Rubinstein-Taybi Syndrome

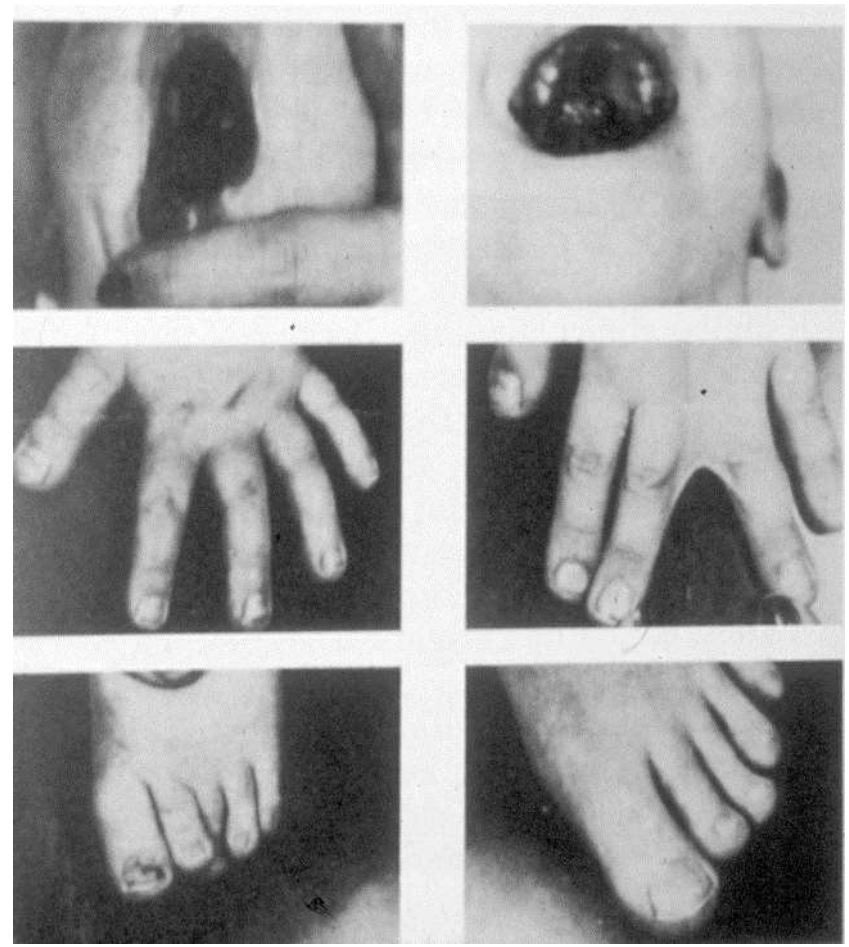
A selected miscellaneous

Raoul CM Hennekam

Academic Medical Center, Amsterdam, The Netherlands

1958

1959-1960



1963

Broad Thumbs and Toes and Facial Abnormalities

A Possible Mental Retardation Syndrome

JACK H. RUBINSTEIN, MD
CINCINNATI
AND
HOOSHANG TAYBI, MD
INDIANAPOLIS

Although a large number of diseases, conditions, and syndromes associated with men- peculiarities along with other physical findings and often resemble neither their parents

