FSHD1 Diagnostics: Molecular Combing (Pt 1)

Molecular combing for FSHD1 D4Z4 deletion testing.

The original genetic testing for FSHD was based on detecting a deletion within the chromosome 4q35 D4Z4 repeat array, and later, assaying for an FSHD permissive allele on the contracted chromosome.

Genomic Vision has developed mostly automated technology to essentially do the same analysis but using a different technique: Molecular combing on the Genomic Vision Molecular Combing Platform.

Molecular combing stretches the DNA and hybridizes to sequence-specific fluorescently labeled probes (CombHeliX FSHD Probes) to provide a direct visualization of the region and simultaneously detect the number of D4Z4 repeat units for all four D4Z4 arrays (2 each on chromosomes 4 and 10) while also identifying the associated 4A and 4B alleles.

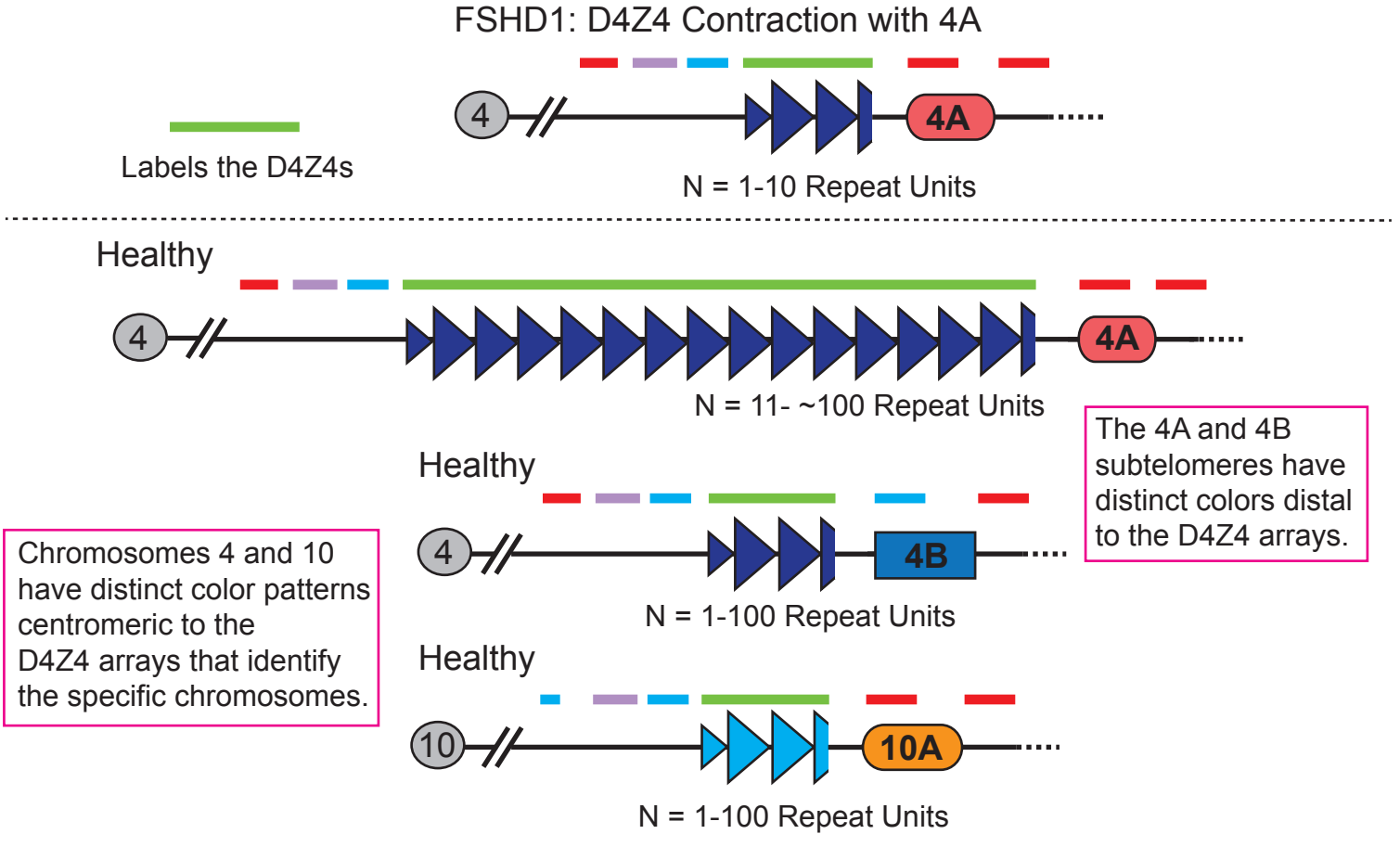
Can detect somatic mosaicism, duplications, and recombination events.

