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Abstract

3,3'-Neotrehalosdiamine (NTD) is a diaminosugar that possesses a rare α,β -1,1'-linked glycosidic bond and has been reported to possess antimicrobial activity against *Staphylococcus aureus*. The *ntdABC* operon contains three structural genes that are necessary for the production of NTD in certain mutants of *Bacillus subtilis*. The gene predicted to be the first in the NTD biosynthetic pathway, *ntdC*, was subcloned into pET-28b as the hexa-histidine tagged fusion. The gene product was expressed, purified to homogeneity, and found to be an NAD⁺-dependent glucose 6-phosphate 3-dehydrogenase, likely operating according to a ternary complex mechanism and possessing a catalytic dyad composed by D176 and H180. The advent of this knowledge suggests that additional genes are required for the biosynthesis of NTD aside from the three encoded by the *ntdABC* operon.

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Dedication

*To the love of my life,
Jae-Eun Kim*

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List of Abbreviations

<i>A. mediterranei</i>	<i>Amycolatopsis mediterranei</i>
Ac	Acetyl
Ac ₂ O	Acetic anhydride
AcOH	Acetic acid
AFR	1,5-Anhydro-D-fructose reductase
AHBA	<i>3-amino-5-hydroxybenzoic acid</i>
AMP	2-amino-2-methyl-1-propanol
AMP·HCl	2-amino-2-methyl-1-propanol titrated with hydrochloric acid
ATP	Adenosine triphosphate
<i>B. circulans</i>	<i>Bacillus circulans</i>
<i>B. pumilis</i>	<i>Bacillus pumilis</i>
<i>B. subtilis</i>	<i>Bacillus subtilis</i>
BLAST	Basic local alignment search tool
Bn	Benzyl
BnBr	Benzyl bromide
bp	Base pair
Bz	Benzoyl
dATP	Deoxyadenosine triphosphate
DCM	Dichloromethane
dCTP	Deoxycytidine triphosphate
dGTP	Deoxyguanosine triphosphate
DMAP	Dimethylaminopyridine
DMF	<i>N,N</i> -Dimethylformamide

DNA	Deoxyribonucleic acid
dNTP	deoxynucleoside phosphate
dTDP	Deoxythymidine diphosphate
dTTP	Deoxythymidine triphosphate
<i>E. Coli</i>	<i>Escherichia coli</i>
EDTA	Ethylenediaminetetraacetic acid
<i>EMBOSS</i>	European molecular biology open software suite
<i>et al.</i>	<i>et alli</i> (and others)
EtOH	Ethanol
G6P	Glucose 6-phosphate
GFOR	Glucose-fructose oxidoreductase
Glucose-PTS	Glucose-specific phosphoenolpyruvate-dependent phosphotransferase system
HAD	Haloacid dehalogenase
IDH	<i>myo</i> -Inositol dehydrogenase
IPTG	Isopropyl- β -D-1-thiogalcopyranoside
<i>J</i>	Coupling constant
K6P	Kanosamine 6-phosphate
kbp	Kilobase pair
LB	Luria broth
LDH	Lactate dehydrogenase
MeOH	Methanol
MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
NAD ⁺	Nicotinamide adenine dinucleotide (oxidized form)
NADH	Nicotinamide adenine dinucleotide (reduced form)
NADP ⁺	Nicotinamide adenine dinucleotide phosphate (oxidized form)

NADPH	Nicotinamide adenine dinucleotide phosphate (reduced form)
NaOMe	Sodium methoxide
<i>N</i> -Boc	<i>N</i> - <i>t</i> -Butoxycarbonyl
NBS	<i>N</i> -Bromosuccinimide
NDP	Nucleoside diphosphate
NEB	New England Biolabs
NMR	Nuclear magnetic resonance
NTD	3,3'-Neotrehalosdiamine
OD	Optical density
PCR	Polymerase chain reaction
Pd/C	10% Palladium on carbon
PDC	Pyridinium dichromate
pH	The negative logarithm of the concentration of protons in an aqueous solution
Ph	Phenyl
pK _a	The negative logarithm of the dissociation constant of an acid
pK _b	The negative logarithm of the equilibrium constant of a base
PLP	Pyridoxal phosphate
PMP	Pyridoxamine phosphate
PP _i	Inorganic pyrophosphate
<i>S. aureus</i>	<i>Staphylococcus aureus</i>
S6PP	Sucrose 6-phosphate phosphatase
S _N 1	Unimolecular nucleophilic substitution
S _N 2	Bimolecular nucleophilic substitution
T6PP	Trehalose 6-phosphate phosphatase
TAE	Tris-acetate-EDTA

TBDMS	<i>t</i> -Butyl-dimethylsilyl
^t BDMSCl	<i>t</i> -Butyl-dimethylsilyl chloride
^t Boc ₂ O	Di- <i>t</i> -butyl dicarbonate
TDP	Thymidine diphosphate
Tf	Trifyl
Tf ₂ O	Triflic anhydride
THF	Tetrahydrofuran
Tris	Tris(hydroxymethyl)aminomethane
Tris·HCl	Tris(hydroxymethyl)aminomethane titrated with hydrochloric acid
Ts	Tosyl (p-toluenesulfonyl)
TsCl	Tosyl chloride
UDP	Uridine diphosphate
UV	Ultraviolet
VISA	Vancomycin-intermediate <i>Staphylococcus aureus</i>
VRSA	Vancomycin-resistant <i>Staphylococcus aureus</i>