MS-MLPA Test

Patient Name:	DUMMY	CRM ID:	NA
Age/DOB:	NA	Sample Type:	EDTA Blood
Sex:	NA	Sample Collected:	DD-MM-YYYY
Referring Clinician:	NA	Sample Received:	DD-MM-YYYY
Test Requested:	MS-MLPA RSS	Report Released:	DD-MM-YYYY

Russell - Silver Syndrome deletion/duplication and methylation analysis by MLPA

CLINICAL DIAGNOSIS/SYMPTOMS

NA

RESULTS

- **No microdeletion and duplication is detected in 11p15 chromosomal region associated with Russell - Silver Syndrome.**

Sr. No.	Gene	Location	Deletion/Duplication	Final Ratio (FR)	Reference
1	*NSD1*	Exon 21 & 23	No deletion and duplication	~1	0.80<FR<1.20
2	*H19*	Exon 5 & Upstream	No deletion and duplication	~1	0.80<FR<1.20
3	*IGF2*	Exon8	No deletion and duplication	1	0.80<FR<1.20
4	*KCNQ1*	Exon 2, 3, 7, 8, 9, 13, 15 & 17	No deletion and duplication	~1	0.80<FR<1.20
5	*CDKN1C*	Exon1 & 3	No deletion and duplication	~1	0.80<FR<1.20

- **Normal methylation pattern is observed in IC2(KvDMR) and IC1(H19 DMR) domains in the 11p15 chromosomal region. Hence, No imprinting abnormalities is detected in IC2 and IC1 domains as compared to Normal control sample.**

Sr. No.	Gene	Location	Methylation Status	Results	Final Ratio (FR)	Reference
1	*H19(301nt)*	H19DMR/IC1	50% Methylated	Normal	0.43	0.4≤FR≤0.65
2	*H19(238nt)*	H19DMR/IC1	50% Methylated	Normal	0.45	0.4≤FR≤0.65
3	*H19(184nt)*	H19DMR/IC1	50% Methylated	Normal	0.54	0.4≤FR≤0.65
4	H19(135nt)	H19DMR/IC1	50% Methylated	Normal	0.52	0.4≤FR≤0.65
5	*IFG2(172nt)*	Exon 4	Unmethylated	Normal	0	FR<0.05
6	*KCNQ1OT1(274nt)*	KvDMR/IC2	50% Methylated	Normal	0.49	0.4≤FR≤0.65
7	*KCNQ1OT1(166nt)*	KvDMR/IC2	50% Methylated	Normal	0.5	0.4≤FR≤0.65
8	*KCNQ1OT1(393nt)*	KvDMR/IC2	50% Methylated	Normal	0.5	0.4≤FR≤0.65
9	*KCNQ1OT1(141nt)*	KvDMR/IC2	50% Methylated	Normal	0.54	0.4≤FR≤0.65
10	*CDKN1C(346nt)*	Exon 1	10% Methylated	Normal	0.11	FR<0.16
11	*ESCO2(355nt)*	Exon 1	Unmethylated	Normal	0	FR<0.05

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Name: DUMMY CRM ID : NA Date:DD-MM-YYYY

INTERPRETATION

No microdeletions and imprinting abnormalities is detected in the IC2(KvDMR) and IC1(H19DMR) domains in the 11p15 chromosomal region associated with Russell-Silver Syndrome in Kamal Noor Kaur. Sample from Kamal Noor Kaur was referred to our laboratory for molecular testing for Russell- Silver Syndrome. Russell-Silver syndrome caused by uniparental disomy (UPD), trisomy 11p15, mutations in the CDKN1C gene and maternal UPD for chromosome 7.

