utilized at this point, this may be useful in a future version of the reconstruction if FAS is 'unlumped'	NJ
malACP	Malonyl-[acyl-carrier protein]	Produced only	Mitochondria	MCOATAm	FA synthesis is lumped, so activation w/ ACP will not be utilized at this point, this may be useful in a future version of the reconstruction if FAS is 'unlumped'	NJ
n4abutn	N4-Acetylaminobutanal	Consumed only	Mitochondria	NABTNOm	knowledge-base gap: not entirely clear how these metabolites are metabolized	SAB
4aabutn	4-Acetamidobutanoate	Produced only	Mitochondria	NABTNOm	knowledge-base gap: not entirely clear how these metabolites are metabolized	SAB
didp	dIDP	Consumed only	Mitochondria	NDPK10m	leave gap; knowledge gap	IT
ditp	dITP	Produced only	Mitochondria	NDPK10m	leave gap; knowledge gap	IT
utp	UTP	Produced only	Mitochondria	NDPK2m	gap eliminated; added UMPKm for modeling purpose: although no activity of such an enzyme has been shown for mitochondria up to dat the UMP kinase function has to be present in order to "restaure" UTP from UMP for/ from mRNA synthesis/degradation. PMID: 11912132 showed that cytosolic CMP-UMP kinase has no mitochondrial activity	IT
idp	IDP	Consumed only	Mitochondria	NDPK9m	leave gap; knowledge gap	IT
itp	ITP	Produced only	Mitochondria	NDPK9m	leave gap; knowledge gap	IT
nmn	NMN	Consumed only	Mitochondria	NMNATm	leave gap; i don't know how to connect rxn in mito with cytosol	IT
nicrnt	Nicotinate D-ribonucleotide	Consumed only	Mitochondria	NNATm	leave gap; i don't know how to connect rxn in mito with cytosol	IT
dnad	Deamino-NAD+	Produced only	Mitochondria	NNATm	leave gap; i don't know how to connect rxn in mito with cytosol	IT
nrvnccoa	nervonyl coenzyme A	Produced only	Mitochondria	NRVNCCPT2	was not removed - technically/physiologically the reaction CAN occur, however long chain fatty acids (>C22) won't be oxidized in the mitochondria so it is unlikely to be used	NJ
o2s	Superoxide anion	Consumed only	Cytosol	O2Stm	gap removed; added rxn for diffusion of o2s	ND
4mptnl	4-Methylpentanal	Produced only	Mitochondria	P45011A1m	metabolized to isocaproic acid and isocapryl alcohol - see PMID: 8645003	NJ
20ahchsterol	20alpha-hydroxy cholesterol	Produced only	Mitochondria	P450SCC1m	knowledge gap, model scope gap - hydroxylated cholesterol metabolism in the mitochondria - no significant literature found	NJ
pcrn	propionyl-carnitine	Produced only	Mitochondria	PCRNtm	CSNAT3m removed and replaced with CSNAT2m, CSNAT3x made reversible	NJ
phe-L	L-Phenylalanine	Consumed only	Mitochondria	PHETA1m	knowledge-base gap: leave in case transporters are found in the future	SAB
phpyr	Phenylpyruvate	Produced only	Mitochondria	PHETA1m	knowledge-base gap: leave in case transporters are found in the future	SAB
pnto-R	(R)-Pantothenate	Consumed only	Mitochondria	PNTKm	leave gap for now: Hoertnagel et al, 2003, Human Mol. genetics, 12(3), 321-327: They also proposed that a complete intramitochondrial pathway for de novo synthesis of CoA exists, but could not find further evidence for this	IT

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
4ppan	D-4'-Phosphopantothenate	Produced only	Mitochondria	PNTKm	leave gap for now: Hoertnagel et al, 2003, Human Mol. genetics, 12(3), 321-327: They also proposed that a complete intramitochondrial pathway for de novo synthesis of CoA exists, but could not find further evidence for this	IT
ppa	Propionate (n-C3:0)	Consumed only	Cytosol	PPAtm	gap removed; added rxn for extracellular -> cytosolic transport based on ref in thuy's mito model	ND
