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APPENDIX A

CONFERENCES AND MEETINGS AT WHICH RESEARCH CONTAINED IN THIS THESIS WERE PRESENTED

Results presented in this thesis were presented at the following national and international meetings. The presenting author's name is underlined in each case.

A.1 RESEARCH PRESENTED AT INTERNATIONAL CONFERENCES

A.1.1 **51th Annual meeting of the American Society of Human Genetics**: San Diego, U.S.A., October 2001.
Van der Merwe A., Schutte C-M., Van der Maarel S.M., Alessandrini M., Honey E., Frants R.R. and Olckers A. DNA rearrangements at the D4Z4 locus in South African facioscapulohumeral muscular dystrophy families (poster presentation).

A.1.2 **FSHD International Consortium Research Meeting**: Philadelphia, U.S.A., October 2001.
Olckers A., Van der Merwe A., Alessandrini M., Wallace D.C., Van der Maarel S.M., Honey E., Frants R.R. and Schutte C-M. FSHD in the South African population: Evidence to date suggest a dual founder effect.

A.1.3 **6th Congress of the World Muscle Society**: Salt Lake City, Utah, U.S.A., September 2001.
Van der Merwe A., Schutte C-M., Van der Maarel S.M., Honey E., Frants R.R. and Olckers A. Deletion fragment analysis in South African FSHD families (poster presentation).

A.1.4 **50th Annual meeting of the American Society of Human Genetics**: Philadelphia, U.S.A., October 2000.
Van der Merwe A., Schutte C-M., Van der Maarel S.M., Honey E., Frants R.R. and Olckers A. Molecular analysis of facioscapulohumeral muscular dystrophy (FSHD) in the South African population (poster presentation).

A.1.5 **FSHD International Consortium Research Meeting**: Philadelphia, U.S.A., October 2000.
Olckers A., Van der Merwe A., Van der Maarel S.M., Honey E., Frants R.R. and Schutte C-M. Segregation of DNA rearrangements at the D4Z4 locus in South African FSHD families.

A.1.6 **5th Congress of the World Muscle Society**: White River, South Africa, June 2000.
Van der Merwe A., Schutte C-M., Honey E. and Olckers A. Molecular investigation of Facioscapulohumeral muscular dystrophy in South African families (platform presentation).

A.1.7 **FSHD International Consortium Research Meeting**: San Francisco, U.S.A., October 1999.
Van der Merwe A., Schutte C-M., Honey E., and Olckers A. Haplotype analysis of South African facioscapulohumeral muscular dystrophy families.

A.2 RESEARCH PRESENTED AT NATIONAL CONFERENCES

A.2.1 **9th South African Society of Human Genetics Congress**: The Kruger National Park, South Africa, August 2001.
Van der Merwe A., Schutte C-M., Van der Maarel S.M., Honey E., Frants R.R. and Olckers A. Southern blot and haplotype analysis of selected facioscapulohumeral muscular dystrophy (FSHD) families (platform presentation).

A.2.2 **Annual congress of the Neurological association of South Africa**: Wild Coast Sun, KwaZulu-Natal, March 2001.
Van der Merwe A., Schutte C-M., Van der Maarel S.M., Honey E., Frants R.R. and Olckers A. Molecular analysis of D4Z4 rearrangements in South African Facioscapulohumeral muscular dystrophy (FSHD) families (platform presentation).

A.2.3 **Muscular Dystrophy Symposium of the Muscular Dystrophy Foundation of South Africa**: Strand, Cape Town, March 1999.
Van der Merwe A. and Olckers A. Facioscapulohumeral muscular dystrophy: the significance of a diagnostic service in South Africa (poster presentation).

A.3 RESEARCH PRESENTED AT THE FACULTY OF MEDICINE, UNIVERSITY OF PRETORIA

A.3.1 **Faculty Day 2001: Faculty of Medicine, University of Pretoria, Pretoria, South Africa**

Van der Merwe A., Schutte C-M., Honey E. and Olckers A. Facioscapulohumeral muscular dystrophy (FSHD) in the South African population: a molecular investigation. August 2000 (platform presentation).

A.4 PUBLISHED ABSTRACTS IN INTERNATIONAL PEER-REVIEWED JOURNALS

A.4.1 Van der Merwe A., Schutte C-M., Van der Maarel S.M., Alessandrini M., Honey E., Frants R.R. and Olckers A. DNA rearrangements at the D4Z4 locus in South African facioscapulohumeral muscular dystrophy families (abstract). *Am. J. Hum. Genet.*, **69**(4), 637, 2001.

A.4.2 Van der Merwe A., Schutte C-M., Van der Maarel S.M., Honey E., Frants R.R. and Olckers A. Deletion fragment analysis in South African FSHD families (abstract). *Neuromusc. Disord.*, **11**(6,7), 633-634, 2001.

A.4.3 Van der Merwe A., Schutte C-M., Van der Maarel S.M., Honey E., Frants R.R. and A. Olckers. Molecular analysis of Facioscapulohumeral muscular dystrophy (FSHD) in the South African population (abstract). *Am. J. Hum. Genet.*, **67**(4), 314, 2000.

A.4.4 Van der Merwe A., Schutte C-M., Honey E., and Olckers A. Molecular investigation of facioscapulohumeral muscular dystrophy (FSHD) in South African families (abstract). *Neuromusc. Disord.*, **10**(4,5), 376, 2000.

APPENDIX B

MODE OF INHERITANCE OF DIFFERENT TYPES OF MUSCULAR DYSTROPHIES

This appendix contains information on the mode of inheritance, gene locus, gene symbol and gene product for all the muscular dystrophies.

Table B.1: Mode of inheritance of different types of muscular dystrophies

Disorder	Inheritance	Gene locus	Gene symbol	Gene product
Muscular dystrophies:				
Duchenne/Becker	XR	Xp21.2	DMD	Dystrophin
Emery Dreifuss	XR	Xq28	EMD	Emerin
Emery Dreifuss	AD	1q11-q23	EDMD-AD (LMNA)	LaminA/C
Facioscapulohumeral	AD	4q35	FSHD	---
Limb-girdle muscular dystrophies (LGMD)				
LGMD, dominant	AD	5q31	LGMD1A	Myotilin
LGMD with cardiac involvement	AD	1q11-21	LGMD1B (LMNA)	LaminA/C
LGMD, dominant	AD	3p25	LGMD1C (CAV3)	Caveolin-3
Familial dilated cardiomyopathy with conduction defect and adult-onset LGMD	AD	6q23	LGMD1D	---
LGMD, dominant	AD	7q	LGMD1E	---
Vocal cord and pharyngeal weakness with autosomal dominant distal myopathy	AD	5q31	VPDMD (possibly allelic to LGMD1A)	---
LGMD, recessive	AR	15q15.1-q21.1	LGMD2A (CAPN3)	Calpain 3
LGMD, recessive	AR	2p13	LGMD2B (FER-1)	Dysferlin
LGMD, recessive	AR	13q12	LGMD2C (SGCG)	γ-sarcoglycan
LGMD, recessive	AR	17q12-q21.33	LGMD2D (SGCA)	α-sarcoglycan

continued ...

Table B.1: continued ...

Disorder	Inheritance	Gene locus	Gene symbol	Gene product
LGMD, recessive	AR	4q12	LGMD2E (SGCB)	β-sarcoglycan
LGMD, recessive	AR	5q33-q34	LGMD2F (SGCD)	δ-sarcoglycan
LGMD, recessive	AR	17q11-q12	LGMD2G (TCAP)	Telethonin
LGMD, Hutterite type	AR	9q31-q34.1	LGMD2H	---
LGMD, recessive	AR	19q13.3	LGMD2I	---
Distal myopathy:				
Autosomal dominant distal myopathy	AD	14	MPD1	---
Distal myopathy with rimmed vacuoles	AR	9p1-q1	DMRV	---
Hereditary inclusion body myopathy	AR	9p1-q1	HIBM	---
Miyoshi myopathy	AR	2p12-14	MM	Dysferlin
Tibial muscular dystrophy	AD	2q31	TMD	Titin?
Other myopathies:				
Autosomal dominant myopathy with proximal muscle weakness and early respiratory muscle involvement (Edstrôm)	AD	2q24-31	MPRM1	---
Autosomal dominant myopathy with proximal muscle weakness and early respiratory muscle involvement	AD	2q21	MPRM2	---
Bethlem myopathy	AD	21q22.3	COL6A1	Collagen VI α1
Bethlem myopathy	AD	21q22.3	COL6A2	Collagen VI α2
Bethlem myopathy	AD	2q37	COL6A3	Collagen VI α3
Desmin-related myopathy	AD	11q22	DRM (CRYAB)	αB-crystallin
Desmin-related myopathy	AD	2q35	DES	Desmin
Epidermolysis bullosa simplex associated with late-onset muscular dystrophy	AR	8q24-qter	MD-EBS	Plectin
Myopathy with excessive autophagy	XR	Xq28	MEAX	---
Oculopharyngeal	AD	14q11.2-q13	OPMD (PABP2)	Poly A binding protein 2
Congenital myopathies:				
Central core	AD	19q13.1	CCD (RYR1)	Ryanodine receptor
Congenital myopathy with excess of thin myofilaments	AR	1q42,1	ACTA1	Actin alpha, skeletal muscle

continued ...

Table B.1: continued ...

Disorder	Inheritance	Gene locus	Gene symbol	Gene product
Congenital muscular dystrophy with merosin deficiency	AR	6q2	LAMA2	Laminin α2 chain of merosin
Congenital muscular dystrophy with secondary merosin deficiency	AR	1q42	CMD1B	---
Congenital muscular dystrophy with integrin deficiency	AR	12q13	ITGA7	Integrin α7
Congenital muscular dystrophy with rigid spine	AR	1p35-36	RSMD-1	---
Fukuyama CMD	AR	9q31-q33	FCMD	Fukutin
Myotubular myopathy	XR	Xq28	MTMX	Myotubularin
Nemaline myopathy	AD	1q21-q23	NEM1 (TPM3)	α tropomyosin
Nemaline myopathy	AR	2q21.1-q22	NEM2	Nebulin
Nemaline myopathy	AD	1q42.1	ACTA1	Actin alpha, skeletal muscle
Myotonic syndromes				
Brody disease	AR	16p12	SERCA1	Sarcoplasmic reti-culum Ca^{2+} ATPase
Myotonic dystrophy (Steinert)	AD	19q13	DM	Myotonin-protein kinase
Myotonic dystrophy type 2	AD	3q	DM2	---
Myotonia, dominant (Thomsen)	AD	7q35	CLC-1	Muscle chloride channel
Myotonia, recessive (Becker)	AR	7q35	CLC-1	Muscle chloride channel
Rippling muscle disease	AD	1q41	RMD	---
Schwartz-Jampel syndrome	AR	1p34-p36.1	SJS	---

XR = X-linked recessive; AR = autosomal recessive; AD = autosomal dominant, --- = no information available. (Adapted from Neuromuscular disorders: gene location, 2001).

APPENDIX C

DIAGNOSTIC CRITERIA FOR FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

The following criteria define facioscapulohumeral muscular dystrophy (FSHD) on a clinical level:

1. Onset of the disorder is in the facial or shoulder girdle muscles; sparing of the extra-ocular, pharyngeal and lingual muscles and the myocardium.
2. Facial weakness in more than 50% of the affected family members.
3. Autosomal dominant inheritance in familial cases.
4. Evidence of a myopathic disorder in electromyography (EMG) and muscle biopsy in at least on affected member without biopsy features specific to alternative diagnoses.

The following clinical definitions apply:

i. **Non-penetrance** refers to an obligate gene carrier without symptoms or signs relating to the disorder.
ii. **Pre-symptomatic** indicated that an individual has no complaints (symptoms) related to the disorder, but has muscle atrophy and weakness upon physical examination.
iii. **Symptomatic** refers to patients with complaints and clinical symptoms related to the weakness and muscle atrophy of FSHD.

The International FSHD consortium has defined the clinical, genetic, laboratory criteria and the criteria for an individual to be included in linkage analysis for FSHD (Padberg *et al.,* 1991 and Padberg *et al.,* 1997). In Table C.1, in the left hand column, the inclusion criteria are indicated with an "I", the exclusion criteria with an "E" and additional comments with a "C".

Table C.1: Diagnostic criteria for FSHD

1.0	**CLINICAL CRITERIA**
1.1	**Onset**
I	Onset of the disorder is in the facial or shoulder-girdle muscles. Presenting symptoms usually relate to weakness or wasting of these muscles.
E	Onset in pelvic girdle muscles suggests alternative diagnoses; although subsequent pelvic girdle involvement is not uncommon in FSHD.
C	Clinically recognizable age at onset is very variable; age at symptomatic presentation is even more so. The mean age at recognizable onset is in the second decade. Onset before the age of 5 years, although rare in families, is not uncommon in the more severe proven new mutation cases, and does not exclude the diagnosis. Infantile or early childhood onset requires facial weakness to be present, since a clinical diagnosis cannot otherwise be reliably made.
1.2	**Facial**
I	Facial weakness affecting eye closure (orbicularis oculi) and peri-oral muscles (orbicularis oris) occurs in the vast majority of patients. In the absence of facial weakness, a diagnosis of FSHD can be accepted only if the majority of affected family members have facial weakness.
E	Extra-ocular, masticatory, pharyngeal and lingual muscle weakness is not part of the disorder.
C	Facial weakness may be very subtle and is sometimes noticeable by asymmetry of facial expression only. There is also some evidence that a dominant scapulohumeral presentation without facial weakness may be due to the same mutation mechanism at 4q35.
1.3	**Shoulders**
C	The scapular fixators are the muscles more prominently involved. Also the pectoralis major muscles will become affected early in most cases. The deltoid muscles remain unaffected for a long period of time and often have a particular pattern of atrophy, i.e. partial and proximal.
1.4	**Asymmetry**
I	Asymmetry of involvement in the shoulder girdle muscle is the rule, usually affecting the right side first.
C	Symmetrical weakness and atrophy at presentation is unusual and necessitates increased caution before accepting the diagnosis as FSHD. Asymmetrical involvement of the facial muscles occurs frequently.
C	NMR, ultrascan or CT-scan may be of help to detect asymmetry of muscle atrophy.
1.5	**Progression**
I	Progression is inevitable, albeit at a rate which is highly variable and in some cases virtually imperceptible.
E	Regression of symptoms and signs does not occur and would exclude the diagnosis.
C	The rate of progression and severity level reached tend to correlate inversely with age at onset.
C	Progression of the disorder usually includes involvement of abdominal and foot extensor muscles at an early stage; pelvic girdle weakness and upper arm weakness may occur at any time after the onset of shoulder girdle weakness.
C	Neck extensor, intrinsic hand and triceps surae muscle weakness is uncommon but can be observed occasionally within families and is not dependent on advance age or severe involvement.
1.6	**Severity**
C	At any age the disorder has a wide range of severity. Five aspect of note are: 1) Overall, between 10-20% of cases have eventual requirement for a wheelchair. 2) Severity in recognised isolated new mutation cases tend to be greater than in large families. 3) Presymptomatic cases occur at any age and appear to comprise approximately 30% of all cases in large families. 4) Once symptomatic, the disorder is progressive in the majority of cases. The rate of progression is variable, although faster rates tend to be seen with earlier ages at onset. Rarely, there can be long periods of apparent arrest of progression.

continued ...

Table C.1: continued ...

	5) There is broad correlation in 4q35 cases between greater clinical severity and smaller residual DNA fragment size at D4F104S1; it is currently uncertain whether this may also be influence by possible generational anticipation.
C	There appears to be no difference in mean age at death between patients and their non-affected sibs.
1.7	**Contractures**
C	Contractures and pseudohypertrophy of muscles may be present.
E	Severe and diffuse contractures exclude the diagnosis of FSHD.
1.8	**Cardiac disorder**
E	Cardiomyopathy is not part of the disorder. When present it suggests and alternative diagnosis.
1.9	**Hearing loss**
C	Hearing loss is part of the disorder; it starts with high tone perceptive deafness and my progress to involve all frequencies. The severity of the hearing loss varies between subjects at any age, but tends to be progressive. It is recommended that the results of hearing assessments be documented for several affected members in each family.
1.10	**Retinal disorder**
C	A retinal vasculopathy with capillary telangiectasis, microaneurysms and capillary closure has been reported in some members of some FSHD families. At present it is unclear whether this is a specific association. It should not be used for diagnostic purposes.
1.11	**Mental retardation**
C	A few cases have been reported with mental retardation. It is recommended that investigation of any such case should include chromosome analysis, concentrating on the distal long arm of chromosome 4. However, no causally associated cytogenetic abnormalities have yet been recorded, and haploinsuffiency of the 4q35 region does not seem to cause FSHD.
2.0.	**GENETIC CRITERIA**
I	The pattern of inheritance in familial cases is autosomal dominant.
C	Sporadic cases occur, their frequency is unknown, but they are not rare. Only if both parents have been examined can a case be accepted as "sporadic".
E	There is no substantiated evidence for recessive inheritance.
C	The mutation rate is unknown due to many uncertainties related to prevalence, penetrance and ascertainment.
C	Published estimates of prevalence remain approximations, the literature suggests widely variable regional differences. A prevalence of 1 in 20,000 in Europe appears a reasonable figure.
C	Penetrance is almost complete. Non-penetrance is estimated at less than 5% beyond the age of 20.
3.0.	**LABORATORY CRITERIA**
C	Serum creatine kinase (SCK) levels can be normal, but are often elevated, though rarely exceed five times the upper limit of normal. Persistently high CK values above this level warrant exclusion of other neuromuscular diagnoses.
C	EMG often shows short duration, low amplitude polyphasic potentials. Some neurogenic features such as high amplitude potentials and positive sharp waves are present occasionally, but do not characterise individual families. Motor and sensory nerve conduction velocities are normal.
E	Giant potentials are not a feature of the disorder.
C	Muscle biopsies may exhibit any of the standard myopathic criteria. In addition, small angular fibres are not uncommon and moth-eaten fibres are frequently found. An occasional small group of atrophic fibres may be observed, in which case another biopsy in the same patient or an affected sib is desirable. Cellular infiltrates are not uncommon in FSHD and can be extensive. Their significance is unknown. In these cases, either an autosomal dominant pattern of inheritance of a deleted DNA fragment at 4q35 is required to establish the diagnosis of FSHD.

continued ...

