ESPE 2015 P3-1255：Analysis of gene methylation difference and evaluation the effect of growth hormone in Silver Russell syndrome

北京儿童医院
BEIJING CHILDREN'S HOSPITAL

Di Wu, Chunxiu Gong*, Yang Zhao, Chang Su, Bingyan Cao

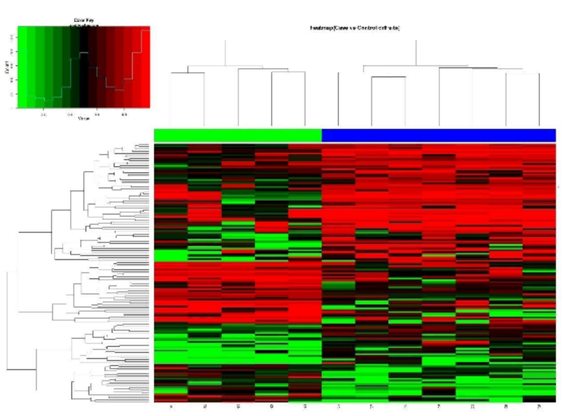
Departments of Endocrinology, Genetics, and Metabolism, Beijing Children's Hospital, Capital Medical University, Beijing 100045, China

OBJECTIVES

To determine novel gene or imprinted gene associated with pathogenicity of SRS through detection genome-wide methylation differences. To observe growth hormone (GH) efficacy in Silver-Russell syndrome (SRS) and the relationship between GH and epigenetic changes.

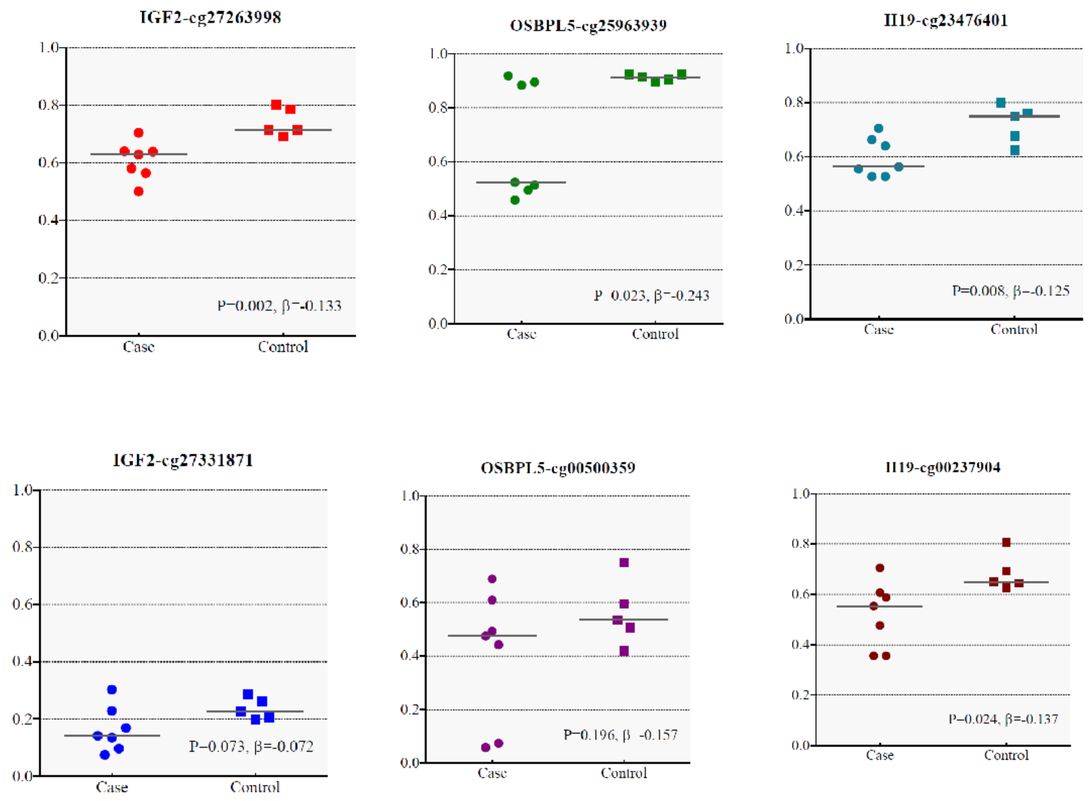
METHODS

To detect genome-wide methylation site through the Illumina 450K methylation chip in 7 SRS and 5 controls matched age. Other 10 cases of SRS were analyzed GH efficacy.