3hpcoa	3-Hydroxypropionyl-CoA	Produced only	Mitochondria	PRPNCOAHYDm	knowledge-base gap: good evidence for inclusion regardless of gap	SAB
pyam5p	Pyridoxamine 5'-phosphate	Produced only	Mitochondria	PYAM5Ptm	leave gap; excedds model	IT
pydx5p	Pyridoxal 5'-phosphate	Produced only	Mitochondria	PYDX5Ptm	leave gap; excedds model	IT
pylald	Perillyl aldehyde	Consumed only	Mitochondria	PYLALDOXm	knowledge-base gap: unknown where this metabolite goes in humans; low priority subsystem also	SAB
peracd	Perillic acid	Produced only	Mitochondria	PYLALDOXm	knowledge-base gap: unknown where this metabolite goes in humans; low priority subsystem also	SAB
sl-L	L-sulfolactate	Consumed only	Mitochondria	SLDxm	knowledge-based gap	MM
t2m26dcoa	trans-2-Methyl-5-isopropylhexa-2,5-dienoyl-CoA	Consumed only	Mitochondria	T2M26DCOAHLm	knowledge-base gap	SAB
tetpent3coa	tetracosapentaenoyl coenzyme A, n-3	Produced only	Mitochondria	TETPENT3CPT2	was not removed - technically/physiologically the reaction CAN occur, however long chain fatty acids (>C22) won't be oxidized in the mitochondria so it is unlikely to be used	NJ
tetpent6coa	tetracosapentaenoyl coenzyme A, n-6	Produced only	Mitochondria	TETPENT6CPT2	was not removed - technically/physiologically the reaction CAN occur, however long chain fatty acids (>C22) won't be oxidized in the mitochondria so it is unlikely to be used	NJ
tettet6coa	tetracosatetraenoyl coenzyme A	Produced only	Mitochondria	TETTET6CPT2	was not removed - technically/physiologically the reaction CAN occur, however long chain fatty acids (>C22) won't be oxidized in the mitochondria so it is unlikely to be used	NJ
thm	Thiamin	Produced only	Mitochondria	THMt2m	leave gap; knowledge based: It is thought that this SLC19A2 is also reponsible for the mitochondrial transport since cells of TRMA patients (thiamine-responive megaloblastic anemia) in this gene show no mitochondrial transport of thiamine. Role of thiamine in mitochondria is not clear (therefore will be a gap) since there is no mitochondrial thiamine diphosphokinase)	IT
trdox	Oxidized thioredoxin	Consumed only	Mitochondria	TRDRm	knowledge gap; thioredoxin is needed by ribonucleotide reductase, however, up to date only cytosolic version has been identified	IT
trdrd	Reduced thioredoxin	Produced only	Mitochondria	TRDRm	knowledge gap; thioredoxin is needed by ribonucleotide reductase, however, up to date only cytosolic version has been identified	IT
tdcoa	Tetradecanoyl-CoA (n-C14:0CoA)	Produced only	Mitochondria	TTDCPT2	FAOXC140 added	NJ
tyr-L	L-Tyrosine	Consumed only	Mitochondria	TYRTAm	knowledge-base gap: not clear how tyr-L enters mitochondria	SAB
xoldiolone	7alpha,12alpha-Dihydroxycholest-4-en-3-one	Consumed only	Mitochondria	XOLDIOLONEtm	no xoldiolone reactions in mitochondria	NJ
co2	CO2	Consumed only	Nucleus	CO2tn	gap is due to transporter rxn in nucleus (not needed now, but ok to leave in)	ND
dna	DNA	Consumed only	Nucleus	DNAMTSEn	model-scope gap: DNA not represented in model so methylation will require sinks	SAB
dna5mtc	DNA 5-methylcytosine	Produced only	Nucleus	DNAMTSEn	model-scope gap: DNA not represented in model so methylation will require sinks	SAB
dna	DNA	Consumed only	Nucleus	DNAMTn	model-scope gap: DNA not represented in model so methylation will require sinks	SAB
dna5mtc	DNA 5-methylcytosine	Produced only	Nucleus	DNAMTn	model-scope gap: DNA not represented in model so methylation will require sinks	SAB
o2s	Superoxide anion	Consumed only	Cytosol	O2Stn	gap removed; added rxn for diffusion of o2s	ND
