A History of Abnormal Dentition, Hair…

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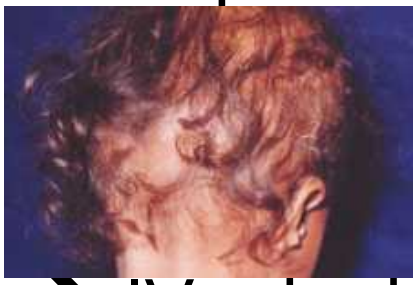
Case n° 1

- 6years
  - Failure to thrive & no catch up
  - Referral for severe AD, thin & sparse hair
- Personal history:



  - IUGR
  - 9mo: severe dehydration ➔ IV rehydration
  - 10mo: adenoidectomy, transmission deafness
  - Ophtalmologic abn., hyposalivation…

Case n° 1 (cont'd)

- Familial history
  - Familial atopy+++
  - Obesity tendancy
  - Mother: IUGR, abnormal dentition, hypotrichiosis

Diagnoses? Exams?

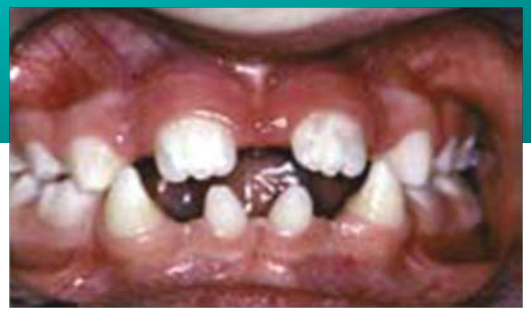
Case n° 1 (cont'd)

- GS disease: salivary glands biopsy: normal
- Auto-immune disease:
  - LE cells (-); Latex-WR (-); Anti-musle ab (-)
  - Prot. electrophoresis, Ig & Cp: Normal
- Hormonal deficiency
  - GH & T_4-TSH: Normal

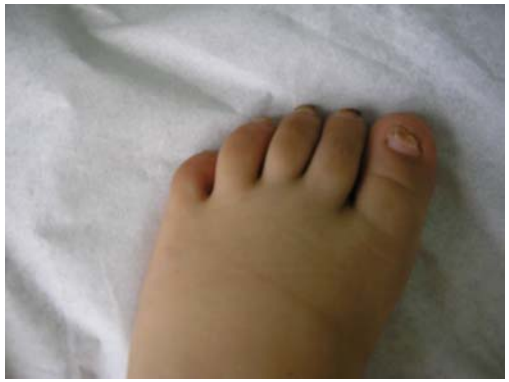
??

Patient had futures of Anhidrotic Ectodermal Dysplasia…

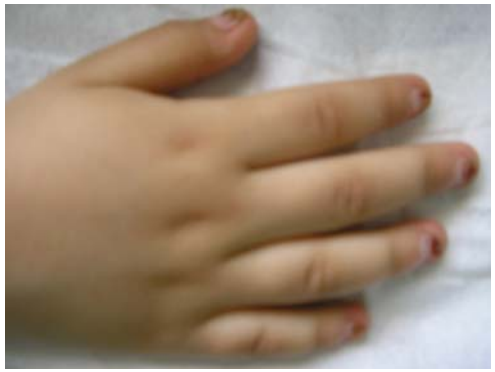
- Reduced sweating
- Abnormal hair patterns: thin, sparse…
- Conical or peg teeth

