Molecular Pathways in Human Cancer

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Förderung:
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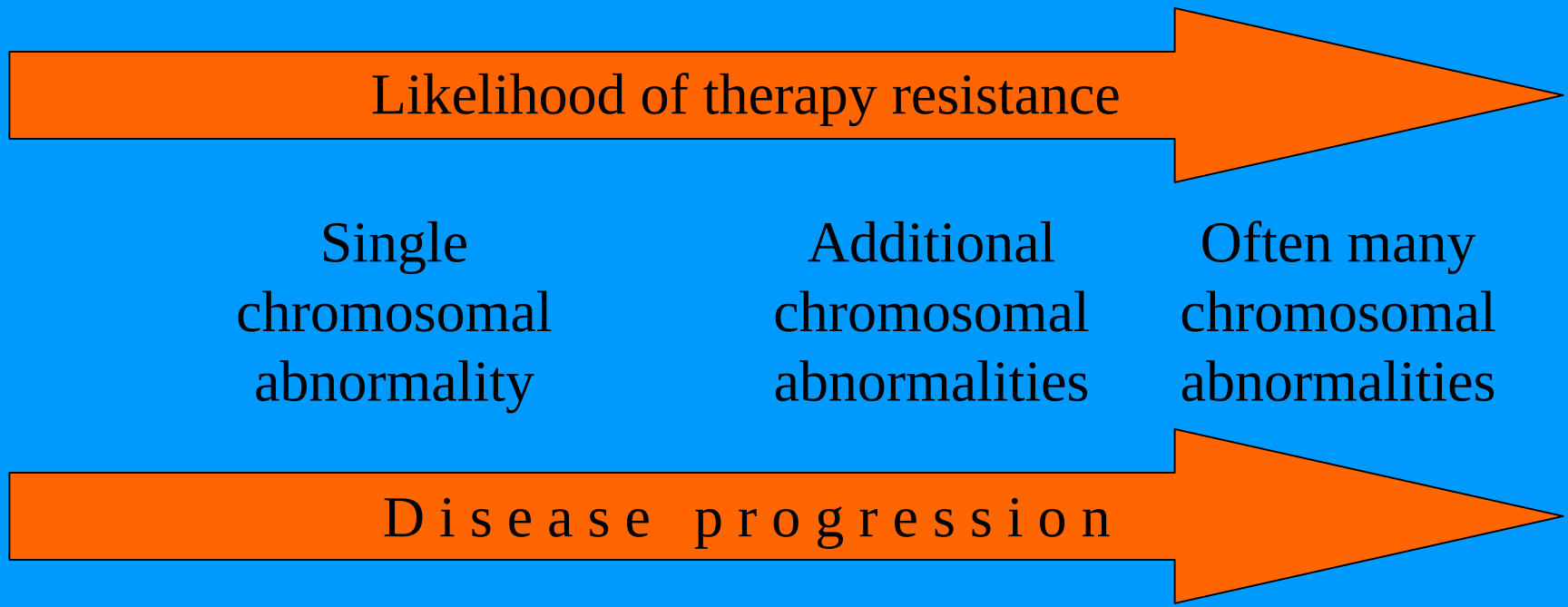
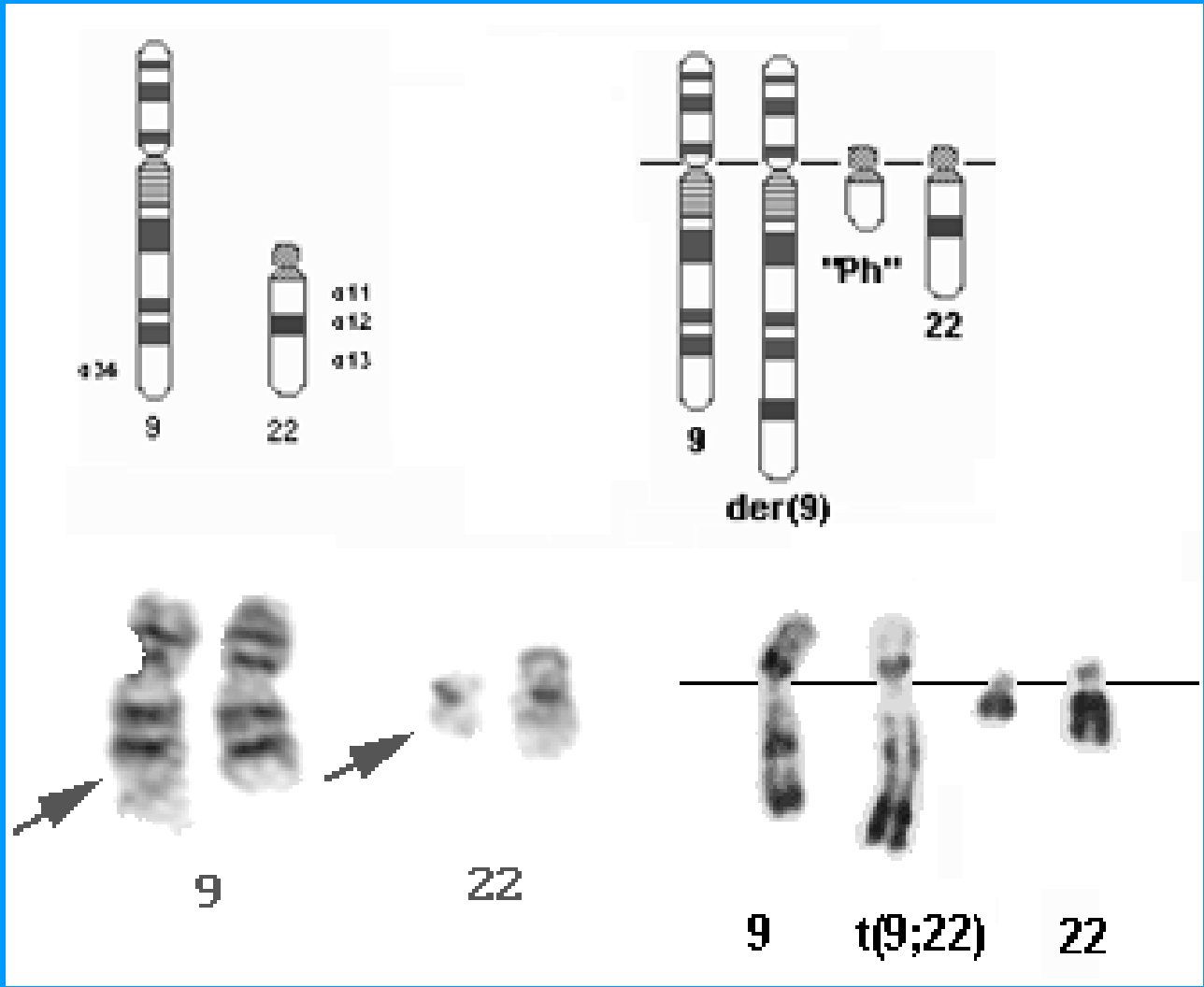
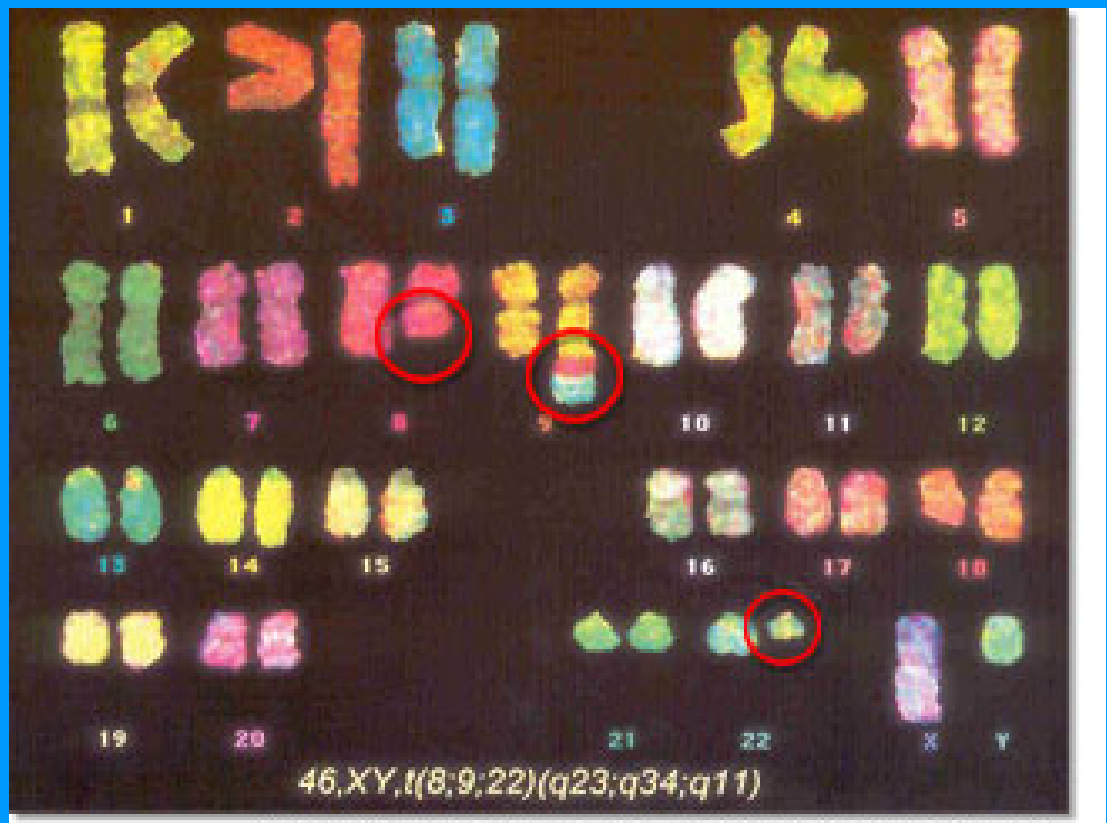
„Stereotypic“ course of chronic myeloid leukemia (CML)