1957

POUCE BOT ARQUÉ EN FORTE ABDUCTION-EXTENSION ET AUTRES SYMPTOMES CONCOMITANTS

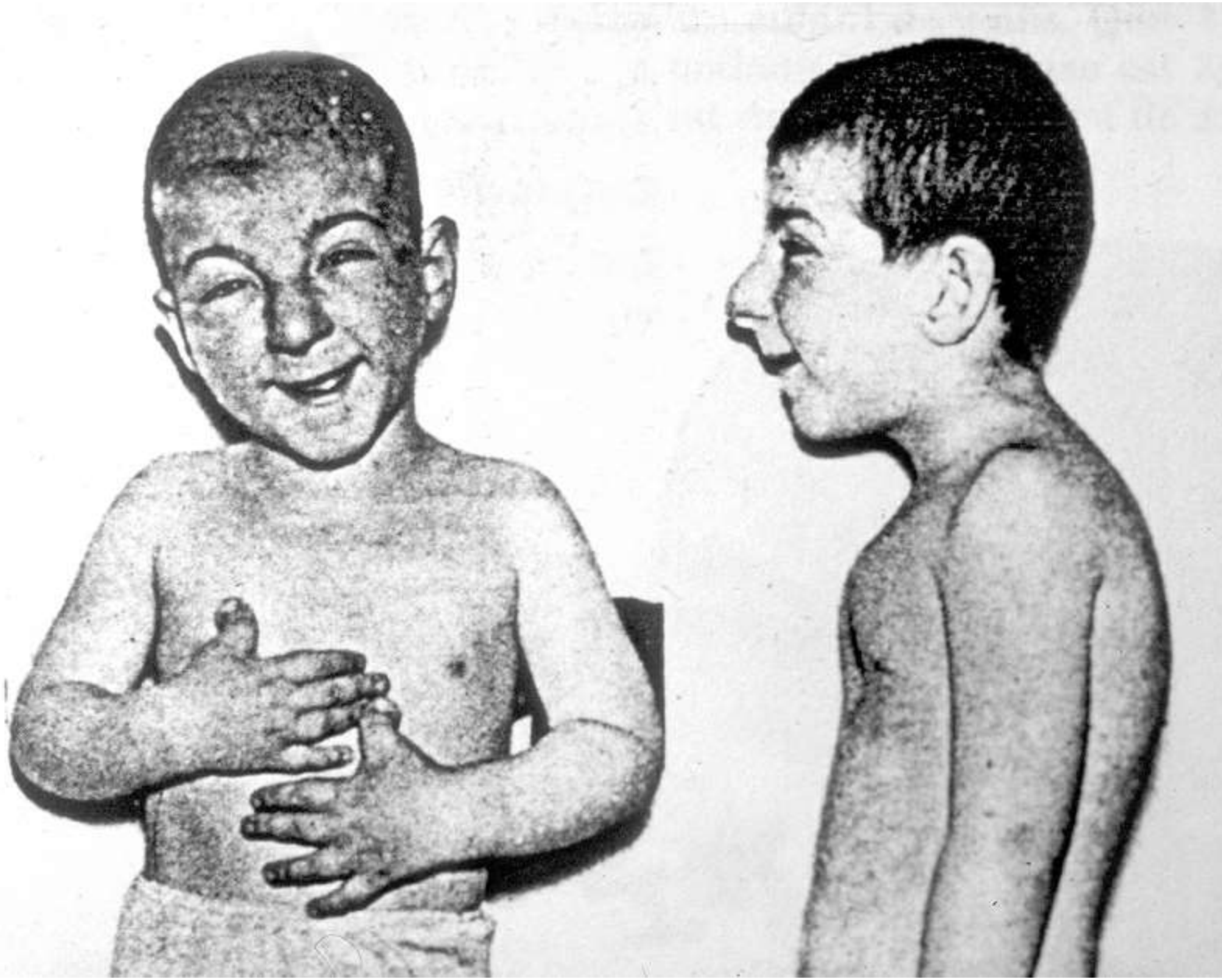
PAR MM.

J. MICHAIL, J. MATSOUKAS et S. THÉODOROU

(Athènes)

Dans une précédente publication (Michail, 1949) (1), nous avons décrit un cas de déformation congénitale et symétrique du pouce avec déformation analogue du gros orteil sous le titre *Pollux varus rigidus et hallux valgus chez un jeune*. Dernièrement, nous avons eu l'occasion d'observer une déformation inverse du pouce (pouce arqué en abduction-extension) dont nous n'avons nulle part trouvé de description. Pour

1957



900 bc

American Journal of Medical Genetics 91:56–61 (2000)

Possible Case of Rubinstein-Taybi Syndrome in a Prehistoric Skeleton From West-Central Illinois

Alicia Kay Wilbur*
Department of Anthropology, University of New Mexico, Albuquerque New Mexico

American Journal of Medical Genetics 91:56–61 (2000)

900 bc

Possible Case of Rubinstein-Taybi Syndrome in a Prehistoric Skeleton From West-Central Illinois

Alicia Kay Wilbur*
Department of Anthropology, University of New Mexico, Albuquerque New Mexico

