Metabolic Glycoengineering: Sialic Acid and Beyond

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This document provides:

(1) A list of the full names of enzymes mentioned in the main text and the figures therein (in Table S1 on Page S2).

(2) a compilation of analogs that intercept the sialic acid pathway and supporting reference (in Table S2 on Page S4).

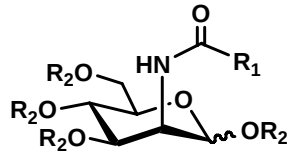
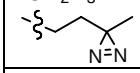
(3) References (on Page S7).

Table S1. Enzymes depicted in the figures and mentioned in the text.

Symbol	Name	EC Number	HGNC ID Number
CMAH	Cytidine monophospho-*N*-acetylneuraminic acid monooxogenase (or CMP-N-acetylneuraminate,NAD(P)H: oxygen oxidoreductase (hydroxylating))	1.14.18.2	2098
CMAS	Cytidine monophospho-*N*-acetylneuraminic acid synthetase	2.7.7.43	18290
CMPNT	CMP-Neu5Ac transporter (the anti-port Golgi transporter)		
DPAGT1	Dolichyl-phosphate (UDP-*N*-acetylglucosamine) *N*-acetylglucosaminephosphotransferase 1 (GlcNAc-1-P transferase)	2.7.8.15	2995
FPGT	Fucose-1-phosphate guanylyltransferase	2.7.7.30	3825
FUK	Fucokinase	2.7.1.52	29500
GALE	UDP-*N*-acetylglucosamine 4-epimerase	5.1.3.2	4116
GALK2	*N*-Acetylgalactosamine 1-kinase; galactokinase 2	2.7.1.157	4119
GALNT	Polypeptide *N*-acetylgalactosaminyltransferase	2.4.1.41	
GNE	Glucosamine (UDP-*N*-acetyl)-2-epimerase/*N*-acetylmannosamine kinase	5.1.3.14/ 2.7.1.60	23657
GNPNAT1	Glucosamine-phosphate *N*-acetyltransferase 1	2.3.1.4	19980
KL	Klotho; β-glucuronidase and putative sialidase (as discussed in (Cha et al. 2008, Kuro-o 2009))	3.2.1.18/ 3.2.1.21	6344
MGAT1	Mannosyl (α1,3-)-glycoprotein β1,2-N-acetylglucosaminyltransferase	2.4.1.101	7044
MGAT2	Mannosyl (α1,6-)-glycoprotein β1,2-N-acetylglucosaminyltransferase	2.4.1.143	7045
MGAT3	Mannosyl (β1,4-)-glycoprotein β1,4-N-acetylglucosaminyltransferase	2.4.1.144	7046
MGAT4A	Mannosyl (α1,3-)-glycoprotein β1,4-N-acetylglucosaminyltransferase, isozyme A	2.4.1.145	7047
MGAT4B	Mannosyl (α1,3-)-glycoprotein β1,4-N-acetylglucosaminyltransferase, isozyme B	2.4.1.145	7048
MGAT4C	Mannosyl (α1,3-)-glycoprotein β1,4-N-acetylglucosaminyltransferase, isozyme C (putative)	2.4.1.145	30871
MGAT5	Mannosyl (α1,6-)-glycoprotein β1,6-N-acetyl-glucosaminyltransferase	2.4.1.155	7049
MGAT5B	Mannosyl (α1,6-)-glycoprotein β1,6-N-acetyl-glucosaminyltransferase, isozyme B	2.4.1.-	24140
NANP	*N*-Acetylneuraminic acid phosphatase	3.1.3.29	16140
NANS	*N*-Acetylneuraminic acid synthase (sialic acid synthase)	2.5.1.57	19237
NEU1	Sialidase 1 (lysosomal sialidase)	3.2.1.18	7758
NEU2	Sialidase 2 (cytosolic sialidase)	3.2.1.18	7759
NEU3	Sialidase 3 (membrane sialidase)	3.2.1.18	7760
NEU4	Sialidase 4	3.2.1.18	21328
OGT	*O*-Linked *N*-acetylglucosamine (GlcNAc) transferase (UDP-*N*-acetylglucosamine:polypeptide-N-acetylglucosaminyl transferase)	2.4.1.94	8127
PGM3	Phosphoacetylglucosamine mutase	5.4.2.3	8907
RENBP	*N*-Acylglucosamine 2-epimerase (renin-binding protein)	5.1.3.8	9959
SAC	Sialic acid cyclase, as proposed by Kannagi and colleagues (Mitsuoka et al. 1999, Kannagi 2002)		

