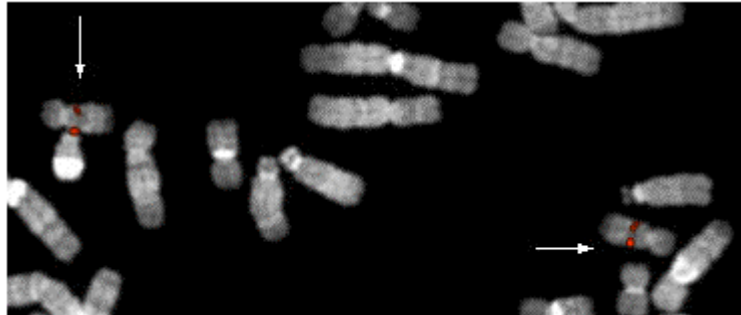


RARA (Retinoic acid receptor, alpha)

Identity

Hugo [RARA](#)

Location 17q12



[c-RARA](#) (17q21) in normal cells: PAC 833D9 - Courtesy Mariano Rocchi, [Resources for Molecular Cytogenetics](#). Laboratories willing to validate the probes are welcome: contact [M Rocchi](#)

DNA/RNA

Description 9 exons; total gene sequence: 7450 bp

Transcription 2.8 and 3.6 kb transcripts

Protein

Description 462 amino acids - 5 functional domains A/B (transcriptional regulation), C (DNA binding domain, contains 2 zinc fingers), D (cellular localization signal), E (ligand-binding domain) and F (function?)

Expression in hematopoietic cells

Localisation nuclear

Function ligand-dependent transcription factor specifically involved in hematopoietic cells differentiation and maturation = receptor for all-trans retinoic acid (ATRA) and 9-cis RA which are intracellular metabolites of vitamin A, active in cellular differentiation and morphogenesis
after linking with ATRA, RARA binds with a high affinity as a heterodimer with RXR (retinoid X receptor protein) to the RARE domain (retinoic acid response elements), a DNA sequence common to a number of genes and located in their promoter
the gene response to RARA binding is modulated by a series of co-repressors and co-activators

Homology with RARB and RARG (retinoic acid receptors ? and ?). 9-cis RA

receptors (RXRs) and receptors for thyroid and steroid hormones and for vitamin D3

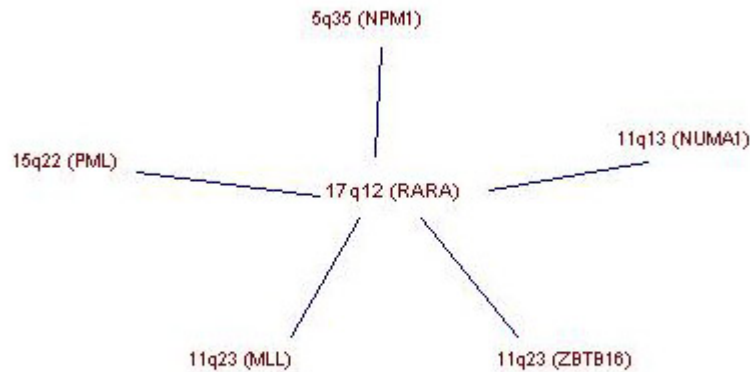
Implicated in

Entity	t(15;17)(q22;q12) / acute promyelocytic leukemia (APL) --> PML - RARA
Disease	typical APL (or M3 ANLL, FAB classification), approximately 98% of APL cases; abnormal promyelocytes with Auer rods and bundles (faggots); disruption of the PODs with a microspeckled pattern; maturation response to all-trans retinoic acid (ATRA) therapy
Prognosis	immediate prognosis impaired by intravascular disseminated coagulopathy; long term prognosis is favorable with treatment combining ATRA plus chemotherapy
Cytogenetics	variant or complex t(15;17) translocation in 5% of cases, no known prognosis implication; secondary chromosomal abnormalities in 30 to 35% of APL at diagnosis; association with +8 in 17 to 28% of cases; other associations are rare but recurrent: del(7q) , del(9q) , ider(17)t(15;17) , +21
Hybrid/Mutated Gene	the crucial fusion transcript is 5'PML-3'RARA, encoded by der(15) chromosome; the counterpart 5'RARA-3'PML encoded by der(17) is inconstant breakpoint in RARA gene is always located in intron between A and B domains three breakpoint clusters in PML gene: bcr1 (70% of patients), bcr2 (10%) and bcr3 (20%), giving rise respectively to the long (L), intermediate (V) and short (S) length hybrid PML-RARAt transcripts; V form would be linked to ATRA decreased sensitivity and S form to association with an excess of secondary chromosome changes.
Abnormal Protein	106 Kda fusion protein; role in the leukemogenic process by probable interference with the signalling pathway leading to differentiation and maturation of myeloid precursors (mainly dysregulation of retinoid-inducible genes involved in myeloid differentiation)
Entity	t(11;17)(q23;q12) / acute promyelocytic leukemia --> PLZF -RARA
Disease	variant acute promyelocytic leukemia (APL) form with atypical cytologic aspects (intermediate morphology between M2 and M3, no Auer rods) and no response to ATRA therapy; less than 1% of APL cases.
Entity	t(5;17)(q35;q12) / acute promyelocytic leukemia --> NPM -RARA
Disease	exceptional; probable response to ATRA
Entity	t(11;17)(q13;q12) / acute promyelocytic leukemia --> NuMA -RARA
Disease	exceptional: probable response to ATRA