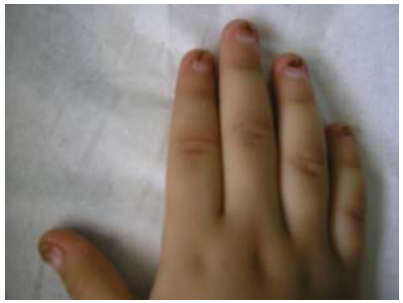


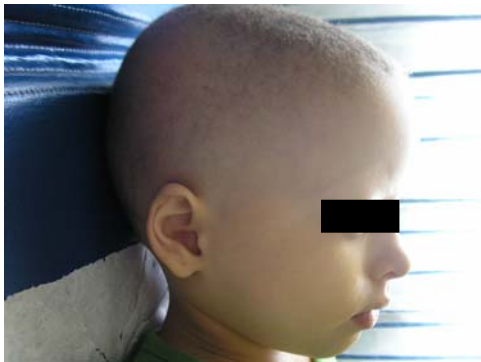
Clinical triad

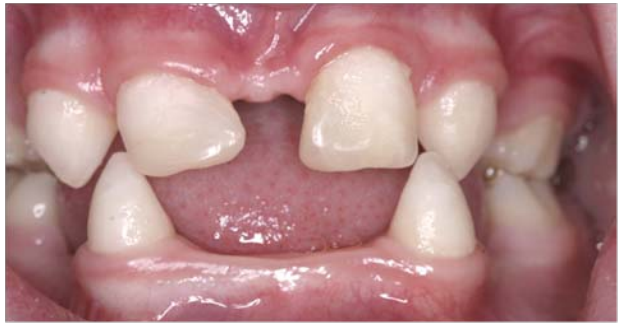


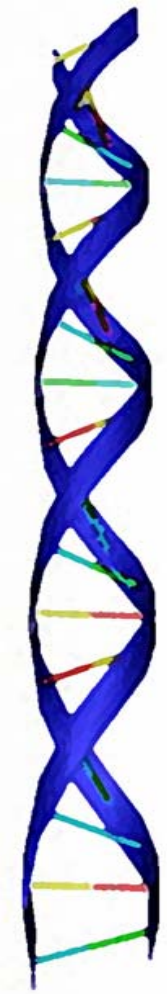
- Genetic disorder
- Defective development of teeth, hair, nails & eccrine sweat glands:
  - Hypodontia/ Anodontia, Conical teeth
  - Hypotrichosis or alopecia
  - Hypohdrosis or anhidrosis