Table C.1: continued ...

4.0	**PHENOTYPIC-GENOTYPIC ANALYSIS**
I	Individuals who have been examined by a physician familiar with this disorder, and classified as affected according to the above criteria.
I	unaffected family members aged 20 yr and over, who have been examined as above.
I	unrelated spouses, whether or not examined.
E	any subject whose clinical status remains in dispute.
E	apparently unaffected individuals under age 20 year.
E	An unaffected individual with a CK level repeatedly above the normal range in the absence of a proven alternative explanation for this.
5.0	**RECOMMENDED INVESTIGATIONS IN AT LEAST ONE MEMBER OF EACH FAMILY INCLUDED IN LINKAGE STUDIES**
The following are recommended investigations:	
a)	Fully documented history and clinical examination,
b)	Serum creatine kinase,
c)	EMG,
d)	Muscle biopsy from an affected muscle for routine analysis,
e)	Audiometry, and
f)	Lymphoblast cell line and/or high molecular weight DNA sample suitable for pulsed field gel studies, and tested for persistence of DNA fragment of size 40 kb at locus D4F104S1, following double digestion of DNA with restriction enzymes *Eco* RI and *Bln* I.

APPENDIX D

NUCLEOTIDE SEQUENCE OF REPEAT UNITS AND FLANKING REGIONS AT THE D4Z4 LOCUS

The nucleotide sequence of the 3.3 kb repeat units and the flanking regions at the D4Z4 locus on chromosome 4q35 is presented in Table D.1.

Table D.1: Nucleotide sequence of repeat units at D4Z4 locus

Nucleotide position	Genomic DNA Sequence
1	gaattctatc tggtacccag agggaagggg gttcccagtg agggcaggac caggcttcat
61	gcacctcttc aggaatgttc tcctcatagt ccagcctcaa ggtgtgcatc ctctgtgtgc
121	atggagtcca tggcaggctc tgcctgggga gccgtccagc tgcacacctg caatgtggtg
181	gtgaccctca tgaatgggtg gttctgggcc ccatggctgg cagcagagag ggagatgttc
241	agccaccaag cccagagccc tgccacaggc ttctgtgagg cctccatctg ctctgggttc
301	ttgccctgag aggctgccct gaagtcaaac agaagcaggt gggcctctct tccagggctg
361	ctctctcccc cactgacagc tccctagagg gagactcaga cagcggggac agattcctca
421	ggcataagca ctggagttta ggctggccag ttcattccat acgcccacat gacatgacac
481	aaggcagagg ctgtgggaca aaggtattgc cttttcttct ggcatgagga atggcttagg
541	aagcagggga tggtggggct ggggttgagt gatgggctgt gggccacaag gagtgggtgg
601	gcgctgagaa agtgtcctgg ttgtctgtcc atagacgcag aatgagtggc atcccaggag
661	cctgtgaggg gctggcagag acttactggt tccagtaaaa gccccatgtg gatgcagtaa
721	tgctgcctgc tggtccttgg ctgtaattac aaacaggtac atgaggtacc catgcatctt
781	gaagctctca gggagtgggt tccagctgct catggtaggc acttttagtc actgaacatg
841	cttcaggcat gtccaagctt gattaagcca ggcatcttgc tgtgaggccc tccacttcac
901	taagaacact cttccttgct tcccctggaa gttggacctt ccagttctgg ttctggagac
961	acgatggccc ctcctggacc cctgggagaa tgtgctcagg tgacacacag ttgatggggc
1021	ccatttccaa gccattcttc catttcccac tgtttgaggg acccgaggcc ggtgacaagc
1081	acagagccac ccaaggccag ctgtctgcac ctaaatgtga tgcttgtctg gatgtctcag
1141	ggccagaacc ctccaggtga gatggcctgg tcctcaccac ctggcgtccg tgctcccttt
1201	tcctctgttc aatcctggcg ccaatgcctc cctcaactct caggtcacca ttggagaaga
1261	tgctcaggaa gaacaagcag ctgcagttaa ccctgctgaa agtggcagat gggtccaggc
1321	tcttgagctc gtcttggaca tggaacatgt ggatacaggc tttgagcagt gtgtgtagct

continued ...

Table D.1: continued ...

Nucleotide position	Genomic DNA Sequence
1381	ctttcaggaa ggaagggaaa agggtgttac ccgggtccta caccctggaa cgacccttct
1441	cagacagtaa atagttggca gggtgcggtc atgtgtgatt ttagttttca actttaggct
1501	ttcattttca aattccacaa taaacacata aggtggagtt ctggtttcag cacacacaca
1561	cacacacaca aacacacaca cacacacaca cacagtctct ctctctgtat gtctctttct
1621	gtctctctct ctctccttcc tgcaaggatc cttgttaaca agaaaccttc tgccaaatgc
1681	ctctgaagca caggcaggtc ttggggagcc acaaggccac ttcctctttg tgcactagtg
1741	tcttgggtag gcatagcttt cagagctctg gggcctccac aaccttgccc tgctgtccag
1801	gggcagccct catgcagggg tgtcctaaga acttttcagg atgcacaagt tcagcactgt
1861	cttccaatgt gtgtttcacg atattttaat ggtggttctt ttgggaaaaa ggaaaggttc
1921	tgtgatcaat tatgggacac attgagctac agatcttttt cacaattgct cttaacaagc
1981	aggtagaccc tgagaacatg agtagcttcc ccgcaggtaa cttgagtgca tgagaacttt
2041	tgctttacaa ccatgccaat ctcacctcag cagttggcag tgctgcacgg ggcagacttc
2101	cctactcaaa ggctgtgaag cttttctttc ttttttttta aacattattt ttctttatag
2161	aattttgttg ggctgatatc aagcctggct tggtactgcc tcatttttt tggaatcaga
2221	acgctgttct ttaactcacg ggttgtgaag ttagaaggtg ctggtgtgac agcctgacaa
2281	gcagagcgca gctccaatcc caccttcatg ctctcatctg acgcagagcc ctcagagaag
2341	tggggaagtg cttcctggcc ctgcttctgg gggccgtccc caaggcagtc caccgaactt
2401	ccaaaacagc cttccctcac acacagccct gagccctcct gccgctcctc aatgttgcac
2461	atctctgaga agtggtccag catgttgctg tccaggggca gtgagaagca ggtgcggtga
2521	cacatgtctt cacggaccat gagcaccggg taaatctcct gcacaatctc cttgggggac
2581	accttgaggg agaaagcccc aacaactgat ggcatgccac atggcagaaa gcaaagactt
2641	acccttccc cagcccaaag tcctgagaat catgccaaaa atccttggtt tcccactttt
2701	taaaaatttt aaaattaaaa tcccaggttc cgcgtataca tgccatgccc acctgcacct
2761	gtgtgtgtgt gtgtgtttgt gcacgcagga cagagcctgg cccattgact attcctgcag
2821	accaagaaaa atccctatgc agagtaaggg gagatggaag aaacgaggga gagaaaatgg
2881	cagccttgcc tcctcccttg cccagtgcta aggtccccag ggcaaatggc ttttgccttc
2941	aacttcacct taacaacata caaaatatat tcatttttac ttccgtcact ttcttaacat
3001	tacaaattgt atctttatat atgatttgta ttttcacaga gatttaagaa tttaatgcac
3061	cattatagta gaaaattgta tatctgtgta tatatttaca ttgaacagag agctttatat
3121	tttcatgtgg ttttatgatg ctgtccagca tcatttaatt tttcaacata attaactctc
3181	tttagcattt tttttcctag ggttattcta gtagttaaca acctcagctt ttttatttta
3241	atctttgaaa gtctttattt ttttctaatt tttgaaatac agtatttccc agatcaatta
3301	ttattggttg ctagtatttt ttctttcatc gctttgaaat ctggaaagtt cttagcatcc
3361	ccgctttttc tctgaaataa tgtttatgcc attttctccc tctattcttt ttaaaagact
3421	ctatctctga atgtattggt ctacttgatg gtgtccagta agtcttatat ttcacccgta
3481	attttcccat tctttaaaat attagtttcc aggactcaat atttgtgaat aatatatgtt
3541	caattttctt ttttctgctc cattgtttgc tgttgtgtct ctgtagtgaa tttataaaac
3601	tcagttatta tattcttcaa ctctatgatt tctgttgggt ttttaaaaat agtttttatc

continued ...

Table D.1: continued ...

Nucleotide position	Genomic DNA Sequence
3661	tctttgttga tattttgctc attcgttatt tttaaatttc actcagttgt ctctttctgt
3721	tatagttttg ctcactgaga atgcataaga tgattatttt aagttctcca tcagatatgc
3781	aaaaatcttt atttgttaaa attcagtttc tgaatattta tgtttttctt ccaatgggga
3841	atattttctg ccttctctgt gtgccttgtg attttttttt ttaaagagat ctggggatct
3901	atacagcact catcaaatct agcatttaaa gactggctca gtaaaggggg ataccgacag
3961	caatagtcca ggctatagat tctaggtgct tcacaaacac attcccaaat atattttctc
4021	tggacttcgc tgtgtttcca agttaaagag aatttttttct caatgtattt tagattctat
4081	tgtatatttt cttccccagt tggctgtctg tggtattgca gtttcactag tgctgtagca
4141	aacactcatc tttcttctca gcagacacaa actgtcatct atatgactcc atcatgtcct
4201	tcagcactcc acatcaggag agaaagaatc tagtcattag acaatttatc aaaaagccaa
4261	acatttcaac acatattcta ctgttttaat tctctcctga aggagatact gggagttggg
4321	cattttctca ttagcccagt tactgttctg ggtgaaaaaa taaactgcag tggacaggct
4381	gtaagccaga cttcatcaaa tttctgcacc aatgaaaaaa aaatttacaa gagaaaaaca
4441	aaaaacccta ttaaacgtca cggacaaggc cagagtttga atatactgtg gtcatctctg
4501	ctccagtgca aactgtttcc agaaagccta cttctatttt ccttgctgta acagaggaac
4561	atttcctgtc ttatgtttat tctactctgc aatcccctaa ggctttttct ctccctccca
4621	gaatcttaaa gtgcattcga actcacaggc aaaatcctcc cagaatcttg tgagaacata
4681	aatgatctga ctagtttggc attgcttttg gggatctggg aaaatctgtg cacacttctg
4741	gagacccttg tcatgccatt ttttataaat ctattgtgcc tcaagtcaga agtgtgtgag
4801	gggagatggg gagacattgg gatgcgcgcg cctggggctc tcccacaggg ggctttcgtg
4861	agccaggcag cgagggccgc ccccgcgctg cagcccagcc aggccgcgac ggcagagggg
4921	gtctcccaac ctgccccggc gcgcggggat ttcgcctacg ccgccccggc tcctccggac
4981	ggggcgctct cccaccctca ggctcctcgg tggcctccgc acccgggcaa aagccgggag
5041	gaccgggacc cgcagcgcga cggcctgccg ggcccctgcg cggtggcaca gcctgggccc
5101	gctcaagcgg ggccgcaggg ccaaggggtg cttgcgccac ccacgtccca ggggagtccg
5161	tggtggggct ggggccgggt ccccaggtcg ccggggcggc gtgggaaccc caagccgggg
5221	caagcttcca cctccccagc ccgcgccccc ggacgcctcc gcctccgcgc ggcaggggca
5281	gatgcaaggc atcccggcgc cctcccaggc gctccaggag ccggcgccct ggtctgcact
5341	cccctgcggc ctgctgctgg atgagctcct ggcgagcccg gagtttctgc agcaggcgca
5401	acctctccta gaaacggagg ccccgggggа gctggaggcc tcggaagagg ccgcctcgct
5461	ggaagcaccc ctcagcgagg aagaataccg ggctctgctg gaggagcttt aggacgcggg
5521	gttgggacgg ggtcgggtgg ttcggggcag ggcggtggcc tctctttcgc ggggaacacc
5581	tggctggcta cggaggggcg tgtctccgcc ccgccccctc caccgggctg accggcctgg
5641	gattcctgcc ttctaggtct aggcccggtg agagactcca caccgcggag aactgccatt
5701	ctttcctggg catcccgggg atcccagagc cggcccaggt accagcaggt gggccgccta
5761	ctgcgcacgc gcgggtttgc gggcagccgc ctgggctgtg ggagcagccc gggcagagct
5821	ctcctgcctc tccaccagcc caccccgccg cctgaccgcc ccctccccac cccccacccc
5881	ccacccccgg aaaacgcgtc gtcccctggg ctgggtggag acccccgtcc cgcgaaacac

continued ...

Table D.1: continued ...

Nucleotide position	Genomic DNA Sequence
5941	cgggccccgc gcagcgtccg ggcctgacac cgctccggcg gctcgcctcc tatgcgcccc
6001	cgcgccaccg tcgcccgccc gcccgggccc ctgcagccgc ccaggtgcca gcacggagcg
6061	cctggcggcg gaacgcagac cccaggcccg gcgcacaccg gggacgctga gcgttccagg
6121	cgggagggaa ggcgggcaga gatggagaga ggaacgggag acctagaggg gcggaaggac
6181	gggcggaggg acgttaggag ggagggaggg aggcagggag gcagggagga acggagggaa
6241	agacagagcg acgcagggac tgggggcggg cgggagggag ccggggaacg gggggaggaa
6301	ggcagggagg aaaagcggtc ctcggcctcc gggagtagcg ggacccccgc cctccgggaa
6361	aacggtcagc gtccggcgcg ggctgagggc tgggcccaca gccgccgcgc cggccggcgg
6421	ggcaccaccc attcgccccg gttccgtggc ccagggagtg ggcggtttcc tccgggacaa
6481	aagaccggga ctcgggttgc cgtcgggtct tcacccgcgc ggttcacaga ccgcacatcc
6541	ccaggctgag ccctgcaacg cggcgcgagg ccgacagccc cggccacgga ggagccacac
6601	gcaggacgac ggaggcgtga ttttggtttc cgcgtggctt tgccctccgc aaggcggcct
6661	gttgctcacg tctctccggc ccccgaaagg ctggccatgc cgactgtttg ctcccggagc
6721	tctgcgggca cccggaaaca tgcagggaag ggtgcaagcc cggcacggtg ccttcgctct
6781	ccttgccagg ttccaaaccg gccacactgc agactcccca cgttgccgca cgcgggaatc
6841	catcgtcagg ccatcacgcc ggggaggcat ctcctctctg gggtctcgct ctggtcttct
6901	acgtggaaat gaacgagagc cacacgcctg cgtgtgcgag accgtcccgg caacggcgac
6961	gcccacaggc attgcctcct tcacggagag agggcctggc acactcaaga ctcccacgga
7021	ggttcagttc cacactcccc tccaccctcc caggctggtt tctccctgct gccgacgcgt
7081	gggagcccag agagcggctt cccgttcccg cgggatccct ggagaggtcc ggagagccgg
7141	ccccgaaac gcgcccccct ccccctccc ccctctcccc cttcctcttc gtctctccgg
7201	ccccaccacc accaccgcca ccacgccctc ccccccacc cccccccccc accaccacca
7261	ccaccacccc gccggccggc cccaggcctc gacgccctgg ggtcccttcc ggggtggggc
7321	gggctgtccc agggggggctc accgccattc atgaaggggt ggagcctgcc tgcctgtggg
7381	cctttacaag ggcggctggc tggctggccg gctgtccggg caggcctcct ggctgcacct
7441	gccgcagtgc acagtccggc tgaggtgcac gggagcccgc cggcctctct ctgcccgcgt
7501	ccgtccgtga aattccggcc ggggctcacc gcgatggccc tcccgacacc ctcggacagc
7561	accctccccg cggaagcccg gggacgagga cggcgacgga gactcgtttg gacccgagc
7621	caaagcgagg ccctgcgagc ctgctttgag cggaacccgt acccgggcat cgccaccaga
7681	gaacggctgg cccaggccat cggcattccg gagcccaggg tccagatttg gtttcagaat
7741	gagaggtcac gccagctgag gcagcaccgg cgggaatctc ggccctggcc cgggagacgc
7801	ggcccgccag aaggccggcg aaagcggacc gccgtcaccg gatcccagac cgccctgctc
7861	ctccgagcct ttgagaagga tcgctttcca ggcatcgccg cccgggagga gctggccaga
7921	gagacgggcc tcccggagtc caggattcag atctggtttc agaatcgaag ggccaggcac
7981	ccgggacagg gtggcagggc gcccgcgcag gcaggcggcc tgtgcagcgc ggccccggc
8041	gggggtcacc ctgctccctc gtgggtcgcc ttcgcccaca ccggcgcgtg gggaacgggg
8101	cttcccgcac cccacgtgcc ctgcgcgcct ggggctctcc cacaggggc tttcgtgagc
8161	caggcagcga gggccgcccc cgcgctgcag cccagccagg ccgcgccggc agaggggatc

continued ...

Table D.1: continued ...

