Cytogenetic alterations in prostate carcinomas

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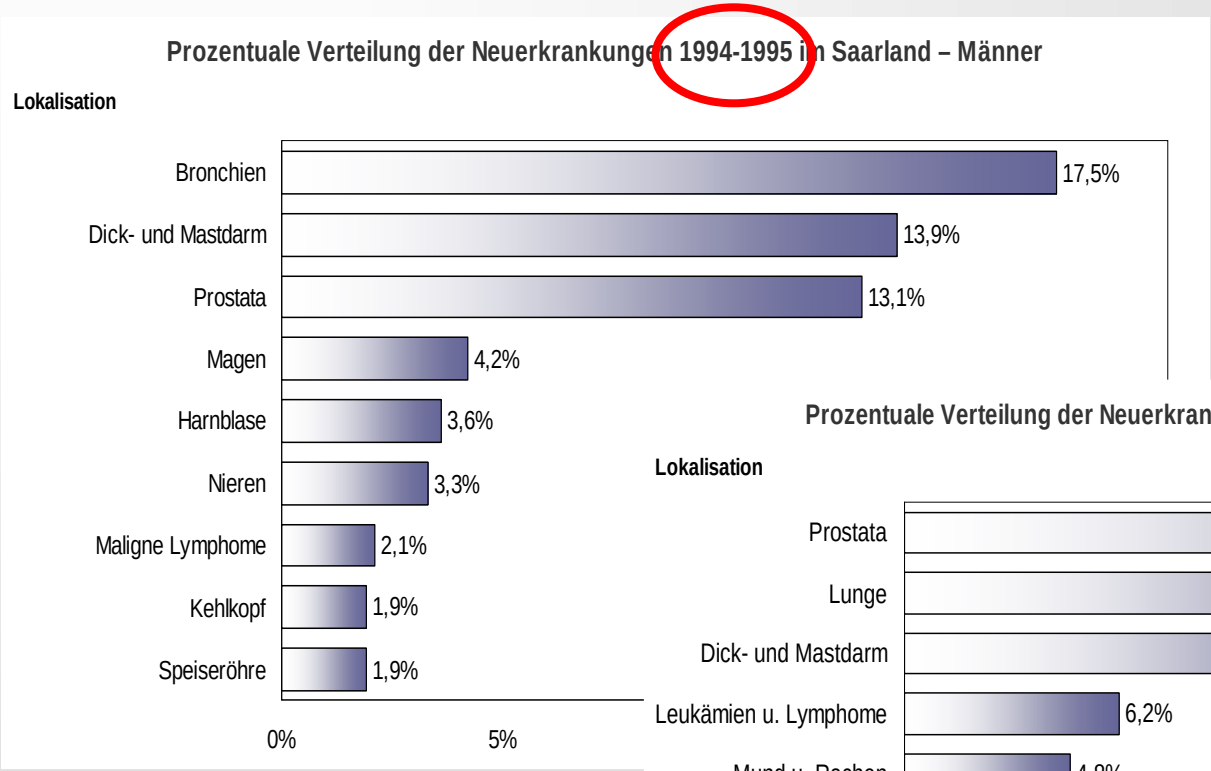
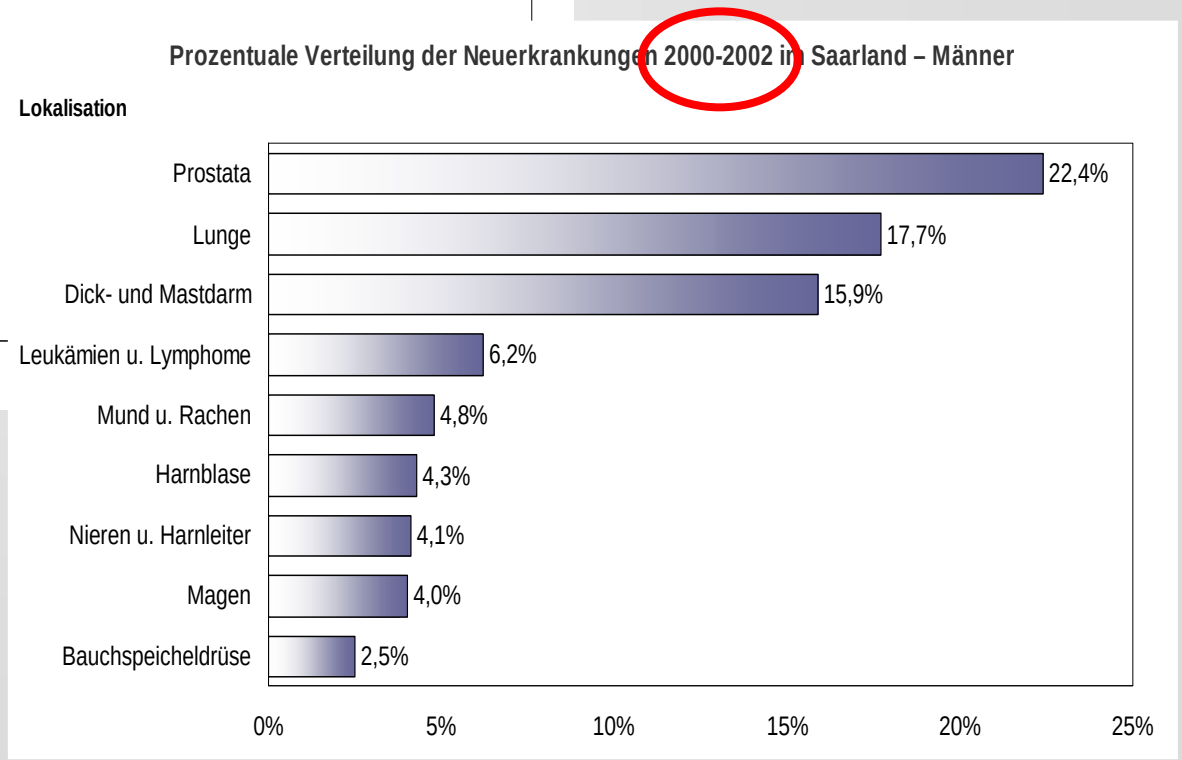
Prostate cancer: epidemiology