This diagnostic technique is highly accurate and is available as a CLIA-approved test. Genetic diagnosis by this method, when CLIA-approved, will qualify you genetically for consideration in clinical trials.

Nguyen *et al*. (2011) Molecular combing reveals allelic combinations in facioscapulohumeral dystrophy. *Annals of Neurology* 70:627-33.

Vasale *et al*. (2015) Molecular combing compared to Southern blot for measuring D4Z4 contractions in FSHD. *Neuromuscular Disorders* 25:945-51.

http://www.genomicvision.com/



FSHD1 Diagnostics: Molecular Combing (Pt 2)

Molecular combing for FSHD1 D4Z4 deletion testing.

Nguyen *et al*. (2011) Molecular combing reveals allelic combinations in facioscapulohumeral dystrophy. *Annals of Neurology* 70:627-33.

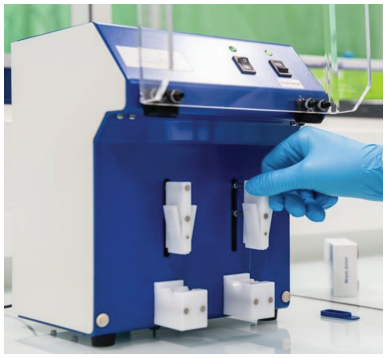
Vasale *et al*. (2015) Molecular combing compared to Southern blot for measuring D4Z4 contractions in FSHD. *Neuromuscular Disorders* 25:945-51.

Nguyen *et al*. (2017) Molecular combing reveals complex 4q35 rearrangements in Facioscapulohumeral dystrophy. *Human Mutation* 38:1432-41.

Nguyen *et al*. (2019) Deciphering the complexity of the 4q and 10q subtelomeres by molecular combing in healthy individuals and patients with facioscapulohumeral dystrophy. *Journal of Medical Genetics* 56:590-601.

http://www.genomicvision.com/

Determining the size of your chromosome 4 D4Z4 arrays by molecular combing:



Collect ~6ml blood sample then isolate cells.

▼

FiberPrep DNA extraction kit for HMW DNA (~300kb)

▼

Load the FiberComb Molecular Combing System for molecular combing

▼

Hybridize with CombHelix FSHD Probes

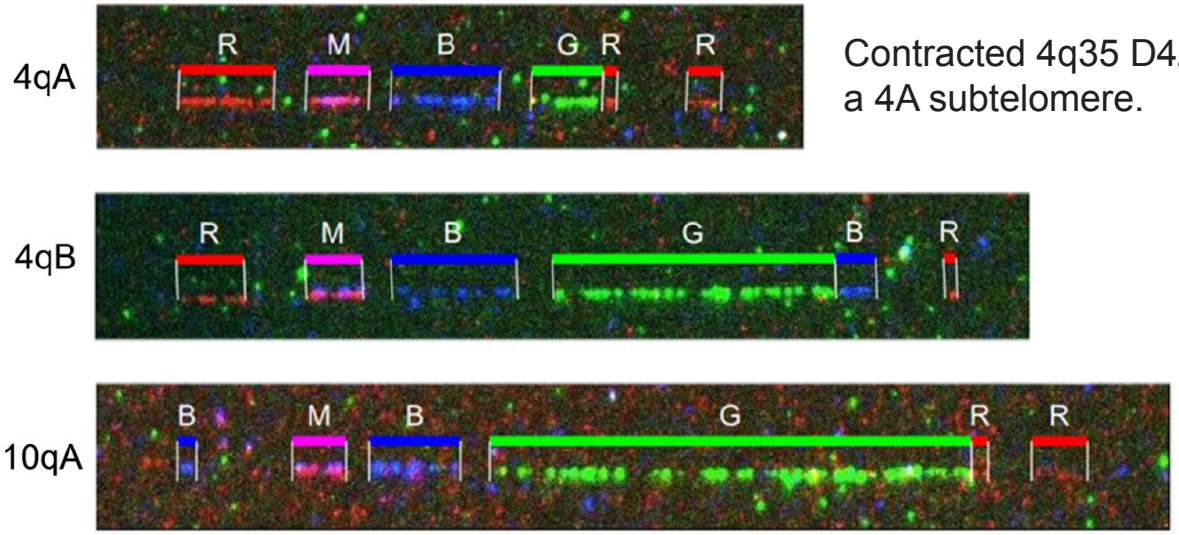
▼

Scan for FSHD1 signals

▼

Analysis with CombiHelix FSHD Software to identify the D4Z4 RUs and subtelomeres for each chromosome 4q35 and 10q26 D4Z4 array.

Not currently available in the USA. Available in France at CHU de Marseille.



Contracted 4q35 D4Z4 with a 4A subtelomere.

Figure modified from: Q. Zhang *et al*., (2019) *Molecular Genetics & Genomic Medicine* 7:e565.