o2s	Superoxide anion	Consumed only	Nucleus	O2Stn	gap removed; added rxn for diffusion of o2s	ND
retn	Retinoate	Produced only	Nucleus	RAtn	leave gap; excedds model	IT
thbpt	Tetrahydrobiopterin	Produced only	Nucleus	SPRn	knowledge-base gap: unknown where selmeth comes from in humans; modeling evidence only, need a source of selenomethionine	IT
ahcys	S-Adenosyl-L-homocysteine	Produced only	Endoplasmic Reticulum	AHCYStr	gap filled, added AHCYStr	NJ
dhcholoylcoa	3alpha,7alpha-Dihydroxy-5beta-cholest-24-enoyl-CoA	Produced only	Endoplasmic Reticulum	AMACR2r	leave gap for now, complete pathway in peroxisome	NJ
cholcoas	3alpha,7alpha,12alpha-Trihydroxy-5beta-cholestanoyl-CoA(S)	Produced only	Endoplasmic Reticulum	AMACRr	leave gap for now, complete pathway in peroxisome	NJ
amet	S-Adenosyl-L-methionine	Consumed only	Endoplasmic Reticulum	AMETr	gap filled, added AMETr	NJ
bz	Benzoate	Consumed only	Cytosol	BZtr	gap filled, added BZt	NJ
nh4	Ammonium	Produced only	Endoplasmic Reticulum	CBPPer	knowledge-base gap; we don't have any rxns which consume nh4 in the ER. If need be one could potentially resolve this gap by adding ER-cytosol transport (but have not come across any evidence for that yin a preliminary search)	ND
coke	cocaine	Consumed only	Endoplasmic Reticulum	COKECBESr	11DOCRTSLtr, 11DOCRTSLtm	NJ

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
crtstrn	Corticosterone	Produced only	Endoplasmic Reticulum	CRTSTRNtr	CRTSTRNtr, CRTSTRNtm	NJ
crn	L-Carnitine	Consumed only	Endoplasmic Reticulum	CSNATer	Not currently used reactions, see PMID: 11257506	NJ
acrn	O-Acetylcarnitine	Produced only	Endoplasmic Reticulum	CSNATer	Not currently used reactions, see PMID: 11257506	NJ
Asn-X-Ser/Thr	protein-linked asparagine residue (N-glycosylation site)	Consumed only	Endoplasmic Reticulum	DOLASNT_Ler	gap OK; represents polypeptide which would be broken down in lysosome	ND
Asn-X-Ser/Thr	protein-linked asparagine residue (N-glycosylation site)	Consumed only	Endoplasmic Reticulum	DOLASNT_Uer	gap OK; represents polypeptide which would be broken down in lysosome	ND
estriol	estriol	Produced only	Cytosol	ESTRIOLtr	no cytosolic estriol reactions	NJ
ru5p-D	D-Ribulose 5-phosphate	Produced only	Endoplasmic Reticulum	GNDer	there has been speculation that the entire PPP occurs in the ER, but there is no direct evidence for any enzymes past this step…. Rather than inferring rest of pathway have left as a knowledge gap	ND
dem2emgacpail_prot_hs	deacylated-(phosphoethanolaminyl-dimannosyl),(phosphoethanolaminyl)-mannosyl-glucosaminyl-acylphosphatidylinositol	Produced only	Endoplasmic Reticulum	GPIDA2er	gap ok, represents additional processing of GPI anchor; this is a modeling dead-end (transport of this metabolite to plasma memebrane is beyond the scope of our network)	ND
dgpi_prot_hs	deacylated-glycophosphatidylinositol (GPI)-anchored protein	Produced only	Endoplasmic Reticulum	GPIDAer	gap ok, represents additional processing of GPI anchor; this is a modeling dead-end (transport of this metabolite to plasma memebrane is beyond the scope of our network)	ND
pre_prot	glycophosphatidylinositol (GPI)-anchored protein precursor	Consumed only	Endoplasmic Reticulum	H7TAer	gap OK; peptide binding site for GPI anchor, its biosynthesis is outside the scope of model	ND
pre_prot	glycophosphatidylinositol (GPI)-anchored protein precursor	Consumed only	Endoplasmic Reticulum	H8TAer	gap OK; peptide binding site for GPI anchor, its biosynthesis is outside the scope of model	ND