Nucleotide position	Genomic DNA Sequence
8221	tcccaacctg ccccggcgcg cggggatttc gcctacgccg ccccggctcc tccggacggg
8281	gcgctctccc accctcaggc tcctcggtgg cctccgcacc cgggcaaaag ccgggaggac
8341	cgggacccgc agcgcgacgg cctgccgggc ccctgcgcgg tggcacagcc tgggcccgct
8401	caagcggggc cgcagggcca aggggtgctt gcgccaccca cgtcccaggg gagtccgtgg
8461	tggggctggg gccggggtcc ccaggtcgcc ggggcggcgt gggaacccca agccgggca
8521	gctccacctc cccagcccgc gcccccggac gcctccgcct ccgcgcggca ggggcagatg
8581	caaggcatcc cggcgccctc ccaggcgctc caggagccgg cgccctggtc tgcactcccc
8641	tgcggcctgc tgctggatga gctcctggcg agcccggagt ttctgcagca ggcgcaacct
8701	ctcctagaaa cggaggcccc gggggagctg gaggcctcgg aagaggccgc ctcgctggaa
8761	gcacccctca gcgaggaaga ataccgggct ctgctggagg agctttagga cgcggggttg
8821	ggacggggtc gggtggttcg gggcagggcg gtggcctctc tttcgcgggg aacacctggc
8881	tggctacgga ggggcgtgtc tccgccccgc cccctccacc gggctgaccg gcctgggatt
8941	cctgccttct aggtctaggc ccggtgagag actccacacc gcggagaact gccattcttt
9001	cctgggcatc ccggggatcc cagagccggc ccaggtacca gcaggtgggc cgcctactgc
9061	gcacgcgcgg gtttgcgggc agccgcctgg gctgtgggag cagcccgggc agagctctcc
9121	tgcctctcca ccagcccacc ccgccgcctg accgcccccc ccccacccca caccccccac
9181	ccccggaaaa cgcgtcgtcc cctgggctgg gtggagaccc ccgtcccgcg aaacaccggg
9241	ccccgcgcag cgtccgggcc tgacaccgct ccggcggctc gcctcctatg cgccccgcg
9301	ccaccgtcgc ccgcccgccc gggcccctgc agccgcccag gtgccagcac ggagcgcctg
9361	gcggcggaac gcagacccca ggcccggcgc acaccgggga cgctgagcgt tccaggcggg
9421	agggaaggcg ggcagagatg gagagaggaa cgggagacct agaggggcgg aaggacgggc
9481	ggagggacgt taggagggag ggagggaggc agggaggcag ggaggaacgg agggaaagac
9541	agagcgacgc agggactggg ggcgggcggg agggagccgg ggaacggggg gaggaaggca
9601	gggaggaaaa gcggtcctcg gcctccggga gtagcgggac ccccgccctc cgggaaaacg
9661	gtcagcgtcc ggcgcgggct gagggctggg cccacagccg ccgcgccggc cggcggggca
9721	ccacccattc gccccggttc cgtggcccag ggagtgggcg gtttcctccg ggacaaaaga
9781	ccgggactcg ggttgccgtc gggtcttcac ccgcgcggtt cacagaccgc acatccccag
9841	gctgagccct gcaacgcggc gcgaggccga cagccccggc cacggaggag ccacacgcag
9901	gacgacggag gcgtgatttt ggtttccgcg tggctttgcc ctccgcaagg cggcctgttg
9961	ctcacgtctc tccggccccc gaaaggctgg ccatgccgac tgtttgctcc cggagctctg
10021	cgggcacccg gaaacatgca gggaagggtg caagcccggc acggtgcctt cgctctcctt
10081	gccaggttcc aaaccggcca cactgcagac tccccacgtt gccgcacgcg ggaatccatc
10141	gtcaggccat cacgccgggg aggcatctcc tctctggggt ctcgctctgg tcttctacgt
10321	cagttccaca ctcccctcca ccctcccagg ctggtttctc cctgctgccg acgcgtggga
10381	gcccagagag cggcttcccg ttcccgcggg atccctggag aggtccggag agccggcccc
10441	cgaaacgcgc ccccctcccc cctccccccc ctcccccttc ctcttcgtct ctccggcccc
10501	accaccacca ccgccaccac gccctccccc ccccccccgc cccccacca ccaccaccac

continued ...

Table D.1: continued ...

Nucleotide position	Genomic DNA Sequence
10201	ggaaatgaac gagagccaca cgcctgcgtg tgcgagaccg tcccggcaac ggcgacgccc
10261	acaggcattg cctccttcac ggagagaggg cctggcacac tcaagactcc cacggaggtt
10561	caccccgccg gccggcccca ggcctcgacg ccctgggtcc cttcggggggt ggggcgggct
10621	gtcccagggg ggctcaccgc cattcatgaa ggggtggagc ctgcctgcct gtgggccttt
10681	acaagggcgg ctggctggct ggctggctgt ccgggcaggc ctcctggctg cacctgccgc
10741	agtgcacagt ccggctgagg tgcacgggag cccgccggcc tctctctgcc cgcgtccgtc
10801	cgtgaaattc cggccggggc tcaccgcgat ggccctcccg acaccctcgg acagcaccct
10861	ccccgcggaa gcccggggac gaggacggcg acggagactc gtttggaccc cgagccaaag
10921	cgaggccctg cgagcctgct ttgagcggaa cccgtacccg ggcatcgcca ccagagaacg
10981	gctggcccag gccatcggca ttccggagcc cagggtccag atttggtttc agaatgagag
11041	gtcacgccag ctgaggcagc accggcggga atctcggccc tggcccggga gacgcggccc
11101	gccagaaggc cggcgaaagc ggaccgccgt caccggatcc cagaccgccc tgctcctccg
11161	agcctttgag aaggatcgct ttccaggcat cgccgcccgg gaggagctgg ccagagagac
11221	gggcctcccg gagtccagga ttcagatctg gtttcagaat cgaagggcca ggcacccggg
11281	acagggtggc agggcgcccg cgcaggcagg cggcctgtgc agcgcggccc ccggcggggg
11341	tcaccctgct ccctcgtggg tcgccttcgc ccacaccggc gcgtggggaa cggggcttcc
11401	cgcaccccac gtgccctgcg cgcctggggc tctcccacag ggggctttcg tgagccaggc
11461	agcgagggcc gcccccgcgc tgcagcccag ccaggccgcg ccggcagagg ggatctccca
11521	acctgccccg gcgcgcgggg atttcgccta cgccgccccg gctcctccgg acggggcgct
11581	ctcccaccct caggctcctc gctggcctcc gcacccgggc aaaagccggg aggaccggga
11641	cccgcagcgc gacggcctgc cgggcccctg cgcggtggca cagcctgggc ccgctcaagc
11701	ggggccgcag ggccaagggg tgcttgcgcc acccacgtcc caggggagtc cgtggtgggg
11761	ctggggccgg ggtccccagg tcgccggggc ggcgtgggaa ccccaagccg gggcagctcc
11821	acctccccag cccgcgcccc cggacgcctc cgcctccgcg cggcaggggc agatgcaagg
11881	catcccggcg ccctcccagg cgctccagga gccggcgccc tggtctgcac tcccctgcgg
11941	cctgctgctg gatgagctcc tggcgagccc ggagtttctg cagcaggcgc aacctctcct
12001	agaaacggag gccccggggg agctggaggc ctcggaagag gccgcctcgc tggaagcacc
12061	cctcagcgag gaagaatacc gggctctgct ggaggagctt taggacgcgg ggttgggacg
12121	gggtcgggtg gttcggggca gggccgtggc ctctctttcg cggggaacac ctggctggct
12181	acggaggggc gtgtctccgc cccgcccccc ccaccgggct gaccggcctg ggattcctgc
12241	cttctaggtc taggcccggt gagagactcc acaccgcgga gaactgccat tctttcctgg
12301	gcatcccggg gatcccagag ccggcccagg tacctgcgca cgcgcgggtt tgcgggcagc
12361	cgcctgggct gtgggagcag cccgggcaga gctctcctgc ctctccacca gcccaccccg
12541	ctccgctccg gcggctcgcc tcctgtgtgc ccccgcgcca ccgtcgcccg cccgcccggg
12601	cccctgcagc ctcccagctg ccagcgcgga gctcctggcg gtcaaaagca tacctctgtc
12661	tgtctttgcc cgcttcctgg ctagacctgc gcgcagtgcg caccccggct gacgtgcaag
12721	ggagctcgct ggcctctctg tgcccttgtt cttccgtgaa attctggctg aatgtctccc
12421	ccgcctgacc gcccccctcc caccccccac cccccacccc cggaaaacgc gtcgtccccc

continued ...

Table D.1: continued ...

Nucleotide position	Genomic DNA Sequence
12481	gggctgggtg gagacccccg tcccgcgaaa caccgggccc cgcgcagcgt ccgggcctga
12781	cccaccttcc gacgctgtct aggcaaacct ggattagagt tacatctcct ggatgattag
12841	ttcagagata tattaaaatg ccccctccct gtggatccta tagaagattt gcatcttttg
12901	tgtgatgagt gcagagatat gtcacaatat cccctgtaga aaaagcctga aattggttta
12961	cataacttcg gtgatcagtg cagatgtgtt tcagaactcc atagtagact gaacctagag
13021	aatggttaca tcacttaggt gatcagtgta gagatatgtt aaaattctcg tgtagacaga
13081	gcctagacaa ttgttacatc acctagtgat cagtgcaggg ataagtcata aagcctcctg
13141	taggcagagt gtaggcaagt gttccctccc tgggctgatc agtgcagaga tatctcacaa
13201	agcccctata agccaaacct tgacaagggt tacatcacct gtttgagcag tggaaatata
13261	tatcacaaag ccccctgtag acaaagccca gacaattttt acatctcctg agtgagcatt
13321	ggagagatct gtcacaatgc ccctgtaggc agagcttaga caagtgttac atcacctggg
13381	tgatcagtgc agagatatgt caaaacgctc ctgtagtctg aacctagaca ggagttacat
13441	caccttgggg atcagtgcag agatacgtga gaattcc

a) DNA sequence was retrieved from Genbank with accession number AF117653 as reported by Gabriels *et al.*, (1999). b) The sequence of p13E-11 is indicated by thick underlining (nt. 3896-4715). c) The start of the 3.3 kb repeat units are indicated by arrows (nt. 5738-9052 and 9034-12329). d) The Lsau and hhspm3 repeats are shown by single (nt. 5719-6036) and dashed underlining (nt. 7055-7523) respectively. e) The double homeodomains are indicated by double underlining (nt. 7588-7767, 7813-7992 and 10883-11062, 11108-11287). f) The black box represents the GC-signal (nt. 7311-7319 and 10607-10615). g) The TATA signal (nt. 7385-7389 and 10681-10685) is represented by the blue box. h) The putative DUX4 gene is represented by the green dot-dash underlining (nt. 7534-8808 and 10829-12103). i) The restriction enzymes are indicated by: gaattc for *Eco* RI; cctagg for *Bln* I; agatct for *Bgl* II; ggtacc for *Kpn* I; and gaattc for *Xap* I.

APPENDIX E

COMPARISON OF NUCLEOTIDE SEQUENCE FROM ONE *Kpn* I REPEAT UNIT DERIVED FROM CHROMOSOMES 4q35 AND 10q26

Sequences derived from the homologous *Kpn* I repeat units on chromosome 4q35 and chromosome 10q26 were compared and are presented in Table E.1.

Table E.1: Comparison of one *Kpn*I repeat unit nucleotide sequence derived from 4q35 and 10q26

Chr 4:	agatctgggg atctatacag cactcatcaa atctagcatt taaagactgg ctcagtaaag
Chr 10:	agatctgggg atctatacag cactcatcaa atctagcatt taaagactgg ctcagtaaag
	Bgl II p13E-11
	ggggataccg acagcaatag tccaggctat agattctagg tgcttcacaa acacattccc
	ggggataccg acagcaatag tccaggctat agattctagg tgcttcacaa acacattccc
	aaatatattt tctctggact tcgctgtgtt tccaagttaa agagaatttt ttctcaatgt
	aaatatattt tctctggact tgggtgtgtt tccaagttaa agagaatttt ttctcaatgt
	attttagatt ctattgtata ttttcttccc cagttggctg tctgtggtat tgcagtttca
	attttagatt ctattgtcta ttttcttccc cagttggctg tctgtggtat tgcagtttca
	ctagtgctgt agcaaacact catctttctt ctcagcagac acaaactgtc atctatatga
	ctagtgctgt agcaaacact catctttctt ctcagcaggc acaaactctc atctatatga
	ctccatcatg tccttcagca ctccacatca ggagagaaag aatctagtca ttagacaatt
	ctccatcatg tccttcagca ctccacatca ggagagaaag aatctagtca ttagacaatt
	tatcaaaaag ccaaacattt caacacatat tctactgttt taattctctc ctgaaggaga
	tatcaaaaag ccaaacattt caacacatat tctactgttt taattctctc ctgaaggaga
	tactgggagt tgggcatttt ctcattagcc cagttactgt tctgggtgaa aaaataaact
	tactgggagt tgggcatttt ctgattagcc cagttactgt tctgggtgaa aaaagaaact
	gcagtggaca ggctgtaagc cagacttcat caaatttctg caccaatgaa aaaaaaattt
	gcagtggaca ggctgtaagc cagacttcat caaatttctg cagcaatgaa aaaaaaattt
	acaagagaaa aacaaaaaac cctattaaac gtcacggaca aggccagagt ttgaatatac
	acaagagaaa aacaaaaaac cctattaaac gtcacggaca aggccagagt ttgaatatac
	tgtggtcatc tctgctccag tgcaaactgt ttccagaaag cctacttcta ttttccttgc
	tgtggtcatc tccgctccag tgcaaactgt tttcagaaag cctgctttta ttttccttgc
	tgtaacagag gaacatttcc tgtcttatgt ttattctact ctgcaatccc ctaaggcttt
	tgtaacagag gaacatttcc tgtcttatgc ttattctact ctgcagtccc ctaaggcttt

continued ...

Table E.1: continued ...

Chr 4: Chr 10:	ttctctccct cccagaatct taaagtgcat tcgaactcac aggcaaaatc ctcccagaat ttctctccct cccagaatct taaagtgcat tcgaacgcac aggcaaaatc ctcccagaaa cttgtgagaa cataaatgat ctgactagtt tggcattgct tttggggatc tgggaaaatc cttgtgaaaa cataaatgat ctgactagtt tggcattgct tttggggatc tgggaaaatc tgtgcacact tctggagacc cttgtcatgc cattttttat aaatctattg tgcctcaagt tgtgcacact tctggagacc cttgtcaggc cattttttat aaatctattg tgcctcaagt cagaagtgtg tgaggggaga tggggagaca ttgggatgcg cgcgcctggg gctctcccac cagcagtgtg tgaggggaga tggggagaca ttgggatgcg cgcgcctggg gctctcccac agggggcttt cgtgagccag gcagcgaggg ccgcccccgc gctgcagccc agccaggccg agggggcttt cgtgagccag gcagcgaggg ccgcccccgc gctgcagccc agccaggccg cgacggcaga gggggtctcc caacctgccc cggcgcgcgg ggatttcgcc tacgccgccc cgccggcaga ggggatctcc caacctgccc cggcgcgcgg ggatttcgcc tacgccgccc cggctcctcc ggacggggcg ctctcccacc ctcaggctcc tcggtggcct ccgcacccgg cggctcctcc ggacggggcg ctctcccacc ctcaggctcc tcggtggcct ccgcacccgg gcaaaagccg ggaggaccgg gacccgcagc gcgacggcct gccgggcccc tgcgcggtgg gcaaaagccg ggaggaccgg gacccgcagc gcgacggcct gccgggcccc tgcgcggtgg cacagcctgg gcccgctcaa gcggggccgc agggccaagg ggtgcttgcg ccacccacgt cacagcctgg gcccgctcaa gcggggccgc agggccaagg ggtgcttgcg ccacccacgt cccaggggag tccgtggtgg ggctggggcc ggg*tcccca ggtcgccggg gcggcgtggg cccaggggag tccgtggtgg ggctggggcc ggggtcccca ggtcgccggg gcggcgtggg aaccccaagc cggggcaagc ttccacctcc ccagcccgcg cccccggacg cctccgcgcg aaccccaagc cggggca*gc t*ccacctcc ccagcccgcg cccccggacg cctccgcgcg gcaggggcag atgcaaggca tcccggcgcc ctcccaggcg ctccaggagc cggcgccctg gcaggggcag atgcaaggca tcccggcgcc ctcccaggcg ctccaggagc cggcgccctg gtctgcactc ccctgcggcc tgctgctgga tgagctcctg gcgagcccgg agtttctgca gtctgcactc ccctgcggcc tgctgctgga tgagctcctg gcgagcccgg agtttctgca gcaggcgcaa cctctcctag aaacggaggc cccgggggag ctggaggcct cggaagaggc gcaggcgcaa cctctcctag aaacggaggc cccgggggag ctggaggcct cggaagaggc cgcctcgctg gaagcacccc tcagcgagga agaataccgg gctctgctgg aggagcttta cgcctcgctg gaagcacccc tcagcgagga agaataccgg gctctgctgg aggagcttta ggacgcgggg ttgggacggg gtcgggtggt tcggggcagg gcggtggcct ctctttcgcg ggacgcgggg ttgggacggg gtcgggtggt tcggggcagg gcggtggcct ctctttcgcg gggaacacct ggctggctac ggaggggcgt gtctccgccc cgcccctcc accgggctga gggaacgcct ggctggctac ggaggggcgt gtctccgccc cgcccctcc accgggctga ccggcctggg attcctgcct tctaggtcta ggcccggtga gagactccac accgcggaga ccggcctggg attcctgcct tctaggccta ggcccggtga gagactccac acagcggaga *Bln I* actgccattc tttcctgggc atcccgggga tcccagagcc ggcccaggta ccagcaggtg actgccattc tttcctgggc atcccgggga tcccagagcc ggcccaggta ccagcaggtg *Kpn I* ggccgcctac tgcgcacgcg cgggtttgcg ggcagccgcc tgggctgtgg gagcagcccg ggccgcctac tgcgcacgcg cgggtttgcg ggcagccgcc tgggctgtgg gagcagcccg

continued ...

Table E.1: continued ...

