Disease	Gene/s	Technique
Alpha-1-antitrypsin	SERPINA1	Sanger sequencing
Alpha thalassaemia	HBA	MLPA [detects ~90% of pathogenic variants]
Alport syndrome	COL4A3, COL4A4, COL4A5	NGS (Illumina MiSeq) with over 95% coverage at 20X. COL4A5 MLPA if required.
Antithrombin Deficiency	SERPINC1	Sanger sequencing, MLPA
Ataxia	ADCK3, AFG3L2, APTX, ATM, ABCB7, ATP7B, ATP1A3, CACNB4,CACNA1A, CYP27A1, FTL, FGF14, FXN, GBA, ITPR1, IFRD1, MTPAP,KCNA1, KCNC3, KCND3, PDYN, PRRT2, PRKCG, SACS, SETX, SIL1,SLC1A3, SLC16A2, SLC2A1, SPTBN2, SPG7, SYNE1, TGM6, TTBK2,TTPA	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger gap fills and confirmations as required.
Bernard Soulier Syndrome	GP1BA, GP1BB, GP9	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
Combined Factor V and Factor VIII Deficiency	LMAN1 & MCFD2	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
C9orf72	C9orf72	Flanking and triplet primed PCR
Coagulation & Fibrinolysis Disorders	F10, F11, F12, F13A1, F13B, F2, F5, F7, F8, F9, FGA, FGB, FGG, GGCX, KNG1, KLKB1, LMAN1, MCFD2, SERPINE1, SERPINF2, THBD, VKORC1, VWF	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence confirmations as required
Combined FV & FVIII Deficiency	LMAN1, MCFD2	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence confirmations as required
Congenital contractural arachnodactyly (CCA) or Beal's syndrome	FBN2 hotspot region	Sanger sequencing

Connective tissues disorders	ABCC6, ACTA2, ACVR1, ADAMTS2, ALPL, ATP6V0A2, B3GALT6,B4GALT7, BMP1, CBS, CHST14, COL11A1, COL1A1, COL1A2, COL2A1,COL3A1, COL5A1, COL5A2, CRTAP, ELN, FBLN5, FBN1, FBN2, FKBP10,FKBP14, IFITM5, LEPRE1 (P3H1), LRP5, MYLK, NOTCH1, NOTCH2,PKD2, PLOD1, PLOD2, PPIB, PRDM5, RIN2, SERPINF1, SERPINH1, SLC2A10, SLC39A13, SMAD3, SP7, TGFB2, TGFBR1, GFBR2, TNXB,ZNF469	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
Cornelia de Lange syndrome (CdLS) including atypical forms	NIPBL, SMC1A, SMC3, HDAC8, RAD21, ANKRD11, KMT2A, BRD4, PUF60 & known pathogenic variants in AFF4 & NAA10 (p.Arg83Cys)	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger confirmations as required.
Craniodiaphyseal dysplasia (AD) / sclerostosis (AR)	SOST	Sanger sequencing
Craniofacial disorders	FGFR1 (NM_023110.2) exon 7, FGFR2 (NM_000141.4) exons 8 & 10, FGFR3 (NM_000142.4) exons 7 & 10 & TWIST1 (NM_00474.3) exon 1	Sanger sequencing
Cystic fibrosis and related conditions: · CFTR-related azoospermia · CFTR-related bronchiectasis	CFTR	CF-EU2, and/or Sanger sequencing, MLPA
Dilated cardiomyopathy (DCM)	ACTC1, ACTN2, BAG3, CSRP3, DES, DMD, DSP, FLNC, LAMP2, LMNA, MYBPC3, MYH7, MYL2 , MYL3, NKX2-5, PLN, RBM20, SCN5A, TNNC1, TNNI3, TNNI3K, TNNT2, TPM1, TTN, VCL	NGS (MiSeq) with over 95% coverage at 20X. Sanger sequence gap fills and confirmations as required.
DRPLA	ATN1	Fluorescent PCR amplification then fragment analysis
Early onset dementia / motor neuron disease	C9orf72	Flanking and triplet-primed fluorescent PCR amplification then fragment analysis