SANAE	*Sialic acid de-N-acetylase (Hanai et al. 1988)*		
ST3GAL1	ST3 β-galactoside α2,3-sialyltransferase 1	2.4.99.4	10862
ST3GAL2	ST3 β-galactoside α2,3-sialyltransferase 2	2.4.99.4	10863
ST3GAL3	ST3 β-galactoside α 2,3-sialyltransferase 3	2.4.99.6	10866
ST3GAL4	ST3 β-galactoside α2,3-sialyltransferase 4	2.4.99.4	10864
ST3GAL5	ST3 β-galactoside α2,3-sialyltransferase 5	2.4.99.9	10872
ST3GAL6	ST3 β-galactoside α2,3-sialyltransferase 6	2.4.99.-	18080
ST6GAL1	ST6 β-galactosamide α2,6-sialyltranferase 1	2.4.99.1	10860
ST6GAL2	ST6 β-galactosamide α2,6-sialyltranferase 2	2.4.99.2	10861
ST6GALNAC1	ST6 (α-*N*-acetyl-neuraminyl-2,3-β-galactosyl-1,3)-*N*-acetylgalactosaminide α2,6-sialyltransferase 1	2.4.99.3	23614
ST6GALNAC2	ST6 (α-*N*-acetylneuraminyl-2,3-β-galactosyl-1,3)-*N*-acetylgalactosaminide α2,6-sialyltransferase 2	2.4.99.7	10867
ST6GALNAC3	ST6 (α-*N*-acetylneuraminyl-2,3-β-galactosyl-1,3)-*N*-acetylgalactosaminide α2,6-sialyltransferase 3	2.4.99.-	19343
ST6GALNAC4	ST6 (α-*N*-acetylneuraminyl-2,3-β-galactosyl-1,3)-*N*-acetylgalactosaminide α2,6-sialyltransferase 4	2.4.99.7	17846
ST6GALNAC5	ST6 (α-*N*-acetylneuraminyl-2,3-β-galactosyl-1,3)-*N*-acetylgalactosaminide α2,6-sialyltransferase 5	2.4.99.-	19342
ST6GALNAC6	ST6 (α-*N*-acetylneuraminyl-2,3-β-galactosyl-1,3)-*N*-acetylgalactosaminide α2,6-sialyltransferase 6	2.4.99.-	23364
ST8SIA1	ST8 α-*N*-acetylneuraminide α2,8-sialyltransferase 1	2.4.99.8	10869
ST8SIA2	ST8 α-*N*-acetylneuraminide α2,8-sialyltransferase 2	2.4.99.-	10870
ST8SIA3	ST8 α-*N*-acetylneuraminide α2,8-sialyltransferase 3	2.4.99.-	14269
ST8SIA4	ST8 α-*N*-acetylneuraminide α2,8-sialyltransferase 4	2.4.99.-	10871
ST8SIA5	ST8 α-*N*-acetylneuraminide α2,8-sialyltransferase 5	2.4.99.-	17827
ST8SIA6	ST8 α-*N*-acetylneuraminide α2,8-sialyltransferase 6	2.4.99.8	23317
UAP1 (AGX1)	UDP-*N*-acteylglucosamine pyrophosphorylase 1	2.7.7.23	12457

Table S2(a). Compilation of representative ManNAc analogs and references.