Chr 4:	ggcagagctc tcctgcctct ccaccagccc accccgccgc ctgaccgccc cctccccacc
Chr 10:	ggcagagctc tcctgcctct ccaccagccc accccgccgc ctgaccgccc cctccccacc
	ccccaccccc caccccggga aaacgcgtcg tcccctgggc tgggtggaga cccccgtccc
	ccc*accccc cgccccggga aaacgcgtcg tcccctgggc tgggtggaga cccccgtccc
	gcgaaacacc gggccccgcg cagcgtccgg gcctgacacc gctccggcgg ctcgcctcct
	gcgaaacacc gggccccgcg cagcgtccgg gcctgacacc gctccggcgg ctcgcctcct
	atgcgccccc gcgccaccgt cgcccgcccg cccgggcccc tgcagccgcc caggtgccag
	ctgcgccccc gcgccaccgt cgcccgcccg cccgggcccc tgcagccgcc caggtgccag
	cacggagcgc ctggcggcgg aacgcagacc ccaggcccgg cgcacaccgg ggacgctgag
	cacggagcgc ctggcggcgg aacgcagacc ccaggcccgg cgcacaccgg ggacgctgag
	cgttccaggc gggagggaag gcgggcagag atggagagag gaacgggaga cctagagggg
	cgttccaggc gggagggaag gcgggcagag atggagagag gaacgggaga cctagagggg
	cggaaggacg ggcggaggga cgttaggagg gagggaggga ggcagggagg cagggagg**
	cggaaggatg ggcggaggga cgttaggagg gagggaggga ggcagggagg cagggaggca
	******aacg gagggaaaga cagagcgacg cagggactgg gggcgggcgg gagggagccg
	gggaggaacg gagggaaaga cagagcgacg cagggactgg gggcgggcgg gagggagccg
	gggaacgggg ggaggaaggc agggaggaaa agcggtcctc ggcctccggg agtagcggga
	ggga*cgggg ggaggaaggc agggaggaaa agcggtcttc ggcctccggg agtagcggga
	cccccgccct ccgggaaaac ggtcagcgtc cggcgcgggc tgagggctgg gcccacagcc
	cccccgccct ccgggaaaac ggtcagcgtc cggcgcgggc tgagggctgg gcccacagcc
	gccgcgccgg ccggcggggc accacccatt cgccccggtt ccgtggccca gggagtgggc
	gccgcgccgg ccggcggggc accacccatt cgccccggtt ccgggccca gggagtgggc
	ggtttcctcc gggacaaaag accgggactc gggttgccgt cgggtcttca cccgcgcggt
	ggtttcctcc gggacaaaag accgggactc gggttgccgt cgggttttca cccgcgcggt
	tcacagaccg cacatcccca ggctgagccc tgcaacgcgg cgcg*ggccg acagccccgg
	tcacagaccg cacatcccca ggctgagccc tgcaacgcgg cgcgaggccg acagccccgg
	ccacggagga gccacacgca ggacgacgga ggcgtgattt tggtttccgc gtggctttgc
	ccacggagga gccacacgca ggacgacgga ggcgtgattt tggtttccgc gtggctttgc
	cctccgcaag gcggcctgtt gctcacgtct ctccggcccc cgaaaggctg gccatgccga
	cctctgcaag gcggcctgtt gctcacgtct ctccggcccc cgaaaggctg gccatgccga
	ctgtttgctc ccggagctct gcgggcaccc ggaaacatgc agggaacagg gtgcaagccc
	ctgtttgctc ccggagctct gcgggcaccc ggaaacatgc aggggacagg gtgcaagccc
	ggcacggtgc cttcgctctc cttgccaggt tccaaaccgg ccacactgga ctccccacgt
	ggcacggtgc cttcgctctc cttgccaggt tccaaaccgg ccacactgga ctccccacgt
	tgccgcacgc gggaatccat cgtcaggcca tcacgccggg gaggcatctc ctctctgggg
	tgccgcacgc gggaatccat cgtcaggcca tcacgccggg gaggcatctc ctctctgggg
	tctcgctctg gtcttctacg tggaaatgaa cgagagccac acgcctgcgt gtgcgagacc
	tctcgctctg gtcttctacg tggaaatgaa cgagagccac acgcctgcgt gtgcgagacc
	gtcccggcaa cggcgacgcc cacaggcatt gcctccttca cggagagagg gcctggcaca
	gtcccggcaa cggcgacgcc cacaggcatt gcctccttca cggagagagg gcctggcaca
	ctcaagactc ccacggaggt tcagttccac actcccctcc accctcccag gctggtttct
	ctcaagactc ccacggaggt tcagttccac actcccctcc accctcccag gctggtttct

continued ...

Table E.1: continued ...

Chr 4: Chr 10:	ccctgctgcc gacgcgtggg agcccagaga gcggcttccc gttcccgcgg gatccctgga ccctgctgcc gacgcgtggg agcccagaga gcggcttccc gttcccgcgg gatccctgga gaggtccgga gagccggccc ccgaaacgcg ccccccctccc ccctcccccc tctccccctt gaggtccgga gagccggccc ccgaaacgcg ccccccctccc ccctcccccc tctccccctt cctcttcgtc tctccggccc caccaccacc accgccacca cgccctcccc ccccaccccc cctcttcgtc tctccggccc caccaccacc accgccacca cgccctcccc caccaccccc ccc*cc**** ********** ccaccaccac caccaccacc ccgccggccg gccccaggcc cccaccccac accaccacca ccaccaccac caccaccacc ccgccggccg gccccaggcc tcgacgccct ggggtccctt ccggggtggg gcgggctgtc ccaggggggc tcaccgccat tcgacgccct ggg*tccctt ccggggtggg gcgggctgtc ccaggggggc tcaccgccat tcatgaaggg gtggagcctg cctgcctgtg ggcctttaca agggcggctg gctggctggc tcatgaaggg gtggagcctg cctgcccgtg ggcctttaca agggcggctg gctggctggc cggctgtccg ggcaggcctc ctggctgcac ctgccgcagt gcacagtccg gctgaggtgc tggctgtccg ggcaggcctc ctggctgcac ctgccgcagt gcacagtccg gctgaggtgc acgggagccc gccggcctct ctctgcccgc gtccgtccgt gaaattccgg ccggggctca acgggagccc gccggcctct ctctgcccgc gtccgtccgt gaaattgcgg ccggggctca *Xap* I ccgcgatggc cctcccgaca ccctcggaca gcaccctccc cgcggaagcc cggggacgag ccgcgatggc cctcccgaca ccttcggaca gcaccctccc cgcggaagcc cggggacgag gacggcgacg gagactcgtt tggaccccga gccaaagcga ggccctgcga gcctgctttg gacggcgacg gagactcgtt tggaccccga gccaaagcga ggccctgcga gcctgctttg agcggaaccc gtacccgggc atcgccacca gagaacggct ggcccaggcc atcggcattc agcggaaccc gtacccgggc atcgccacca gagaacggct ggcccaggcc atcggcattc cggagcccag ggtccagatt tggtttcaga atgagaggtc acgccagctg aggcagcacc cggagcccag ggtccagatt tggtttcaga atgagaggtc acgccagctg aggcagcacc ggcgggaatc tcggccctgg cccgggagac gcggcccgcc agaaggccgg cgaaagcgga ggcgggaatc tcggccctgg cccgggagac gcggcccgcc agaaggccgg cgaaagcgga ccgccgtcac cggatcccag accgccctgc tcctccgagc ctttgagaag gatcgctttc ccgccgtcac cggatcccag accgccctgc tcctccgagc ctttgagaag gatcgctttc caggcatcgc cgcccgggag gagctggcca gagagacggg cctcccggag tccaggattc caggcatcgc cgcccgggag gagctggcca gagagacggg cctcccggag tccaggattc agatctggtt tcagaatcga agggccaggc acccgggaca gggtggcagg gcgcccgcgc agatctggtt tcagaatcga agggccaggc acccgggaca gggtggcagg gcgcccgcgc *Bgl* II aggcaggcgg cctgtgcagc gcggcccccg gcgggggtca ccctgctccc tcgtgggtcg aggcaggcgg cctgtgcagc gcggcccccg gcgggggtca ccctgctccc tcgtgggtcg ccttcgccca caccggcgcg tggggaacgg ggcttcccgc accccacgtg ccctgcgcgc ccttcgccca caccggcgcg tggggaacgg ggcttcccgc accccacgtg ccctgcgcgc ctggggctct cccacagggg gctttcgtga gccaggcagc gagggccgcc cccgcgctgc ctggggctct cccacagggg gctttcgtga gccaggcagc gagggccgcc cccgcgctgc agcccagcca ggccgcgccg gcagagggga tctcccaacc tgccccggcg cgcggggatt agcccagcca ggccgcgccg gcagagggga tctccca*cc tgccccggcg cgcggggatt

continued ...

Table E.1: continued ...

Chr 4:	tcgcctacgc cgccccggct cctccggacg gggcgctctc ccaccctcag gctcctcggt
Chr 10:	tcgcctacgc cgccccggct cctccggacg gggcgctctc ccaccctcag gctcctcggt
	ggcctccgca cccgggcaaa agccgggagg accgggaccc gcagcgcgac ggcctgccgg
	ggcctccgca cccgggcaaa agccgggagg accgggaccc gcagcgcgac ggcctgccgg
	gcccctgcgc ggtggcacag cctgggcccg ctcaagcggg gccgcagggc caaggggtgc
	gcccctgcgc ggtggcacag cctgggcccg ctcaagcggg gccgcagggc caaggggtgc
	ttgcgccacc cacgtcccag gggagtccgt ggtggggctg gggccggggt ccccaggtcg
	ttgcgccacc cacgtcccag gggagtccgt ggtggggctg gggccggggt ccccaggtcg
	ccggggcggc gtgggaaccc caagccgggg cagctccacc tccccagccc gcgcccccgg
	ccggggcggc gtgggaaccc caagccgggg cagctccacc tccccagccc gcgcccccgg
	acgcctccgc ctccgcgcgg caggggcaga tgcaaggcat cccggcgccc tcccaggcgc
	acgcctccg* *****cgcgg caggggcaga tgcaaggcat cccggcgccc tcccaggcgc
	tccaggagcc ggcgccctgg tctgcactcc cctgcggcct gctgctggat gagctcctgg
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	cggtggcctc tctttcgcgg ggaacacctg gctggctacg gaggggcgtg tctccgcccc
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	gcccctcca ccgggctgac cggcctggga ttcctgcctt ctaggcctag gcccggtgag
	Bln I
	agactccaca ccgcggagaa ctgccattct ttcctgggca tcccggggat cccagagccg
	agactccaca cagcggagaa ctgccattct ttcctgggca tcccggggat cccagagccg
	gcccaggtac c
	gcccaggtac c
	Kpn I

a) The 4q35 sequence was retrieved from Genbank with accession number AF117653 as reported by Gabriels *et al.*, (1999) and the 10q26 sequence was retrieved from Genbank with accession number NT_028298. b) The restriction enzymes are indicated by: cctagg for *Bln* I; agatct for *Bgl* II; aaattc for Xap I; and ggtacc for *Kpn* I. c) The sequence of p13E-11 is indicated by single underlining. d) The sequence indicated in green and the * = differences observed in the two compared sequences.

APPENDIX F

EXTENDED FAMILY PEDIGREES

This appendix contains the full pedigrees of the core FSHD families (F10, F20, F30, F40 and F60), which were selected for genotyping as discussed in chapter three. Symbols utilised within the pedigrees are listed below and were assigned as reported by the Pedigree Standardization Task Force [PSTF] (Bennet *et al.*, 1995).

male/female: tested FSHD normal

male/female: FSHD equivocal

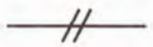
male/female: never tested for FSHD (phenotypical status unknown)

male/female: tested FSHD positive

male/female: deceased

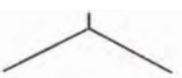
Sex unknown

multiple individuals, exact number of individuals unknown



Divorced

Proband



dizygotic twins

monozygotic twins

Figure F.1: Full pedigree of South African FSHD family F10

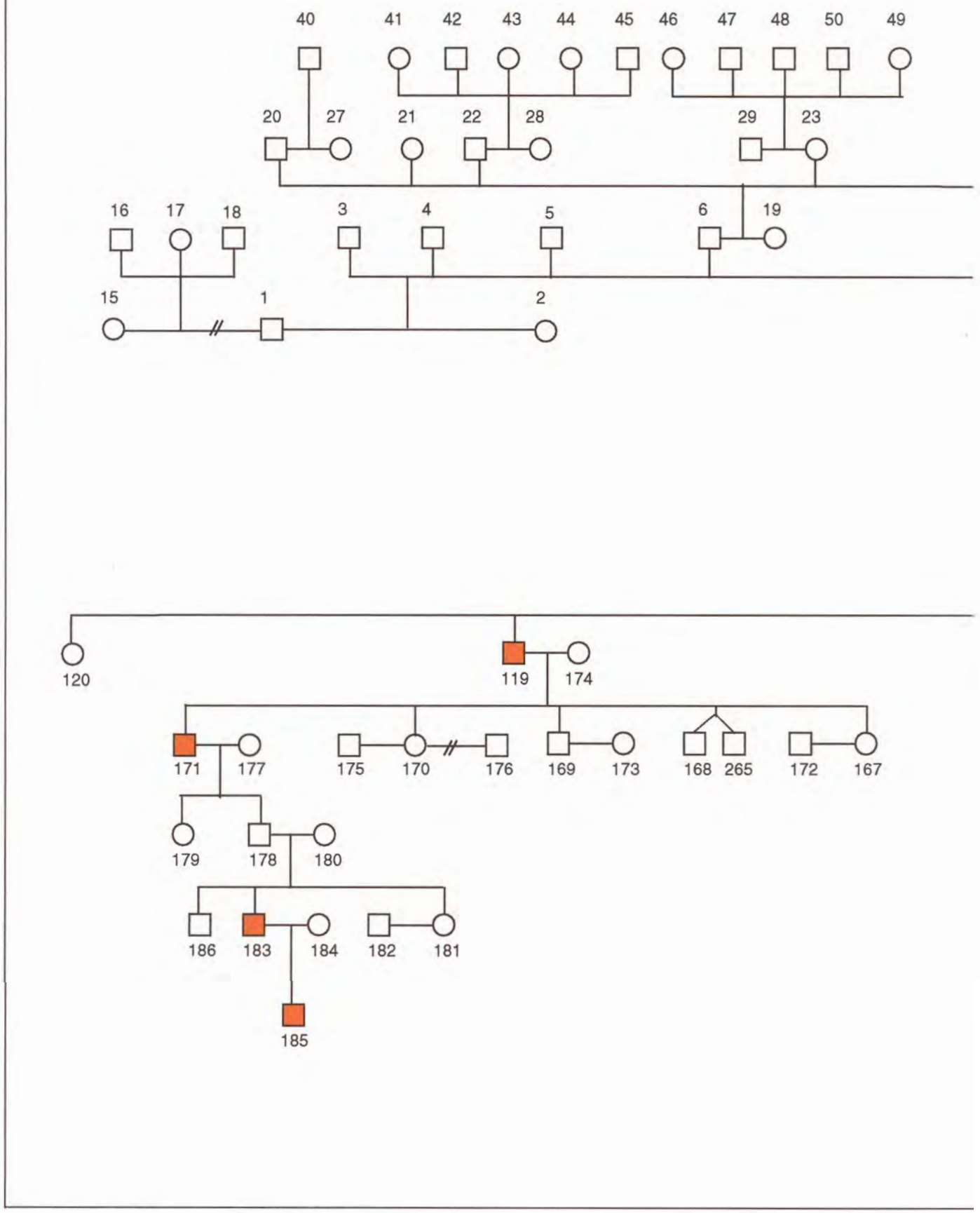
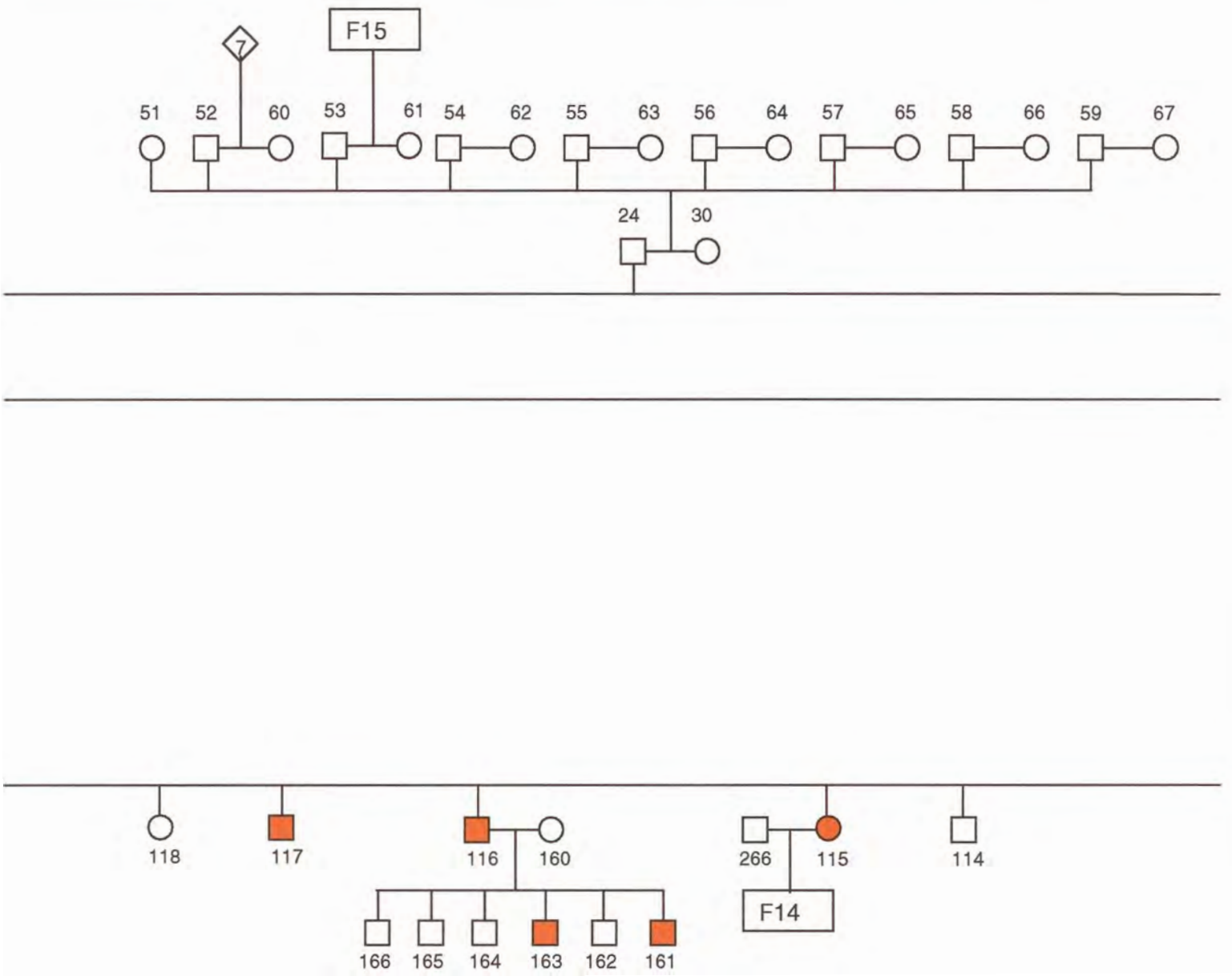


