



SINGULA™
PRECISION MEDICINE

Clinical ID: XYZ-98765

Cellworks ID: 999999

Ref Physician: Dr.John

Biopsy Sequence: 1

Gender/Age: - / -

Date of Report: 06th Aug 2018

Indication: Myelodysplastic Syndrome(MDS)

1. Drug Response Prediction

Therapies of Interest	Patient Predicted Response
AZACITIDINE	Responder
DECITABINE	Responder
LENALIDOMIDE	Non-Responder

*For more details of actionable molecular target(s) and pathway(s), please check this [link](#).

2. Patient Disease Characteristics: Key Biomarker(s)

PARP1	AURKB
CHEK2	TP53
CHEK1	PPARG
CSNK2A1	
MYC	

*For more details on selected biomarker(s) and its impact on patient's disease profile, please check this [link](#).

3. Biomarker Impact Score

Therapies of Interest	Patient Biomarker Characteristics								Biomarker Impact Score
	PARP1	CHEK2	CHEK1	CSNK2A1	MYC	AURKB	TP53	PPARG	
AZACITIDINE	✓			✓	✓	✓	✓		5 / 8
DECITABINE	✓			✓	✓	✓	✓		5 / 8
LENALIDOMIDE	✓				✓	✓			3 / 8

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4. Summary of Patient Genomic Profile

Input Data Type	Mutations, CNV and Cytogenetics
Genetic Mutation(s)	5
Copy Number Variation(s)	373
Gene(s) Methylated	0

4.1 Detailed Information of Genomic Aberration(s) Modeled

4.1.1 Gene Mutation(s) with Gain of Function

NCOR1	PTPN11	TCF7L2
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4.1.2 Gene Mutation(s) with Loss of Function

KMT2C	MSH6
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4.1.3 Gene(s) with Increase in Copy Number Variation [CNV]

ABHD12	ABHD16A	ACSS1	ADRM1	AGER	ALG12	ANGPT1	ANGPT2
ARHGAP8	ASAHI	ASH2L	ATP6V1H	BAALC	BAG4	BIK	BLK
CCNE2	CDC25B	CEBPD	CERK	CHKB	CLU	CNOT7	COPS5
CSGALNACT1	CSNK2A1	CSNK2B	CTSB	CYP7A1	DDR1	DDX39B	DEPTOR
DERL1	DGATI	DHX16	DLC1	DPYS	E2F5	EGR3	EHMT2
EIF3E	EIF3H	EIF4EBP1	ELP3	EPHX2	ESRP1	EYA1	FABP5
FBXO32	FBXO43	FDFT1	FGFR1	FKBP1A	FKBPL	FNTA	FOXA2
GATA4	GFRA2	GFRA4	GGH	GPT	GSR	GTSE1	GZF1
HAS2	HDAC10	HEY1	HSF1	ID1	IDH3B	IDO1	IDO2
IKBKB	IL7	JAG1	KAT6A	LAMA5	LOXL2	LPL	LTA



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LTB	LY96	LYN	LYPLA1	MAPK11	MAPK12	MAVS	MCM4
MDC1	MICA	MICB	MMP16	MTDH	MYC	NBN	NCOA2
NDRG1	NEIL2	NOTCH4	NRG1	NSFL1C	NSMAF	NUDT18	OPLAH
PAG1	PBK	PCNA	PDLIM2	PDP1	PIM3	PLAT	PLCB1
PLXNB2	POLB	POU5F1	PPARA	PPP2R2A	PREX2	PRKDC	PRNP
PRR5	PSMA7	PTDSS1	PTK2	PTK2B	PTP4A3	RAB2A	RAD21
RALGAPA2	RASSF2	RB1CC1	RBCK1	RGS19	RIPK2	RRM2B	RUNX1T1
SCO2	SCRIB	SDC2	SFRP1	SFTPC	SGK3	SIRPA	SLC23A2
SLC25A32	SLC2A4RG	SNAI2	SNAP25	SPTLC3	SQLE	SRXN1	ST3GAL1
STK3	TASP1	TCEA1	TNF	TNFRSF10A	TNFRSF10B	TNFRSF10C	TNFRSF10D
TNFRSF11B	TRIB3	TRIM26	TYMP	UBR5	WNT7B	WRN	XKR4
XKR9	YWHAZ	ZDHHC2	ZFPM2	ZNF703			

