Journal of Genetics and Genomes

Liehr et al., J Genet Genom 2017, 1:1

Editorial Open Access

Modern High Throughput Approaches are not meant to Replace 'Old Fashioned' but Robust Techniques

Thomas Liehr*, Kristin Mrasek, Elisabeth Klein and Anja Weise

Institute of Human Genetics, Jena University Hospital, Friedrich Schiller University, Jena, Germany

Genetics and Genomes: A Brief Discussion

Presently, there are major discussions in the field of genetics and genomes if some approaches may be outdated and to be replaced by more recent and modern ones. Especially if it is on human genetics, one easily finds papers claiming that e.g., banding or molecular cytogenetics could or should best be replaced by array comparative genomic hybridization (aCGH) and next generation sequencing (NGS) technologies [1-5]. Often there is also the claim that aCGH is cheaper and NGS more reliable than the 'old-fashioned' approaches, even though both allegations already showed to be not true [6,7].

Besides, one should remember that in most countries around the world it will be practically impossible to adapt aCGH and NGS during the next decades due to limited financial resources. Furthermore, it is questionable if e.g., a clinically suspected a Down syndrome should really be characterized by a high throughput approach instead of single cell oriented techniques like cytogenetics. Apart from cost efficiency aspects, for correct genetic counselling a translocation trisomy 21 must always be distinguished from free trisomy 21 – thus chromosome analyses cannot be skipped in such cases, as neither aCGH nor NGS can separate them.

Just to pinpoint the misleadingness of some of the recent papers, exclusively glorifying new, and condemning old approaches we compared our own data on detection rates in a specific application achieved with 'standard methods' to data of a recent 'glorifying' paper [1]. The latter [1] claimed, that in miscarriage-samples from women who had an early spontaneous abortion, the application of SNP-aCGH and NGS would lead to most comprehensive results with detection rates of ~50%. In our laboratory, we do a combination of banding cytogenetics and microsatellite analyses of maternal blood and DNA isolated from abortion-tissues to answer this question. Surprisingly, we found comparable detection rates of ~48% as when using much more expensive and not everywhere available high throughput approaches.

In detail: By banding cytogenetics we studied overall 237 tissues derived from miscarriages. 50 of them did not show any growth (18.3%), 28 revealed normal male (11.8%), 74 normal female (31.2%) and the remainder 85 abnormal karyotypes (38.7%). In a second step only those cases without a result explaining the miscarriage (i) and those with normal female karyotype (ii) were studied by microsatellite analyses. Group (i) was studied to detect triploidy, trisomies or monosomies 13, 15, 16, 18, 21 and 22. Thus, in 19 additional cases (8%) causative chromosomal imbalances could be found. Group (ii) was studied to exclude those cases with complete maternal contamination. Thus, the final result was: 63 cases (26.6%) did not contain any fetal material and thus showed a normal female karyotype. The number of here studied cases had thus to be corrected down to 174 miscarriages. 57/174 cases revealed normal male (32.8%), 33/174 normal female (19.0%) and the remainder 104/174 abnormal karyotypes (48.2%). In conclusion, the detection rate of this 'low throughput'-approach is in the same range as that of the study of Shen et al. [1], which is given as 225/436 (51.6%) cases, and by far less expensive. Also in [1] no conclusion was possible, how many of the 110 normal female tested samples were of maternal origin. Overall, in this example it may be the best strategy, especially in case of being reimbursed by the corresponding national health insurance, first to apply GTG-banding, second microsatellite analyses and third, only in then still unclear cases aCGH. NGS may be considered after exclusion of all aCGH positive cases.

In summary, as novel approaches being advertised as mature and robust, like NGS, may show in practice low concordance if comparing different platforms [7], it might be wise to consider not only always and exclusively brand-new approaches. Especially, when it is not about research but about diagnostics this is an important point. Some conservativeness in staying with and remembering the advantages of the well-established standard approaches supports usage of available resources thoughtfully.

References

1. Shen J, Wu W, Gao C, Ochin H, Qu D, et al. (2016) Chromosomal copy number analysis on chorionic villus samples from early spontaneous miscarriages by high throughput genetic technology. Molecular Cytogenetics 9: 7.

2. Sireteanu A, Covic M, Gorduza EV (2012) Array CGH: technical considerations and applications. Rev Med Chir Soc Med Nat Iasi 116: 545-551.

3. Ahn JW, Bint S, Bergbaum A, Mann K, Hall RP, et al. (2013) Array CGH as a first line diagnostic test in place of karyotyping for postnatal referrals - results from four years' clinical application for over 8,700 patients. Mol Cytogenet 6: 16.

4. Sagoo GS, Mohammed S, Barton G, Norbury G, Ahn JW, et al. (2015) Cost effectiveness of using array-CGH for diagnosing learning disability. Appl Health Econ Health Policy 13: 421-432.

5. Liang D, Wang Y, Ji X, Hu H, Zhang J, et al. (2017) Clinical application of whole-genome low-coverage next-generation sequencing to detect and characterize balanced chromosomal translocations. Clin Genet 91: 605-610.

***Corresponding author:** Thomas Liehr, Institute of Human Genetics, Jena University Hospital, Friedrich Schiller University, Postfach, D-07740 Jena, Germany, Tel: +493641935533; Fax: +493641935582; E-mail: Thomas.Liehr@med.uni-jena.de

Received August 30, 2017; **Accepted** September 01, 2017; **Published** September 05, 2017

Citation: Liehr T, Mrasek K, Klein E, Weise A (2017) Modern High Throughput Approaches are not meant to Replace 'Old Fashioned' but Robust Techniques. J Genet Genom 1: e101.

6. Liehr T, Lauten A, Schneider U, Schleussner E, Weise A (2017) Noninvasive prenatal testing (NIPT) – when is it advantageous to apply. Biomed Hub 2: 10.

7. Yao R, Zhang C, Yu T, Li N, Hu X, et al. (2017) Evaluation of three read-depth based CNV detection tools using whole-exome sequencing data. Mol Cytogenet 10: 30.