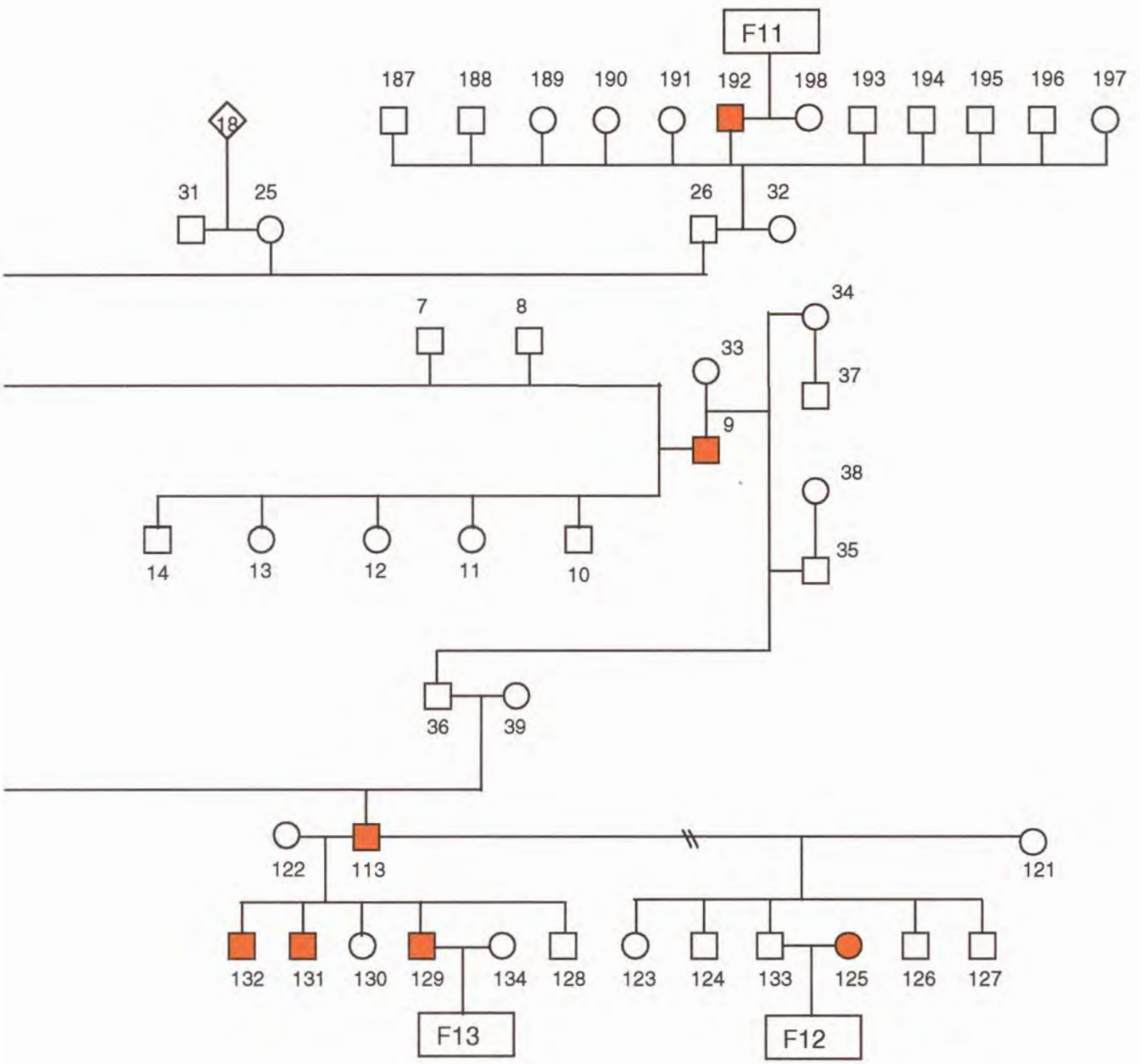
Figure F.1: Full pedigree of South African FSHD family F10 continued ...



F14 : Subfamily F14 of family F10 as presented in Figure F.5

F15 : Subfamily F15 of family F10 as presented in Figure F.6

Figure F.1: Full pedigree of South African FSHD family F10 continued ...



F11	: Subfamily F11 of family F10 as presented in Figure F.2
F12	: Subfamily F12 of family F10 as presented in Figure F.3
F13	: Subfamily F13 of family F10 as presented in Figure F.4

Figure F.2: Full pedigree of South African FSHD family F11

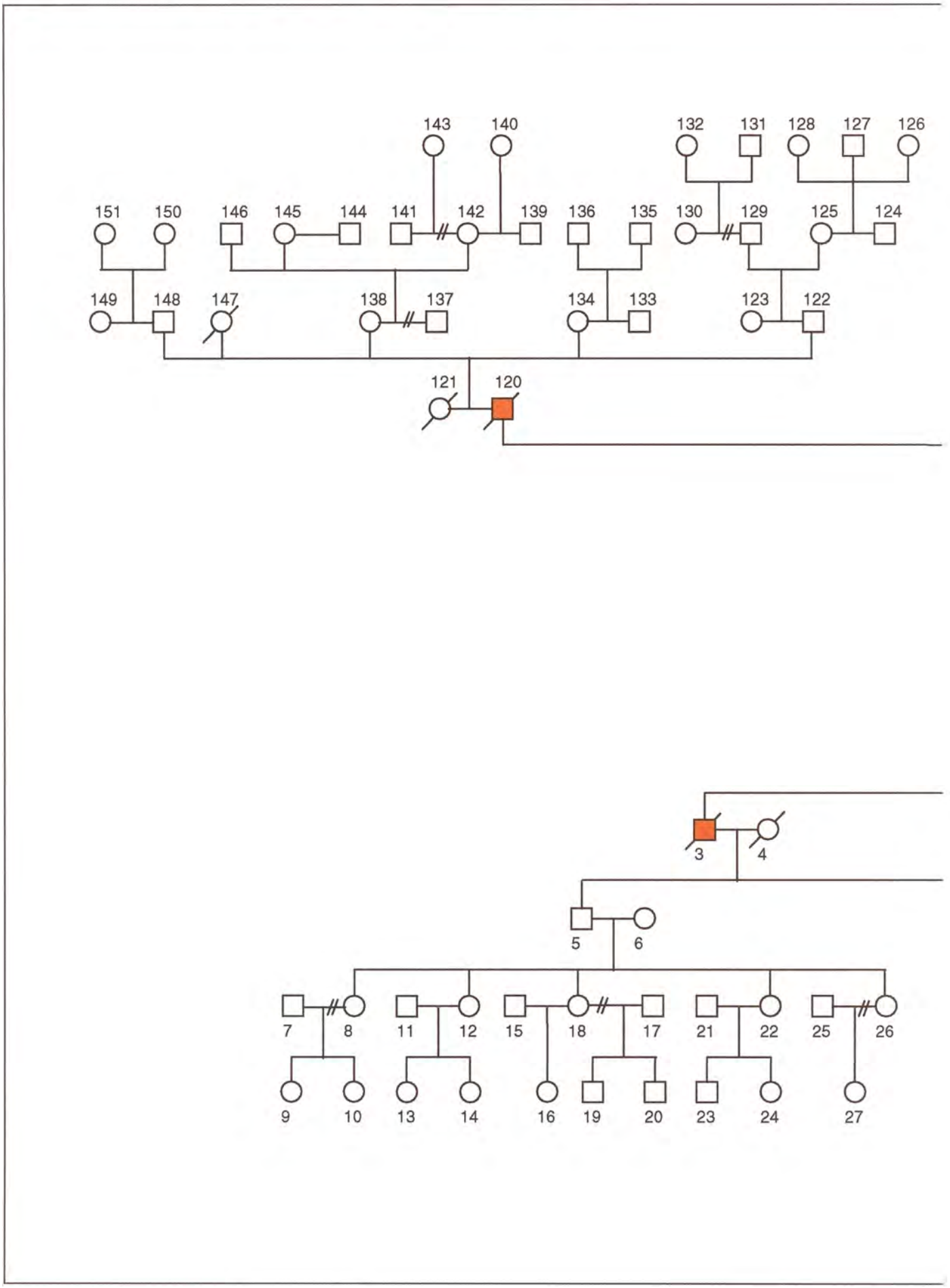


Figure F.2: Full pedigree of South African FSHD family F11 continued ...

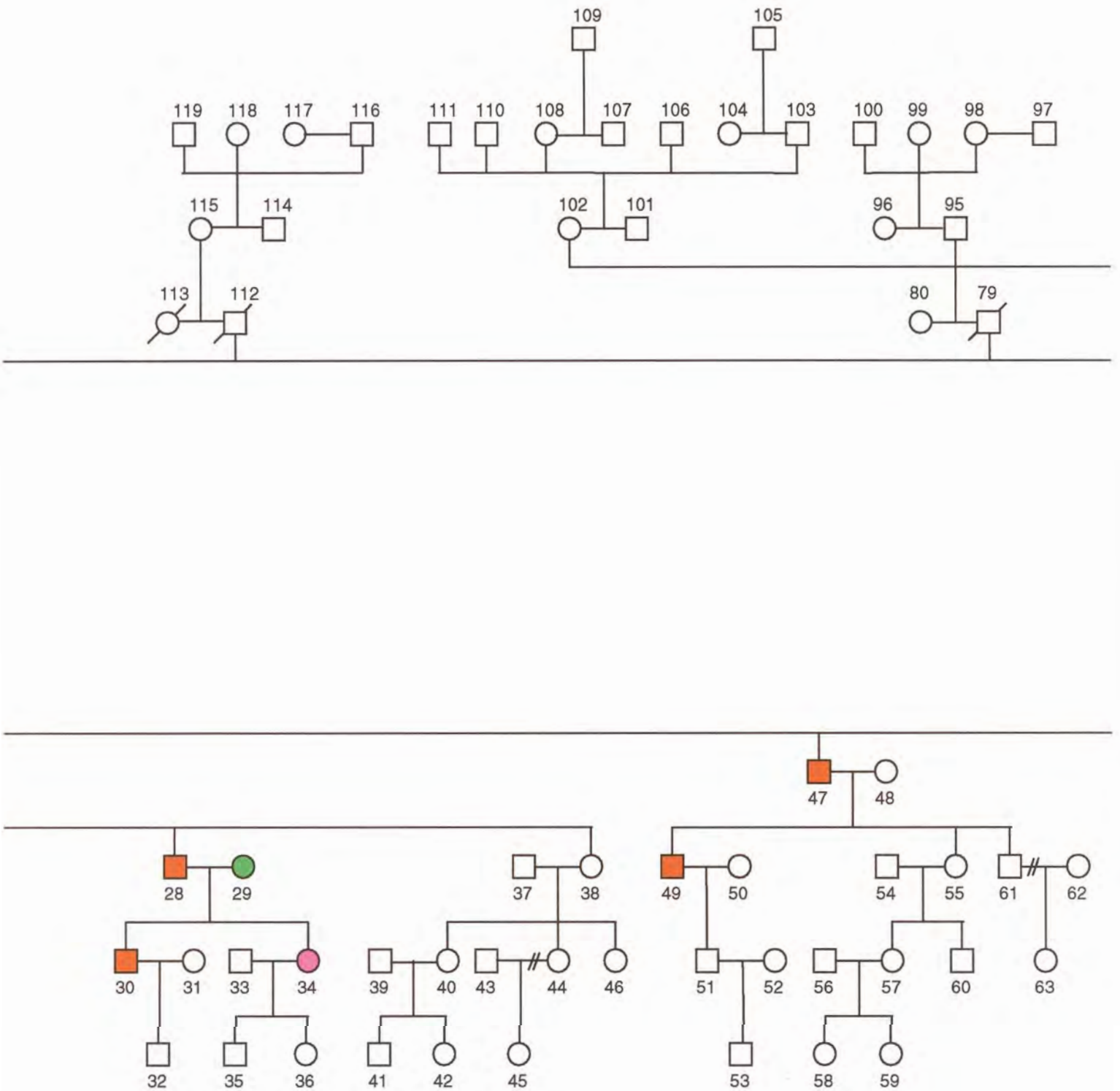


Figure F.2: Full pedigree of South African FSHD family F11 continued ...