hmgcoa	Hydroxymethylglutaryl-CoA	Consumed only	Endoplasmic Reticulum	HMGCOARr	complete reaction in peroxisomal version	NJ
mev-R	(R)-Mevalonate	Produced only	Endoplasmic Reticulum	HMGCOARr	complete reaction in peroxisomal version	NJ
pre_prot	glycophosphatidylinositol (GPI)-anchored protein precursor	Consumed only	Endoplasmic Reticulum	M4ATAer	gap OK; peptide binding site for GPI anchor, its biosynthesis is outside the scope of model	ND
m(em)3gacpail_prot_hs	mannosyl-3-(phosphoethanolaminyl-mannosyl)-glucosaminyl-acylphosphatidylinositol-Protein (M4A)	Produced only	Endoplasmic Reticulum	M4ATAer	gap OK; this is an alternative GPI structure which has recently been suggested as a substrate of human GPI transamidase	ND
pre_prot	glycophosphatidylinositol (GPI)-anchored protein precursor	Consumed only	Endoplasmic Reticulum	M4BTAer	gap OK; peptide binding site for GPI anchor, its biosynthesis is outside the scope of model	ND
mem2emgacpail_prot_hs	({[(mannosyl),(phosphoethanolaminyl)]-dimannosyl},{phosphoethanolaminyl})-mannosyl-glucosaminyl-acylphosphatidylinositol-Protein (M4B)	Produced only	Endoplasmic Reticulum	M4BTAer	gap OK; this is an alternative GPI structure which has recently been suggested as a substrate of human GPI transamidase	ND
acald	Acetaldehyde	Produced only	Endoplasmic Reticulum	P45017A2r	ACALDtr - knowledge gap, unknown mechanism	NJ
acald	Acetaldehyde	Produced only	Endoplasmic Reticulum	P45017A4r	ACALDtr - knowledge gap, unknown mechanism	NJ
whtststerone	w hydroxy testosterone	Produced only	Endoplasmic Reticulum	P4503A43r	WHTSTSTERONEte - unkown transporter and metabolism	NJ
12harachd	12 hydroxy arachidonic acid	Produced only	Endoplasmic Reticulum	P4504B1r	knowledge gap > model scope limitation, final location of many of the hydroxylated arachidonic acid products not well defined - many of these have short half-lives and are quickly metabolized	NJ
wharachd	w-hydroxyl arachidonic acid	Produced only	Endoplasmic Reticulum	P4504F121r	knowledge gap > model scope limitation, final location of many of the hydroxylated arachidonic acid products not well defined - many of these have short half-lives and are quickly metabolized	NJ
18harachd	18 hydroxy arachidonic acid	Produced only	Endoplasmic Reticulum	P4504F81r	knowledge gap > model scope limitation, final location of many of the hydroxylated arachidonic acid products not well defined - many of these have short half-lives and are quickly metabolized	NJ
leuktrB4wcooh	w-carboxy leukotriene B4	Produced only	Endoplasmic Reticulum	P450LTB4r	principally knowledge gap, partial scope limitations	NJ
pecgoncoa	Pseudoecgonyl-CoA	Produced only	Endoplasmic Reticulum	PECGONCOATr	modeling-gap: this is the end of the line in KEGG for cocaine degradation	SAB
prostgd2	Prostaglandin D2	Produced only	Endoplasmic Reticulum	PGDIr	principally a knowledge gap problem - further metabolism, etc unknown, since at the 'fringes' partial model scope gap also - see Goodman and Gilman, Murray Biochem for overall pathway	NJ

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
prostge2	Prostaglandin E2	Produced only	Endoplasmic Reticulum	PGESr	principally a knowledge gap problem - further metabolism, etc unknown, since at the 'fringes' partial model scope gap also - see Goodman and Gilman, Murray Biochem for overall pathway	NJ
prostgi2	Prostaglandin I2	Produced only	Endoplasmic Reticulum	PGISr	principally a knowledge gap problem - further metabolism, etc unknown, since at the 'fringes' partial model scope gap also - see Goodman and Gilman, Murray Biochem for overall pathway	NJ