The Philadelphia Chromosome

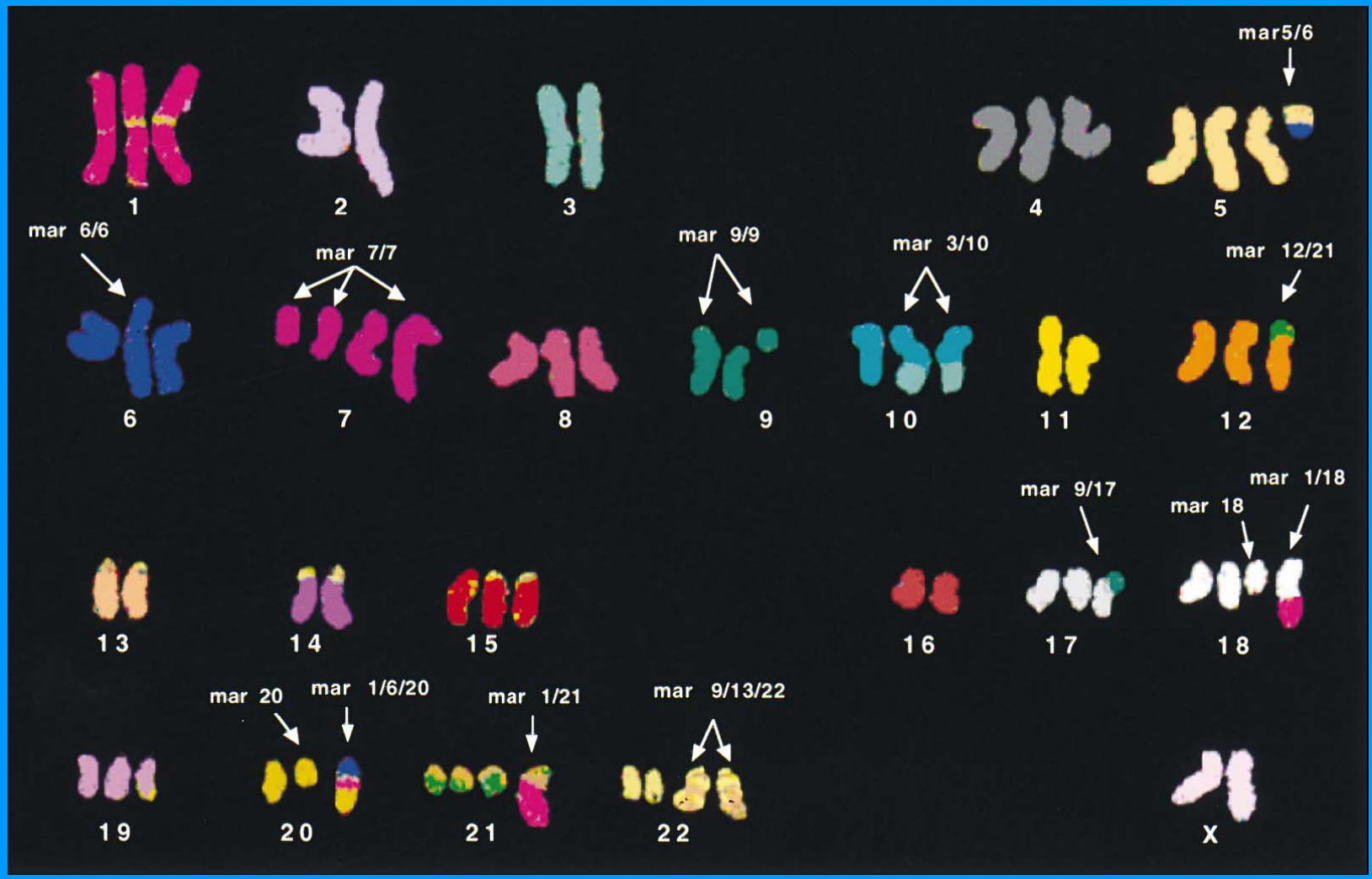


An „almost normal“ karyotype in CML (chronic phase)

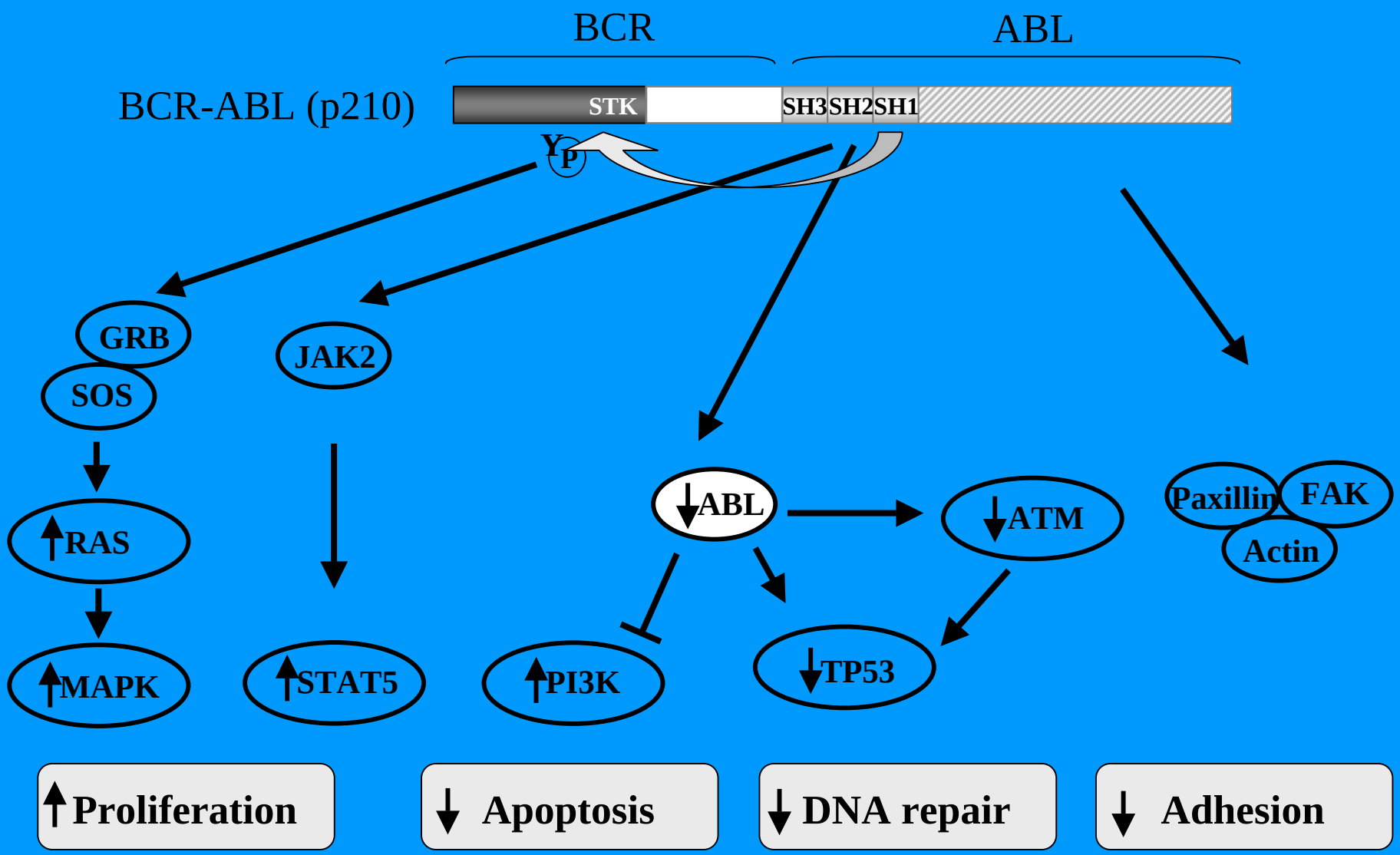


Note: This karyotype was prepared using a FISH technique known as “chromosome painting”. As well as having a translocation from chromosome 22, chromosome 9 also has translocated material from chromosome 8.

An extremely aberrant karyotype in CML (Cell line from blast crisis)



Pleiotropic effects of BCR-ABL fusion

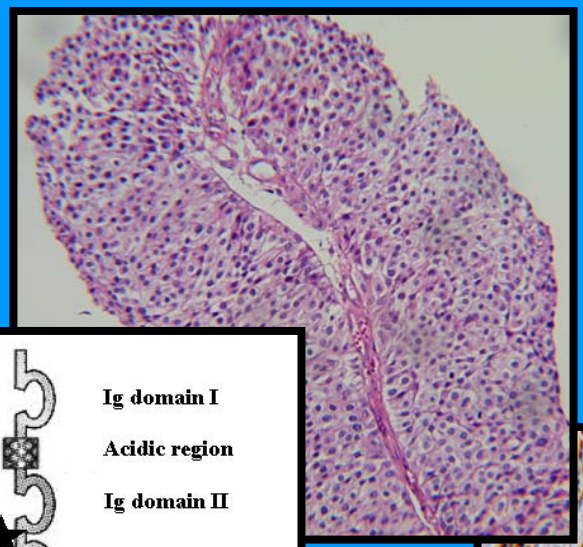


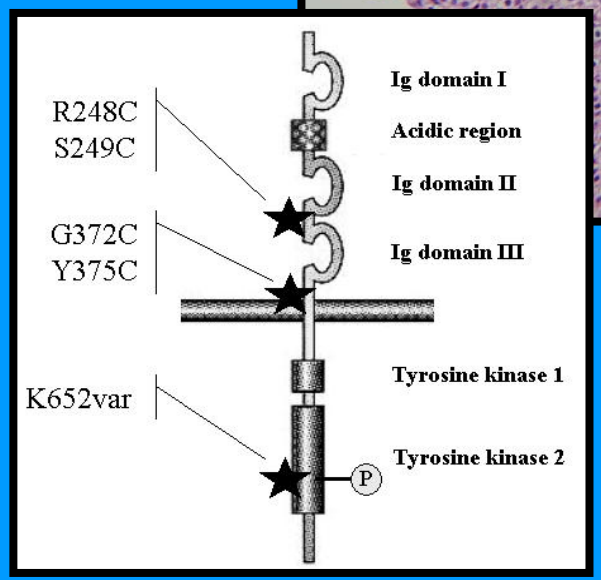
Summary I:
Why CML is (usually) easy to predict