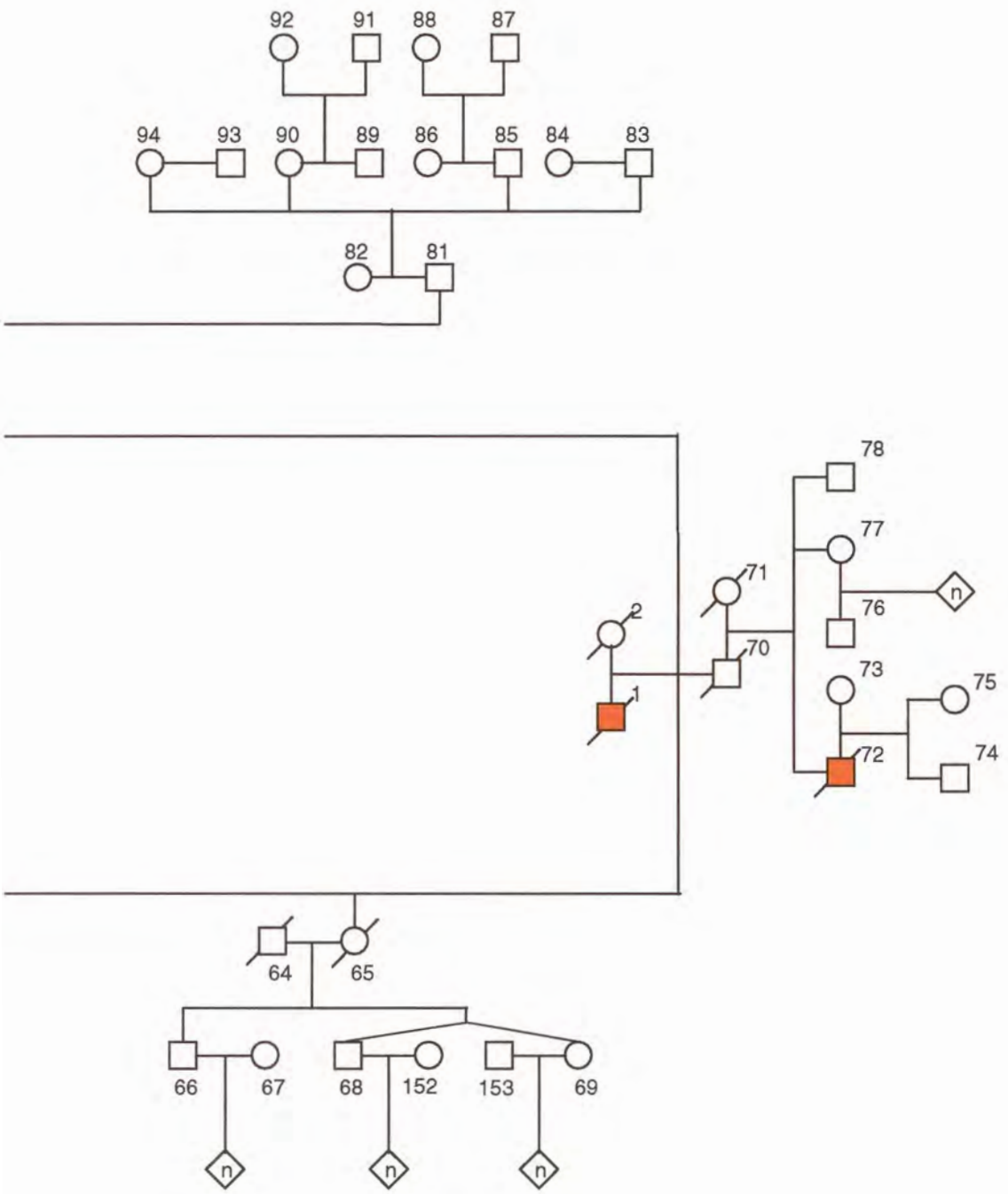


Figure F.3: Full pedigree of South African FSHD family F12

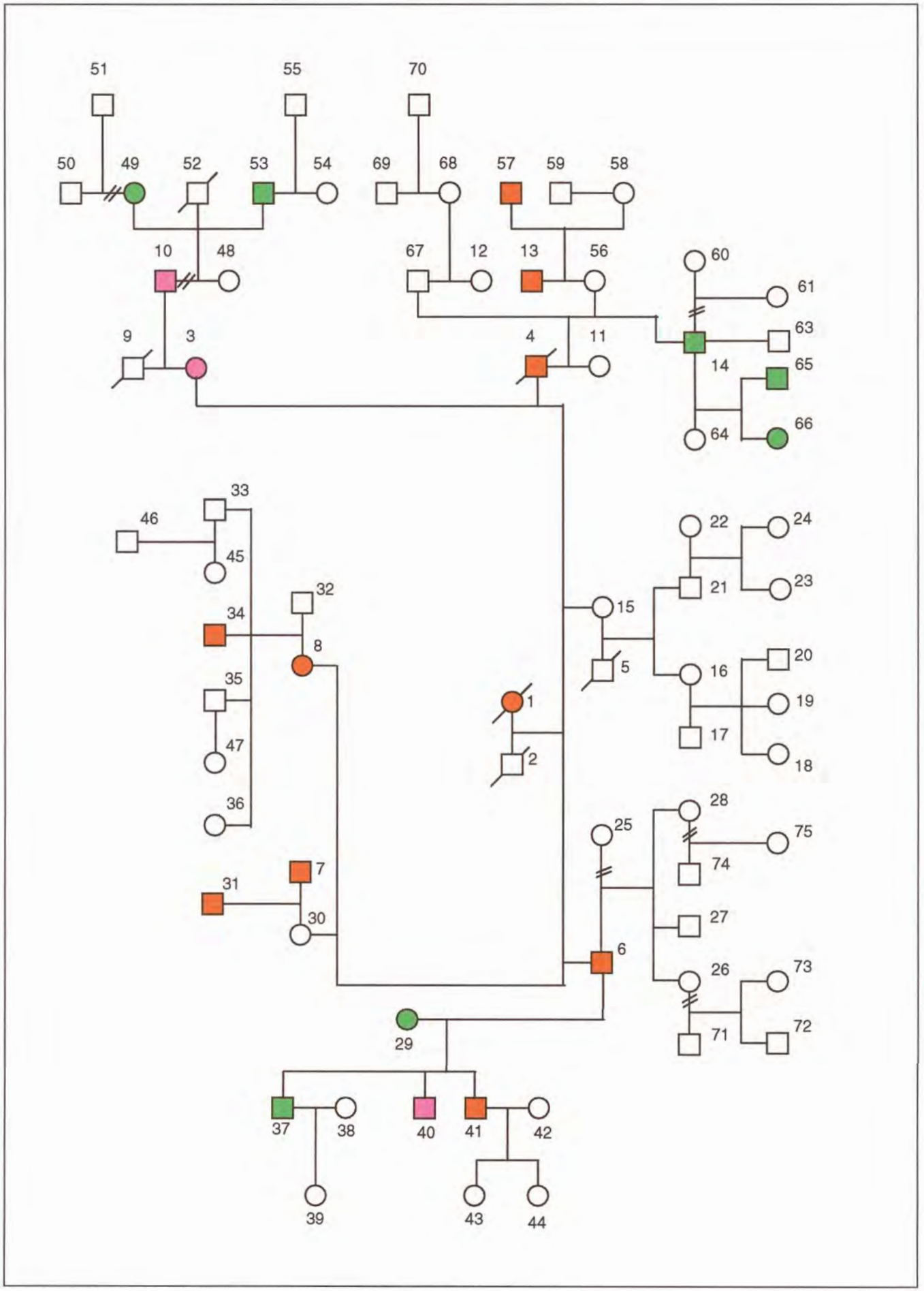


Figure F.4: Full pedigree of South African FSHD family F13

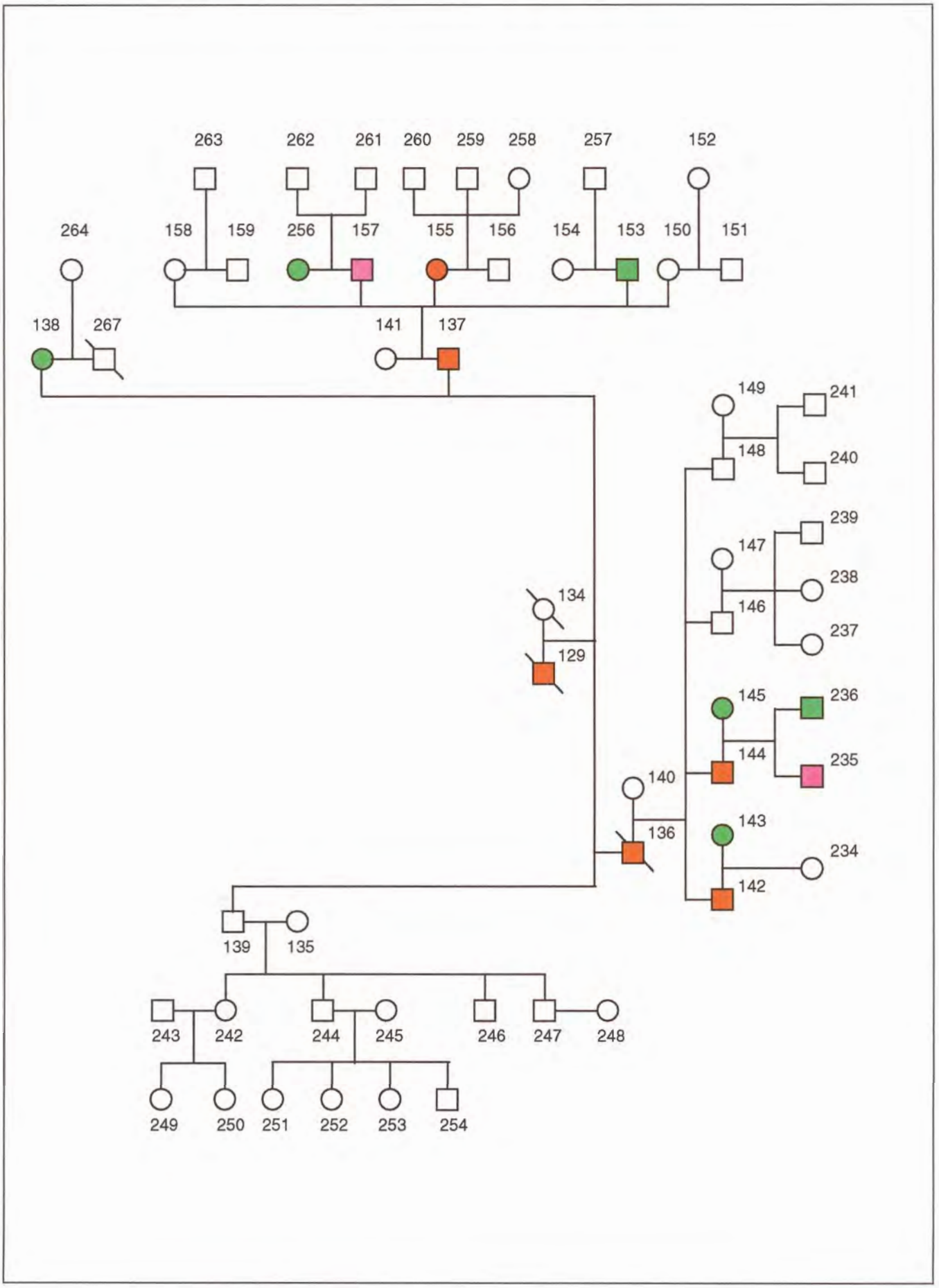


Figure F.5: Full pedigree of South African FSHD family F14

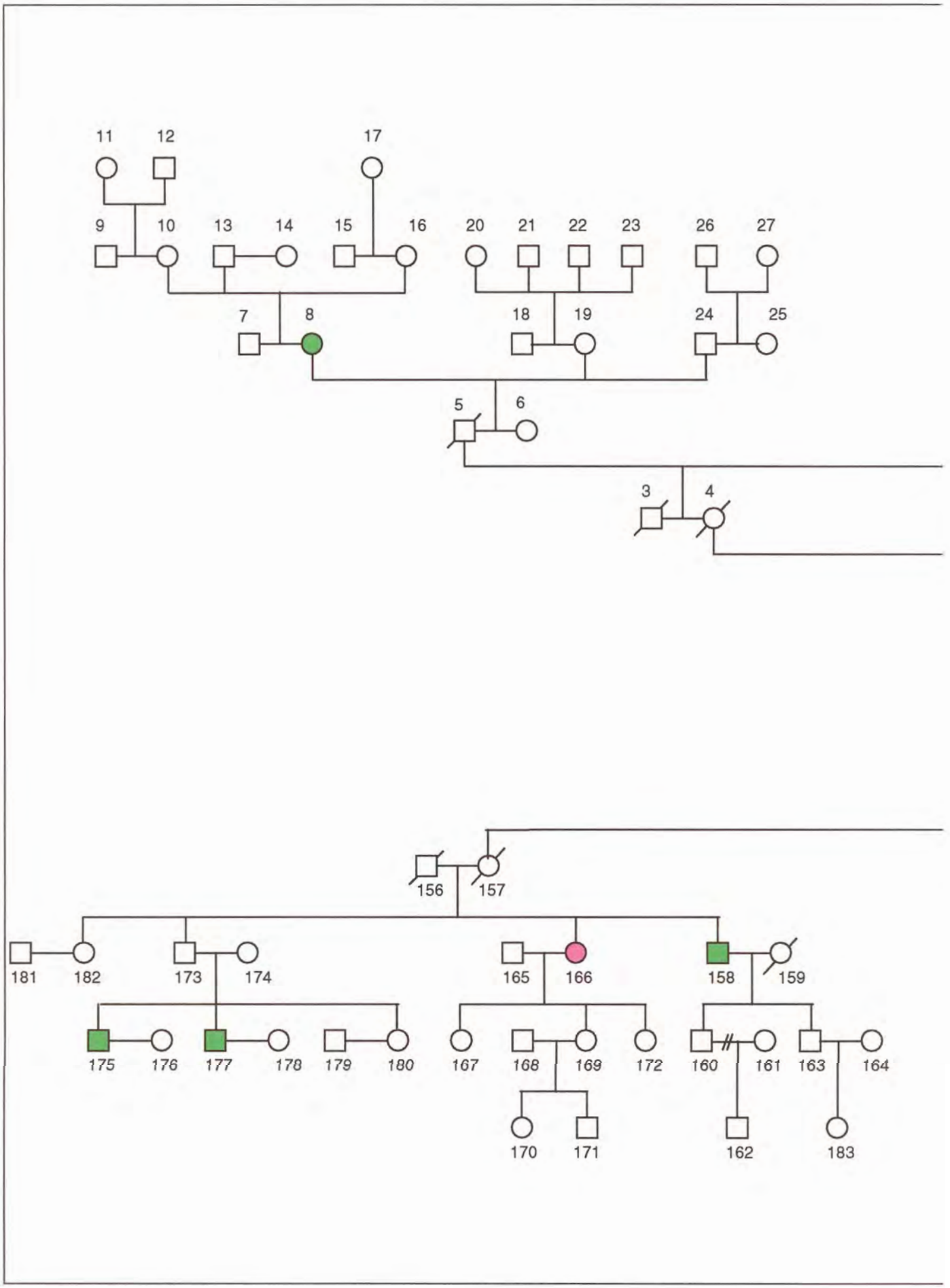


Figure F.5: Full pedigree of South African FSHD family F14 continued ...

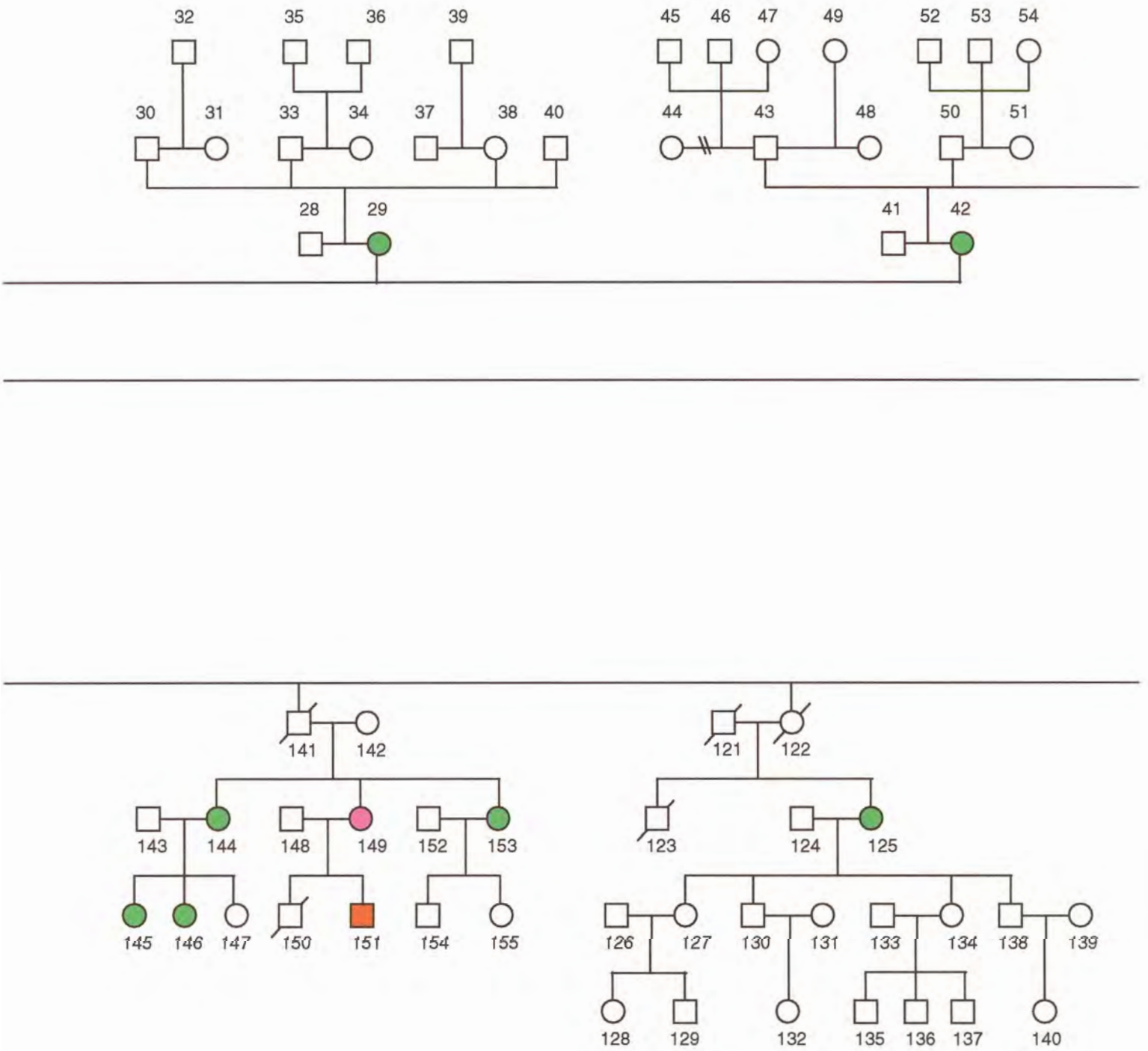


Figure F.5: Full pedigree of South African FSHD family F14 continued ...