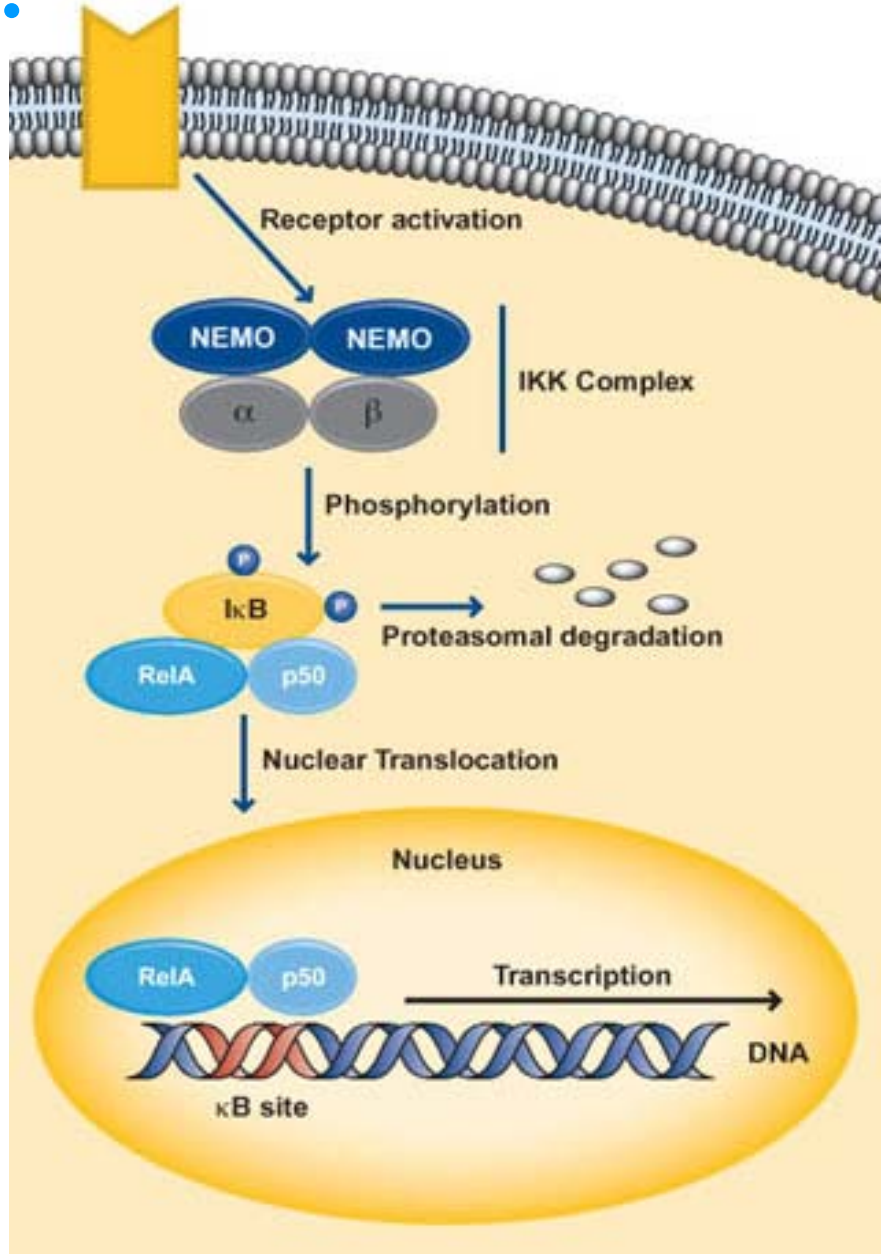




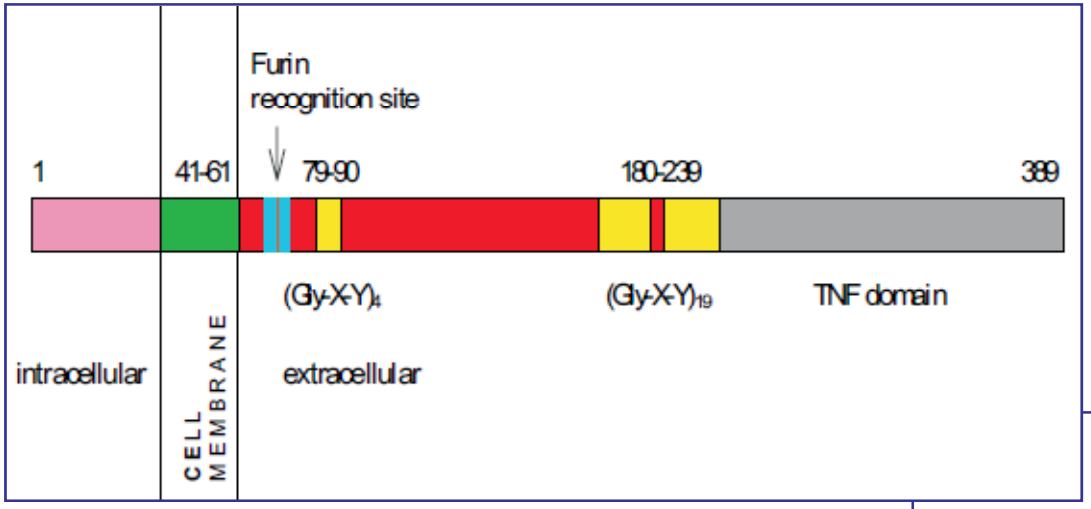
- Genetic background:
  - Inherited X linked form+++
  - Autosomal dominant (AD) & Autosomal recessive (AR)
- Three interacting proteins
  - Ectodysplasin: Xq12-q13.1
    - EDA-A1: essentiel for skin appendages
    - EDA-A2: development timing & completion
  - EDAR: 2q11-q13
  - EDARADD: 1q42.2-q43