www.krebsregister-saarland.de





Lifetime risk ...

... of being diagnosed with prostate cancer

17.8%

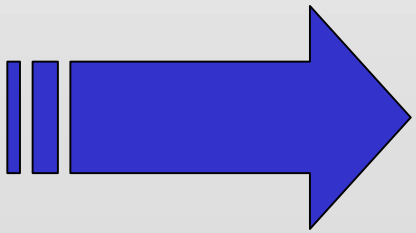
... of dying from prostate cancer

3.0%

SEER Cancer Statistics Review 1975-2001

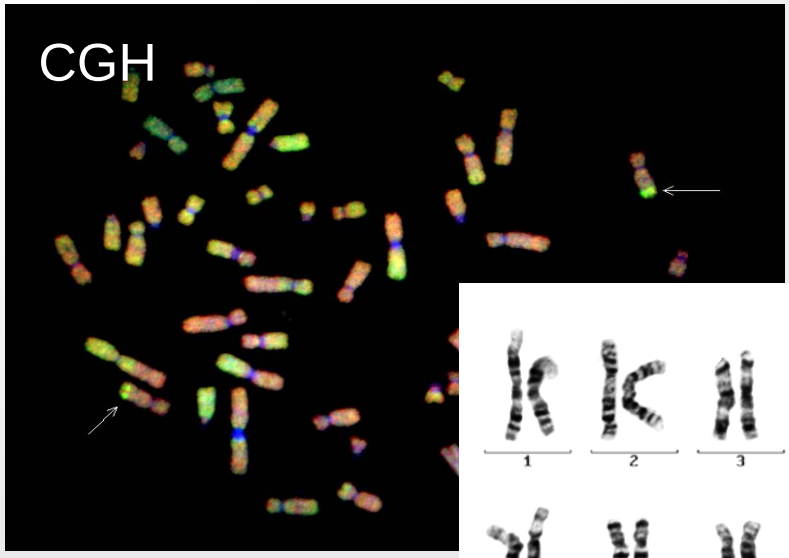
...