Early onset dementia / motor neuron disease	APP, CHMP2B, FUS, GRN, LRRK2, MAPT, PARK2, PSEN1, PSEN2, SOD1, SQSTM1, TARDBP, UBQLN2, VAPB, VCP	NGS (Ion Torrent PGM) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
Ehlers-Danlos syndrome	ADAMTS2, B3GALT6, B4GALT7, COL1A1, COL1A2, COL3A1, COL5A1,COL5A2, CHST14, PLOD1, FKBP14, RIN2, PRDM5, ZNF469, SLC39A13,TNXB, C1R, C1S	NGS (MiSeq) with over 95% coverage at 20X. Sanger sequence gap fills and confirmations as required.
Fabry disease	GLA	Sanger sequencing and MLPA analysis
Factor V Deficiency	F5	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
Factor VII Deficiency	F7	Sanger sequencing, MLPA
Factor X Deficiency	F10	Sanger sequencing, MLPA
Factor XI Deficiency	F11	Sanger sequencing, MLPA
Factor XIII Deficiency	F13A1 & F13B	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
Fibrinogen deficiency	FGA, FGB, FGG	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
Familial amyloid polyneuropathy	TTR	Sanger sequencing
FGFR3-related skeletal dysplasia: · Achondroplasia · Camptodactyly, tall stature and scoliosis and hearing loss (CATSHL) syndrome · Crouzon syndrome with acanthosis nigricans · Hypochondroplasia · Lacrimoauriculodentodigital (LADD) syndrome · Muenke syndrome · Severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN)	FGFR3 (NM_000142.4) exon 7, 10, 13, 15, 19	Sanger sequencing of exon(s) containing common variant(s)

· Thanatophoric dysplasia types I and II		
FGFR3-related skeletal dysplasia: · Achondroplasia · Camptodactyly, tall stature and scoliosis and hearing loss (CATSHL) syndrome · Crouzon syndrome with acanthosis nigricans · Hypochondroplasia · Lacrimoauriculodentodigital (LADD) syndrome · Muenke syndrome · Severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN) · Thanatophoric dysplasia types I and II	FGFR3 (NM_000142.4) exon 7, 10, 13, 15, 19	Sanger sequencing of exon(s) containing common variant(s)
Fragile-X syndrome and related conditions: · Fragile X tremor ataxia syndrome · Premature ovarian failure/insufficiency	FMR1	Flanking and triplet-primed fluorescent PCR amplification then fragment analysis
Friedreich ataxia	FXN	Fluorescent PCR amplification then fragment analysis and Sanger sequencing for point mutation analysis
Glanzmann Thrombasthenia	ITGA2B, ITGB3	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
Haemoglobinopathies and beta thalassaemia	HBB	Sanger sequencing and MLPA analysis
Haemophilia A	F8	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required. MLPA

Haemophilia B	F9	Sanger sequencing, MLPA
Hereditary haemorrhagic telangiectasia (HHT)	ACVRL1, ENG, EPHB4, GDF2, RASA1, SMAD4	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger gap fills and confirmations as required and MLPA analysis.
Hereditary Spastic Paraplegia	ATL1, BSCL2, CYP7B1, FA2H, GJC2, HSPD1, KIAA0196, KIF5A, L1CAM,NIPA1, PLP1, REEP1, SLC33A1, SPG11, SPG20, SPG21, SPAST, SPG7,ZEB2, ZFYVE27	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger gap fills and confirmations as required and MLPA analysis.
Huntington disease (HD)	HTT	Fluorescent PCR amplification of repeat for diagnostic and predictive referrals. Exclusion work-ups by linked markers.
Hypertrophic cardiomyopathy (HCM)	ACTC1, ACTN2, CSRP3, FHL1, FLNC, GLA, JPH2, LAMP2, MYBPC3, MYH7, MYL2, MYL3, PLN , PRKAG2, TNNC1, TNNI3, TNNT2, TPM1, TTR	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
Infantile myofibromatosis Type 1	PDGFRB common variants c.1681C>T, p.(Arg561Cys) & c.1978C>A, p.(Pro660Thr)	Sanger sequencing
Infantile myofibromatosis Type 2	NOTCH3 c.4556T>C, p.(Leu1519Pro)	Sanger sequencing
Juvenile polyposis syndrome (JPS) and JPS/HHT	BMPR1A & SMAD4	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required and MLPA analysis.
Late onset retinal macular degeneration	C1QTNF5 (CTRP5) c.489C>G or c.489C>A p.(Ser163Arg)	Sanger sequencing
Lynch syndrome / Hereditary non polyposis colorectal cancer (HNPCC)	MLH1, MSH2, MSH6, MUTYH exons 7 & 13, PMS2	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence confirmations, as required, and MLPA N.B. PMS2 only when isolated loss of PMS2 has been detected by IHC or when Turcot syndrome is suspected.
Myotonic dystrophy (DM1)	DM1	Flanking and triplet-primed fluorescent PCR amplification then fragment analysis
Nocturnal frontal lobe epilepsy (AD)	CHRNA4 (NM_000744.6) exon 5 & CHRNB2 (NM_000748.2) exon 5	Sanger sequencing
	ACTB, ACTG1, ALDH1A3, BCOR, C12ORF57, CHD7, COL4A1, FOXC1, FOXE3, FZD5, GJA8,	

