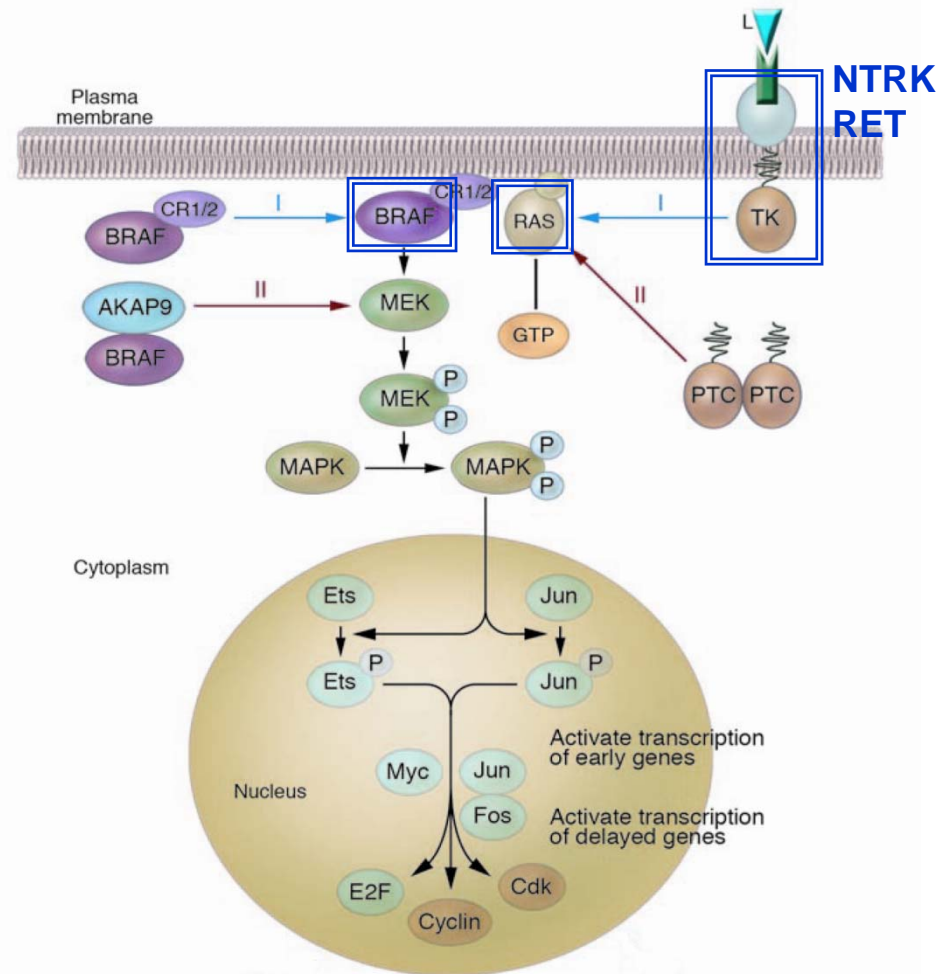


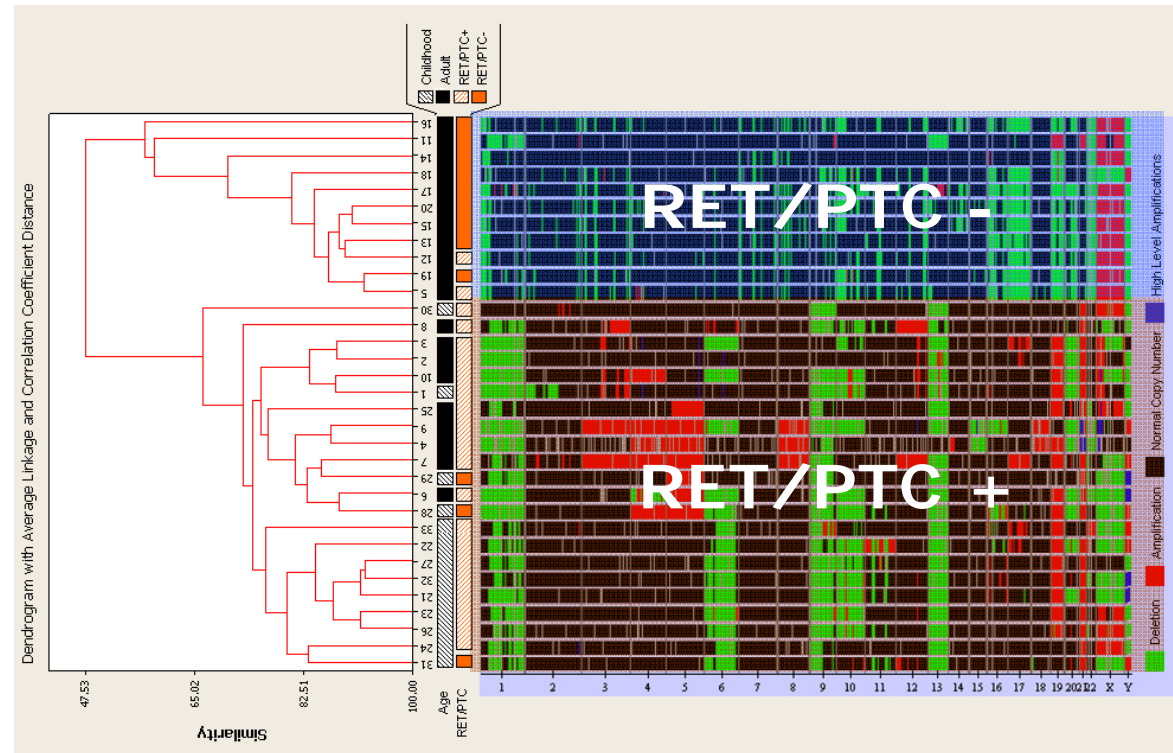
Mitogen-activated MAP kinase pathway in papillary thyroid cancer