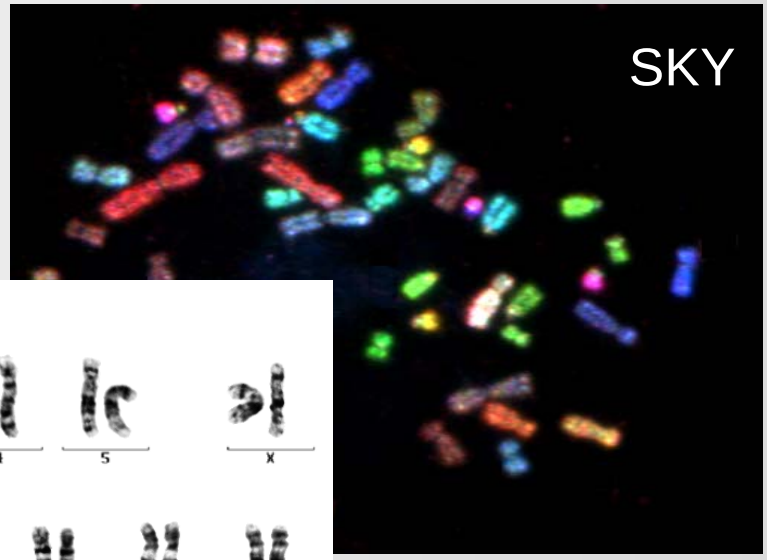
reliable prognostic markers are needed for individualized prostate cancer management