	**ManNAc Analogs**		
R_1	**R_2**	**Name**	**Reference(s)**
Analogs with alkyl *N*-acyl groups			
$-CH_3$	-H	ManNAc	
$-CH_2CH_3$	-H	ManNProp	(Kayser et al. 1992)
$-(CH_2)_2CH_3$	-H	ManNBut	(Kayser et al. 1992)
$-(CH_2)_3CH_3$	-H	ManNPent	[(Kayser et al. 1992)
$-(CH_2)_4CH_3$	-H	ManNHex	(Goon et al. 2003)
$-(CH_2)_5CH_3$	-H	ManNHept	(Goon et al. 2003)
$-(CH_2)_6CH_3$	-H	ManNOct	(Goon et al. 2003)
$-CH_3$	$-COCH_3$	Ac_4ManNAc	(Jones et al. 2004)
$-CH_2CH_3$	$-COCH_3$	Ac_4ManNProp	(Jacobs et al. 2001, Kim et al. 2004)
$-(CH_2)_2CH_3$	$-COCH_3$	Ac_4ManNBut	(Jacobs et al. 2001, Kim et al. 2004)
$-(CH_2)_3CH_3$	$-COCH_3$	Ac_4ManNPent	(Lemieux et al. 1999)
$-(CH_2)_4CH_3$	$-COCH_3$	Ac_4ManNHex	(Jacobs et al. 2001, Kim et al. 2004)
$-(CH_2)_5CH_3$	$-COCH_3$	Ac_4ManNHept	(Jacobs et al. 2001, Kim et al. 2004)
$-(CH_2)_6CH$	$-COCH_3$	Ac_4ManNOct	(Jacobs et al. 2001)
$-CH_3$	$-COCH_2CH_3$	Pr_4ManNAc	(Kim et al. 2004)
$-CH_3$	$-CO(CH_2)_2CH_3$	Bu_4ManNAc	(Kim et al. 2004, Sampathkumar et al. 2006a)
N-Glycolyl and *N*-thioglycolyl analogs			
$-CH_2OH$	-H	ManNGc	
$-CH_2OH$	$-COCH_3$	Ac_5ManNGc	(Collins et al. 2000, Sampathkumar et al. 2006c)
$-CH_2SCOCH_3$	$-COCH_3$	Ac_5ManNTGc	(Sampathkumar et al. 2006b, Sampathkumar et al. 2006c)
$-(CH_2)_2SCOCH_3$	$-COCH_3$	Ac_5ManNTPr	K.J.Yarema, unpublished
$-(CH_2)_3SCOCH_3$	$-COCH_3$	Ac_5ManNTBu	K.J.Yarema, unpublished
Azide- and diazirine-containing analogs			
$-CH_2N_3$	-H	ManNAz	(Saxon and Bertozzi 2000, Saxon et al. 2002)
$-CH_2N_3$	$-COCH_3$	Ac_4ManNAz	(Saxon and Bertozzi 2000, Saxon et al. 2002)
	$-COCH_3$	Ac_4ManNDAz	(Tanaka and Kohler 2008, Bond et al. 2009)
Ketone-containing analogs			
$-CH_2COCH_3$	-H	-	(Jacobs et al. 2001)
$-CH_2CH_2COCH_3$	-H	ManNLev	(Mahal et al. 1997, Jacobs et al. 2001)
$-CH_2CH_2COCH_2CH_3$	-H	ManNHomoLev	(Kim et al. 2004)
$-CH_2(CH_2)_2COCH_3$	-H	ManNOxoHex	(Kim et al. 2004)
$-CH_2(CH_2)_3COCH_3$	-H	ManNOxoHept	(Kim et al. 2004)
$-CH_2(CH_2)_4COCH_3$	-H	ManNOxoOct	[(Kim et al. 2004)
$-CH_2COCH_3$	$-COCH_3$	-	(Jacobs et al. 2001)
$-CH_2CH_2COCH_3$	$-COCH_3$	Ac_4ManLev	(Lemieux et al. 1999, Jacobs et al. 2001)
$-CH_2CH_2COCH_2CH_3$	$-COCH_3$	Ac_4ManNHomoLev	(Jacobs et al. 2001, Kim et al. 2004)
$-CH_2(CH_2)_2COCH_3$	$-COCH_3$	Ac_4ManNOxoHex	(Jacobs et al. 2001)[(Kim et al. 2004)
$-CH_2(CH_2)_3COCH_3$	$-COCH_3$	Ac_4ManNOxoHept	(Jacobs et al. 2001, Kim et al. 2004)
$CH_2(CH_2)_4COCH_3$	$-COCH_3$	Ac_4ManNOxoOct	(Jacobs et al. 2001, Kim et al. 2004)
$-CH_2CH_2COCH_3$	$-CO(CH_2)_2CH_3$	Bu_4ManNLev	(Aich et al. 2008)
Miscellaneous			
$-CH_2Ph$	-H	ManNPhAc	(Pan et al. 2004, Chefalo et al. 2006)
$-CH(CH_3)_2$	-H	ManNiBu	(Pan et al. 2004, Chefalo et al. 2006)
$-C(CH_3)$	-H	ManNPiv	(Pan et al. 2004, Chefalo et al. 2006)
-Ph	-H	ManNBz	(Pan et al. 2004, Chefalo et al. 2006)
$-CH_2CF_3$	-H	ManNTFP	(Pan et al. 2004, Chefalo et al. 2006)
$-CH(CH_3)CH_2COCH_3$	-H	-	(Jacobs et al. 2001)