Ocular malformations	ITPA, ITPR1, MAB21L1, MAB21L2, NAA10, OTX2, PAX2, PAX6, PITX2, PITX3, RAB18, RAB3GAP1, RAB3GAP2, RARB, RAX, RBP4, SALL2, SALL4, SHH, SIX3, SMCHD1, SMOC1, SOX2, STRA6, TBC1D20, VAX1, VSX2, YAP1, ZEB2, ZIC2.	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence confirmations as required.
Ornithine transcarbamylase deficiency (OTC)	OTC	Sanger sequencing and MLPA analysis
Osteogenesis imperfecta	BMP1, COL1A1, COL1A2, CRTAP, FKBP10, IFITM5, LEPRE1 (P3H1), PLOD2, PPIB, SERPINF1, SERPINH1, SP7, SPARC, TMEM38B, WNT1	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations, as required, and MLPA analysis.
Pagets disease of bone	SQSTM1 (NM_003900.4) exons 7 & 8.	Sanger sequencing
Peutz Jegher syndrome	STK11	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations, as required, and
Primary pulmonary hypertension (PPH)/ Pulmonary arterial hypertension (PAH)	ACVRL1, ATP13A3, BMPR2, CAV1, EIF2AK4, ENG, GDF2, KCNK3, SMAD9, SOX17, TBX4.	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger confirmations as required and BMPR2 MLPA analysis.
PGD	Please enquire	Pre-implantation Genetic Haplotyping (PGH)
Platelet disorders	ABCG5, ABCG8, ACTB, ACTN1, ANKRD26, ANO6, AP3B1, AP3D1, ARPC1B, BLOC1S3, BLOC1S6, CDC42, CYCS, DIAPH1, DTNBP1, ETV6, FERMT3, FLI1, FLNA, FYB1, GATA1, GBA, GFI1B, GNE, GP1BA, GP1BA, GP1BB, GP1BB, GP6, GP9, HOXA11, HPS1, HPS3, HPS4, HPS5, HPS6, ITGA2B, ITGA2B, ITGB3, ITGB3, KDSR, LYST, MECOM, MPIG6B, MPL, MYH9, NBEA, NBEAL2, P2RY12, PLA2G4A, PLAU, RASGRP2, RBM8A, RNU4ATAC, RUNX1, SLFN14, SRC, STIM1, STXBP2, TBXA2R, TBXAS1, THPO, TUBB1, VIPAS39, VPS33B, VWF, WAS	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence confirmations as required
Platelet-type von Willebrand Disease	GP1BA	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.