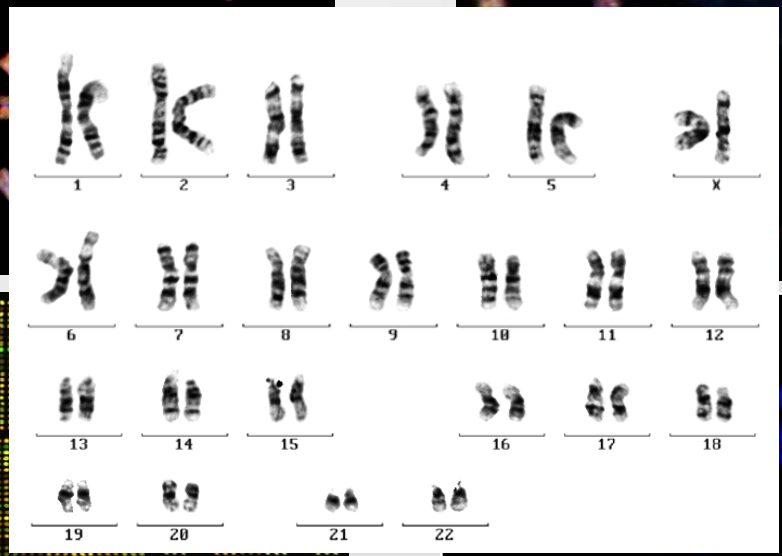


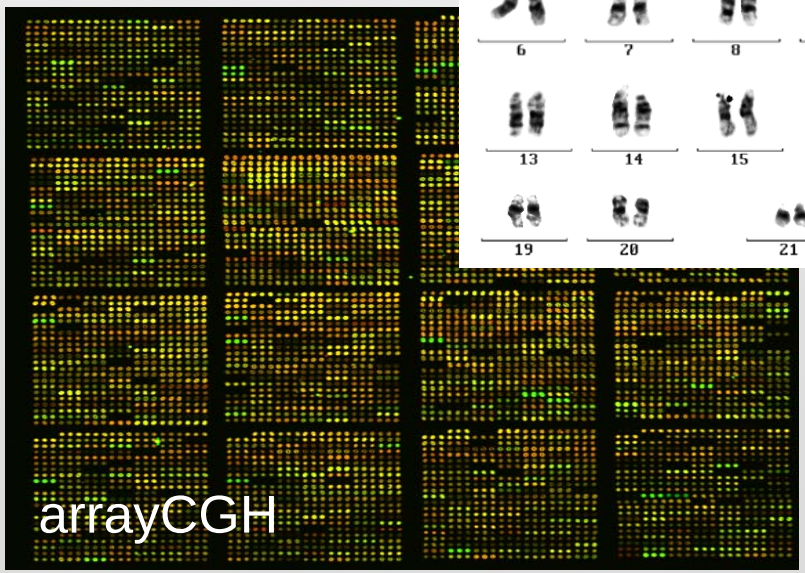
genetic risk assessment

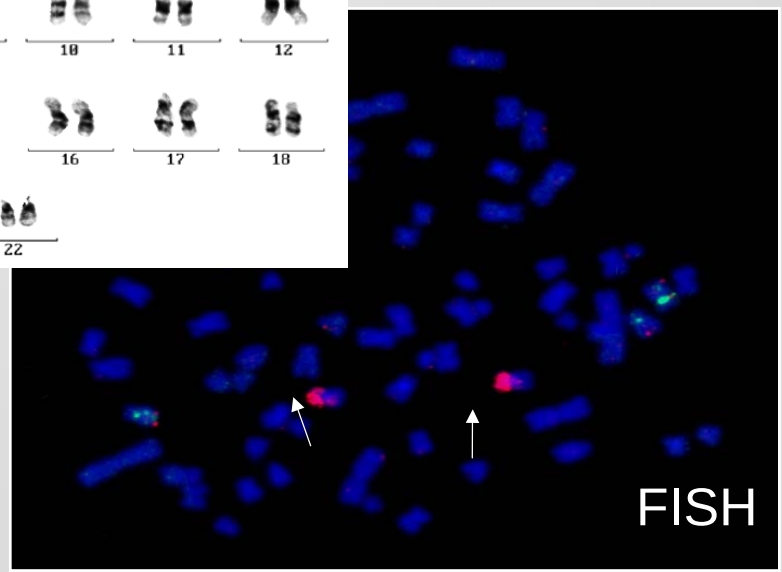