4.1.4 Gene(s) with Decrease in Copy Number Variation [CNV]

ABCB1	ABCB5	ACSS2	ACTB	ADA	ADCY1	ADCYAPIR1	AHCY
AHR	AKAP9	AKR1B10	ARPC1A	ASB4	ASL	ASNS	ATG9B
AURKA	B4GALT5	BAZ1B	BCL7B	BHLHA15	BLVRA	BRAF	CAMK2B
CARD11	CASP2	CAV1	CCL26	CD36	CD40	CDK5	CDK6
CEBPB	CHN2	CLDN4	CNOT4	COL1A2	COPS6	CREB3L2	CUL1
CUX1	CYCS	CYP24A1	CYP51A1	DAGLB	DBF4	DDC	DGKB
DGKI	DMTF1	DNAJB6	DNAJB9	DNMT3B	DOCK4	DSN1	E2F1
EGFR	EIF2S2	EIF3B	ELMO1	ELMO2	EPB41L1	EPHA1	EPHB4
EPHB6	EPO	ETV1	EXOC4	EZH2	FSCN1	FZD1	FZD9
GGCT	GGT7	GLI3	GRB10	GSS	GSTK1	GTF2I	HBP1
HDAC9	HGF	HIPK2	HNF4A	HNRNPA2B1	HOXA1	HOXA10	HOXA11



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HOXA13	HOXA3	HOXA5	HOXA7	HOXA9	HSPB1	HTR5A	HUS1
IGFBP1	IGFBP3	IKZF1	IL6	IMPDH1	INSIG1	ITCH	ITGB8
L3MBTL1	LAMB1	LBP	LEP	LIMK1	MAD1L1	MAFB	MAFK
MAGI2	MCM7	MDH2	MET	MIOS	MIR182	MIR29A	MIR29B1
MLXIPL	MMP9	MNX1	MYBL2	NAMPT	NCF1	NCOA3	NCOA6
NDRG3	NFATC2	NOS3	NRF1	NUDT1	NUP205	OGDH	PAXIP1
PDGFA	PDIA4	PDK4	PHF20	PIK3CG	PLCG1	PMS2	PODXL
POLD2	POLM	PPP1R3A	PREX1	PRSS1	PSMA2	PSMC2	PSMG3
PSPH	PTGIS	PTN	PTPN1	PTPRZ1	RAC1	RALA	RASA4
RBL1	RHEB	RPA3	SAMHD1	SDC4	SEC61G	SEMA3E	SERPINE1
SFRP4	SH2B2	SHH	SLA2	SLC29A4	SMO	SMURF1	SNAI1
SNX13	SRC	SRPK2	STEAP1	STEAP4	STK4	STX1A	TBXAS1
TFPI2	TOP1	TRIM24	TWIST1	UBE3C	UPP1	USP42	VIPR2
WASL	WEE2	WIPI2	WISP2	XRCC2	ZC3HC1	ZDHHC4	ZNF217



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5. Therapy Rationale(s)

Rationales provided in this section highlight the pathways connected to drug sensitivity and resistance and include references to supporting published literature.

Species in **red** denote drug impact points. Species highlighted in **blue** are the key biomarkers.

STATUS: **GOF:** Gain of Function Mutations; **LOF:** Loss of Function Mutations; **SOF:** Switch of Function Mutations; **AMP:** CNV Over-expression; **DEL:** CNV Knock-down;

TYPE: **R:** Resistant Gene/Loop for the Drug; **S:** Sensitive Gene/Loop for the Drug