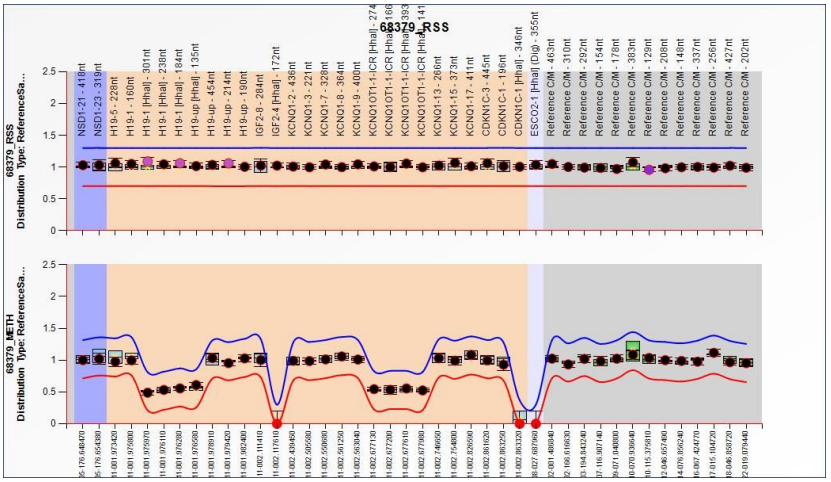

Fig-1: 7585324/MD068379_Kamal Noor Kaur RATIO CHART:ME030Probemix

Comment: The result must be interpreted in the context of the individual's clinical and biochemical profile.

Genetic counselling is advised.

METHODOLOGY

Mutational analysis has been performed on genomic DNA by Methylation-Specific Multiplex ligation probe dependent amplification (MS-MLPA, MRC Holland) using SALSA MLPA probe mix ME030, SALSA Hha 1, EKFAM kit for *BWS/RSS* (OMIM#180860).
Analysis was done by Coffalyser (designed by MRC-Holland) .

DISCLAIMER

- Methylation variants and copy number variations (CNVs) discovered by many sequential ME030 Russell - Silver probes should be verified using a separate method. Particularly, CNVs discovered by a single probe always need to be confirmed by an additional technique.
- The MLPA test will not detect the point mutations in the 11p15 chromosomal region. It is therefore recommended to use MLPA in combination with sequence analysis. Thus, it is advised to employ this SALSA MLPA probemix in conjunction with a sequence analysis of the H19 and KCNQ1OT1 genes to diagnose Russell - Silver Syndrome.
- A point mutation or polymorphism in the sequence detected by a probe, which results in reduced probe binding efficiency, can also cause a reduction in relative peak area. Therefore, single exon deletions detected by MLPA should always be confirmed by other methods like multiplex PCR or sequencing.
- MLPA cannot detect any changes that lie outside the target sequence of the probes and will not detect most inversions or translocations. Even when MLPA did not detect any aberrations, the possibility remains that biological change in that gene or chromosomal region do exist but remain undetected.

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References:

- Priolo, M., Sparago, A., Mammì, C., Cerrato, F., Lagana, C., & Riccio, A. (2008). MS-MLPA is a specific and sensitive technique for detecting all chromosome 11p15. 5 imprinting defects of BWS and SRS in a single-tube experiment. European journal of human genetics, 16(5), 565-571.
- Lukova, M., Todorova, A., Todorov, T., & Mitev, V. (2013). Different methylation patterns in BWS/SRS cases clarified byMS-MLPA. *Molecular biology reports*, *40*, 263-268.
- Scott, R. H., Douglas, J., Baskcomb, L., Nygren, A. O., Birch, J. M., Cole, T. R., ... & Rahman, N. (2008). Methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA) robustly detects and distinguishes 11p15 abnormalities associated with overgrowth and growth retardation. *Journal of Medical Genetics*, *45*(2), 106-113.
- https://support.mrcholland.com/downloads/files/1

#this test is not under NABL scope.

Disclaimer: Method given in report are only indicative and can be changed depending upon type of machine and kit available at time of testing.

Not all tests at all locations are under NABL scope. Availability of tests under NABL scope varies from lab to lab.

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