RTS control control RTS control

1993

2013

Topics

- Genes

- Defining RTS

- Natural history site

- Keloids

- Behavior

Topics

- Genes

- Defining RTS

- Natural history site

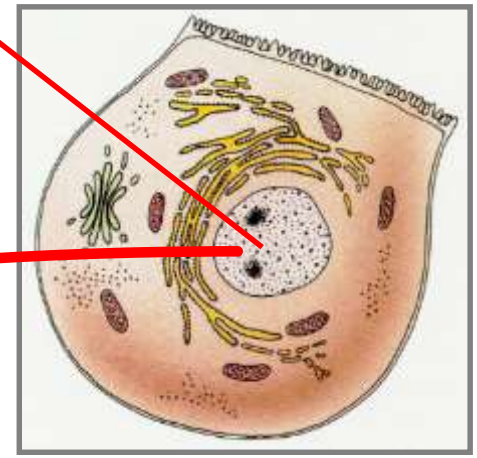
- Keloids

- Behavior

Basics

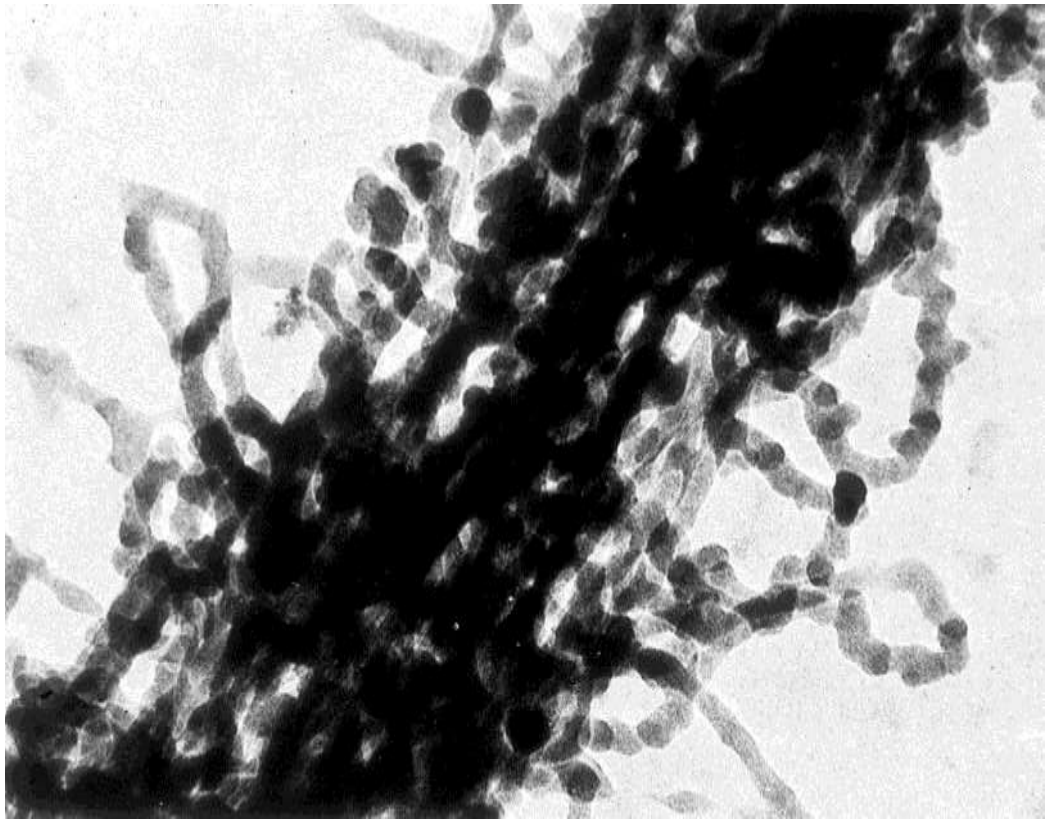
cell

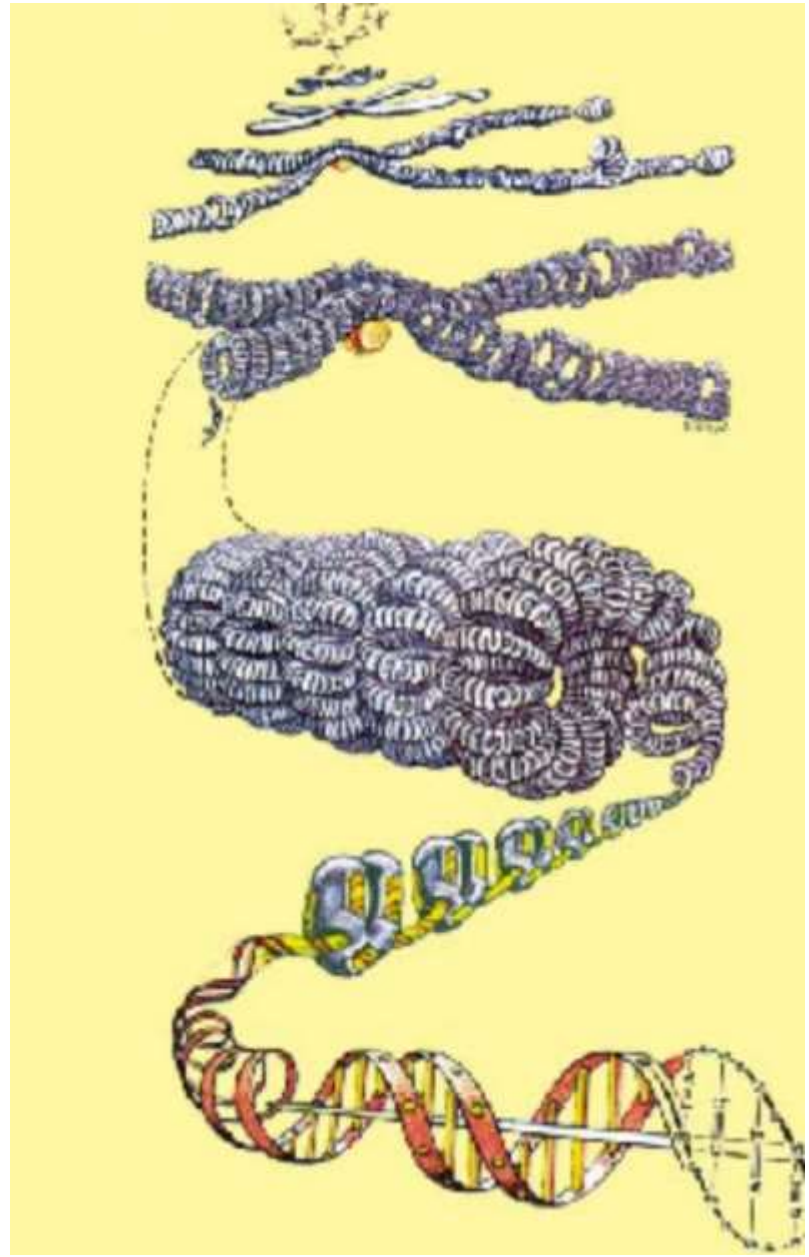
nucleus
(center)