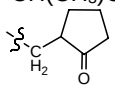
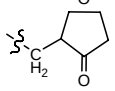
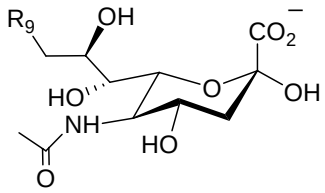
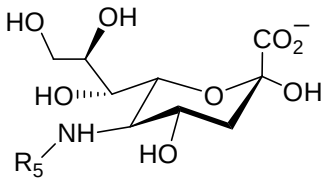
-CH(CH$_3$)CH$_2$COCH$_3$	-COCH$_3$	-	(Jacobs et al. 2001)
	-H	-	(Jacobs et al. 2001)
	-COCH$_3$	-	(Jacobs et al. 2001)
-CH=CHCH$_3$	-H	-	(Keppler et al. 2001)
-CH$_3$CH$_2$CCH (alkyne)	-COCH$_3$	Ac$_4$ManNAlkyne	{Sawa, 2006 #3293}{Hsu, 2007 #3445}

Table 2(b). Compilation of representative Neu5Ac analogs and references.

		**Sialic acid (Neu5Ac) analogs with modified C9OH (i.e., "R_9") groups**
R_9	**Name**	**Reference(s)**
-OH	Neu5Ac	(Oetke et al. 2002)
-H	9-deoxy-Neu5Ac	(Oetke et al. 2002)
-NH$_2$	9-amino-Neu5Ac	(Oetke et al. 2002)
-NHCOCH$_3$	9-acetamido-Neu5Ac	(Oetke et al. 2002)
-NHCOCH$_2$NH$_2$	9-*N*-Gly-Neu5Ac	(Oetke et al. 2002)
-NHCO(CH$_2$)$_2$COOH	9-N-Succ-Neu5Ac	(Oetke et al. 2002)
-I	9-Iodo-Neu5Ac	(Oetke et al. 2002)
-SH	9-Thio-Neu5Ac	(Oetke et al. 2002)
-SCH$_3$	9-SCH$_3$-Neu5Ac	(Oetke et al. 2002)
-SO$_2$CH$_3$	9-SO$_2$CH$_3$-Neu5Ac	(Oetke et al. 2002)
-NHCOPhN$_3$	9-AAz-Neu5Ac	(Han et al. 2005)
		**Sialic acid (Neu5Ac) analogs with modified *N*-acyl (i.e., "R_5") groups**
R_5	**Name**	**Reference(s)**
-COCH$_3$	Neu5Ac	
-COCH$_2$F	5-N-Fluoroac-Neu	(Oetke et al. 2002)
-COCF$_3$	5-N-Trifluoroac-Neu	(Oetke et al. 2002)
-COCH$_2$NH$_2$	5-N-Gly-Neu	(Oetke et al. 2002)
-CO(CH$_2$)$_2$COOH	5-N-Succ-Neu	(Oetke et al. 2002)
-CSCH$_3$	5-N-thioac-Neu	(Oetke et al. 2002)
-CO(CH$_2$)$_2$COCH$_3$	Sia5Lev	(Chefalo et al. 2004)
-CO(CH$_2$)$_3$COCH$_3$	Sia5OxoHex	(Chefalo et al. 2004)
-CO(CH$_2$)$_4$COCH$_3$	Sia5OxoHept	(Chefalo et al. 2004)
-COCH$_2$N$_3$	Sia5Az	(Chefalo et al. 2004)
-COCH$_2$PhN$_3$	Sia5PhAz	(Chefalo et al. 2004)
-COCH$_2$OH	Neu5Gc	(Bardor et al. 2005, Tangvoranuntakul et al. 2003)
-COCH$_2$PhN$_3$	Sia5AAz	{Tanaka, 2008 #4238}

