

Appendix e-1

Supplemental methods online

Genetic Analysis

Whole exome sequencing (WES) was completed using 50ng of genomic DNA extracted from peripheral blood of this case. WES library preparation was completed using Nextera rapid capture exome library preparation kit (Illumina), as per manufacturers instructions, and sequencing was completed using HiSeq 1000 platform (Illumina). Sequence data were mapped using Galaxy (1-3) and Human Genome Reference Consortium build 37/hg19 (GRCh37/hg19) as a reference. Over 95% of reads were aligned to the reference genome. SNPs were called using wANNOVAR. Annotated sequencing data was screened in the first instance for rare non-synonymous variants in any of following known candidate genes associated with arteriopathies:

ACTA2

BMPR2

COL3A1

FBN1

SLC2A10

TGFBR1

TGFBR2

MYH11

RNF213

GUCY1A3

MYLK

PRKG1

SMAD3

SMAD4

TGFB2

HFE

RHOD

ELN

FBN2

NOTCH1

SKI

MAFP5

Sanger sequencing of *MYH11* was performed using the primers shown below. FastStart PCR master mix (Roche) was used for amplification and BigDye Terminator V3.1 cycle sequencing kit (Applied Biosystem) was used for the sequencing reaction. Sanger sequencing was completed using Applied Biosystem 3730 DNA Analyser and calls were made using Applied Biosystem 5.2 software. The sequencing output was analysed using CodonCode Aligned 5.1 to align and visualise the reads.

Primers for amplification of MYH11 exon 33

Forward: CTGAGGCAGGAGGTGGAG

Reverse: CAGTCGAGGATGGGTCTGAG