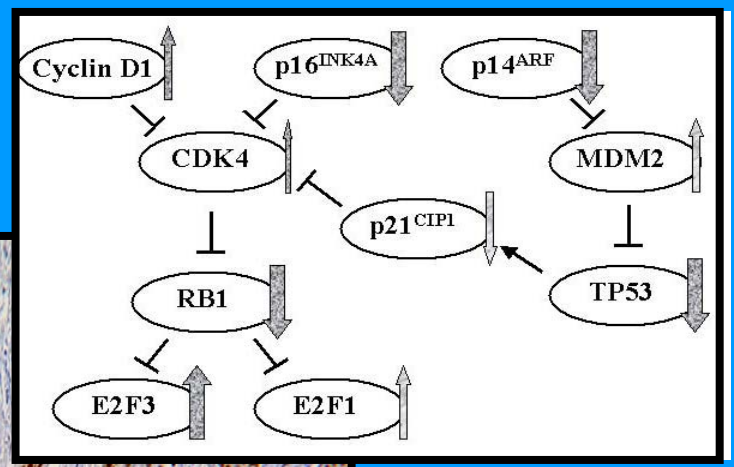
- A recurrent chromosomal alteration is its cause
- Tumor progression is indicated by the appearance of additional changes
  although these are not as homogeneous
- Probability of resistance to therapy increases essentially with disease progression
  although there can be various mechanisms

