Application of a targeted low density BAC-based array CGH platform for prenatal diagnosis in South Korea

Dong Hyun Cha[1], Ji Hyun Park[1], Jung Hoon Woo[2], Song-Ju Yang[2], Kap-Seok Yang[2], Won Bo Hahn[1], Sung Han Shim[1]

Department of Ob and Gyn, CHA General Hospital, CHA University[1], Macrogen, Inc., Bio Chip Service Department[2]

Objectives (목적)

While conventional G-banded karyotyping still remains a gold standard in prenatal genetic diagnoses, the widespread adoption of array CGH technology for postnatal genetic diagnoses has led to increasing interest in the use of this same technology for prenatal diagnosis. Here, we describe the development and application of a BAC-based DNA chip that is being used for prenatal diagnosis in South Korea.

Methods (연구 방법)

We have designed a target BAC-based array CGH platform (MacArrayTM M-chip) This array CGH platform specifically targets submicroscopic deletions and duplications for 26 known genetic syndromes of medical significance as well as frequently-observed common chromosomal aneuploidies that are observed prenatally. To validate the array, we obtained genomic DNA from 132 cell lines containing relevant genomic imbalances and specific chromosomal aneuploidies. Experiments were performed in a blinded manner and all known genomic alterations were successfully identified. We then applied this array CGH platform to 94 amniotic fluid specimens and 2 abortus cases that were also subjected to conventional karyotyping.

Results (결과)

We can detect the genetic alterations from all 132 cell lines including the microdeletions and aneuploidies. Also, the same results can be obtained with conventional cytogenic technique in the all clinical specimens (94 AF and 2 abortus) with some exceptions. Due to the targeted nature of this array CGH platform, certain chromosomal aberrations could not be detected by array CGH, but were identified via conventional karyotyping including balanced chromosomal rearrangements: 2 cases of inv (9) and 1 case of t (8;11). However, certain chromosomal aberrations were detected with this array platform that were not oberserved by G-banded chromosomal analysis. For example, we identified eight cases of microdeletions in the Yq11.23 chromosomal region, which harbors the DAZ gene, and may lead to non-obstructive spermatogenesis. FISH analysis confirmed the deletion in all eight cases.

Conclusions (결론)

We have successfully designed and applied a BAC-based array CGH platform for prenatal diagnosis. This array CGH platform can be used in conjunction with conventional karyotyping and will provide rapid and accurate diagnosis for the targeted genomic regions while eliminating the need to interpret clinically-uncertain genomic regions – certain copy number variants (CNVs).