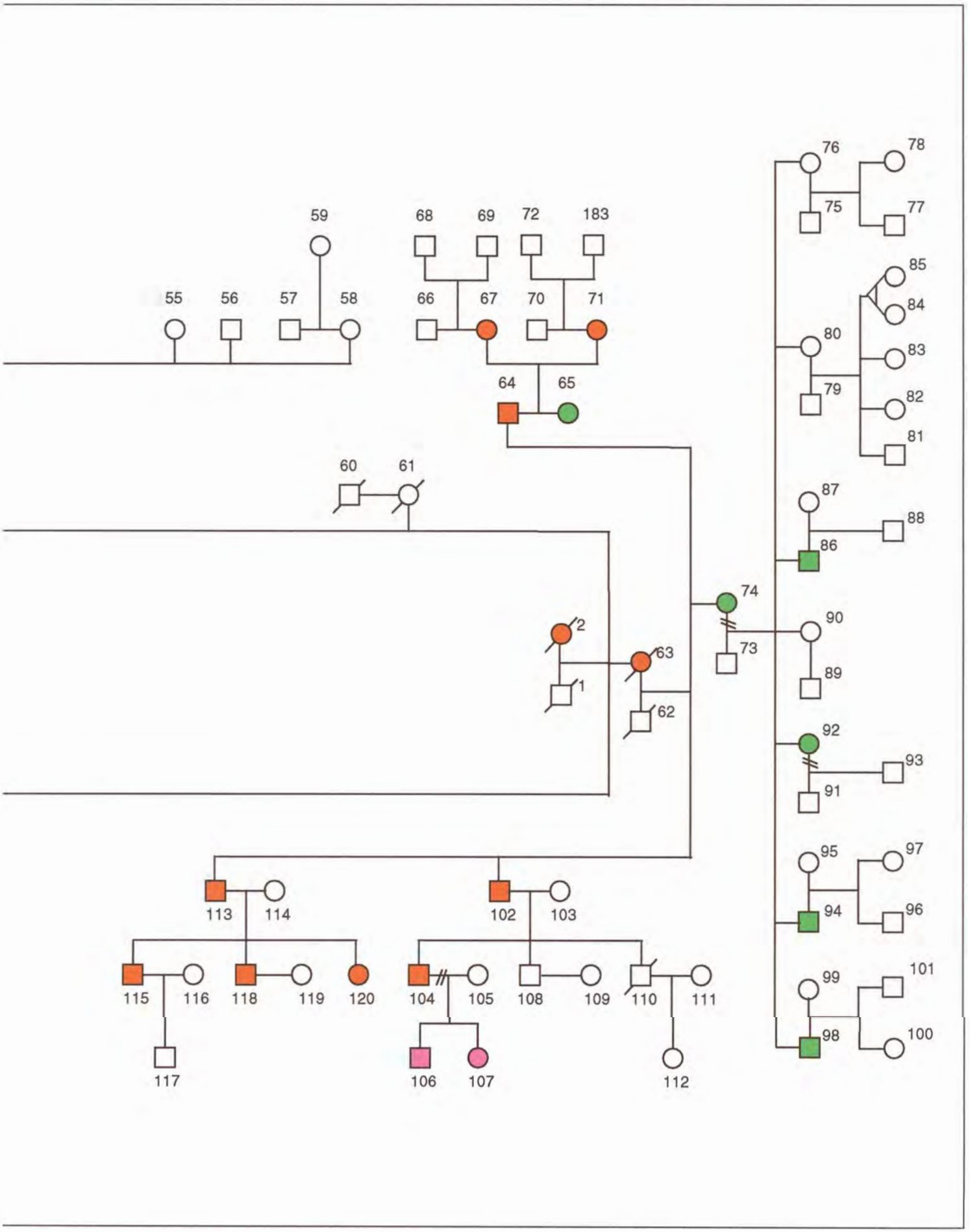


Figure F.6: Full pedigree of South African family F15

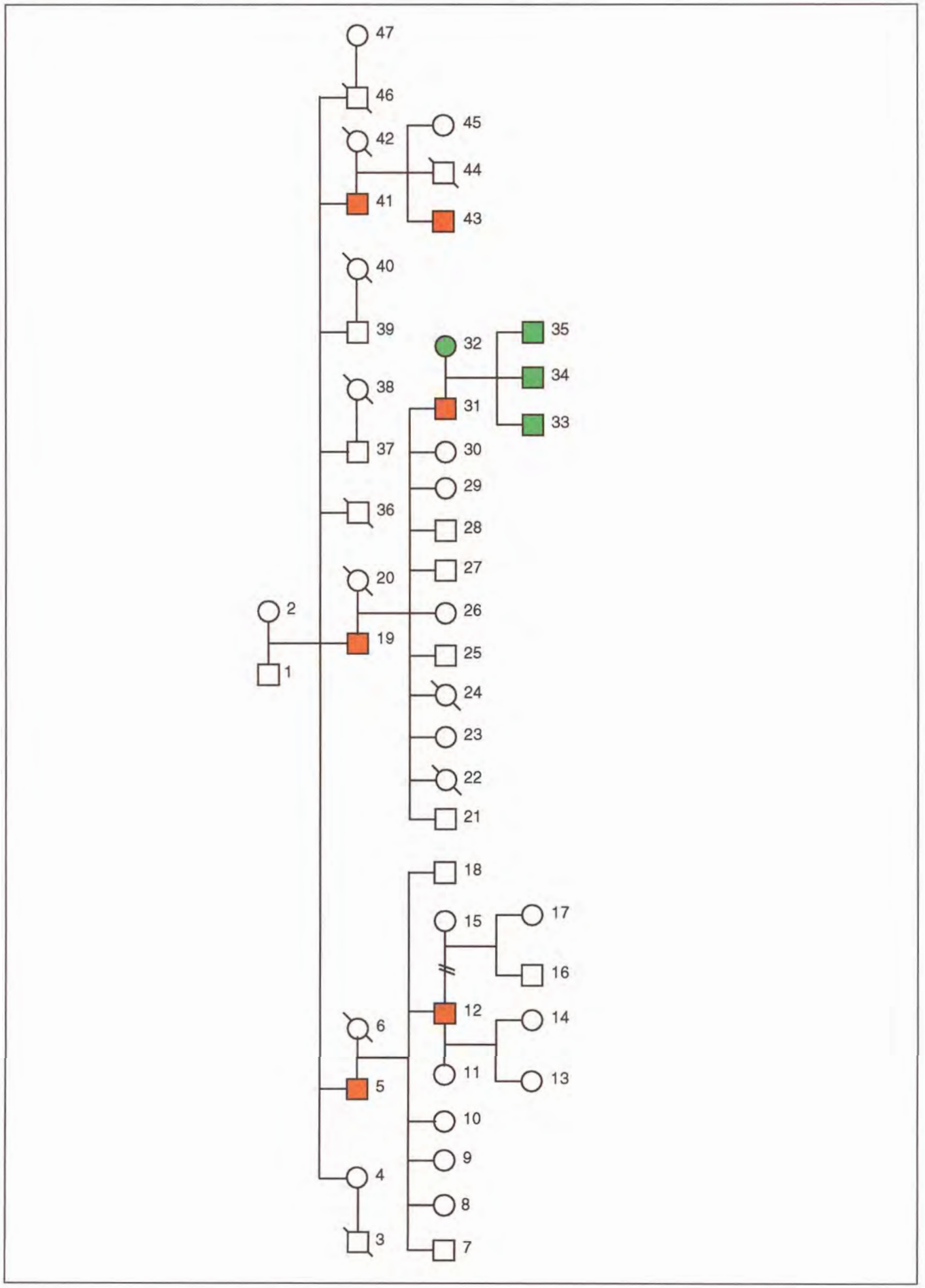


Figure F.7: Full pedigree of South African family F21

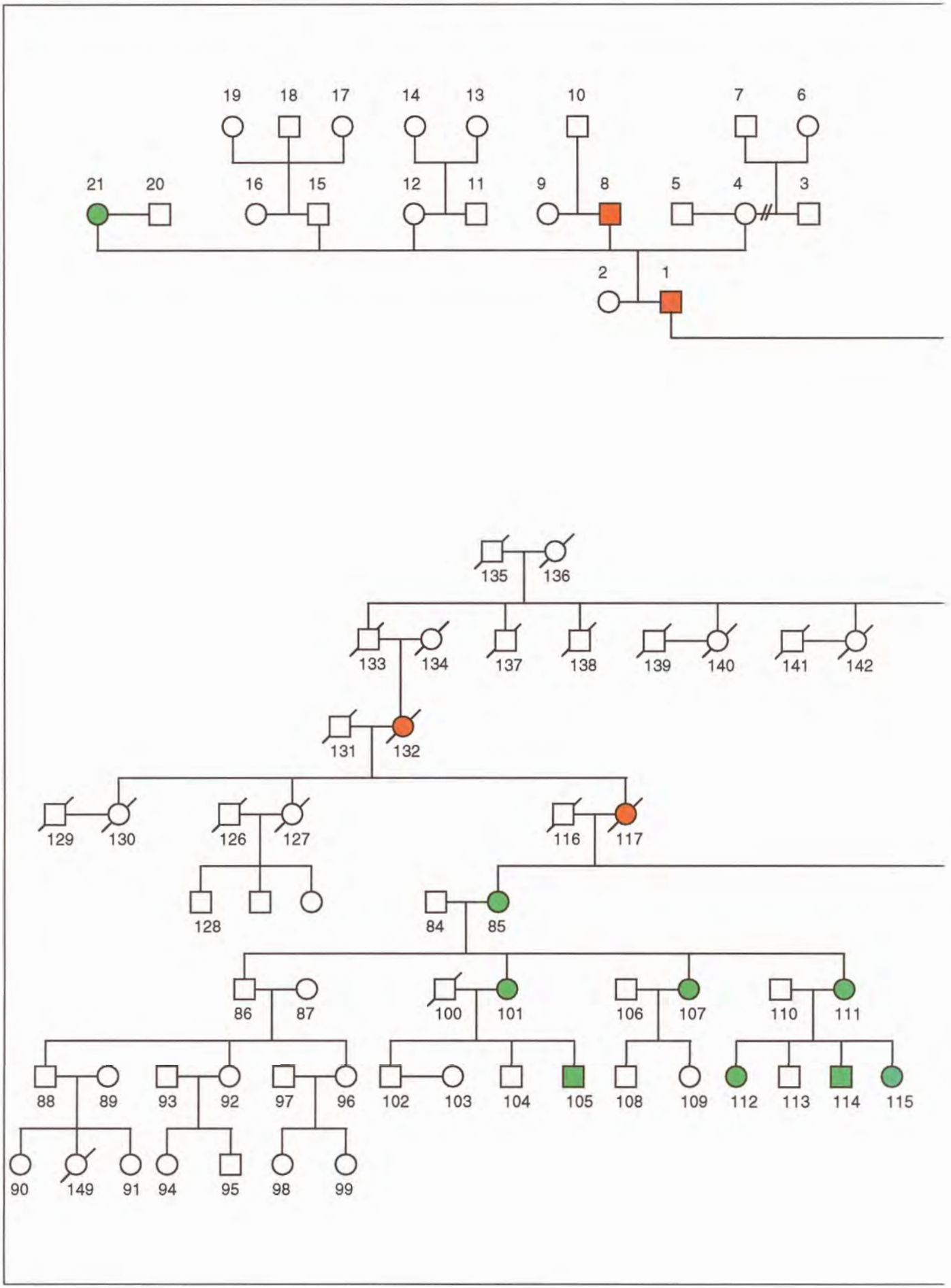


Figure F.7: Full pedigree of South African family F21 continued ...

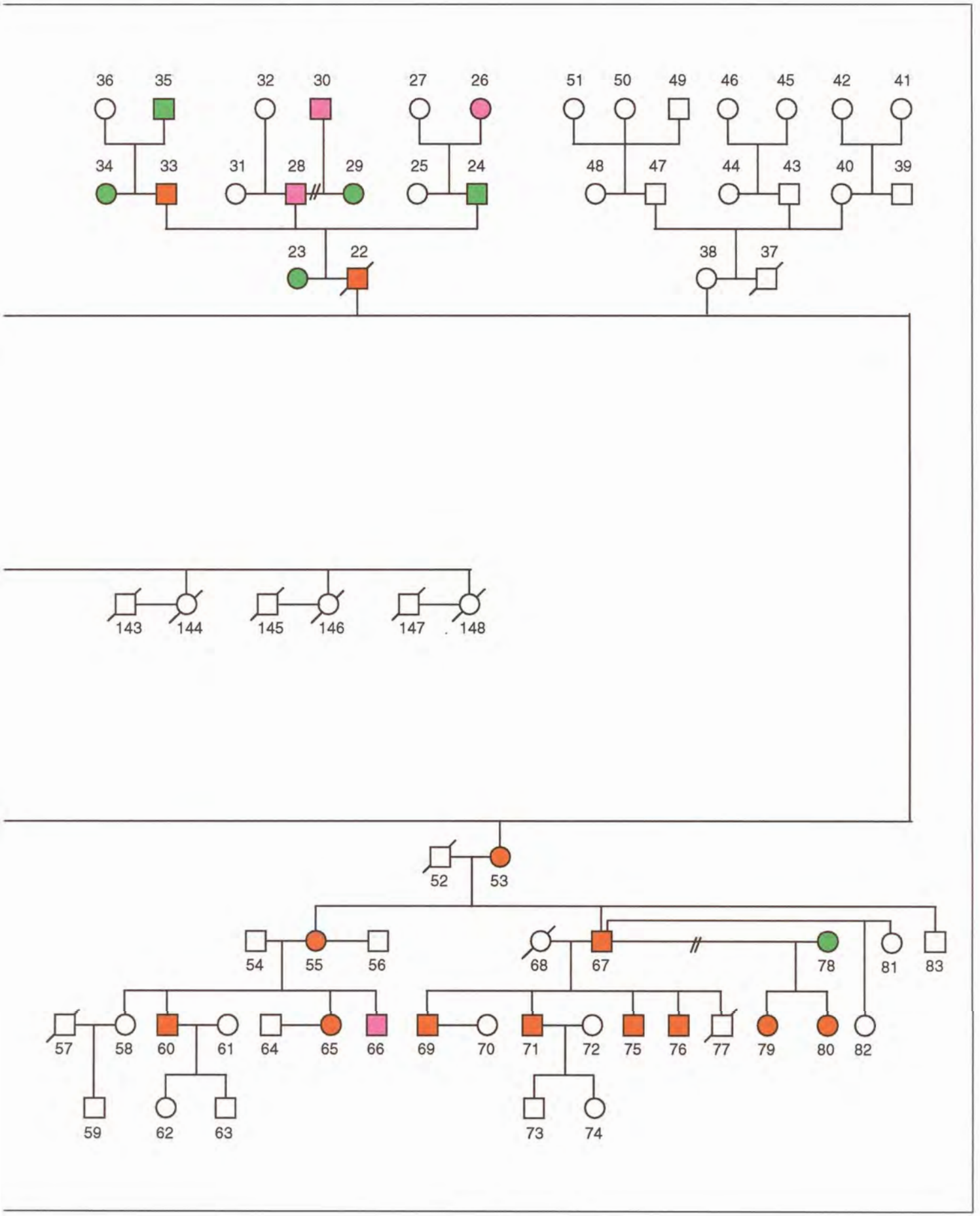


Figure F.8: Full pedigree of South African FSHD family F30

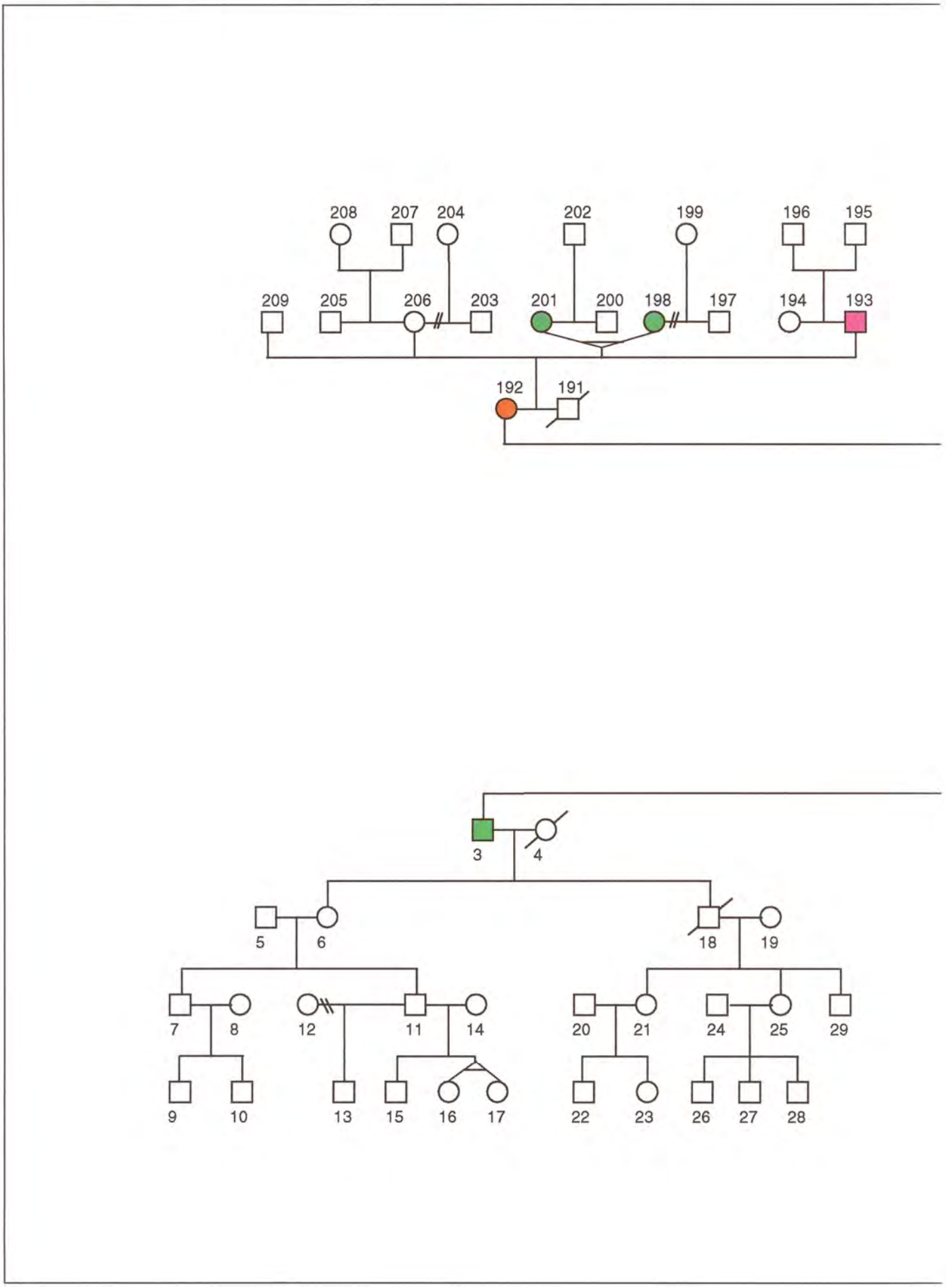
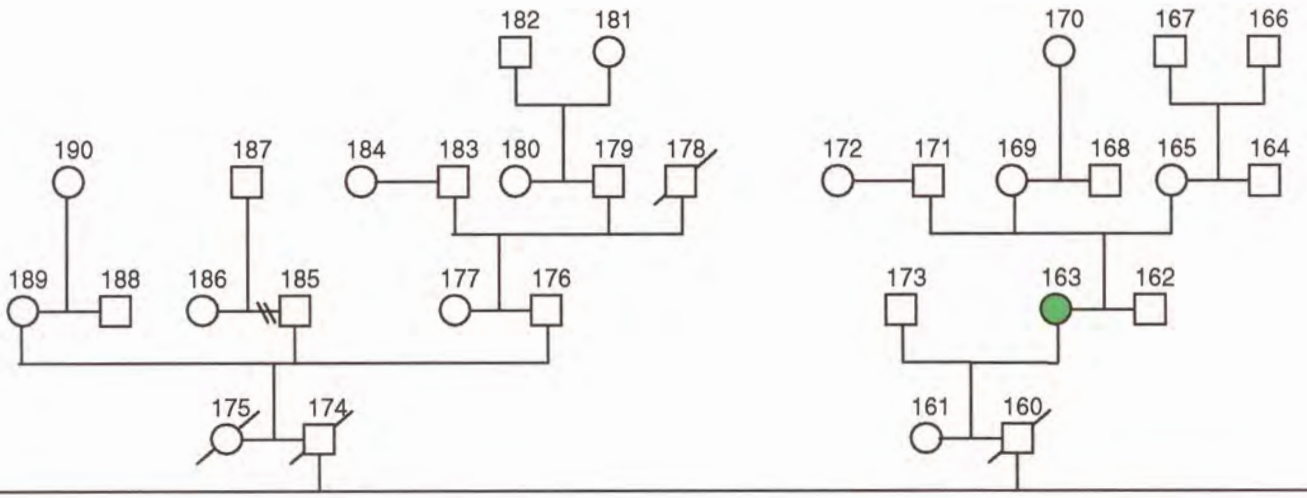


Figure F.8: Full pedigree of South African FSHD family F30 continued ...