Polymerase proofreading-associated polyposis (PPAP).	POLD1 (NM_000748.2)exon 12 & POLE (NM_006231.2) exon 13	Sanger sequencing
Primary pulmonary hypertension	ACVRL1, ATP13A3, BMPR2, CAV1, EIF2AK4, ENG, GDF2, KCNK3, SMAD9, SOX17, TBX4.	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence confirmations as required and MLPA analysis.
Primordial dwarfism and microcephaly disorders	ASPM, ATR, ATRIP, BLM, CASC5, CASK, CDC45, CDC6, CDK5RAP2, CDT1, CENPE, CENPF, CENPJ, CEP135, CEP152, CEP63, CREBBP, DNA2, DPP6, DYRK1A, EP300, GMNN, IGF1, IGF1R, KIF11, LARP7, LIG4, MCPH1, MRE11A, NBN, NDE1, ORC1, ORC4, ORC6, PCNT, PHC1, PLK4, POC1A, RAD50, RBBP8, RNU4ATAC, SRCAP, STIL, TCF4, TRAIP, TUBGCP6, VPS13B, WDR4, WDR62, XRCC4.	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence confirmations as required and MLPA analysis.
Prion disease and related conditions: · Creutzfeldt-Jakob disease (CJD) · Gerstmann-Straussler disease · Huntington disease-like 1 · Fatal familial insomnia	PRNP	Sanger sequencing and octapeptide repeat sizing by flanking fluorescent PCR
Protein C deficiency	PROC	Sanger sequencing, MLPA
Protein S deficiency	PROS1	Sanger sequencing, MLPA
RAS-MAPK related: · Noonan syndrome · Cardio-facio-cutaneous svndrome · Costello syndrome · LEOPARD syndrome · Neurofibromatosis type 1	RAS-MAPK pathway (BRAF, CBL, HRAS, KRAS, LZTR1, MAP2K1, MAP2K2, MRAS, NF1, NRAS, PPP1CB, PTPN11, RAF1, RIT1, SHOC2, SOS1, SOS2, SPRED1)	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required
Retinal dystrophy: · Stargardt disease 1		

· Cone rod dystrophy 3 · Fundus flavimaculatus · Retinitis pigmentosa 19	ABCA4	NGS (Illumina MiSeq) with 100% coverage of coding and flanking intronic region
Skeletal dysplasia	ACAN, ACP5, ADAMTS10, ADAMTSL2, AGPS, ALPL, ANKH, ARSE,B3GALT6, BMP1, BMPR1B, CA2, CANT1, CDC6, CDKN1C, CDT1,CHST3, CLCN7, COL10A1, COL11A1, COL11A2, COL1A1, COL1A2,COL2A1, COL9A1, COL9A2, COL9A3, COMP, CRTAP, CTSK, CUL7,CYP27B1, DHCR24, DLL3, DYM, DYNC2H1, EBP, EIF2AK3, ENPP1,ESCO2, EVC, EVC2, FAM20C, FGF23, FGFR1, FGFR2, FGFR3, FKBP10, FLNA, FLNB, GDF5, GNPAT, GPC6, HSPG2, IFT122, IFT140, IFT43,IFT80, IHH, KAT6B, LBR, LEPRE1, LIFR, LMX1B, LRP5, LTBP2, MATN3,MMP9, NEK1, NPR2, OBSL1, ORC1, ORC4, ORC6, OSTM1, PAPSS2,PCNT, PEX7, PHEX, PLOD2, PPIB, PTH1R, RMRP, RNU4ATAC, ROR2,RUNX2, SBDS, SERPINF1, SERPINH1, SHOX, SLC26A2, SLC34A3, SLC35D1, SLC39A13, SMAD4, SMARCAL1, SNX10, SOX9, TCIRG1,TGFB1, TNFRSF11A, TNFRSF11B, TNFSF11, TRAPPC2, TRIP11, TRPV4,TTC21B, VDR, WDR19, WDR35, WISP3, WNT5A, XYLT1	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required
Spinal muscular atrophy	SMN1	MLPA analysis
Spinocerebellar ataxia 8 (SCA8)	ATXN8	Fluorescent PCR amplification then fragment analysis
Spinocerebellar ataxia 17 (SCA17)	TBP	Fluorescent PCR amplification then fragment analysis
Spinocerebellar ataxia screen (SCA 1,2,3,6,7)	ATXN1, ATXN2, ATXN3, CACNA1A, ATXN7	Fluorescent PCR amplification then fragment analysis

Stickler Syndrome/Cleft palate	ANKRD11, COL11A1, COL11A2, COL2A1, COL9A1, COL9A2, COL9A3,FLNA, FLNB, FOXE1, FOXC2, IRF6, IRF7, PLOD3, SATB2, SLC26A2,SOX9, TP63, TBX1, TBX22	
TruSight One analysis- multiple disorders	Analysis of genes within the TruSight One list	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required.
Variant validation	Variant dependent	Sanger sequencing
Von Willebrand Disease	VWF	NGS (Illumina MiSeq) with over 95% coverage at 20X. Sanger sequence fill in and confirmations as required, MLPA
X-linked spinal bulbar muscular atrophy (X-SBMA, Kennedy disease)	AR	Fluorescent PCR amplification then fragment analysis