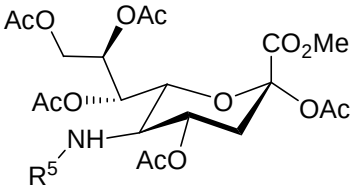
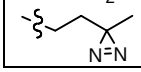
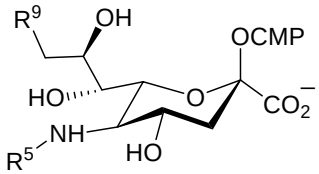
$-COCH_2CH_3$	Sia5Prop	(Goon et al. 2003)
$-CO(CH_2)_2CH_3$	Sia5But	(Goon et al. 2003)
$-CO(CH_2)_3CH_3$	Sia5Pent	(Goon et al. 2003)
$-CO(CH_2)_4CH_3$	Sia5Hex	(Goon et al. 2003)
$-CO(CH_2)_5CH_3$	Sia5Hept	(Goon et al. 2003)
$-CO(CH_2)_6CH_3$	Sia5Oct	(Goon et al. 2003)
		**Peracetylated, methylated sialic acid analogs with modified *N*-acyl (i.e., "R_5") groups**
R_5	**Name**	**Reference(s)**
$-COCH_3$	Ac_5Neu5Ac	(Luchansky et al. 2004)
$-COCH_2COCH_3$	-	(Luchansky et al. 2004)
$-CO(CH_2)_2COCH_3$	Ac_5Sia5Lev	(Luchansky et al. 2004)
$-CO(CH_2)_3COCH_3$	Ac_5Sia5OxoHex	(Luchansky et al. 2004)
$-COCH_2N_3$	Ac_5Sia5Az	(Luchansky et al. 2004)
$-COCH_2PhN_3$	Ac_5Sia5AAz	(Luchansky et al. 2004)
	Ac_5Sia5DAz	(Tanaka and Kohler 2008, Bond et al. 2009)

Table 2(c). CMP-sialic acid analogues used in MOE

		**CMP-Sialic acid Analogs**	
R_9	**R_5**	**Name**	**Ref**
$-N_3$	$-COCH_3$	CMP-9-azido-Sia5Ac	(Kosa and Gross 1993)
$-NH_3^+$	$-COCH_3$	CMP-9-amino-Sia5Ac	(Kosa and Gross 1993, Gross et al. 1989)
-NHAc	$-COCH_3$	CMP-9-acetamido-Sia5Ac	(Kosa and Gross 1993, Gross et al. 1989)
$-NHCSCH_3$	$-COCH_3$	CMP-9-thioacetamidoSia5Ac	(Brossmer and Gross 1994, Gross et al. 1989)
-NHCOPh	$-COCH_3$	CMP-9-benzamidoSia5Ac	(Brossmer and Gross 1994)
N-fluoresceinyl) thioureide	$-COCH_3$	CMP-9-deoxy-9-*N*-*N*-fluoresceinyl) thioureido-Sia5Ac	
$-NHCO(CH_2)_4CH_3$	$-COCH_3$	CMP-9-hexanoylamidoSia5Ac	(Gross et al. 1989)
-OH	$-COCH_2NH_3$	CMP-5-*N*- aminoacetylNeu5Ac	(Brossmer and Gross 1994)
-OH	$-CSCH_3$	CMP-5-*N*-thioacetylSia5Ac	(Brossmer and Gross 1994)
-OH	-CHO	CMP-5-*N*-formylSia5Ac	(Brossmer and Gross 1994)

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