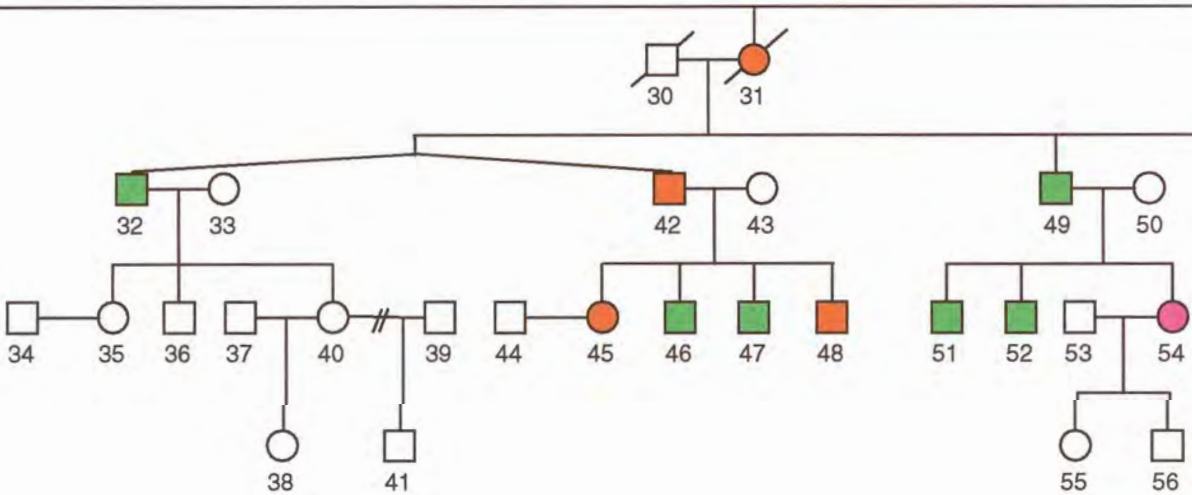


Figure F.8: Full pedigree of South African FSHD family F30 continued ...

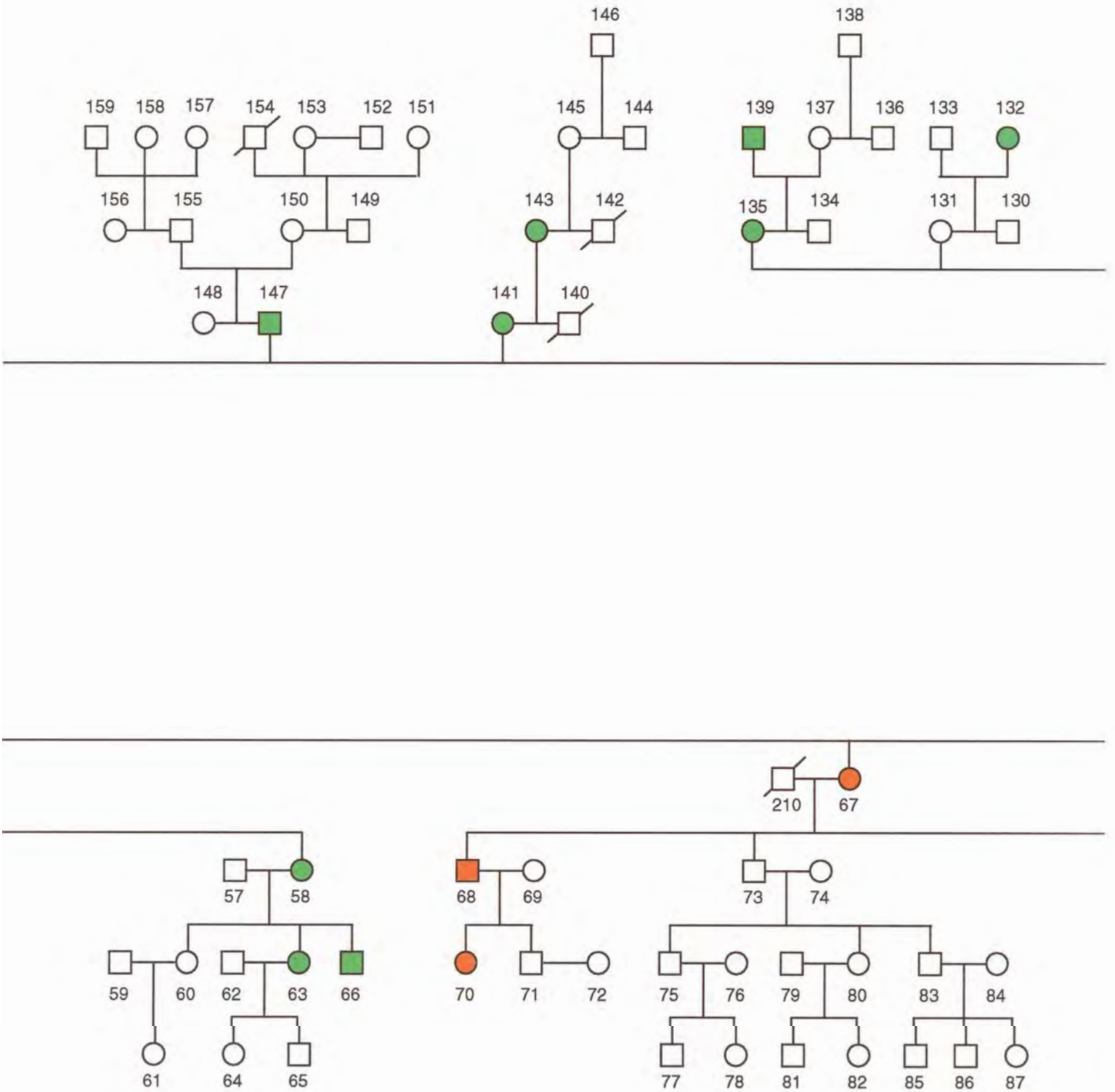


Figure F.8: Full pedigree of South African FSHD family F30 continued ...

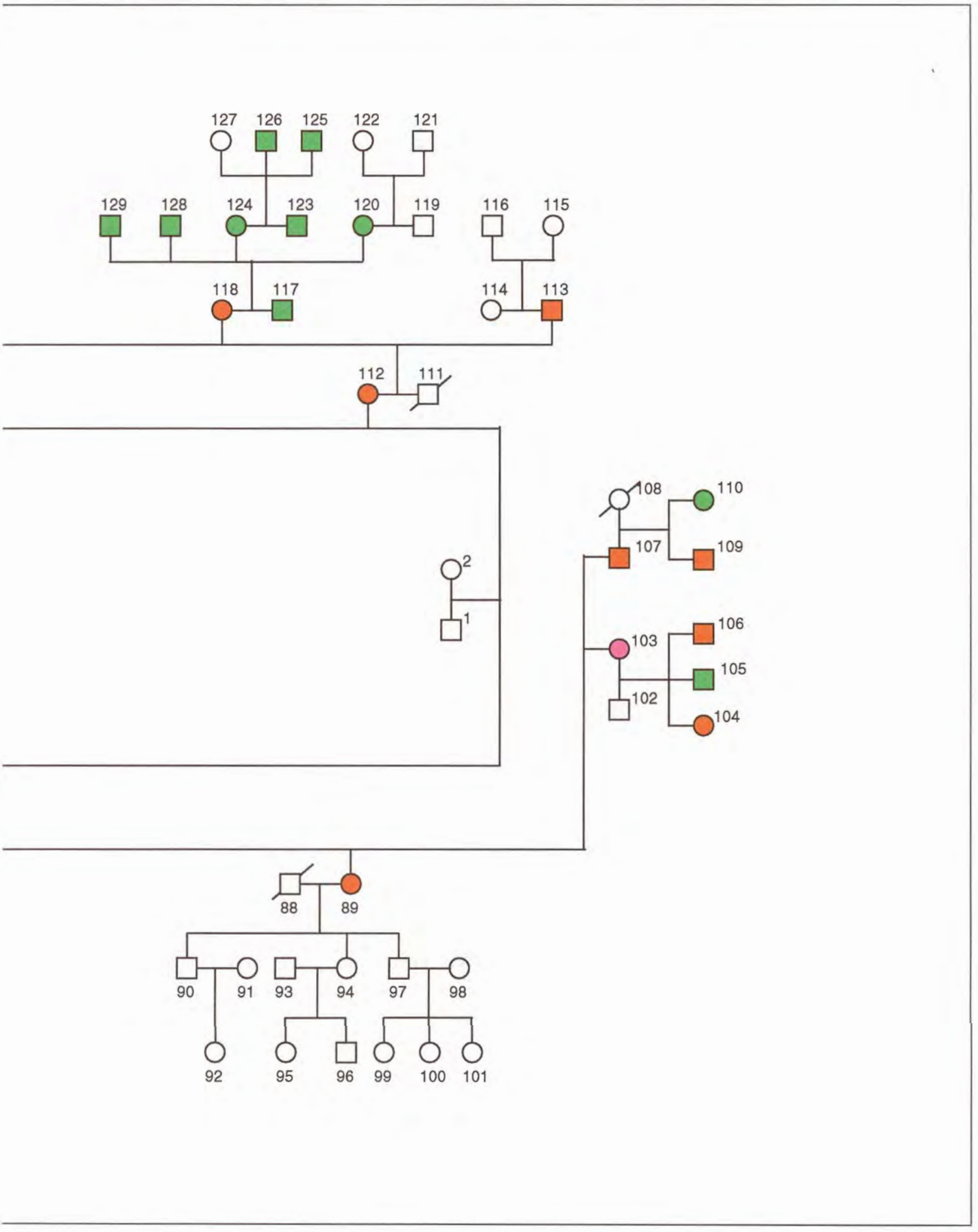


Figure F.9: Full pedigree of South African FSHD family F40

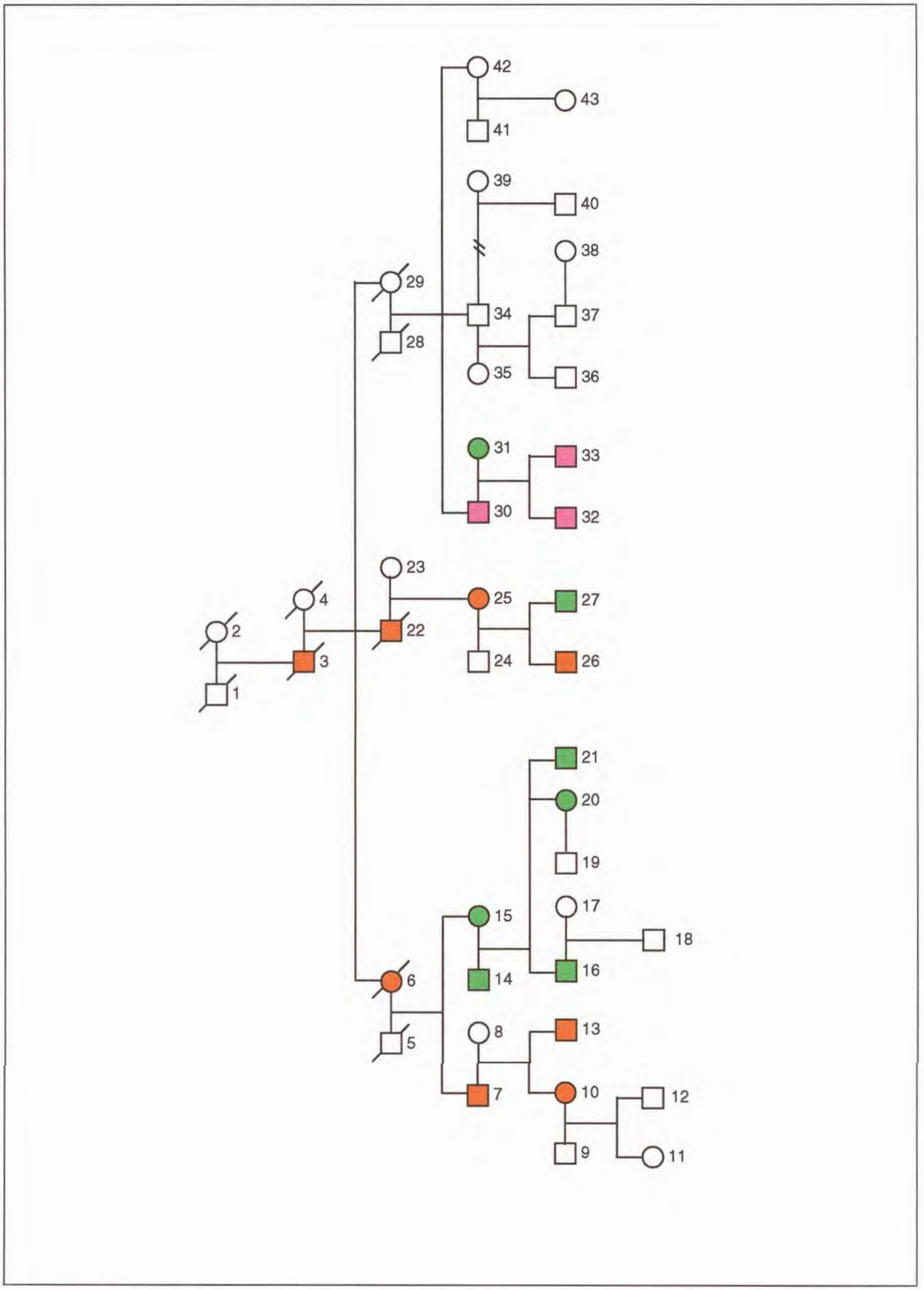


Figure F.10: Full pedigree of South African FSHD family F60

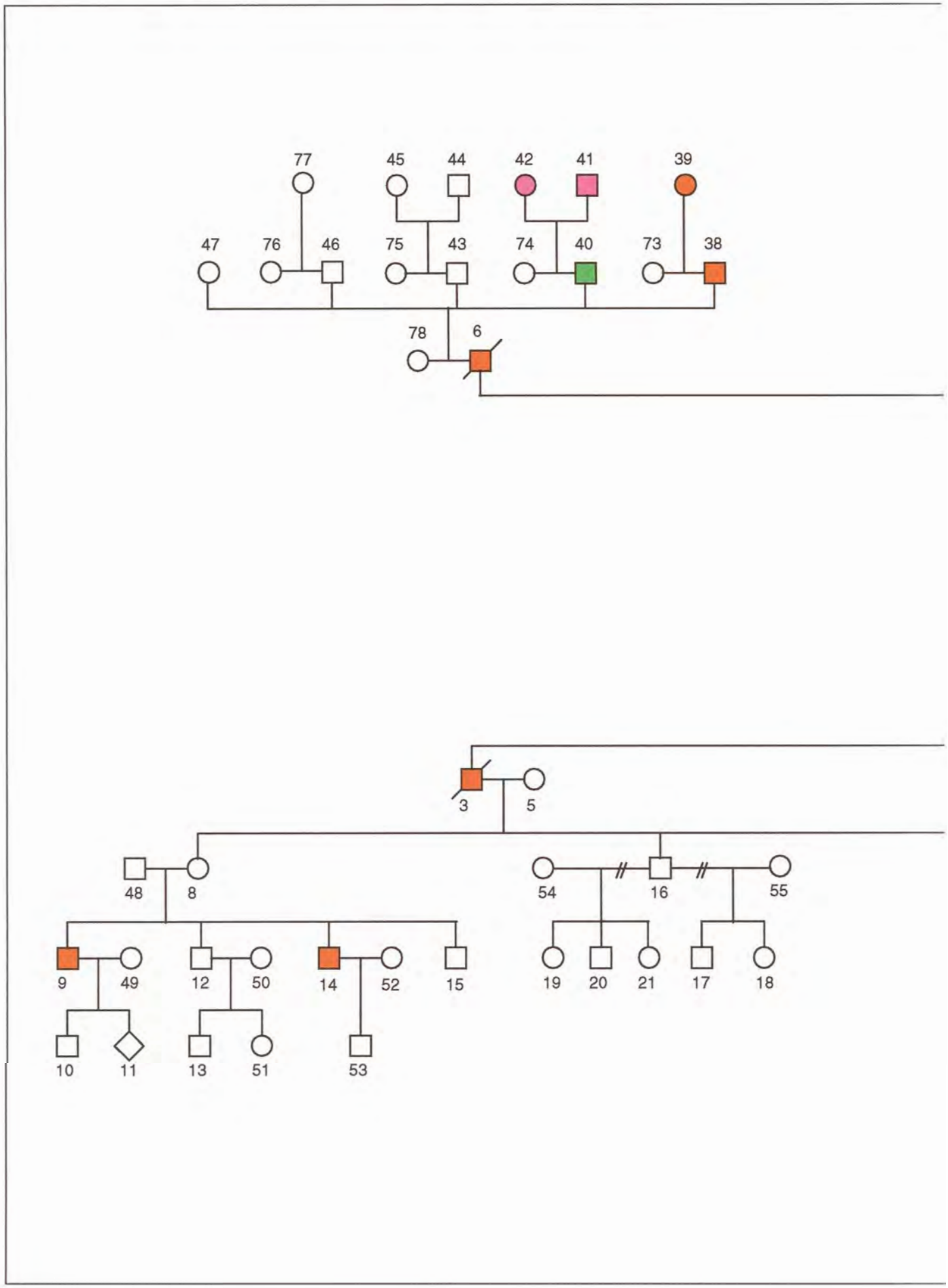


Figure F.10: Full pedigree of South African FSHD family F60 continued ...