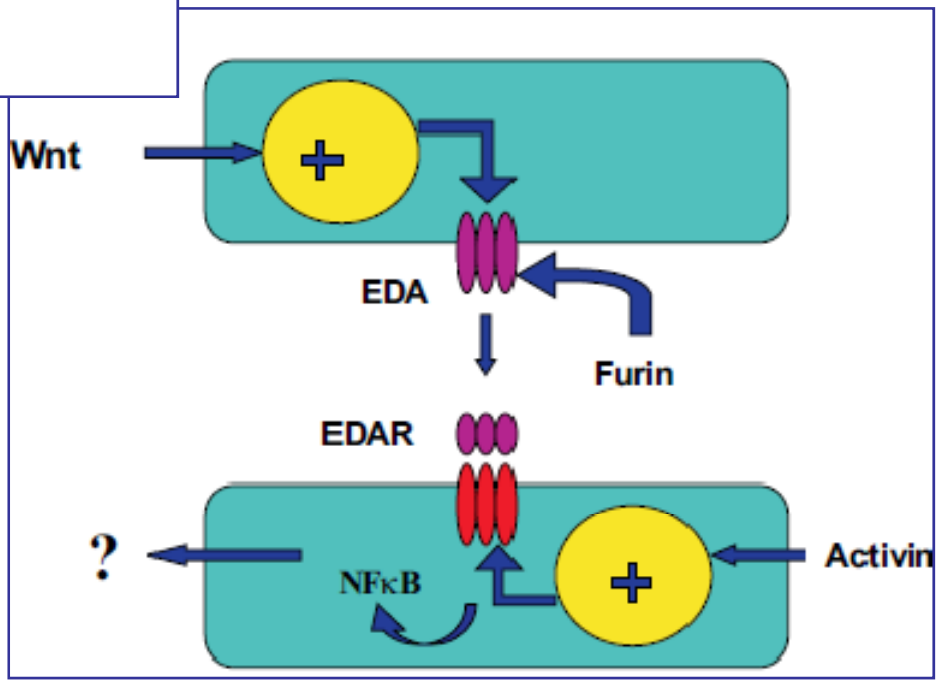
Help finding NEMO…

NEMO is critical for activation for a transcription factor, critical for immune responses



Hypothetic signalling of EDA_1 & EDAR

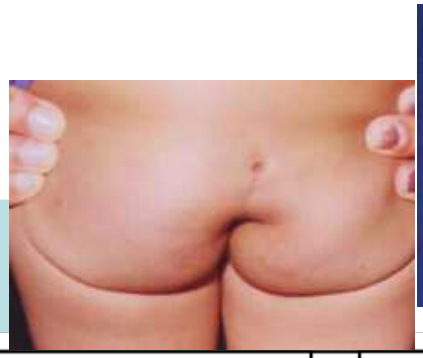


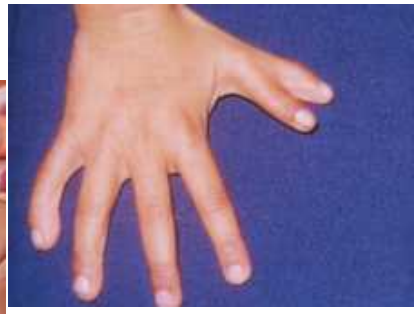


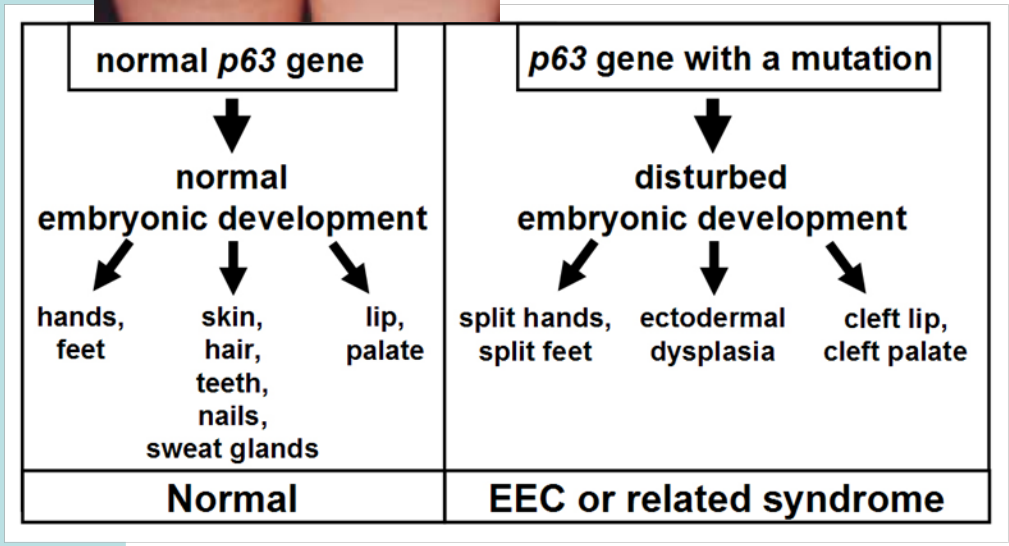
Wisniewski et *al*. J Appl Genet 2002; 43(1)

