
CONTENTS

	Page No
ACKNOWLEDGEMENTS	I
LIST OF FIGURES	III
LIST OF TABLES	IX
LIST OF ABBREVIATIONS	XII
ABSTRACT	XXI
Chapter 1	
INTRODUCTION	1
Overview of Development of Skin Appendages	1
Ectodermal Appendages	2
• Hairs	2
• Teeth	3
• Nails	4
• Sweat Glands	4
Major Signaling Pathways Involved in Ectodermal Appendages Disorders	5
I) Wnt/ β -catenin Signaling Pathway	5
II) Ectodysplasin/NF κ B (EDA/EDAR/EDARADD) Signaling Pathway	6
III) A Lipid (LIPH/LPA/LPAR6) Signaling Pathway	7
Disorders of Ectodermal Appendages	8
➤ Alopecias	8

continued

continued from the previous page

	Page No
a) Non-Syndromic forms of Alopecias	8
Marie Unna Hereditary Hypotrichosis	8
Monilethrix	9
Congenital Atrichia	10
Autosomal Dominant Woolly Hair	10
Hypotrichosis Simplex	11
Autosomal Recessive Hypotrichosis	11
b) Syndromic forms of Alopecias	13
Alopecia with Mental Retardation	13
Hypotrichosis with Juvenile Macular Dystrophy	14
Netherton Syndrome	14
➤ Ectodermal Dysplasias	15
Classification of Ectodermal Dysplasias	15
a) Pure Ectodermal Dysplasias	15
Hypohidrotic Ectodermal Dysplasia	15
Ectodermal Dysplasia of Hair, Nail and Teeth	16
Ectodermal Dysplasia of Pure Hair and Nail	16
Odonto-Onycho-Dermal Dysplasia	17
Witkop/Tooth and Nail Syndrome	17
Congenital Anonychia	17
Isolated Congenital Nail Dysplasia	18
Isolated Congenital Nail Clubbing	18

continued

continued from the previous page

	Page No
b) Associated Ectodermal Dysplasias	18
Ectodermal Dysplasia, Ectrodactyly, Macular Dystrophy Syndrome	18
Cleft-lip/Palate Ectodermal Dysplasia Syndrome	19
Ectodermal Dysplasia Cutaneous Syndactyly Syndrome	19
Ectodermal Dysplasia Syndactyly Syndrome	19
Ectodermal Dysplasia Skin Fragility Syndrome	20
Pachyonychia Congenita	20
Ankyloblepharon Ectodermal Defects Cleft-lip/Palate Syndrome	20
Acantholytic Ectodermal Dysplasia	20
Genetic Linkage Studies to Identify Genes	21
Research Work Presented in the Dissertation	22
Chapter 2	
MATERIALS AND METHODS	23
Pedigree Analysis	23
Collection of Blood Samples and Clinical Studies	23
Extraction of Genomic DNA	24
1. Phenol-Chloroform Method	24
2. GenElute™ Blood Genomic DNA Kit Method	25
DNA Quantification and Polymerase Chain Reaction	25
Linkage Analysis	26
a: Exclusion Mapping	26
b: Human Genome Scan	26

continued

continued from the previous page

	Page No
1. Genome Scan Using Microsatellite Markers	26
2. Genome Scan Using Single Nucleotide Polymorphism (SNP) Markers	27
Gel Electrophoresis	27
• Agarose Gel Electrophoresis	27
• Polyacrylamide Gel Electrophoresis	28
Statistical Analysis	28
Screening of Candidate Genes	29
Sequencing of Candidate Genes	29
• Purification	30
• Sequencing Reactions	30
• Ethanol Precipitation	30
Functional Studies of Frizzled 6 (FZD6)	31
Isolation of Total RNA from Human Hair Follicle	31
Reverse Transcription of mRNA into cDNA	32
Cloning Frizzled 6 (FZD6) Cdna	32
a) Production of Competent TOP10 <i>E. coli</i>	32
b) Cloning FZD6 cDNA	33
c) Transformation	33
d) Extraction of Plasmid DNA	33
Western/Protein Blot Analysis	34
a) Preparation of Cells for Transfection	34
b) Preparation of Cell Lysates	34

continued

continued from the previous page

	Page No
c) Discontinuous Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis (SDS-PAGE)	35
d) Transfer to Proteins to Polyvinylidene Fluoride (PVDF) Membrane	35
e) Chemiluminescence Method	35
Immunofluorescence Analysis	36
Immunohistochemistry	37
Chapter 3	
HEREDITARY ALOPECIAS	76
Mapping Genes Responsible for Autosomal Recessive Hypotrichosis	78
• Description of the Families Studied	78
Family A	78
Family B	79
Family C	80
Family D	80
Family E	81
Family F	81
Family G	82
• Genetic Linkage Analysis and Mutational Screening	82
Human Genome Scan in Family A	83
Linkage of Family B to Chromosome 3q27.2	84
Linkage of three Families (C, D, E) to Chromosome 13q14.2	85

continued

continued from the previous page

	Page No
Linkage of Family F to Desmoglein and Desmocollin Genes Cluster on Chromosome 18q12.1	86
Linkage of Family G to Hairless Gene on Chromosome 8p21.3	86
• Discussion	86
 Chapter 4	
HEREDITARY ECTODERMAL DYSPLASIAS	127
Mapping Gene Responsible for Autosomal Recessive Nail Dysplasia	128
• Clinical Features of Affected Individuals in Family H	128
• Linkage of Family H on Chromosome 8q22.3 and Identification of the Gene	129
• Discussion	132
Mapping Gene Responsible for Autosomal Recessive Hair and Nail Dysplasia	154
• Clinical Features of Affected Individuals in Family I	154
• Linkage of Family I to Chromosome 12q13.13 and Mutational Screening	154
• Discussion	155
Conclusion	165
 Chapter 5	
REFERENCES	167
Electronic Database Information	199