The experimental group *vs* control group methylation sites clustering image

Comparison of IGF2, OSBPL5 and H19 methylation difference in experimental group and control group



RESULTS

Imprinted gene OSBPL5 has the most significant methylation difference site in case group and normal control group (P= 0.023,β= -0.243). And the gene is located on 11p15-4 5 'UTR, it is quite possible pathogenic. Five important genes were found might related with SRS: TGFβ3, GAP43, HSF1, NOTCH4 and MYH14.

10 SRS with GH treatment, the average follow-up period was 13.2 months.
The average GH dosages was 0.15 IU/kg.d.
Growth velocity (GV) was 9.53 + 3.918 cm/y. which was higher than normal children's GV (5cm/y), P=0.005.

5 out of 10 cases did epigenetic detection.
One patient was matUPD (7) positive and his GV was 11.13cm/y.
Two patients were 11p15 ICR1 hypomethylation and their GV were 8cm/y, 9.141cm/y, respectively.
The other two cases were not found in epigenetic changes, whose GV were 14.4 cm/y and 9.54 cm/y.

CONCLUSIONS

The imprinted gene OSBPL5 is quite possible pathogenicity of SRS. Other 5 important genes, TGFβ3, HSF1, GAP43, NOTCH4, MYH14 may be related to SRS.
We confirmed that the most important epigenetic methylation changes of SRS are located in the 11p15.
This group of SRS have good GH efficacy. One case of UPD (7) mat was higher GV than two patients who were 11p15 ICR1 hypomethylation.

References

Eggermann T, Spengler S, Gogiel M, Begemann M, Elbracht M. Epigenetic and genetic diagnosis of Silver-Russell syndrome. Expert Rev Mol Diagn 2012,12:459-471.
Binder G, Liebl M, Woelfle J, Eggermann T et al. Adult height and epigenotype in children with Silver-Russell syndrome treated with GH. Horm Res Paediatr 2013,80:193-200.
Toumba M, Albanese A, Azcona C, Stanhope R. Effect of long-term growth hormone treatment on final height of children with Russell-Silver syndrome. Horm Res Paeditr 2010,74:212-217.
Bartholdi D, Krajewska-Walasek M, Ounap K, et al. Epigenetic mutations of the imprinted IGF2-H19 domain in Silver-Russell syndrome (SRS): results from a large cohort of patients with SRS and SRS-like phenotypes. J Med Genet 2009,46:192–197.
Docherty LE, Rezwan F, Poole R, et al. Genome-wide DNA methylation analysis of patients with imprinting disorder identifies differentially methylated regions associated with novel candidate imprinted genes. J Med Genet 2014,51:229-238.
Eggermann T, Heilsberg AK, Bens S, et al. Additional molecular findings in 11p15-associated imprinting disorder: an urgent need for multi-locus testing. J Mol Med 2014,92:769-777.
Azzi S, Steunou V, Tost J et al. Exhaustive methylation analysis revealed uneven profiles of methylation at IGF2/ICR1/H19 11p15 loci in Russell Silver syndrome. J Med Genet 2015,52:53-60.
Prickett A.R, Ishida M, Bohm S et al. Genome-wide methylation analysis in Silver-Russell syndrome patients. Hum Genet 2015,134:317-332.

ESPE 2015 1255--P3
Misc 3
DI WU
DOI: 10.3252/pso.eu.54espe.2015
Poster presented at: 54th Annual Meeting 7-9 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology
PosterSessionOnline.com