chromosomes

Basics





Basics

- Two genes in RTS

    a. *CREBBP*

        located on chromosome 16

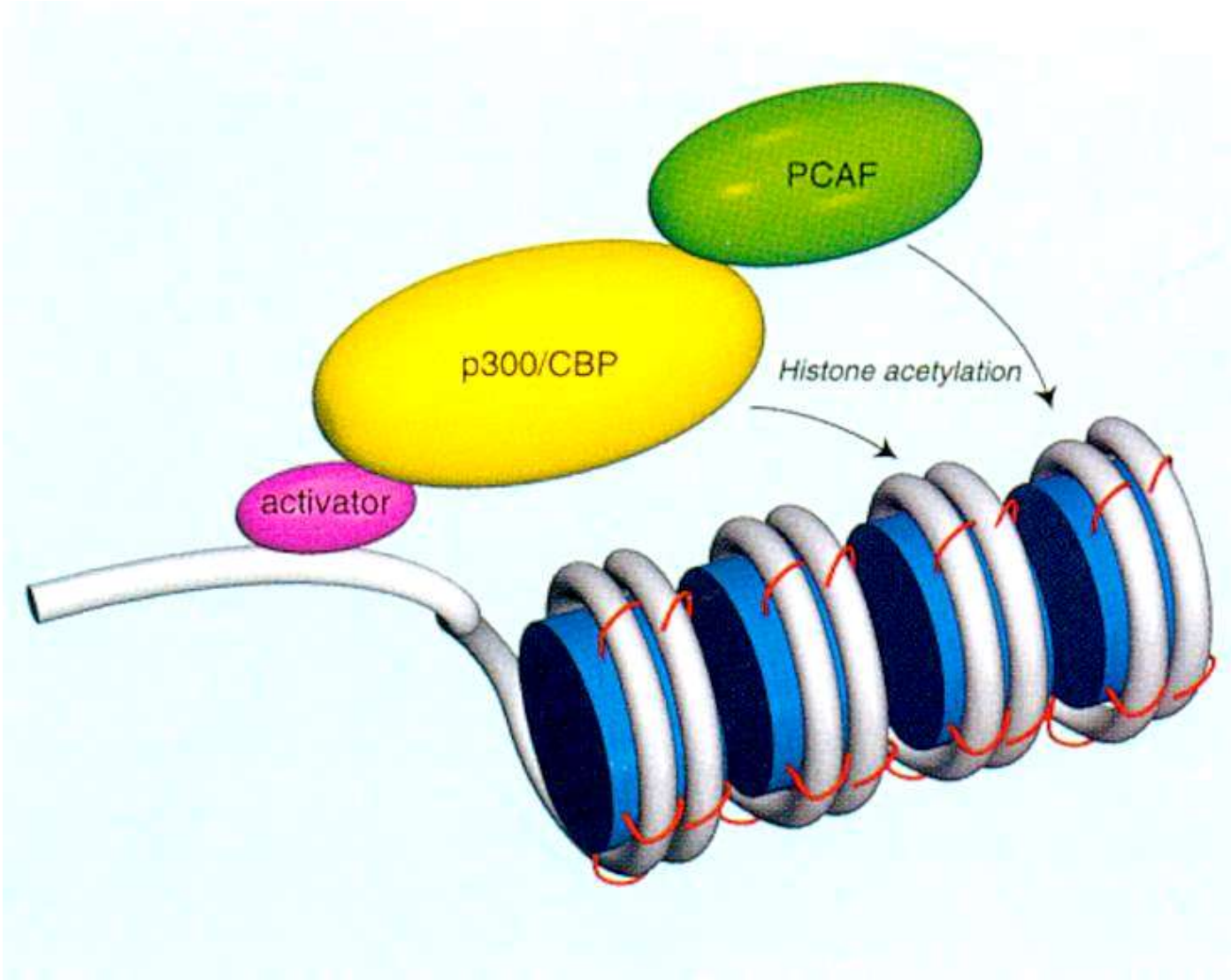
        60-65%

    b. *EP300*

        located on chromosome 22

        8-10%

Basics



Differences CREBBP – EP300

	CREBBP	*EP300*
	(n=308)	(n=52)
small head	54%	86%
more hair	76%	52%
typical smile	94%	47%
broad thumbs	96%	70%
thumb not straight	49%	2%

Fergelot, Am J Med Genet 2016

Differences CREBBP – EP300

	CREBBP	*EP300*
	(n=308)	(n=52)
mild delay	14%	61%
more delay	48%	32%
marked delay	36%	7%
autism	49%	25%
pm pre-eclampsia	3%	23%

Fergelot, Am J Med Genet 2016

What about the other ~30%?

- mosaicism (= change in CREBBP/EP300

  cannot be detected in blood)

- one candidate (unpublished)

- studies for other genes

Topics

- Genes

- Defining RTS

- Natural history site

- Keloids

- Behavior

Changes

- new “screening” DNA techniques

- unexpected gene changes

- is this still RTS?

