

CHIMERAHID™ AND ARMEDXPert™: MIXTURE DECONVOLUTION PROGRAMS FOR SHORT TANDEM REPEAT DATA

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NicheVision Inc. (Akron, OH) has released two mixture deconvolution programs for short tandem repeat data analysis: ChimeraHID™ and ArmedXpert™. These mixture deconvolution programs are designed to automate the tedious and numerous calculations required to thoroughly review a mixed STR DNA result. ChimeraHID™ has unique features for bone marrow transplant monitoring and ArmedXpert™ has matchless features for the analysis of mixed samples commonly encountered in forensic casework. Both programs offer tools for quality control testing where contamination has been observed.

Following a bone marrow transplant, patients are monitored closely for evidence of graft rejection or recurrence of the original disease. Bone marrow transplantation creates a donor-recipient cellular chimerism in the patient, which can be quantitatively measured through short tandem repeat (STR) analysis of peripheral whole blood to determine the percent chimerism of the sample. Increasing recipient chimerism is an indication of graft rejection or relapse. ChimeraHID™, a software program with functionality originally designed to analyze forensic mixture samples, has the potential to be useful in analyzing post-transplant mixed chimeric samples. In this study, post-transplant samples were analyzed using this mixture deconvolution software program. ChimeraHID™ is fast, accurate, and consistent in determining the mixing proportions of the samples and has the ability to apply the profiles of both the donor and recipient.

The peripheral whole blood of a bone marrow recipient is drawn weekly, bi-weekly or monthly post-transplant to evaluate chimerism. Quantification of the percentage, or proportion, of donor and host DNA in the post-transplant sample is calculated manually using peak height or peak area comparisons – a procedure commonly used by forensic laboratories in cases such as sexual assaults. If an allele is shared in chimerism testing, only the allele which distinguishes the donor from the recipient is used.

Fewer STR markers are needed for chimerism analysis than traditional forensic analysis; recipient-donor alleles can be distinguished using between two and six loci. Loci which contain more polymorphisms are more “informative,” or able to distinguish the two contributors to the mixture, than those with fewer polymorphisms. However, it is common that the bone marrow recipient and donor are biologically related; therefore, it is more likely that there will be shared alleles than if the patient and donor are unrelated. If both alleles are shared, that locus is considered “uninformative” and cannot be used to calculate mixture statistics. Shared alleles as well as stutter must be considered in data interpretation. When either a donor or recipient allele is in a stutter position to another peak, this can alter the percent chimerism calculation because it is not known how much of the peak height is due to the true allele and how much is due to stutter. Often, laboratories will completely exclude a locus if a donor or recipient allele is in a stutter position. ChimeraHID™ has an additional feature to adjust for stutter in the data.

ChimeraHID™ automates interpretation and documentation of DNA results for bone marrow recipient peripheral blood samples. The software automatically calculates and displays the peak height ratio for each combination and the mixing proportions. Similar data will be presented with ArmedXpert™ for the analysis of mixed forensic casework DNA samples. ☘