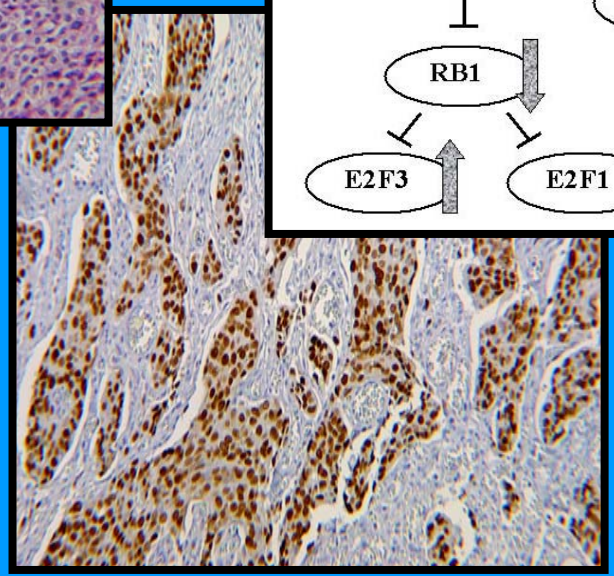
Two types of bladder cancer

Papillary urothelial cancer



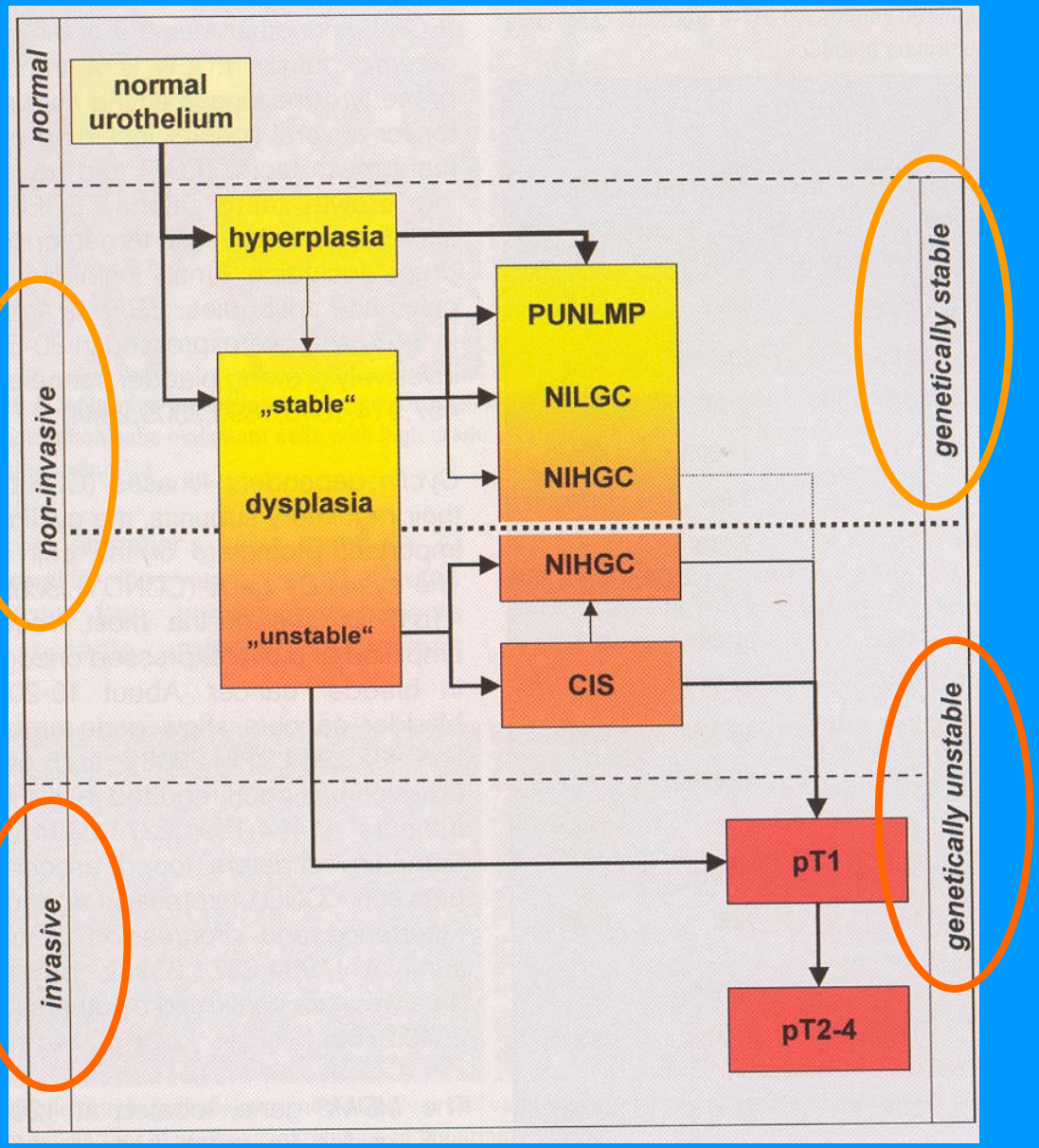






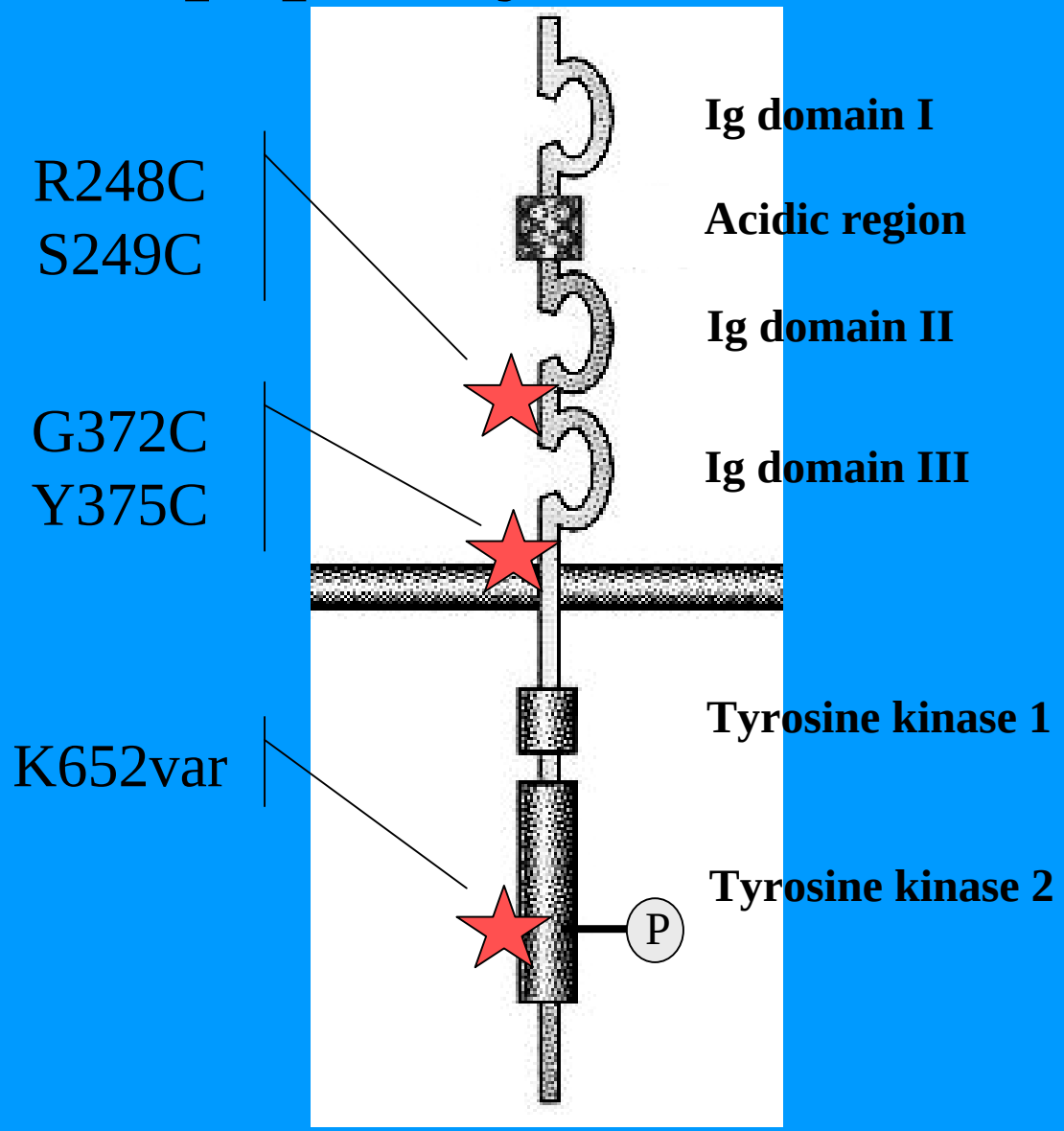
Invasive urothelial cancer

Urothelial cancer progression and genomic stability

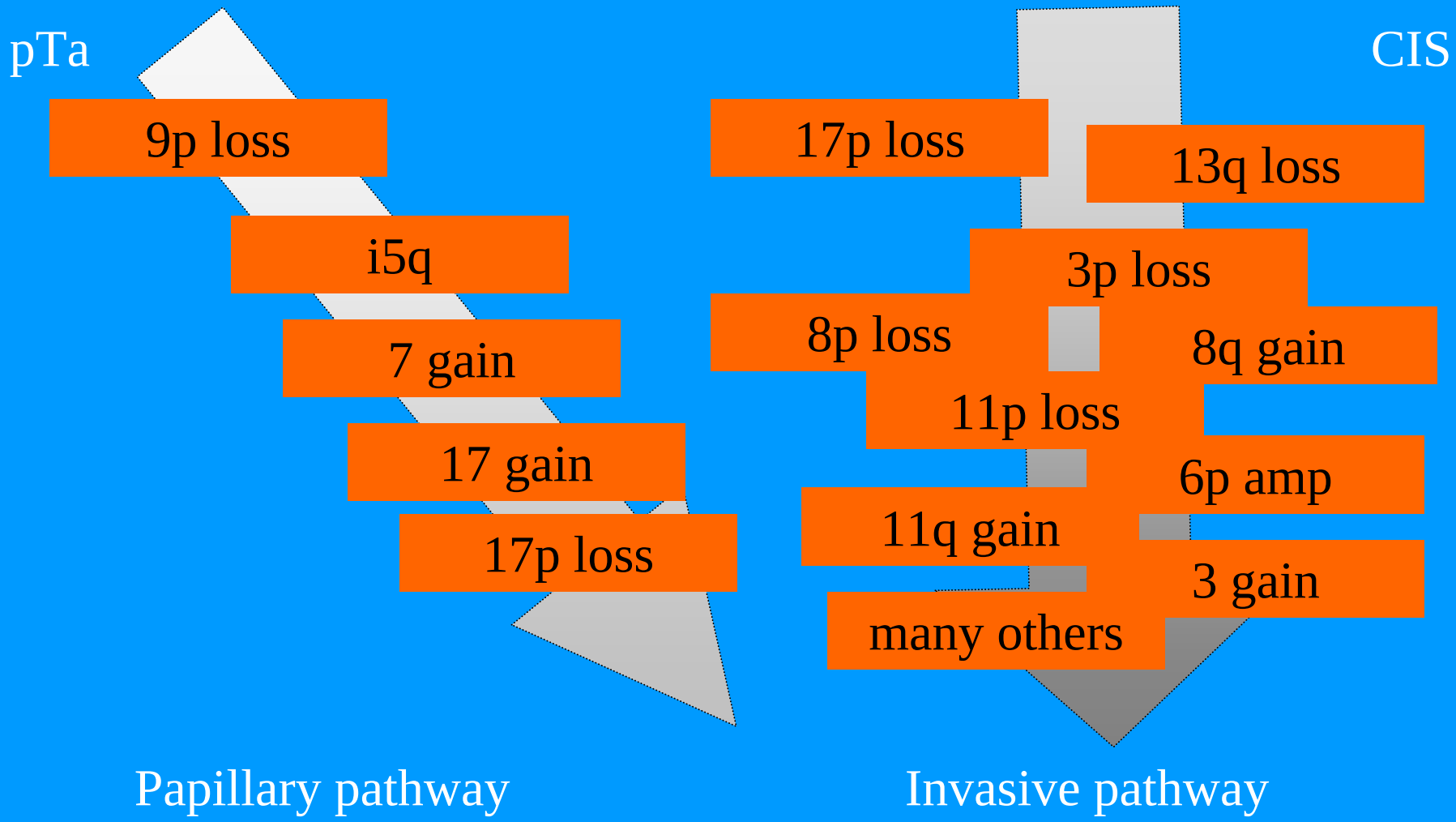


WHO classification 2004

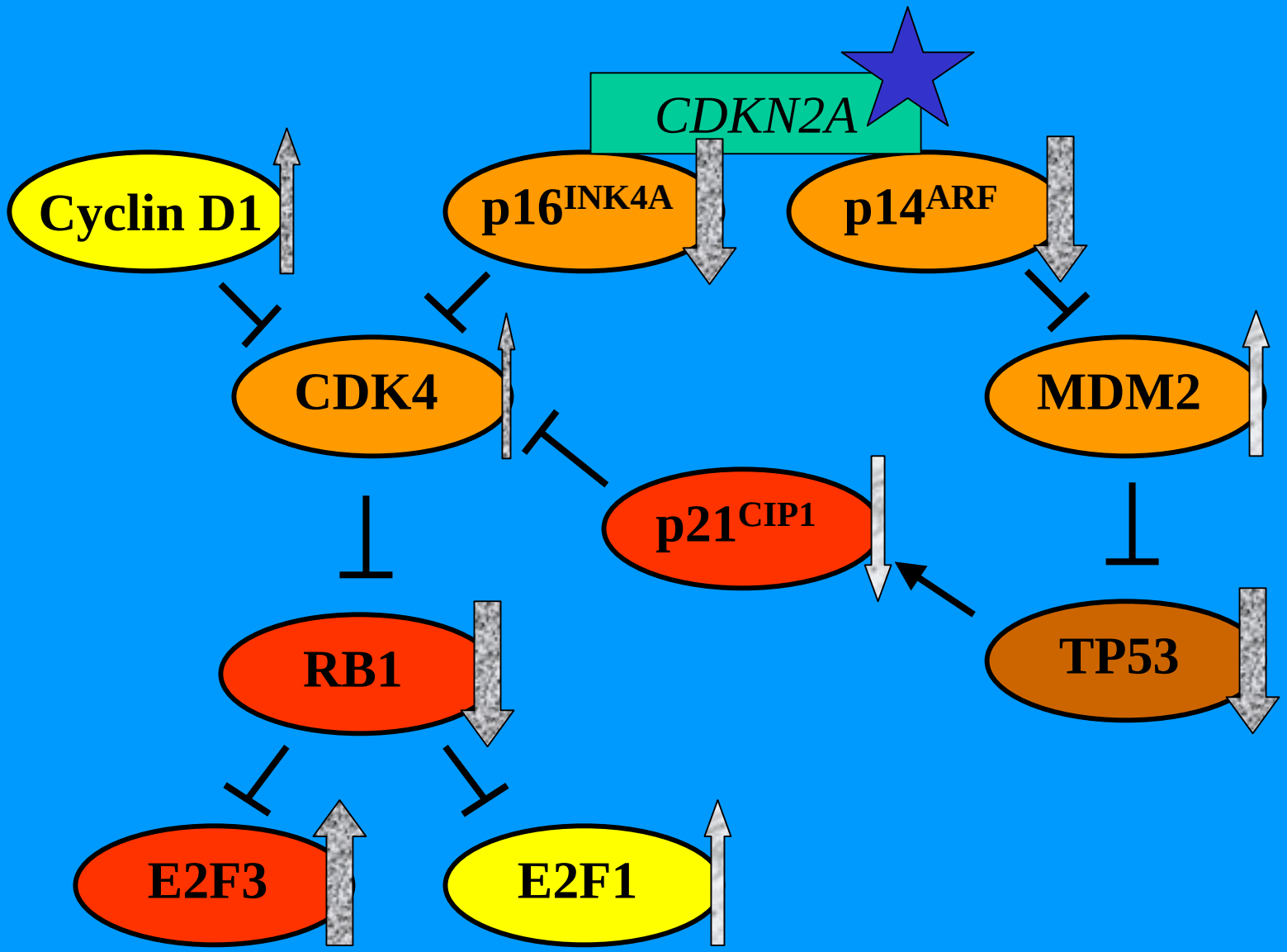
Mutations of FGFR3 in papillary bladder cancer



