CARRIERTEST GENNET - THE EXPANDED PRECONCEPTION CARRIER SCREENING

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Abstract Body

Introduction CarrierTest GENNET is a custom NGS panel testing 889 key mutations causing 68 severe genetic disorders that can affect progeny of healthy individuals (genetic compatibility test). The test was designated for patients undergoing an IVF program and for gamete donors. Results are grouped according to clinical impact: (1) mutations in genes associated with severe recessive disorders in offspring (e.g. *SMN1, CFTR, GJB2* genes), (2) mutations in set of genes predisposing to blood hypercoagulation- trombophilic profile (*F2, F5, MTHFR, ANXA5*- M2 haplotype), (3) ovarian response to gonadotrophin stimulation (*FSHR* polymorphism).
Methods: We have developed a bioinformatic pipeline using local installation of Ensembl genomic database for annotation and SQL server variant database for data handling and clinical reporting. To replace MLPA and fragmentation analysis methods we developed coverage analysis-based CNV detection of frequent large deletions of *SMN1* and *CFTR* genes and also microdeletions on chromosome Y (AZF region). The report contains in addition to general information on found variants and associated disorders residual risk estimation and couple´s preconception compatibility
Results: So far 8258 samples were analyzed. These include 3196 couples before conception, 1388 gamete donors and 478 patients with reproduction impairment without compatibility testing. Frequent occurrence of carriers was observed in the commonly screened genes (*SMN1 2,4%, CFTR 3,7%, GJB2 6,2%*) but also in other genes previously not tested (e.g. *ABCA4* 4,2%, *DHCR7* 2,7%, *SERPINA1* 2,7%, *PAH* 2,5%, *ACADM* 1,5%, *ATP7B* 1,2%, *AR* 1,1%). We identified 79 pairs (2,4%) with a reproduction risk, which is twofold increase detection rate in comparison with only basic *CFTR/SMN1/GJB2* testing.
Conclusion: CarrierTest can contribute to individualization and therefore more effective treatment of infertility and prevention of rare genetic disorders. There is a clinical option of preimplantation (PGT-M) or prenatal diagnostics or using compatible donor gametes for couples with significant risk of having affected offspring.