Defining RTS



CREBBP mutation

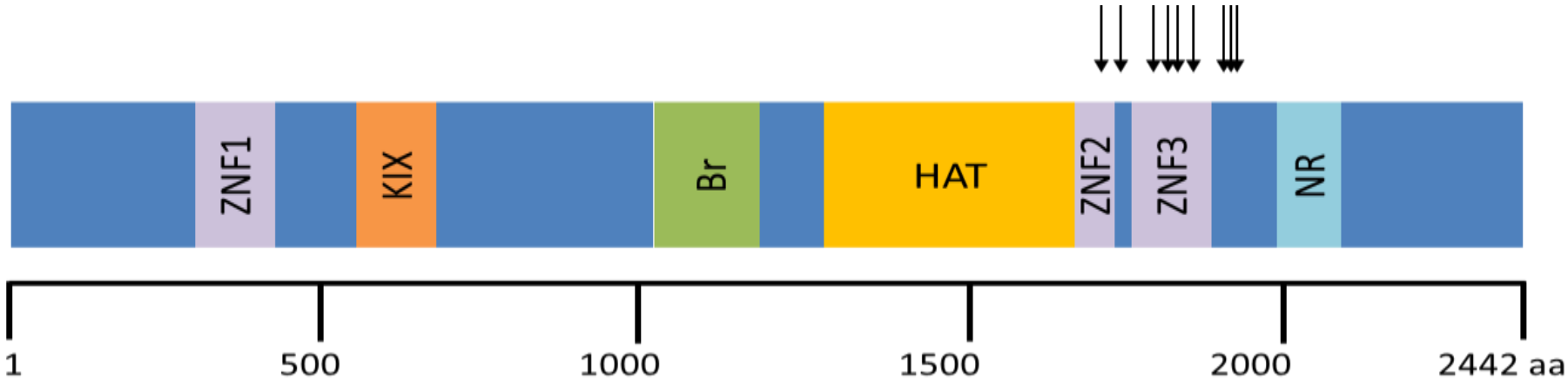
But RTS??

Defining RTS

All CREBBP mutation

Menke, Am J Med Genet 2016

Defining RTS



Menke, Am J Med Genet 2016

Defining RTS

- one has RTS if one has clinically RTS

- need for definition

- internationally accepted

Topics

- Genes

- Defining RTS

- Natural history site

- Keloids

- Behavior

Natural History Site

- information!

- what will the future bring

- future therapies

Natural History Site

- many rare disorders, few doctors

- and the true specialists are…

- Internet

- Wiki

Natural History Site

- once (!) all early data

- pdf

- follow-up questionnaires

- behavior

- translations in 8 languages

Natural History Site

- wikipedia

wiki = Hawaiian for fast

Natural History Site

- waihonapedia

waihona = Hawaiian for treasure

Natural History Site

Contents lists available at ScienceDirect

European Journal of Medical Genetics

journal homepage: http://www.elsevier.com/locate/ejmg

Genetic forum

Building treasures for rare disorders

Melanie Baas [a,1], Sylvia Huisman [a,1], John van Heukelingen [b], Gerritjan Koekkoek [c], Henk-Willem Laan [d], Raoul C. Hennekam [e,*]

[a] Department of Paediatrics, AMC, University of Amsterdam, The Netherlands
[b] Pitt-Hopkins Parents Support Group, Leidschendam, The Netherlands
[c] Cornelia de Lange Syndrome Support Group, Ijmuiden, The Netherlands
[d] Marshall-Smith Syndrome Foundation, The Hague, The Netherlands
[e] Department of Paediatrics and Translational Genetics, AMC, University of Amsterdam, The Netherlands

European Journal of Medical Genetics 58 (2015) 11–13

Natural History Site

de Winter *et al. Orphanet Journal of Rare Diseases* (2016) 11:37
DOI 10.1186/s13023-016-0422-2

Orphanet Journal of Rare Diseases

RESEARCH Open Access

Phenotype and natural history in 101 individuals with Pitt-Hopkins syndrome through an internet questionnaire system

Channa F. de Winter[1†], Melanie Baas[2†], Emilia K. Bijlsma[3], John van Heukelingen[4], Sue Routledge[5] and Raoul C. M. Hennekam[2*]