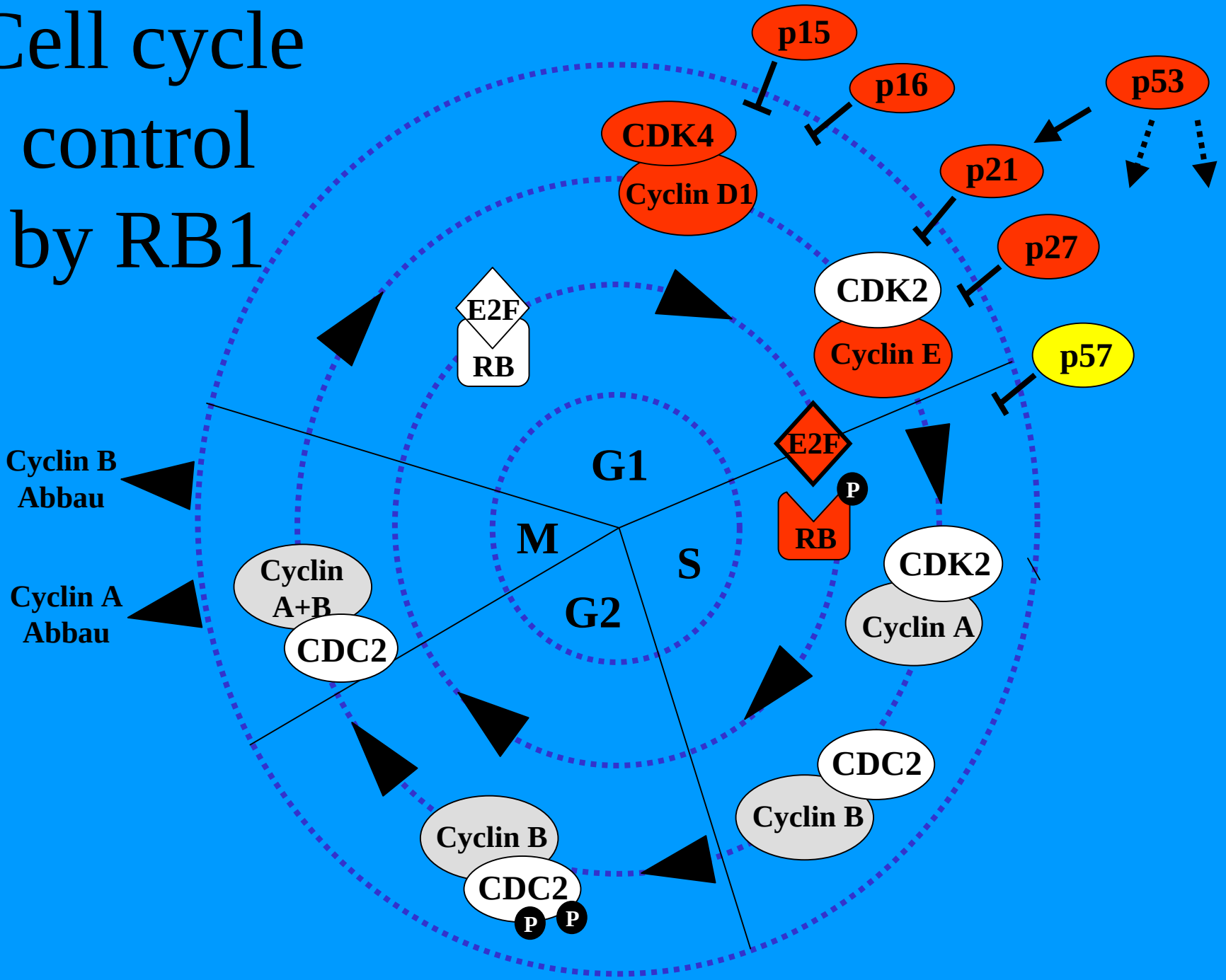
Chromosomal changes in bladder cancers



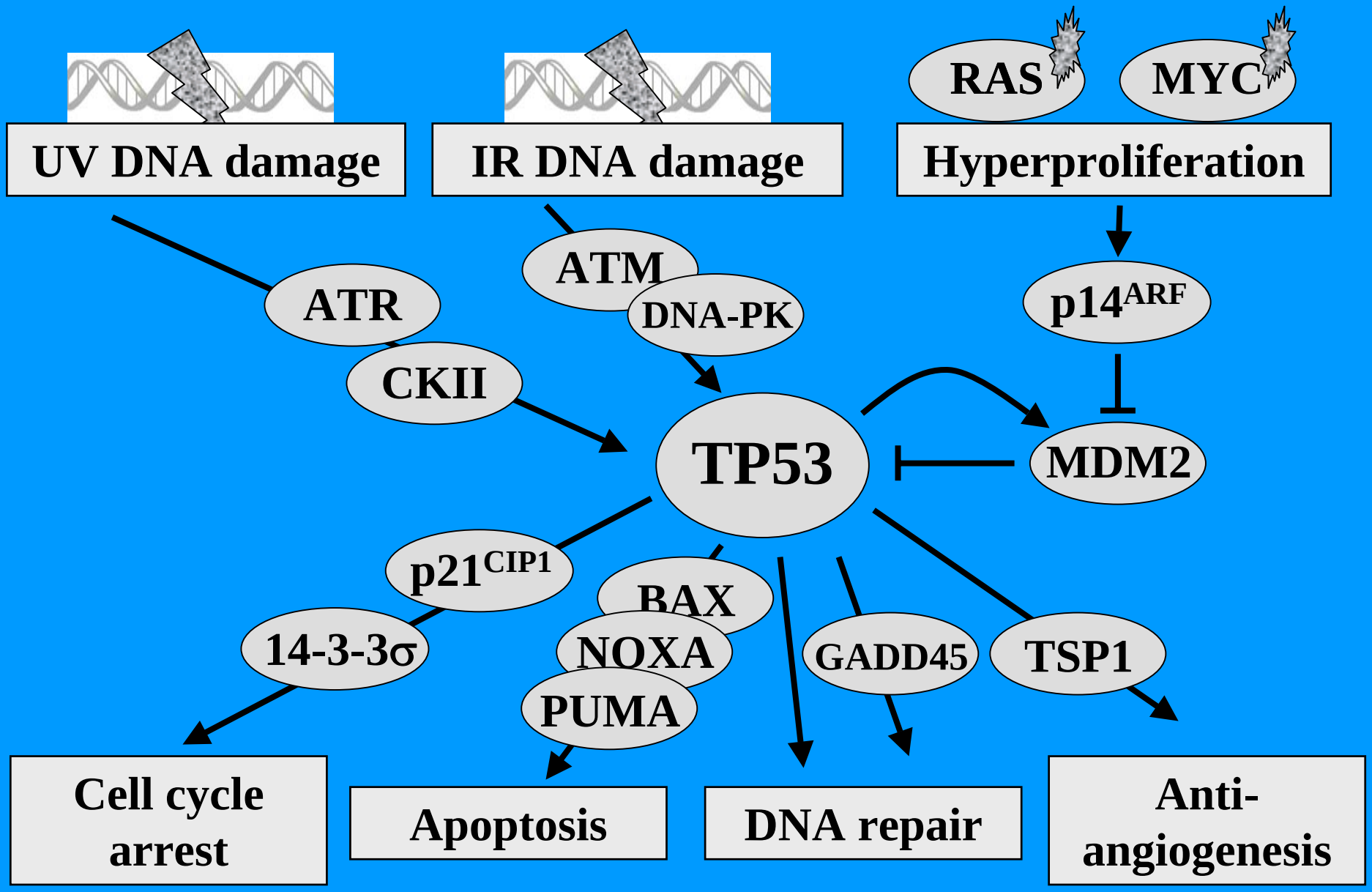
The interlinked RB1 and TP53 networks are regularly compromised in bladder cancer