AZACITIDINE				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
L3MBTL1	DEL	S	AZACITIDINE — DNMT1	12154409 23671287 17540172 16357870 14532106 15824892 19363521 28928282 17015478 22024163
			L3MBTL1 — E2F1 —> EZH2 —> DNMT1 —> CPGMET	
			— TP53 — CANCER PROGRESSION	
			L3MBTL1 — E2F1 —> EZH2 —> DNMT1 —> CPGMET	
			— CDKN1A — CSNK2A1 —> API —> CTNNB1 —>	
			CANCER PROGRESSION	
KAT6A	AMP	S	AZACITIDINE — DNMT1 —> CPGMET	25772242 12154409 23671287 16357870 19363521 28928282 17015478 22024163 15824892
			KAT6A —> EZH2 —> DNMT1 —> CPGMET — TP53	
			— CANCER PROGRESSION	
			KAT6A —> EZH2 —> DNMT1 —> CPGMET — CDKN1A	
			— CSNK2A1 —> API —> CTNNB1 —> CANCER	
			PROGRESSION	
L3MBTL1	DEL	S	L3MBTL1 — E2F1 —> EZH2 —> DNMT1 —> CPGMET	19363521 28928282 17015478 22024163
			— DUSP6 — MAPK1 —> MYC —> CANCER	
			PROGRESSION	
			L3MBTL1 — E2F1 —> EZH2 —> DNMT1 —> CHEK1	
			—> AURKB —> SP1 —> CANCER PROGRESSION	
			PROGRESSION	
KAT6A	AMP	S	AZACITIDINE — DNMT1 —> CPGMET	25772242 12154409 23671287 16357870 19363521 28928282 17015478 22024163 15824892
			KAT6A —> EZH2 —> DNMT1 —> CPGMET — TP53	
			— CANCER PROGRESSION	
			KAT6A —> EZH2 —> DNMT1 —> CPGMET — CDKN1A	
			— CSNK2A1 —> API —> CTNNB1 —> CANCER	
			PROGRESSION	
KAT6A	AMP	S	KAT6A —> EZH2 —> DNMT1 —> CPGMET — DUSP6	17015478 22024163 15824892
			— MAPK1 —> MYC —> CANCER PROGRESSION	
			PROGRESSION	
			KAT6A —> EZH2 —> DNMT1 —> CHEK1 —> AURKB	
			—> SP1 —> CANCER PROGRESSION	
			PROGRESSION	



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Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
EZH2	DEL	R	<p>AZACITIDINE — DNMT1 —> CPGMET</p> <p>EZH2 —> DNMT1 —> CPGMET — TP53 — CANCER PROGRESSION</p> <p>EZH2 —> DNMT1 —> CPGMET — CDKN1A — CSNK2A1</p> <p>—> API —> CTNNB1 —> CANCER PROGRESSION</p> <p>EZH2 —> DNMT1 —> CPGMET — DUSP6 — MAPK1</p> <p>—> MYC —> CANCER PROGRESSION</p> <p>EZH2 —> DNMT1 —> CHEK1 —> AURKB —> SP1 —> CANCER PROGRESSION</p>	<p>12579297 12154409</p> <p>16357870 19363521</p> <p>28928282 17015478</p> <p>22024163 15824892</p>
GGH	AMP	R	<p>AZACITIDINE — DNMT1 —> CPGMET</p> <p>GGH — S ADENOSYL METHIONINE —> CPGMET — TP53 — CANCER PROGRESSION</p> <p>GGH — S ADENOSYL METHIONINE —> CPGMET — </p> <p>CDKN1A — CSNK2A1 —> API —> CTNNB1 —> CANCER PROGRESSION</p> <p>GGH — S ADENOSYL METHIONINE —> CPGMET — </p> <p>DUSP6 — MAPK1 —> MYC —> CANCER PROGRESSION</p>	<p>12154409 23671287</p> <p>25502219 25224413</p> <p>19363521 28928282</p>



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DECITABINE				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
L3MBTL1	DEL	S	<p>DECITABINE — DNMT1</p> <p>L3MBTL1 — E2F1 —> EZH2 —> DNMT1 —> CPGMET</p> <p>— TP53 — CANCER PROGRESSION</p> <p>L3MBTL1 — E2F1 —> EZH2 —> DNMT1 —> CPGMET</p> <p>— CDKN1A — CSNK2A1 —> API —> CTNNB1 —></p> <p>CANCER PROGRESSION</p> <p>L3MBTL1 — E2F1 —> EZH2 —> DNMT1 —> CPGMET</p> <p>— DUSP6 — MAPK1 —> MYC —> CANCER</p> <p>PROGRESSION</p> <p>L3MBTL1 — E2F1 —> EZH2 —> DNMT1 —> CHEK1</p> <p>—> AURKB —> SPI —> CANCER PROGRESSION</p>	12154409 23671287 17540172 16357870 14532106 15824892 19363521 28928282 17015478 22024163
KAT6A	AMP	S	<p>DECITABINE — DNMT1 —> CPGMET</p> <p>KAT6A —> EZH2 —> DNMT1 —> CPGMET — TP53</p> <p>— CANCER PROGRESSION</p> <p>KAT6A —> EZH2 —> DNMT1 —> CPGMET — CDKN1A</p> <p>— CSNK2A1 —> API —> CTNNB1 —> CANCER</p> <p>PROGRESSION</p> <p>KAT6A —> EZH2 —> DNMT1 —> CPGMET — DUSP6</p> <p>— MAPK1 —> MYC —> CANCER PROGRESSION</p> <p>KAT6A —> EZH2 —> DNMT1 —> CHEK1 —> AURKB</p> <p>—> SPI —> CANCER PROGRESSION</p>	25772242 12154409 23671287 16357870 19363521 28928282 17015478 22024163 15824892
EZH2	DEL	R	<p>DECITABINE — DNMT1 —> CPGMET</p> <p>EZH2 —> DNMT1 —> CPGMET — TP53 — CANCER</p> <p>PROGRESSION</p> <p>EZH2 —> DNMT1 —> CPGMET — CDKN1A — CSNK2A1</p> <p>—> API —> CTNNB1 —> CANCER PROGRESSION</p> <p>EZH2 —> DNMT1 —> CPGMET — DUSP6 — MAPK1</p> <p>—> MYC —> CANCER PROGRESSION</p> <p>EZH2 —> DNMT1 —> CHEK1 —> AURKB —> SPI —></p> <p>CANCER PROGRESSION</p>	12579297 12154409 16357870 19363521 28928282 17015478 22024163 15824892