Topics

- Genes

- Defining RTS

- Natural history site

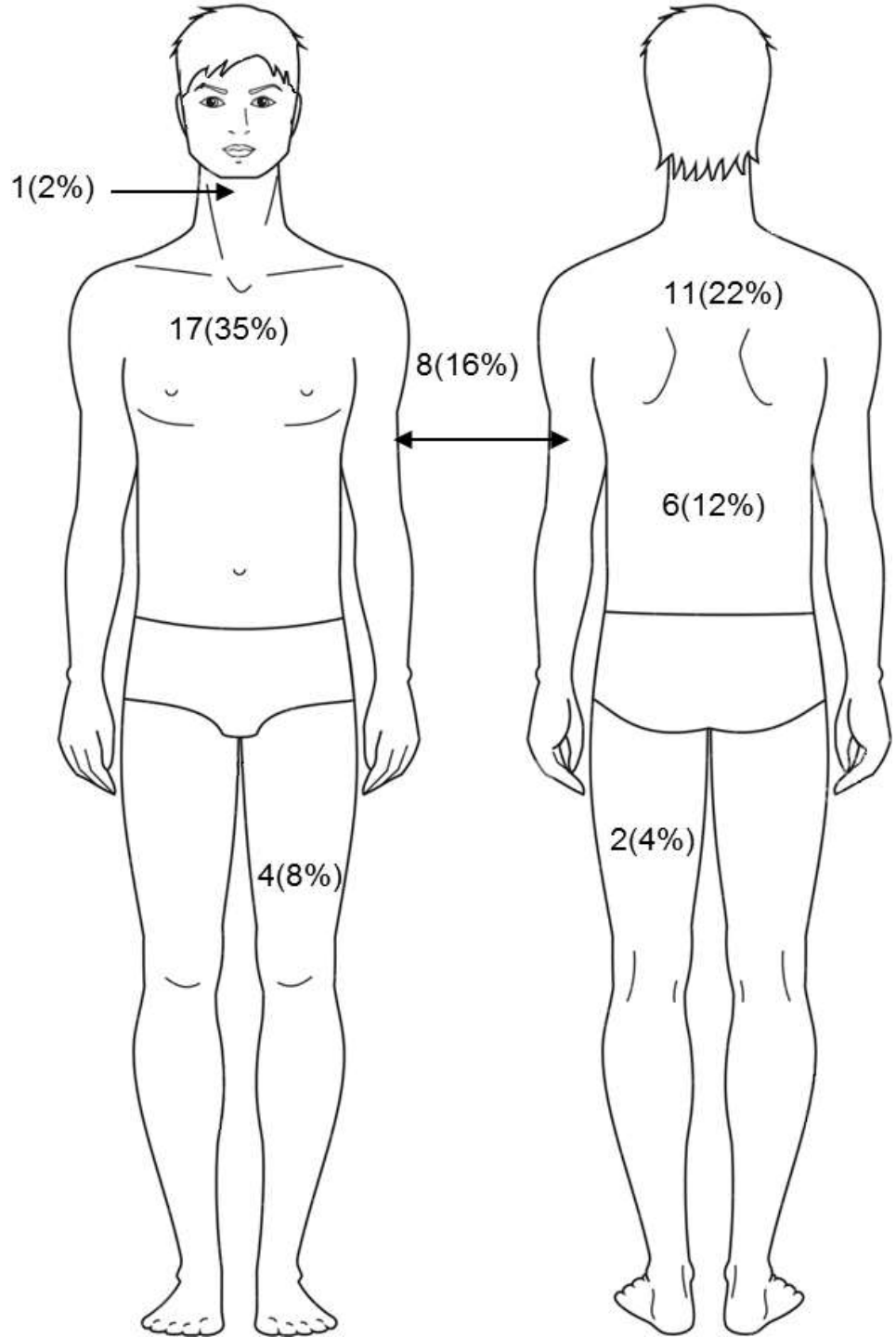
- Keloids

- Behavior

Keloids

Van de Kar, Br J Dermatol 2014;171:615

Keloids



Van de Kar, Br J Dermatol 2014;171:615

Keloids

- 15/62 Dutch RTS individuals had keloids

- mean age 1st keloid 11.9yr

- 1: 18%; 1-5: 52%; >5: 30%

- after surgery: 13; spontaneous 8

Van de Kar, Br J Dermatol 2014;171:615

Keloids

Complaint	n (%)
Itching	24 (89)
Pain	5 (19)
Restriction in movements	2 (7)
Infection	4 (15)
Difficulties falling asleep	7 (27)
Waking up during the night	3 (11)
Differences in behaviour	10 (37)