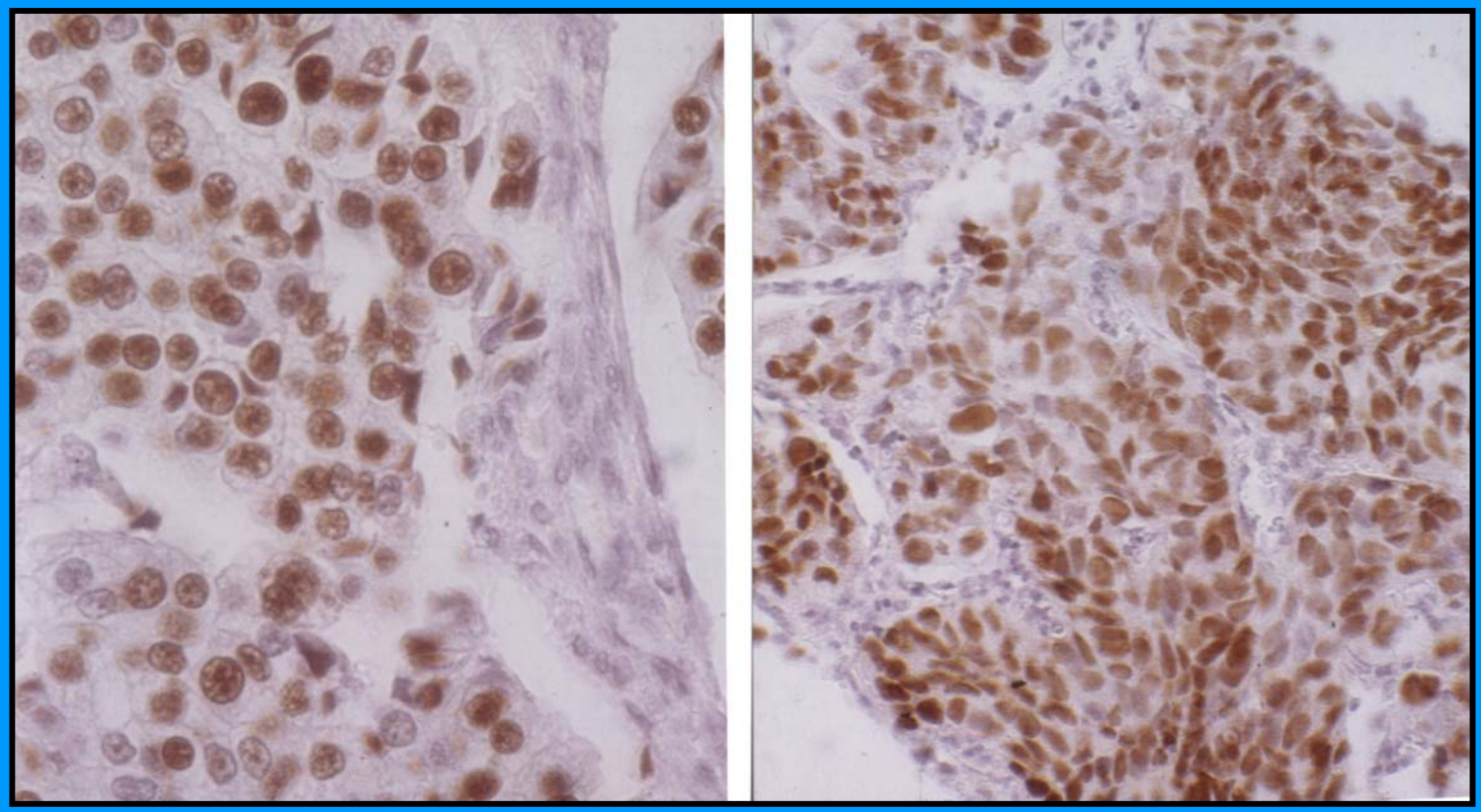
Cell cycle control by RB1



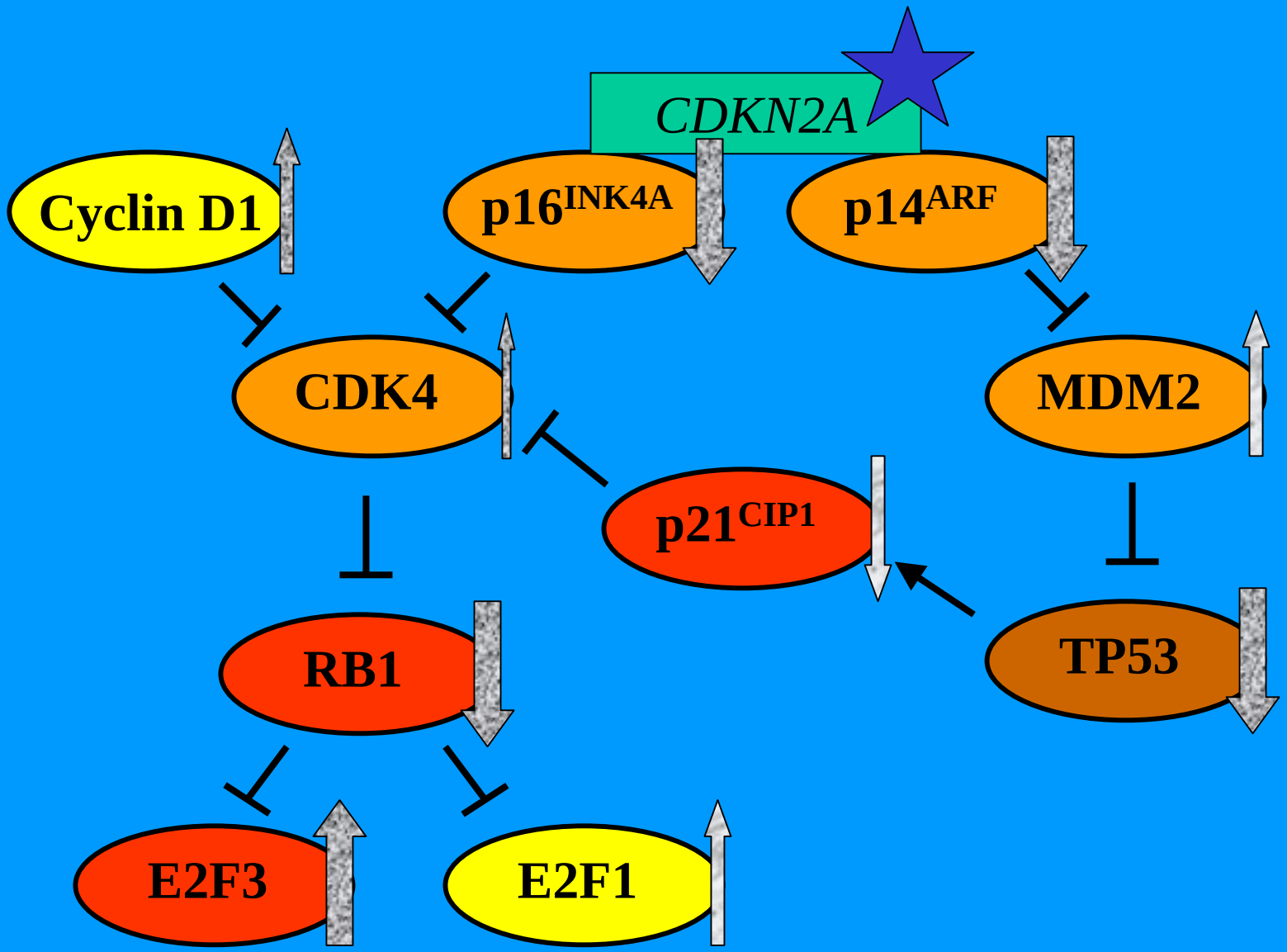
The TP53 network



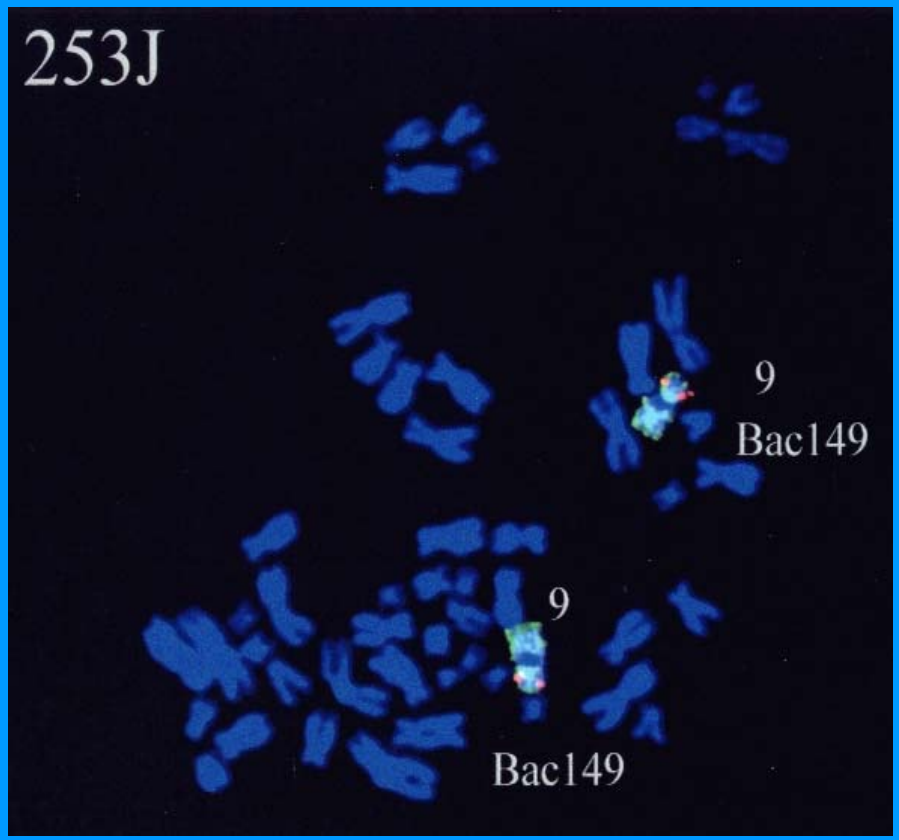
TP53 immunohistochemistry for bladder cancer classification?

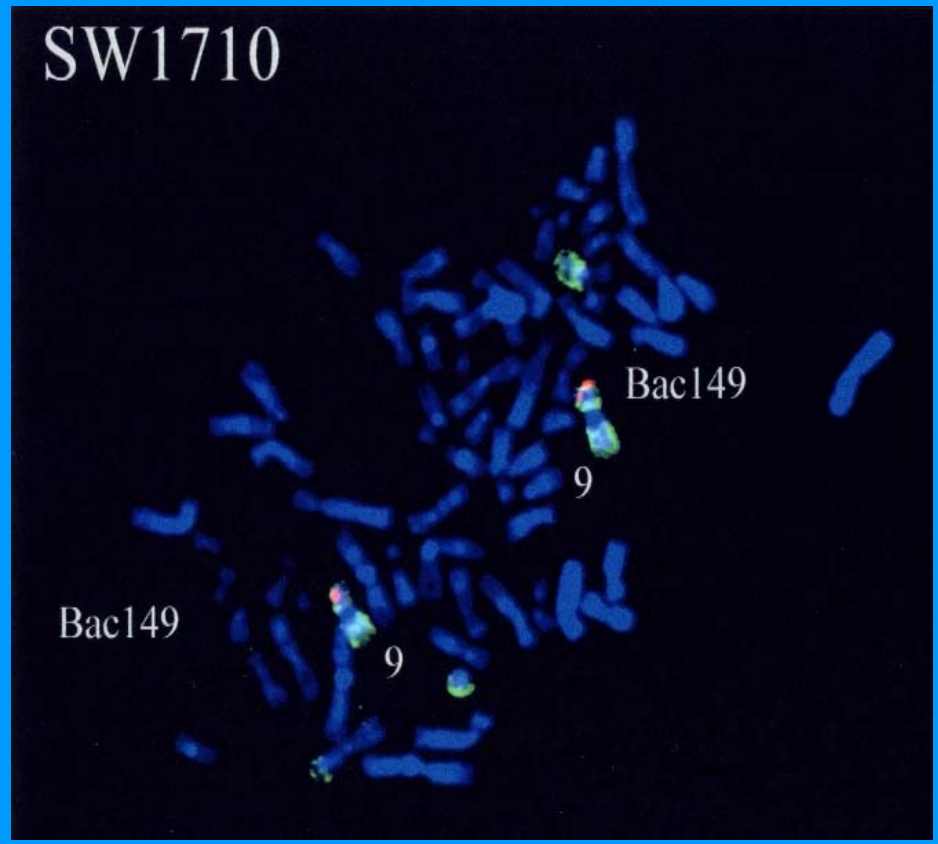


Different disturbances of the RB1 and TP53 network in bladder cancer



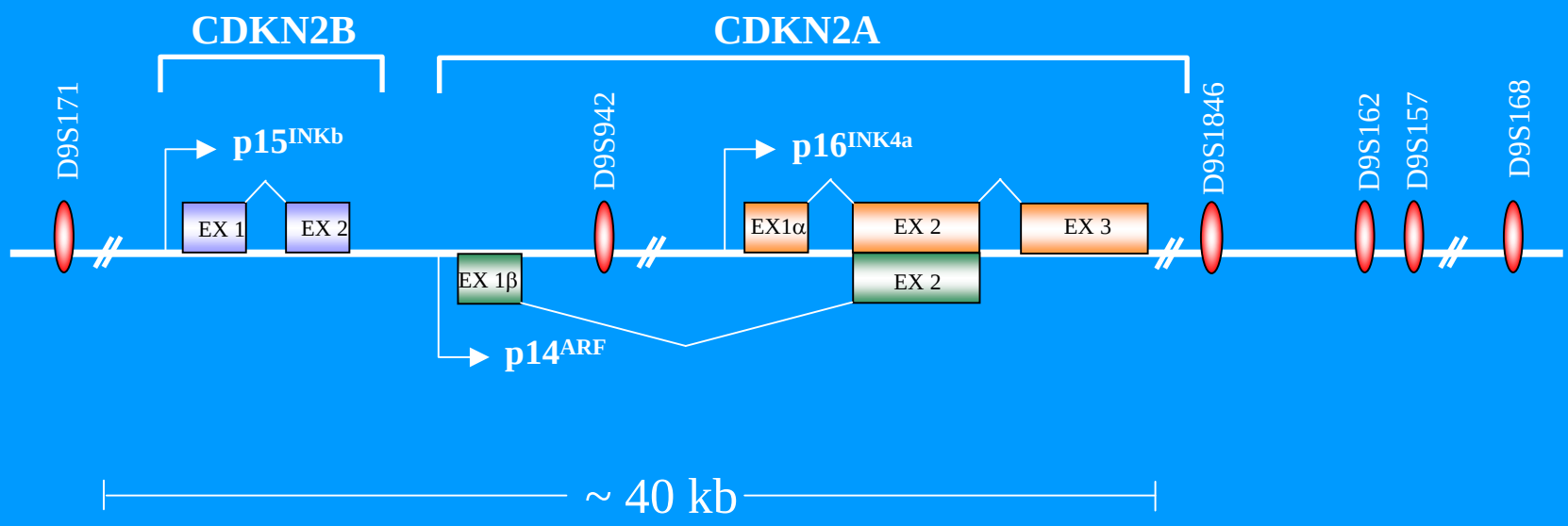
Chromosome 9 in bladder cancer cell lines