Why are EDs so diverse?

- Same genes involved in devpt. of ectodermal structures
- Nature & location of mutation
- Syndromic forms (same genes involved in devpt. of other structures)
  - EEC: Ectrodactyly, Ectodermal Dysplasia, Cleft/ lip palate
  - SHFM: Split Hand/ Foot Malformations
  - Hay-Wells syndrome
  - Rapp-Hodgkin syndrome…







Clinical diagnosis (1)

- Trichogram examination

  3 shaft abnormalities (Pili torti, Tricorrhexis nodosa, variable shaft thickness)

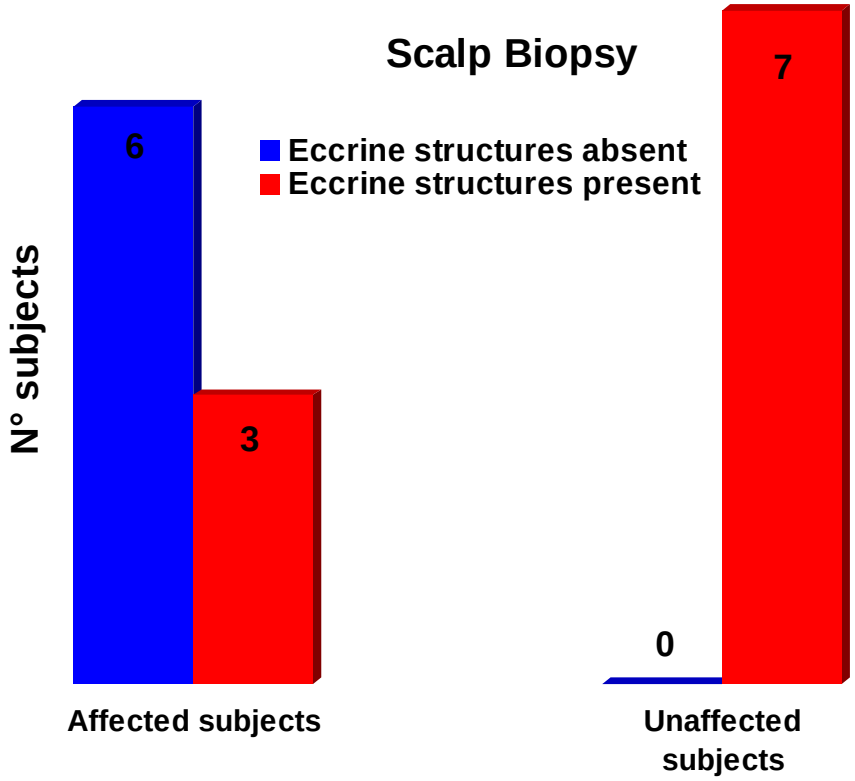
- Starch-iodide paper palm imprint

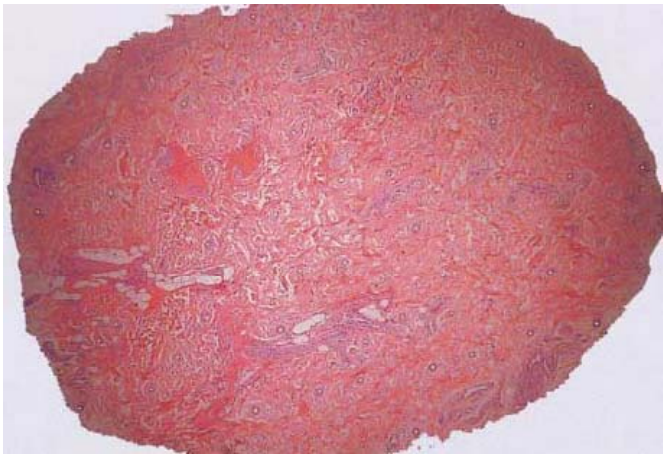
- **Skin biopsy** (horizontal section,palmar)