pail4p_hs	1-Phosphatidyl-1D-myo-inositol 4-phosphate (Homo sapiens)	Consumed only	Endoplasmic Reticulum	PI4P3Ker	leave gap; this is just an alternative localization for enzyme in complet (functional) cytosolic pathway	ND
pail34p_hs	phosphatidylinositol-3,4-bisphosphate (Homo sapiens)	Produced only	Endoplasmic Reticulum	PI4P3Ker	leave gap; this is just an alternative localization for enzyme in complet (functional) cytosolic pathway	ND
pail5p_hs	1-Phosphatidyl-1D-myo-inositol 5-phosphate (Homo sapiens)	Consumed only	Endoplasmic Reticulum	PI5P3Ker	leave gap; this is just an alternative localization for enzyme in complet (functional) cytosolic pathway	ND
pail35p_hs	phosphatidylinositol-3,5-bisphosphate (Homo sapiens)	Produced only	Endoplasmic Reticulum	PI5P3Ker	leave gap; this is just an alternative localization for enzyme in complet (functional) cytosolic pathway	ND
pail_hs	phosphatidylinositol (homo sapiens)	Consumed only	Endoplasmic Reticulum	PIK3er	leave gap; this is just an alternative localization for enzyme in complet (functional) cytosolic pathway	ND
pail3p_hs	1-Phosphatidyl-1D-myo-inositol 3-phosphate (Homo sapiens)	Produced only	Endoplasmic Reticulum	PIK3er	leave gap; this is just an alternative localization for enzyme in complet (functional) cytosolic pathway	ND
pepslys	peptide sans lysine	Produced only	Endoplasmic Reticulum	PLYSPSer	model-scope gap; this is just a generic peptide	MM
akg	2-Oxoglutarate	Consumed only	Endoplasmic Reticulum	PROAKGOX1r	modeling gap: hydroxproline isn't currently used in the model so this reaction isn't (yet) important	SAB
pro-L	L-Proline	Consumed only	Endoplasmic Reticulum	PROAKGOX1r	modeling gap: hydroxproline isn't currently used in the model so this reaction isn't (yet) important	SAB
4hpro-LT	trans-4-Hydroxy-L-proline	Produced only	Endoplasmic Reticulum	PROAKGOX1r	modeling gap: hydroxproline isn't currently used in the model so this reaction isn't (yet) important	SAB
succ	Succinate	Produced only	Endoplasmic Reticulum	PROAKGOX1r	modeling gap: hydroxproline isn't currently used in the model so this reaction isn't (yet) important	SAB
ps_hs	phosphatidylserine (homo sapiens)	Produced only	Endoplasmic Reticulum	PS_HSter	ps_hs not used in any ER reactions currently	NJ
hxdcal	Hexadecanal	Produced only	Endoplasmic Reticulum	SGPL11r	removed due to SGPL12r	NJ
R1coa_hs	R group 1 Coenzyme A homo sapiens	Consumed only	Endoplasmic Reticulum	SOAT11r	complete reaction in cytosolic version	NJ
xolest_hs	cholesterol ester	Produced only	Endoplasmic Reticulum	SOAT11r	complete reaction in cytosolic version	NJ
R2coa_hs	R group 2 Coenzyme A homo sapiens	Consumed only	Endoplasmic Reticulum	SOAT12r	complete reaction in cytosolic version	NJ
xolest_hs	cholesterol ester	Produced only	Endoplasmic Reticulum	SOAT12r	complete reaction in cytosolic version	NJ
so4	Sulfate	Produced only	Endoplasmic Reticulum	STS1r	- knowledge gap, unknown mechanis	NJ
estrones	Estrone 3-sulfate	Consumed only	Endoplasmic Reticulum	STS2r	STS2 is completed, intracellular transport of estrones not known - knowledge gap	NJ
so4	Sulfate	Produced only	Endoplasmic Reticulum	STS2r	- knowledge gap, unknown mechanis	NJ
chsterols	cholesterol sulfate	Consumed only	Endoplasmic Reticulum	STS3r	STS3 is completed, intracellular transport of chsterols not known - knowledge gap	NJ
so4	Sulfate	Produced only	Endoplasmic Reticulum	STS3r	- knowledge gap, unknown mechanis	NJ
prgnlones	pregnenolone sulfate	Consumed only	Endoplasmic Reticulum	STS4r	STS4 is completed, intracellular transport of prgnlones not known - knowledge gap	NJ
