

S005 Single cell genetic analysis for preimplantation genetic diagnosis of inherited disease

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Preimplantation genetic diagnosis (PGD) is now possible for any known single gene defect using multiplex fluorescent PCR to amplify multiple DNA target sequences from single or small numbers of cells biopsied from cleavage or blastocyst stage human embryos, respectively. Typically, amplification of the appropriate region of the affected gene and mini-sequencing for mutation detection is combined with linkage analysis of one or more closely linked, preferably flanking or intragenic, short tandem repeat (STR) markers to avoid errors caused by allele dropout or contamination. Indeed, high order multiplexing (10- to 15-plex) allows linkage analysis of multiple markers across the HLA region, combined with single gene defect diagnosis if appropriate, where the aim is to identify and transfer disease-free, HLA matched embryos and isolate umbilical cord blood stem cells at delivery for treatment of an existing affected child. For women of advanced maternal age requesting PGD, it is also possible to include markers for a limited number of other chromosomes to identify common maternal age related trisomies, including chromosomes 21, 18 and 13, which can result in a viable but abnormal pregnancy. Recent developments including the use of whole genome amplification by isothermal multiple displacement amplification (MDA) as a universal first step and the prospects for genome wide analysis will be reviewed.