Courtesy: Horst Hameister, Ulm

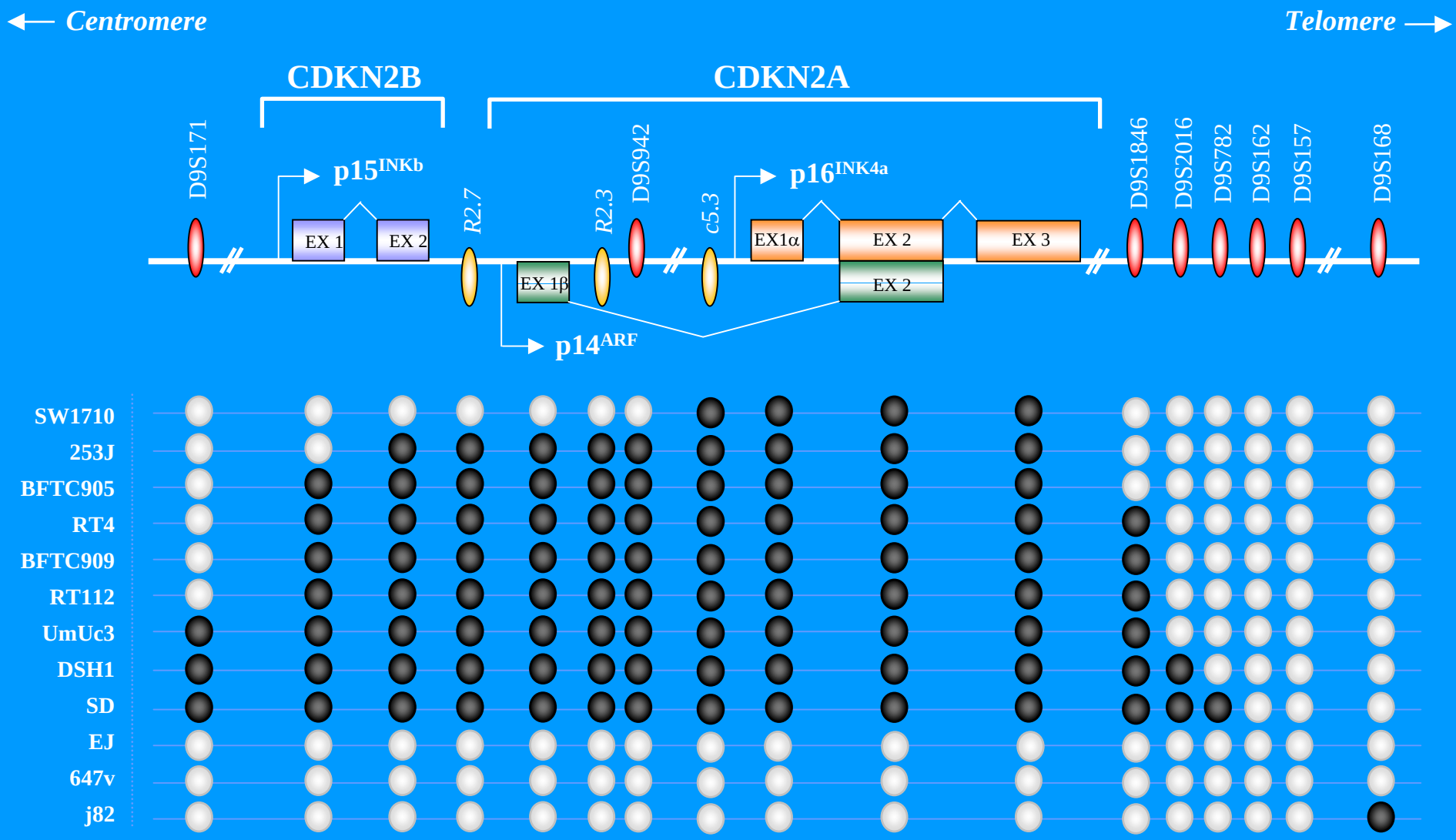
The *CDKN2* Locus at 9p21



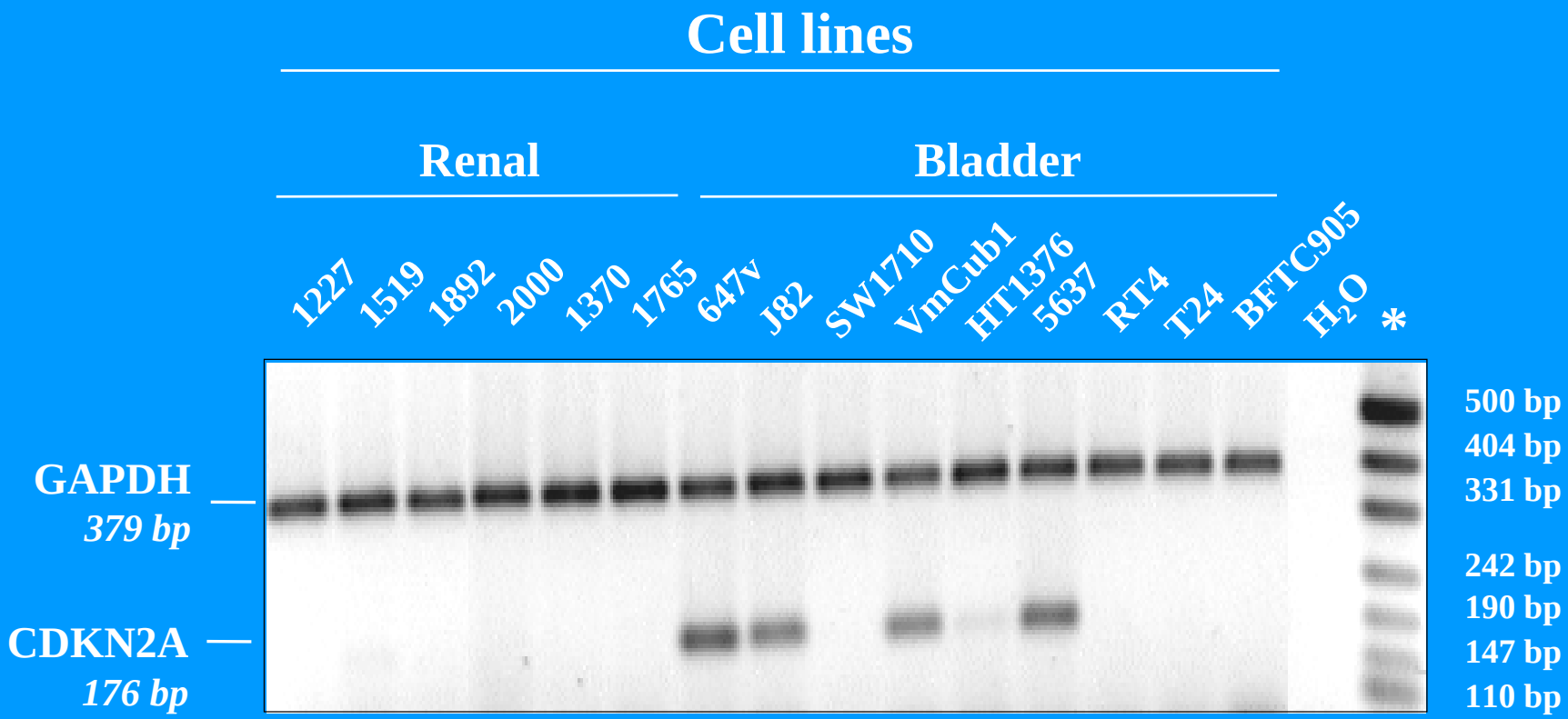
← *Centromere*

Telomere →

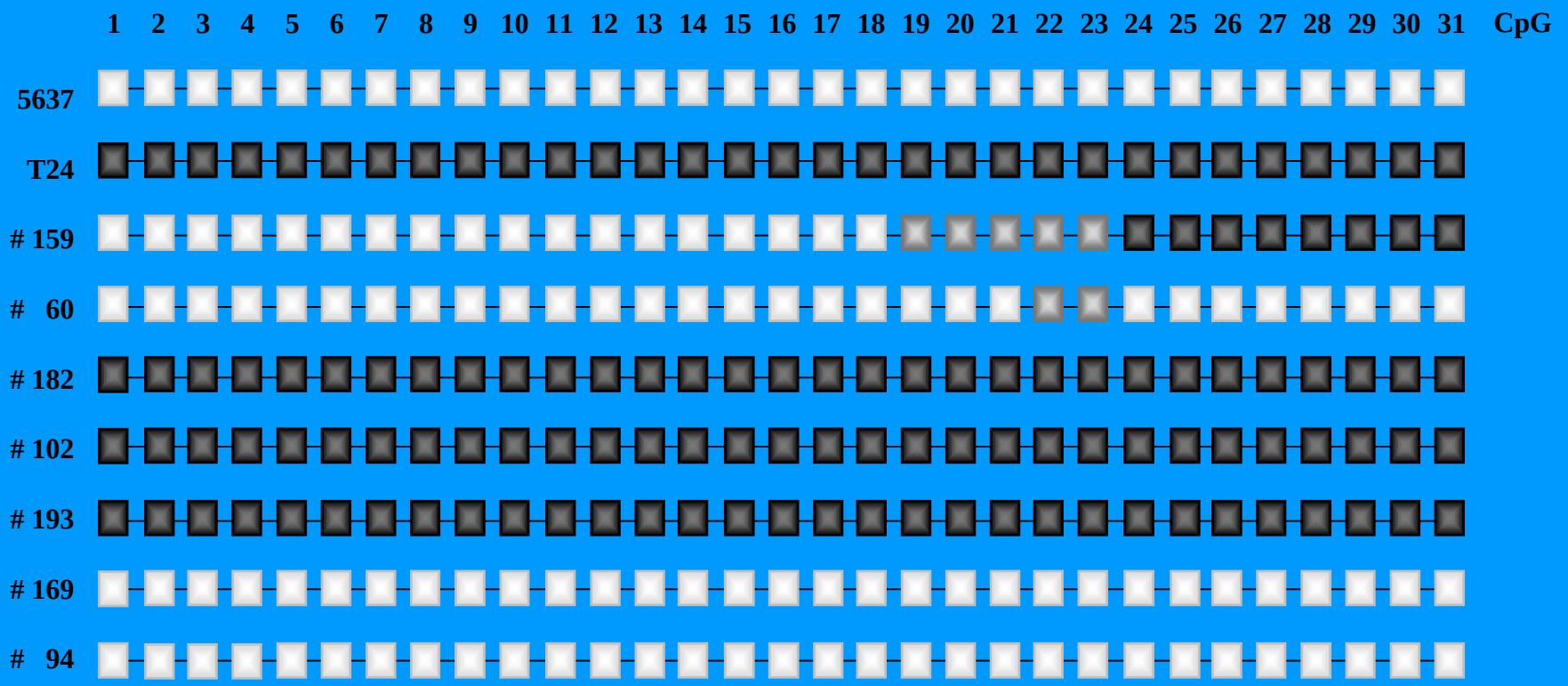
Homozygous deletions at 9p21 in bladder cancer cell lines



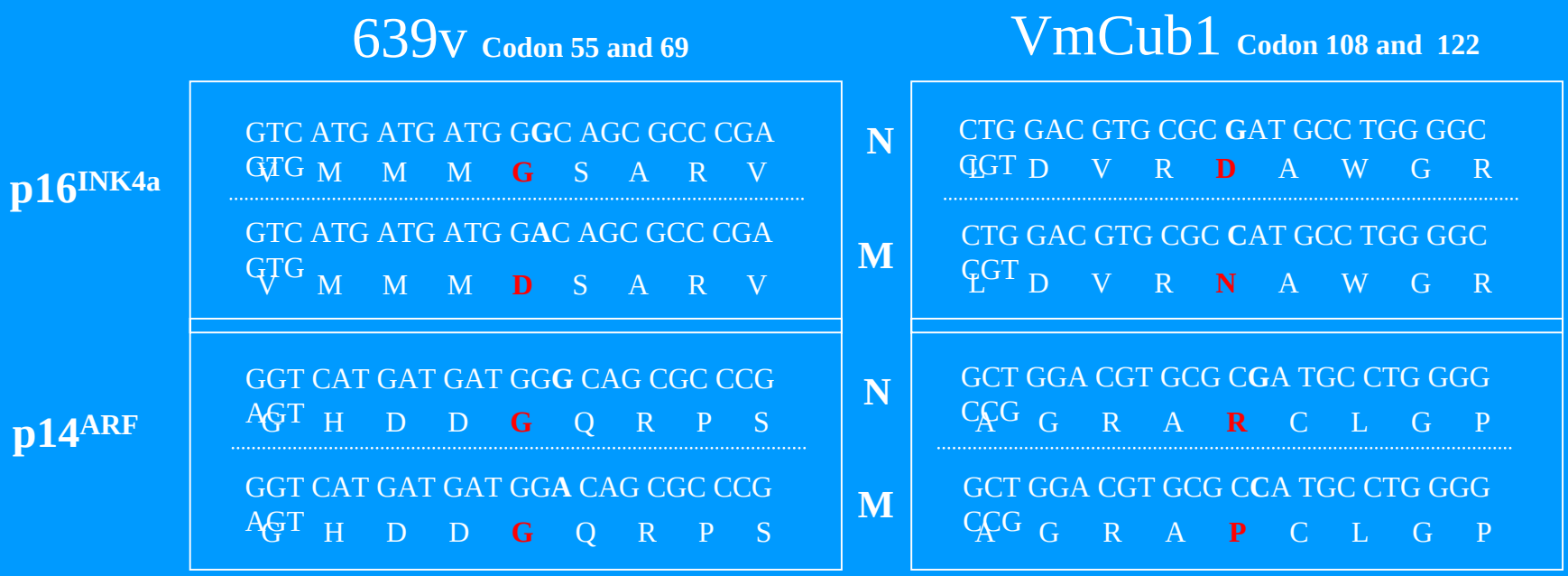
Loss of $p16^{INK4A}$ expression in urological cancer cell lines



Hypermethylation of the p16 gene promoter in bladder cancer



Mutations of p16^{INK4A} in bladder cancer



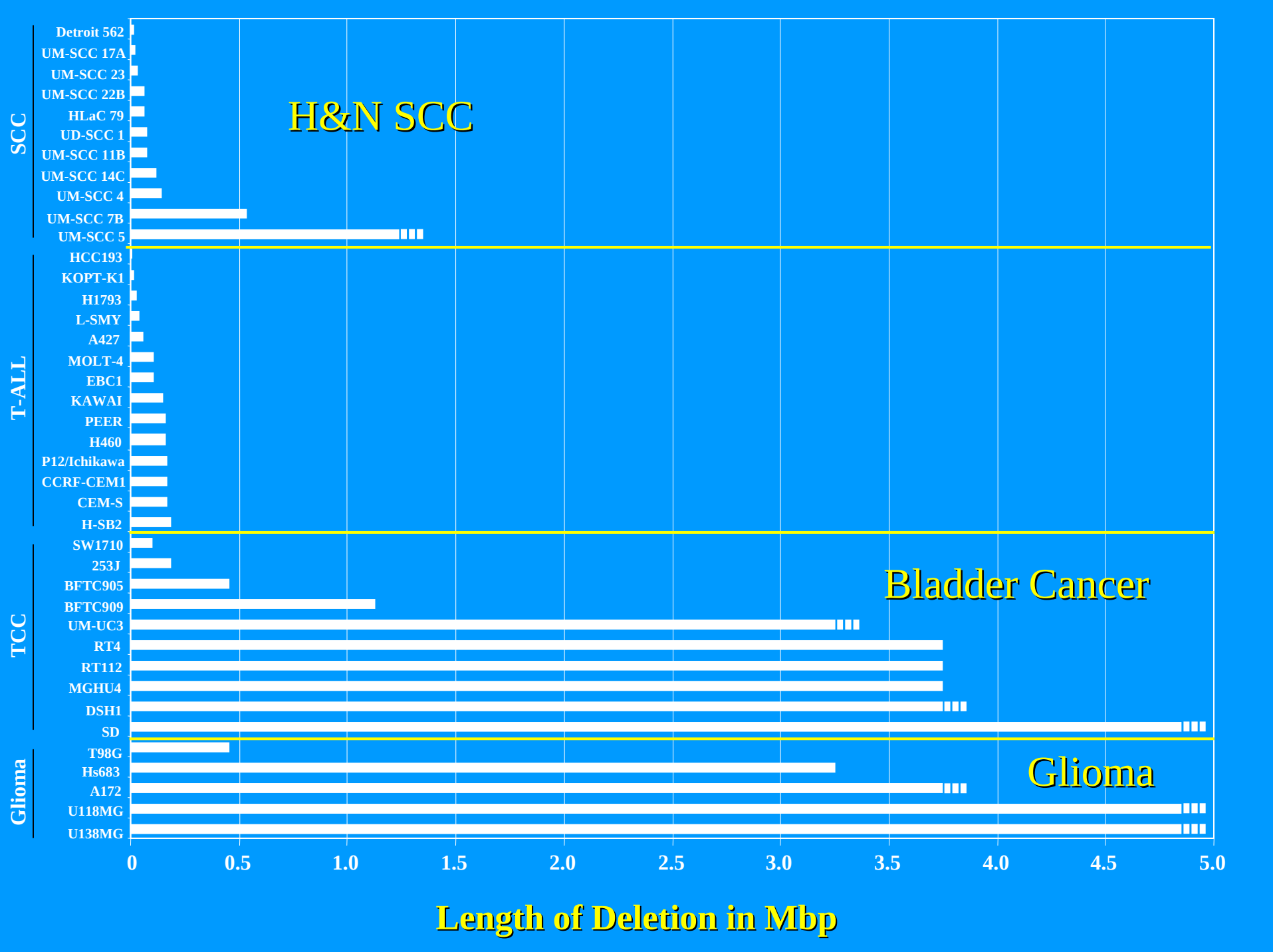
Summary II:
Why bladder cancer is not easy to predict (in many cases)

- A subtype of bladder cancer comprising many cases of papillary urothelial carcinoma contains a limited number of chromosomal changes and often one specific oncogene activation. It is rarely, but still in some cases progressive.
- Multiple chromosomal changes are indicative of more invasive subtypes; chromosomal instability generally increases with progression. However, the relationship is not simple.
- Specific regulatory systems (the RB1 and TP53 networks) are compromised in all invasive bladder cancers. However, the extent of inactivation may differ and different genetic and epigenetic mechanisms can be involved. Prediction by a single alteration is therefore not robust.

Vielen Dank für Ihr Interesse!

Literaturhinweis zu den molekularbiologischen Grundlagen:

W.A. Schulz: Molecular Biology of Human Cancers, Springer 2005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H&N SCC
T-ALL
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MOLT-4
EBC1
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PEER
H460
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CCRF-CEM1
CEM-S
H-SB2
TCC
SW1710
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BFTC909
UM-UC3
RT4
RT112
MGHU4
DSH1
SD
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Glioma
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A172
U118MG
U138MG
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2.5
3.0
3.5
4.0
4.5
5.0
Length of Deletion in Mbp