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DECITABINE				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
GGH	AMP	R	DECITABINE — DNMT1 —> CPGMET	12154409 23671287 25502219 25224413 19363521 28928282
			GGH — S ADENOSYL METHIONINE —> CPGMET — TP53 — CANCER PROGRESSION	
			GGH — S ADENOSYL METHIONINE —> CPGMET — CDKN1A — CSNK2A1 —> AP1 —> CTNNB1 —> CANCER PROGRESSION	
			GGH — S ADENOSYL METHIONINE —> CPGMET — DUSP6 — MAPK1 —> MYC —> CANCER PROGRESSION	



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LENALIDOMIDE				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
IKZF1	DEL	R	<p>LENALIDOMIDE → CUL4-CRBN-DDB1-RBX1 — IKZF1</p> <p>IKZF1 → IRF4 → CARD11 → BCL10 → MALTI →</p> <p>CHUK_IKBKB → NFKB1 → CANCER PROGRESSION</p>	24292625 22698399 25043012 24914135 24292625
MYC	AMP	S	<p>LENALIDOMIDE → CUL4-CRBN-DDB1-RBX1 — IKZF1/3</p> <p>→ IRF4</p> <p>MYC → IRF4 — IRF7 → IFNA → TYK2 → STAT1</p> <p>→ CDKN1A — CANCER PROGRESSION</p>	18568025 25610725 10910100 22698399 25108355 25043012 24914135



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6. Genomic Aberration to Key Biomarker Pathway(s)

This section provides a snapshot of paths connecting the most significant gene aberrations with patient biomarkers and references to published research supporting these pathways.

RED: Gain of Function/Switch of Function Mutation(s) or Amplified Gene(s)

BLUE: Loss of Function Mutation(s) or Deleted Gene(s)

TRANSCRIPTION FACTORS:

Key Biomarker(s)	Molecular Pathway Rationale for Biomarker(s)	Reference PMID(s)
MYC		10373534 10550055 10783165 10866324 11255227 12149649 14701743 18438430 22319212 22850745 25101980 2663470 9788437
		17540172
		28729862
TP53		10373534 10550055 10783165 10866324 14701743 19377469 22319212 9582019
		19433796 22034226
PPARG		10373534 10550055 10783165 10866324 11255227 12479814 14701743 15832170 16127449 22319212 22850745 25101980 9030579
		16029943



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KINASE**:

Key Biomarker(s)	Molecular Pathway Rationale for Biomarker(s)	Reference PMID(s)
CSNK2A1	CUX1 → ATM → BRCA1 → CDKN1A — CSNK2A1	10373534 10550055 10783165 10866324 11255227 14701743 22319212 22850745 25101980
AURKB	CUX1 → ATM → BRCA1 → CDKN1A — CSNK2A1 → HDAC3 → AURKB	10373534 10550055 10783165 10866324 11255227 14701743 19287963 22319212 22751009 22850745 25101980

** Assayable key kinase biomarkers identified for this patient.



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7. Terms of Usage

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Therapeutic agents associated with potential benefit or lack of benefit, as indicated in the Test Report are based on biomarker results provided in the report and on published evidence with PMID references. This evidence in some cases may have been obtained from studies performed in the cancer type present in the tested patient's sample.

No Guarantee of Clinical Benefit

The finding of a biomarker expression does not necessarily indicate pharmacologic effectiveness or lack thereof. The agents identified may or may not be suitable for use with a particular patient and the Test Report does not guarantee or suggest that any particular agent will be effective with the treatment of any particular condition. The user of this Test Report remains responsible for the conduct of patient care and for evaluating the clinical relevance of information provided by the prediction software.

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