Van de Kar, Br J Dermatol 2014;171:615

Keloids

- no effective treatment

- further studies in Norway

Van de Kar, Br J Dermatol 2014;171:615

Topics

- Genes

- Defining RTS

- Natural history site

- Keloids

- Behavior

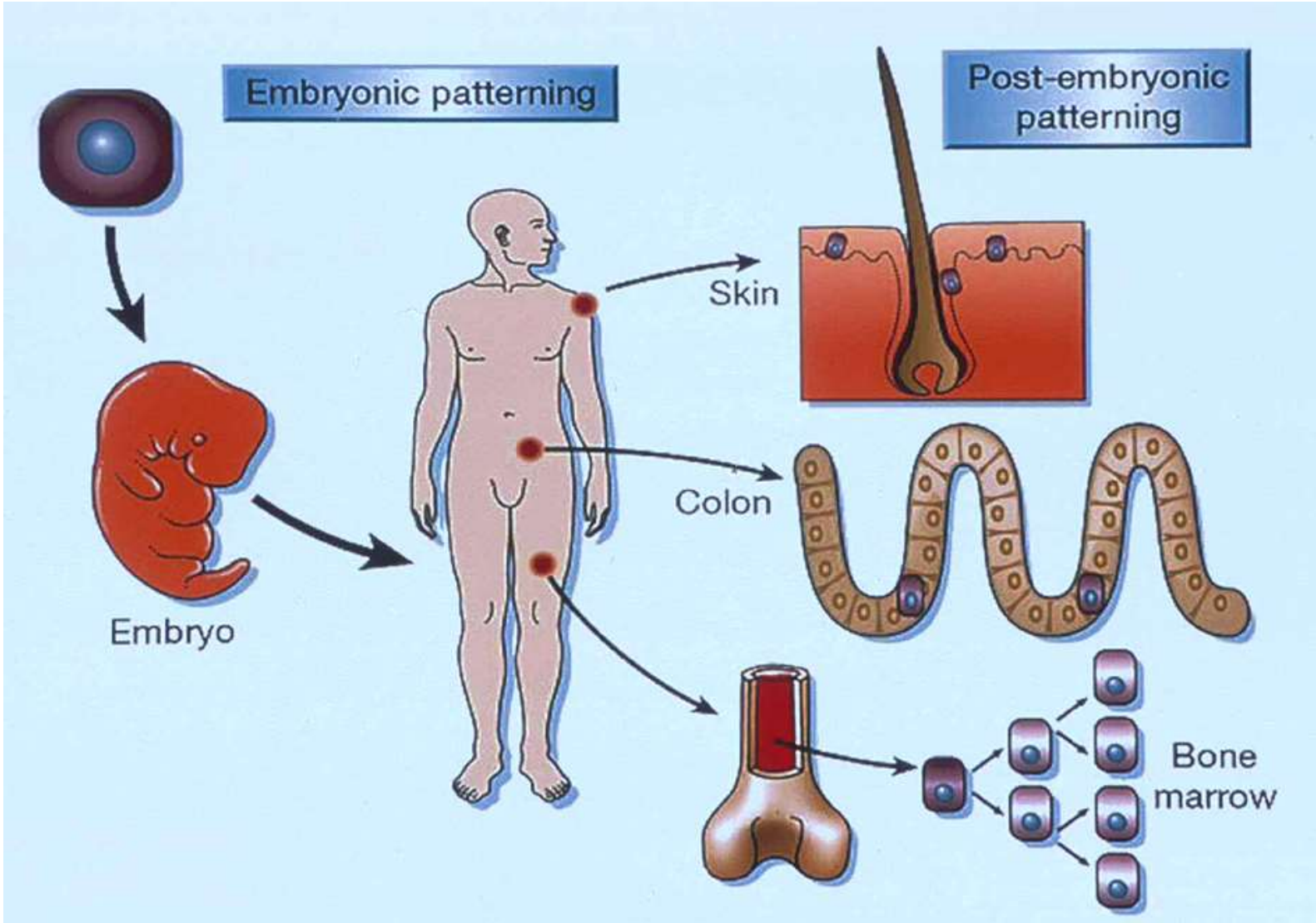
Behavior

- 24/7

- influence on daily life

- earlier lectures

Behavior: progression?



Behavior: progression?

- CBP has brain functions

- function: clearing ‘used’ proteins

- in some more ‘used’ proteins, in others less

- determined by genes

→ compare - CREBBP mutation

- genes that regulate protein use

- behavior