Identification of a novel mutation genes causing thalassemia in Chinese people

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Objective

There was a high frequency of α-thalassemia in Southeast Asia and South China populations. Approximatly 50 deletions from the α-globin cluster were found either completely or partially delete both α-globin genes, and the deletions varied from 2. 4kb to the whole α-globin gene cluster. In this study, we describe a case of a rare, novel 44. 6 kb deletion that eliminated both of the duplicated α-globin genes causing α0- thalassaemia in two members of a Chinese family.

Methods

The probands were Siblings, both of them had a typical hypochromic microcytosis. The common α-thalassemia deletion mutations(--SEA/, -a3. 7/ and -a4. 2/, --FIL/, --Thai/) and three non-deletion mutations (aQSa/, aCSa/, aWSa/) were scanned and revealed negative. The breakpoint of the deletion was determined by the combination of MLPA, custom CGH and direct sequencing.

Results

In the family, the proband II2, proband II3, represents a typical hypochromic microcytosis trait. According to the MLPA result, a new large deletion including the α-globin gene cluster was showed, the 5' breakpoint were between chr16: 193637- 199336 and the 3' breakpoint were between chr16: 237170-256305. Based on the array CGH result, a deletion of the α-globin gene cluster was found, the deletion region were chr16: 194277-237673. The position of the breakpoints was further identified by Gap-PCR throughout the breakpoint regions, Sanger sequencing showed that the exact deletion region were chr16: 194214-238840 44627deletion.

Conclusion

We describe a novel 44. 6 kb deletion that eliminated both of the duplicated a globin genes. This rare mutation constitutes an additional heterogeneous defect causing α-thalassaemia in the Chinese population. We developed an CGH array to detect CNVs in the α-globin gene clusters and surrounding, and allowing high resolution characterization of novel deletions that are not readily detected by PCR-based methods.