so4	Sulfate	Produced only	Endoplasmic Reticulum	STS4r	- knowledge gap, unknown mechanis	NJ
txa2	Thromboxane A2	Consumed only	Cytosol	TXA2tr	removed gap, replaced TXA2te	NJ
udpacgal	UDP-N-acetyl-D-galactosamine	Produced only	Endoplasmic Reticulum	UGALNACter	udpacgal is not used in any ER reactions currently	NJ
andrstrnglc	androsterone glucuronide	Produced only	Endoplasmic Reticulum	UGT1A3r	ANDRSTRNGLCtr, ANDRSTRNGLCte	NJ
ahandrostan	3alpha-Hydroxy-5beta-androstan-17-one	Consumed only	Endoplasmic Reticulum	UGT1A7r	model scope and knowledge limitations	NJ
dhcholestanate	3alpha,7alpha-Dihydroxy-5beta-cholestanate	Consumed only	Endoplasmic Reticulum	VLCS2r	leave - gap in ER, complete in mit-> peroxisome	NJ
thcholstoic	3alpha,7alpha,12alpha-Trihydroxy-5beta-cholestanoate	Consumed only	Endoplasmic Reticulum	VLCSr	leave - gap in ER, complete in mit-> peroxisome	NJ
xol7ah2	3alpha,7alpha-Dihydroxy-5beta-cholestane	Produced only	Endoplasmic Reticulum	XOL7AH2tr	no xol7ah2 reactions in ER right now	NJ
xoldiolone	7alpha,12alpha-Dihydroxycholest-4-en-3-one	Consumed only	Mitochondria	XOLDIOLONEtm	no xoldiolone reactions in mitochondria	NJ
xoltriol	3alpha,7alpha,12alpha-Trihydroxy-5beta-cholestane	Produced only	Endoplasmic Reticulum	XOLTRIOLtr	no xoltriol reactions in ER right now	NJ

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
Ser-Gly/Ala-X-Gly	protein-linked serine residue (glycosaminoglycan attachment site)	Consumed only	Endoplasmic Reticulum	XYLTer	gap ok; represents peptide binding site for GAG chains	ND
3odcoa	3-Oxodecanoyl-CoA	Consumed only	Peroxisome	ACACT4p	knowledge-based gap	NJ
3oddcoa	3-Oxododecanoyl-CoA	Consumed only	Peroxisome	ACACT5p	model-scope gap: presumably will be a cellular demand	NJ
dcacoa	Decanoyl-CoA (n-C10:0CoA)	Produced only	Peroxisome	ACACT5p	peroxisomal thioesterases are known to exist, they hydrolyze acyl-CoA to their respective free FA and coa, it is believed that they may regulat FA content of perox membranes and perox prolif, at this point no info to add transporters or new reactions	NJ
3otdcoa	3-Oxotetradecanoyl-CoA	Consumed only	Peroxisome	ACACT6p	knowledge-base gap	NJ
ddcacoa	Dodecanoyl-CoA (n-C12:0CoA)	Produced only	Peroxisome	ACACT6p	peroxisomal thioesterases are known to exist, they hydrolyze acyl-CoA to their respective free FA and coa, it is believed that they may regulat FA content of perox membranes and perox prolif, at this point no info to add transporters or new reactions	NJ
3ohdcoa	3-Oxohexadecanoyl-CoA	Consumed only	Peroxisome	ACACT7p	model-scope gap	NJ
tdcoa	Tetradecanoyl-CoA (n-C14:0CoA)	Produced only	Peroxisome	ACACT7p	peroxisomal thioesterases are known to exist, they hydrolyze acyl-CoA to their respective free FA and coa, it is believed that they may regulat FA content of perox membranes and perox prolif, at this point no info to add transporters or new reactions	NJ
3ohodcoa	3-Oxooctadecanoyl-CoA	Consumed only	Peroxisome	ACACT8p	knowledge-base gap: KEGG is the only evidence for this reaction	NJ
3ohxccoa	3-Oxohexacosyl-CoA	Consumed only	Peroxisome	ACACT9p	knowledge-base gap	NJ
ttccoa	tetracosanoyl-CoA (n-C24:0CoA)	Produced only	Peroxisome	ACACT9p	peroxisomal thioesterases are known to exist, they hydrolyze acyl-CoA to their respective free FA and coa, it is believed that they may regulat FA content of perox membranes and perox prolif, at this point no info to add transporters or new reactions	NJ