Entity t(11;17)(q23;q12) / M5 acute non lymphocytic leukemia --> MLL-RARA

Disease 1 case to date; not to be confused with the t(11;17)(q23;q12) mentioned above; not found in APL; belongs to the [MLL/11q23 leukemias](#)

Breakpoints



RARA and partners. Editor 08/2004; last update 08/2005.

External links

Nomenclature

[Hugo](#) [RARA](#)

[GDB](#) [RARA](#)

[Entrez Gene](#) [RARA 5914](#) retinoic acid receptor, alpha

Cards

[Atlas](#) [RARAID46](#)

[GeneCards](#) [RARA](#)

[Ensembl](#) [RARA](#)

[Genatlas](#) [RARA](#)

[GeneLynx](#) [RARA](#)

[eGenome](#) [RARA](#)

[euGene](#) [5914](#)

Genomic and cartography

[GoldenPath](#) [RARA - 17q12 chr17:35718972-35767420 + 17q21.2](#) (hg18-Mar_2006)

[Ensembl](#) [RARA - 17q21.2 \[CytoView\]](#)

[NCBI](#) [Genes Cyto](#) [Gene Seq](#) [Map View - NCBI]

[OMIM](#) [Disease map \[OMIM\]](#)

[HomoloGene](#) [RARA](#)

Gene and transcription

[Genbank](#) [AK098172](#) [ENTREZ]

[Genbank](#) [AK130192](#) [ENTREZ]

[Genbank](#) [AL834159](#) [ENTREZ]

[Genbank](#) [BC008727](#) [ENTREZ]

[Genbank](#) [BC071733](#) [ENTREZ]

[RefSeq](#) [NM_000964](#) [SRS] [NM_000964](#) [ENTREZ]

[RefSeq](#) [NM_001024809](#) [SRS] [NM_001024809](#) [ENTREZ]

[RefSeq](#) [NM_001033603](#) [SRS] [NM_001033603](#) [ENTREZ]

[AceView](#) [RARA](#) AceView - NCBI

[TRASER](#) [RARA](#) Traser - Stanford

[Unigene](#) [Hs.535499](#) [SRS] [Hs.535499](#) [NCBI] [HS535499](#) [spliceNest]

Protein : pattern, domain, 3D structure

[SwissProt](#) [P10276](#) [SRS] [P10276](#) [EXPASY] [P10276](#) [INTERPRO]

[Prosite](#) [PS00031 NUCLEAR_REC_DBD_1](#) [SRS] [PS00031 NUCLEAR_REC_DBD_1](#) [Expasy]

[Prosite](#) [PS51030 NUCLEAR_REC_DBD_2](#) [SRS] [PS51030 NUCLEAR_REC_DBD_2](#) [Expasy]

[Interpro](#) [IPR001628 Hrmn_rcpt_DNA_bd](#) [SRS] [IPR001628 Hrmn_rcpt_DNA_bd](#) [EBI]

[Interpro](#) [IPR000536 Hrmn_rcpt_lig_bd](#) [SRS] [IPR000536 Hrmn_rcpt_lig_bd](#) [EBI]

[Interpro](#) [IPR003078 Rtnoid_receptor](#) [SRS] [IPR003078 Rtnoid_receptor](#) [EBI]

[Interpro](#) [IPR001723 Stdhrmn_receptor](#) [SRS] [IPR001723 Stdhrmn_receptor](#) [EBI]

[CluSTr](#) [P10276](#)

[Pfam](#) [PF00104 Hormone_recep](#) [SRS] [PF00104 Hormone_recep](#) [Sanger] [pfam00104](#) [NCBI-CDD]

