Molecular Genetics, Genomics, Mechanisms of Diseases

AB066. The association between *GATA1* mutations in Down syndrome newborns and transient abnormal myelopoiesis

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Background: Children with Down syndrome (DS) are 500 times more likely to develop acute myeloid leukemia (AML-DS), compared to children without DS. One of the potential risk factors for AML-DS is a history of transient abnormal myelopoiesis (TAM) in the newborn period, which is found in approximately 10% of DS neonates. TAM, a specific condition, presents in only DS newborns, although it can spontaneously resolve within 3–6 months of age. However, 20–30% of DS newborns with TAM will develop AML-DS. *GATA1* gene encodes hematopoietic transcription factor. Somatic truncating *GATA1* mutation is associated with most TAM cases and a potential marker for future AML-DS. Currently, the GATA1 test is not applied in clinical practice guidelines. However, it would be beneficial for predicting the risk of AML-DS. Therefore, we decided to study whether *GATA1* mutation will present in DS newborns with TAM, and will increase the risk of developing AML-DS.

Methods: Blood samples from four DS newborns, confirmed by chromosome analysis with a clinical diagnosis of TAM, were collected and isolated for genomic DNA. All coding regions of *GATA1*, exon 2 to 6, were amplified and sequenced.

Results: Of the 4 patients, a mutation was observed in 1 patient. We identified a heterozygous mutation, 17 nucleotides duplication, from the nucleotide 154 to 170 (c.154_170 dup) in exon 2. This frame shift mutation predicted the change of amino acid at codon 58 from alanine to glutamine, and introduced shift of the following 84 amino acids leading to a truncated GATA1 protein (p.Ala58Glnfs*85).

Conclusions: The low frequency of *GATA1* mutation in our cohort may not be precise due to small sample size, or having other genetic predisposing of TAM in our population. However, DS newborns with TAM who have *GATA1* mutations have an increased risk of developing AML-DS, and therefore should be closely monitored.

Keywords: Down syndrome (DS); transient abnormal myelopoiesis (TAM); *GATA1*; mutation; acute myeloid leukemia of Down syndrome (AML-DS)

doi: 10.21037/atm.2017.s066

Cite this abstract as: Chukua K, Netsawang C, Padungthai K, Khetkham T, Surapolchai P, Rojnueangnit K. The association between *GATA1* mutations in Down syndrome newborns and transient abnormal myelopoiesis. Ann Transl Med 2017;5(Suppl 2):AB066. doi: 10.21037/atm.2017.s066