- **Scalp biopsy**

Rouse et *al*. Arch Dermatol 2004;140

Clinical diagnosis (2)





Rouse et *al*. Arch Dermatol 2004;140

Centre for Arab Genomic Studies

A Division of Sheikh Hamdan Award for Medical Sciences

The Catalogue for Transmission Genetics in Arabs

CTGA Database

- Kabbaj et *al.* J Med Genet 1998; 35(12)
  - 14 family members, common ancestor
  - 6 deaths in early childhood/ dehydration
  - Hypotrichosis,Hypodontia, Anhidrosis
- Baala et al. Am J Hum Genet 1999; 64(2)
  - DNA collected in 32 members, 8 were affected
  - Linkage to chromosome 2q11-q13

UNIVERSITE DE PARIS ILE DE FRANCE
UFR NECKER-ENFANTS MALADES

N°

MANIFESTATIONS RESPIRATOIRES AU COURS DE LA DYSPLASIE ECTODERMIQUE ANHIDROTIQUE DE L'ENFANT : A PROPOS DE TROIS OBSERVATIONS et REVUE DE LA LITTERATURE.

MEMOIRE POUR L'OBTENTION DU DIPLÔME INTER-UNIVERSITAIRE DE PNEUMOLOGIE PEDIATRIQUE.

ANNEE1996-1997

Présenté et soutenu publiquement
le 27 juin 1997 par

Mohamed BAYARI

	Stéphane	Anne	Jérémy
Age at diagnosis	10 days	10 months	6 months
Presentation	Severe obst. rhinitis	W & H: -3SD	ENT sx
Other sx	Hyperthermia, abn. swallowing	GERD+++, Oph. abn., Hyposalivation	Anorexia
DA	+	+	+
Dentition	Anodontia	Hypodontia	2 conical incisors
Mother: Abn. dentition Abn. hair	 + +	 + +	 + 0

- Respiratory onset sx between 3-6 years
- First repsiratory assessment at 2, 5 & 6 years
  - IgA: -1,3 to -2SD except Anne; other normal.
  - Complement system normal
- Flexible endoscopy: Inflammatory pattern (I-II), Absence of mucosal secretions, Acquired ciliary abnormalities (viral)

	Stéphane	Anne	Jérémy
SPT	+	+	+
Total IgE	465	Normal	800-1300
Specific IgE	-	-	ND

ND: not done

	11/1982	01/1990	04/1990	07/1991
FVC	-	2,01(81)	2,19(85)	2,47(89)
RFC	0,605(106)	1,24(96)	1,24(93)	-
FEV_1	-	1,38(66)	1,52(70)	1,77(76)
MEF_{25-75}	-	**1,25(47)**	**1,44(54)**	**1,81(64)**
PEF	-	2,81(67)	3,89(89)	4,61(99)
MEF_{50}	-	**1,45(50)**	**1,69(56)**	**2,15(67)**
MEF_{25}	-	**0,61(41)**	**0,73(47)**	**0,89(54)**
Pulm. Res.	13,24(149)	-	-	-
DC	30(68)	-	-	-
ABG	Hypoxia	N	N	Hypoxia

() are % of theoric values

Severe Distal Obstruction, partially reversible

Conclusions

- Antenatal counselling+++
  - Fetoscopy: skin & palmar biopsy/ 20th gest.week
- cDNA probes ➔ gene mapping
- Villous biopsy/10th gest.week

- But…sporadic cases have been described
  (de novo mutation)