[Pfam](#) [PF00105 zf-C4](#) [SRS] [PF00105 zf-C4](#) [Sanger] [pfam00105](#) [NCBI-CDD]

[Smart](#) [SM00430 HOLI](#) [EMBL]

[Smart](#) [SM00399 ZnF_C4](#) [EMBL]

[Prodom](#) [PD000035 Znf_C4steroid](#) [INRA-Toulouse]

[Prodom](#) [P10276 RARA_HUMAN](#) [Domain structure] [P10276 RARA_HUMAN](#) [sequences sharing at least 1 domain]

[Blocks](#) [P10276](#)

[PDB](#) [1DKF](#) [SRS] [1DKF](#) [PdbSum], [1DKF](#) [IMB]

[PDB](#) [1DSZ](#) [SRS] [1DSZ](#) [PdbSum], [1DSZ](#) [IMB]

Protein Interaction databases

[DIP](#) [P10276](#)

IntAct	P10276
	Polymorphism : SNP, mutations, diseases
OMIM	180240 [map]
GENECLINICS	180240
SNP	RARA [dbSNP-NCBI]
SNP	NM_000964 [SNP-NCI]
SNP	NM_001024809 [SNP-NCI]
SNP	NM_001033603 [SNP-NCI]
SNP	RARA [GeneSNPs - Utah] RARA [HGBASE - SRS] RARA [SNP - HAPMAP]
	General knowledge
Family Browser	RARA [UCSC Family Browser]
SOURCE	NM_000964
SOURCE	NM_001024809
SOURCE	NM_001033603
SMD	Hs.535499
SAGE	Hs.535499
Amigo	transcription factor activity
Amigo	transcription factor activity
Amigo	steroid hormone receptor activity
Amigo	retinoic acid receptor activity
Amigo	retinoic acid receptor activity
Amigo	transcription coactivator activity
Amigo	nucleus
Amigo	transcription
Amigo	regulation of transcription, DNA-dependent
Amigo	signal transduction
Amigo	zinc ion binding
Amigo	sequence-specific DNA binding
Amigo	metal ion binding
PubGene	RARA
	Other databases
	Probes
Probe	RARA (17q21) in normal cells (Bari)
Probe	RARA Related clones (RZPD - Berlin)
	PubMed
PubMed	88 Pubmed reference(s) in LocusLink
	Bibliography

The t(15;17) translocation of acute promyelocytic leukaemia fuses the retinoic acid receptor alpha gene to a novel transcribed locus.

de The H, Chomienne C, Lanotte M, Degos L, Dejean A.

Nature. 1990; 347: 558-561.

Medline [91015360](#)

Chromosomal translocation t(15;17) in human acute promyelocytic leukemia fuses RAR alpha with a novel putative transcription factor, PML.

Kakizuka A, Miller WH Jr, Umesono K, Warrell RP Jr, Frankel SR, Murty VV, Dmitrovsky E, Evans RM.

Cell. 1991; 66: 663-674.

Medline [91347368](#)

Characterization of the PML-RAR alpha chimeric product of the acute promyelocytic leukemia-specific t(15;17) translocation.

Nervi C, Poindexter EC, Grignani F, Pandolfi PP, Lo Coco F, Avvisati G, Pelicci PG, Jetten AM.

Cancer Res. 1992; 52: 3687-3692.

Medline [92315212](#)

Genetics of APL and the molecular basis of retinoic acid treatment.

Casini T, Grignani F, Pelicci PG.

Int J Cancer. 1997; 70: 473-474. Review.

Medline [97185977](#)

The pathogenesis of acute promyelocytic leukaemia: evaluation of the role of molecular diagnosis and monitoring in the management of the disease.

Grimwade D.

Brit J Haematol, 1999; 106: 591-613. Review.

Deconstructing a disease: RARalpha, its fusion partners, and their roles in the pathogenesis of acute promyelocytic leukemia.

Melnick A, Licht JD.

Blood. 1999; 93: 3167-3215. Review.

Medline [99252073](#)

[REVIEW articles](#)

automatic search in PubMed

[Last year publications](#)

automatic search in PubMed

[BiblioGene - INIST](#)

Contributor(s)

Written 10-
2000 Franck Viguié

Citation

This paper should be referenced as such :

Viguié F . RARA (Retinoic acid receptor, alpha). Atlas Genet Cytogenet Oncol Haematol. October 2000 .

URL : <http://AtlasGeneticsOncology.org/Genes/RARAI46.html>

© *Atlas of Genetics and Cytogenetics in Oncology and Haematology*