alkylR1oh	hydroxy alkyl chain	Consumed only	Peroxisome	AGPSx	knowledge gap and model scope limitation - when tissue specific models are developed and specific FA of interested are identified, specific pathways (rather than general FA) can be picked and described	NJ
c2m26dcoa	cis-2-Methyl-5-isopropylhexa-2,5-dienoyl-CoA	Consumed only	Peroxisome	C2M26DCOAHLx	model-scope gap: unimportant	SAB
arg-D	D-Arginine	Consumed only	Peroxisome	DARGOp	model-scope gap: relatively unimportant at this stage	SAB
5g2oxpt	5-Guanidino-2-oxopentanoate	Produced only	Peroxisome	DARGOp	model-scope gap: relatively unimportant at this stage	SAB
oaa	Oxaloacetate	Produced only	Peroxisome	DASPO1p	knowledge-based gap	MM
Rtotalcoa	R total Coenzyme A	Consumed only	Peroxisome	DHAPAx	model-scope gap	NJ
dhap	Dihydroxyacetone phosphate	Consumed only	Peroxisome	DHAPAx	DHAPA in cytosol should be complete w/ ADHAPtx	NJ
orn-D	D-Ornithine	Consumed only	Peroxisome	DORNOp	model-scope gap: relatively unimportant at this stage	SAB
5a2opntn	5-Amino-2-oxopentanoate	Produced only	Peroxisome	DORNOp	knowledge-based gap	SAB
pro-D	D-Proline	Consumed only	Peroxisome	DPROOp	model-scope gap: relatively unimportant at this stage	SAb
1p2cbxl	1-Pyrroline-2-carboxylate	Produced only	Peroxisome	DPROOp	model-scope gap: relatively unimportant at this stage	SAB
b2coa	trans-But-2-enoyl-CoA	Produced only	Peroxisome	ECOAH1x	knowledge-base gap: localization is by enzyme similarity	SAB
icit	Isocitrate	Consumed only	Peroxisome	ICDHyp	known gap; the source of intraperoxisomal isocitrate has not been determined [Geisbrecht 1999]	ND
malcoa	Malonyl-CoA	Consumed only	Peroxisome	MCDp	peroxisomal thioesterases are known to exist, they hydrolyze acyl-CoA to their respective free FA and coa, it is believed that they may regulat FA content of perox membranes and perox prolif, at this point no info to add transporters or new reactions	NJ
mmcoa-S	(S)-Methylmalonyl-CoA	Consumed only	Peroxisome	MMCDp	knowledge-based gap	MM
o2s	Superoxide anion	Consumed only	Cytosol	O2Stx	gap removed; added rxn for diffusion of o2s	ND
o2s	Superoxide anion	Consumed only	Peroxisome	O2Stx	gap removed; added rxn for diffusion of o2s	ND
prpncoa	Propenoyl-CoA	Consumed only	Peroxisome	PRPNCOAHYDx	knowledge-base gap	SAB
3hpcoa	3-Hydroxypropionyl-CoA	Produced only	Peroxisome	PRPNCOAHYDx	knowledge-base gap	SAB
hdca	Hexadecanoate (n-C16:0)	Produced only	Peroxisome	PTE2x	peroxisomal thioesterases are known to exist, they hydrolyze acyl-CoA to their respective free FA and coa, it is believed that they may regulat FA content of perox membranes and perox prolif, at this point no info to add transporters or new reactions	NJ
phyt	phytanic acid	Produced only	Peroxisome	PTE4x	PHYTt	NJ
adrn	adrenic acid	Produced only	Peroxisome	PTE5x	peroxisomal thioesterases are known to exist, they hydrolyze acyl-CoA to their respective free FA and coa, it is believed that they may regulat FA content of perox membranes and perox prolif, at this point no info to add transporters or new reactions	NJ
fald	Formaldehyde	Produced only	Peroxisome	SARCOXp	knowledge-based gap	MM

Metabolite Abbreviation	Metabolite Name	Gap Type	Compartment	Reaction Abbreviation	Notes	Reviewer
dmnoncoa	4,8 dimethylnonanoyl-CoA	Consumed only	Cytosol	SCP22x	Will leave gap at present time, sterol carrier protein can move fatty acid derivatives (usually steroid precursors) into different compartments, details about specific substrates and mechanisms not known	NJ
t2m26dcoa	trans-2-Methyl-5-isopropylhexa-2,5-dienoyl-CoA	Consumed only	Peroxisome	T2M26DCOAHLx	knowledge-base gap	SAB