Research Unit for
Radiation
Cytogenetics



Specific aberration patterns lead to separation of papillary thyroid cancers into two clusters

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Cytogenetics



Chromosomal imbalances separate PTC according RET/PTC status

- ▶ Candidate genes are derived from recurrently altered chromosome regions by database mining (www.ensembl.org)

Candidate genes in different tumor subgroups

<i>Chromosomal region</i>	<i>Candidate genes</i>	<i>Type of aberration</i>	<i>Characteristic for tumour group</i>
1p33-cen	RAB3B, JAK1, TGFBR3	Deletion	+
1p35.3-36.31	TNFRSF25, CASP9	Deletion	+ (adults)
3q29	MUC4, PPP1R2, TFRC	Amplification	+
7p22.1	RBAK	Deletion	-
4p14-13.1	RHOH	Amplification	+
9p21.2-24.3	JAK2, TUSC1	Deletion	+
9q22.33-31.1	STX17	Deletion	+
9q32-33.1	TNFSF15, DEC1, DBC1	Deletion	+
10q23.2-23.32	PTENP1, PTEN	Deletion	+
12q24.23-24.31	CAMKK2, PXN, RNF34	Amplification	+
13q12.11-21.2	LATS2, RASL11A, FOXO1A, RB1, DLEU7	Deletion	+
13q22.1-34	SLITRK1, SLITRK5, SLITRK6, INGI	Deletion	+
21q21.3-22.3	TIAM1, ERG	Amplification	+

Candidate genes in commonly altered regions

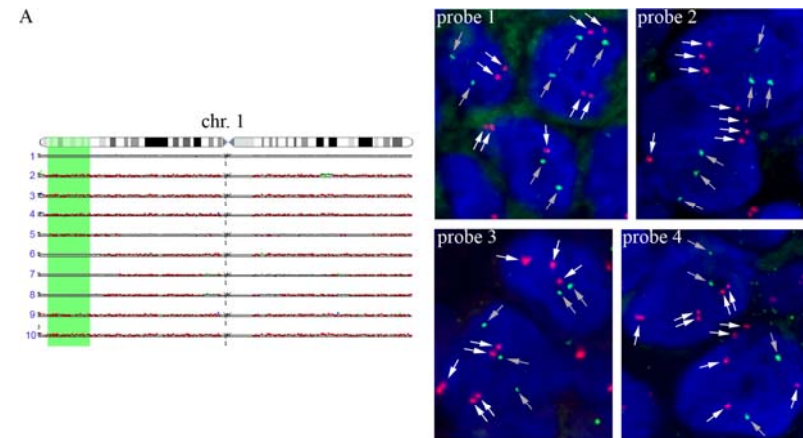
<i>Chromosomal region</i>	<i>Candidate genes</i>	<i>Type of aberration</i>
9q21.33	RMI1, GAS1	Deletion
9q22.2	SHC3, SYK	Deletion
9q22.32-22.33	FANCC, PTCH1	Deletion
10p15.1-14	KLF6, NET1	Deletion
10p13-p12.1	RSU1	Deletion
10q11.21-11.22	NRP1, PARD3, RET	Deletion
10q22.2	ANXA7	Deletion
10q24.1-24.32	SLIT1	Deletion
22q12.3	TIMP3	Deletion

- ▶ 46 Candidate genes involved in PI 3K/MAPK-, apoptosis-, interleukin-27-, and angiopoietin receptor pathways (Pathway Interaction Database, <http://pid.nci.nih.gov/>)

Array CGH and FISH evaluation:

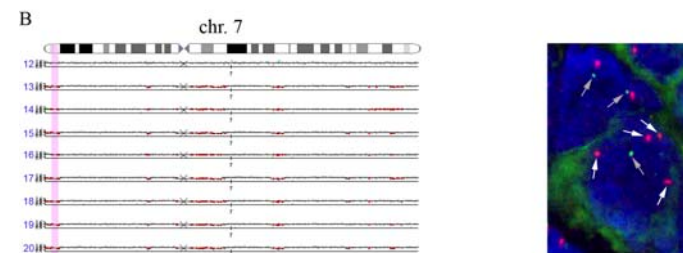
Deletion on 1p35.3-36.31

region-specific (**green**) and reference (**red**) FISH signals confirm the deletion from array CGH with four different BAC clones



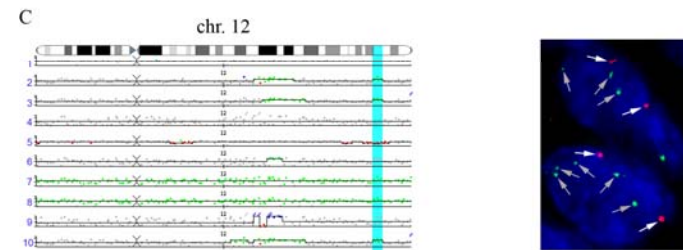
Deletion on 7q21-22

two pooled BAC clones specific for 7q22.1 (**green**) and a reference BAC (**red**) confirm the deletion from array CGH



Amplification on 12q24

two pooled BAC clones specific for 12q24 (**green**) and two reference BAC clones (**red**) confirm the amplification from array CGH



Functional studies to investigate the role of selected candidate genes in thyroid tumorigenesis

Comparison of genom-wide genomic alterations with proteomic changes (MALDI Imaging)

Investigation of aberration patterns dependent on the BRAF status of papillary thyroid carcinomas