Cytogenetic techniques



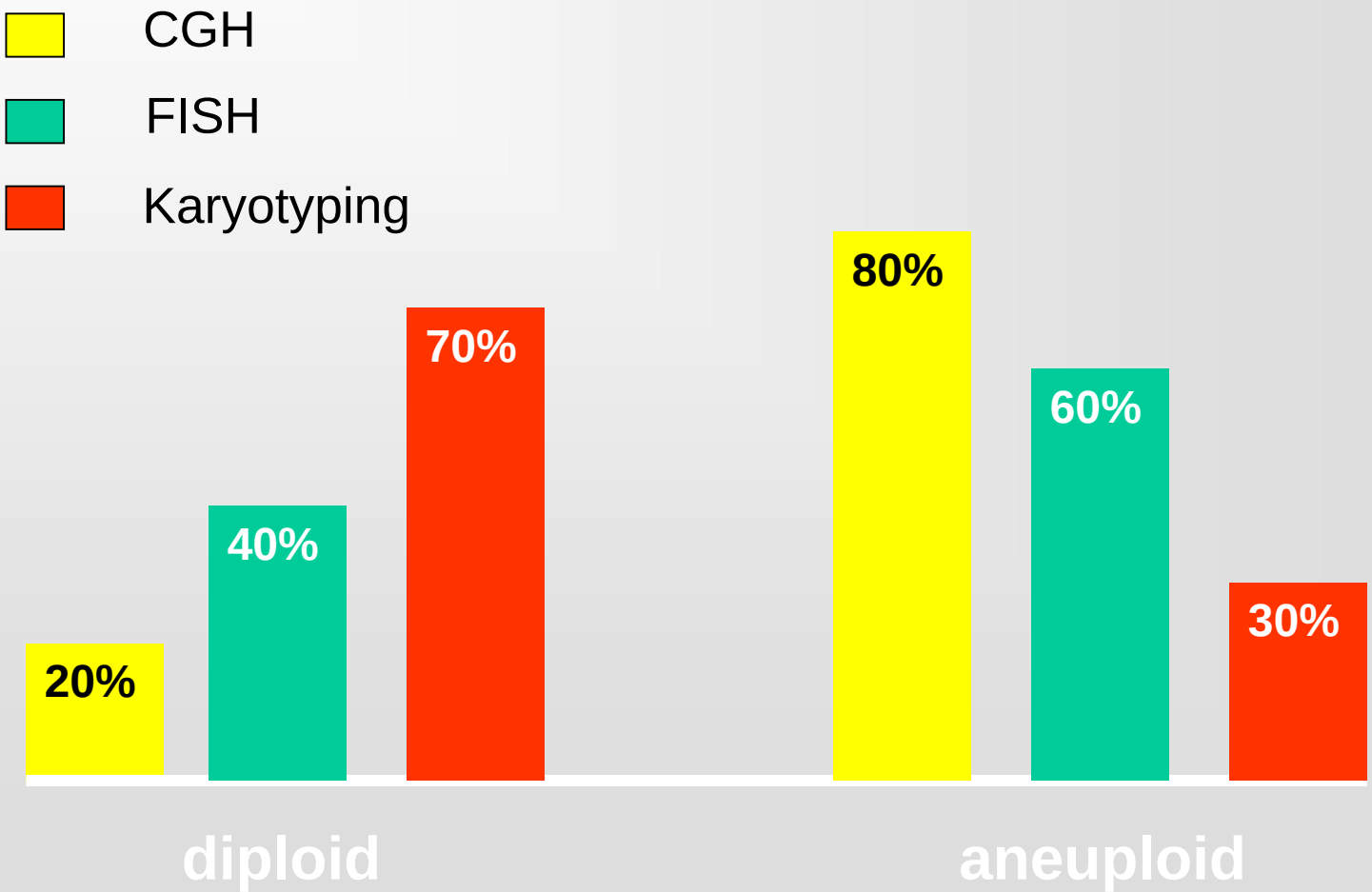








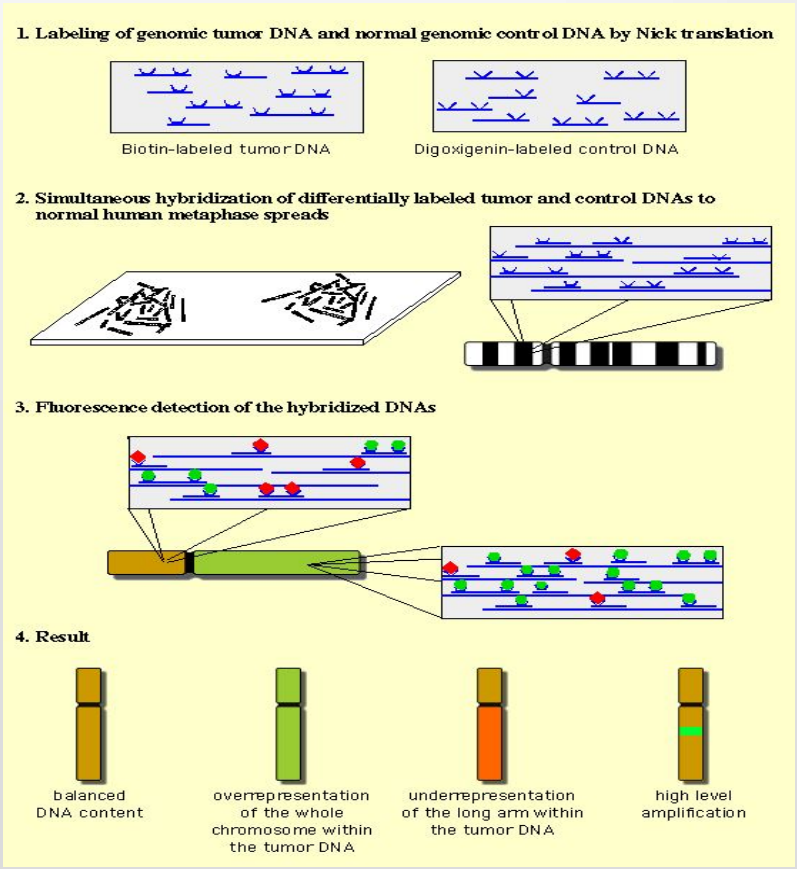
“Cytogenetic alterations“ depend on methodology

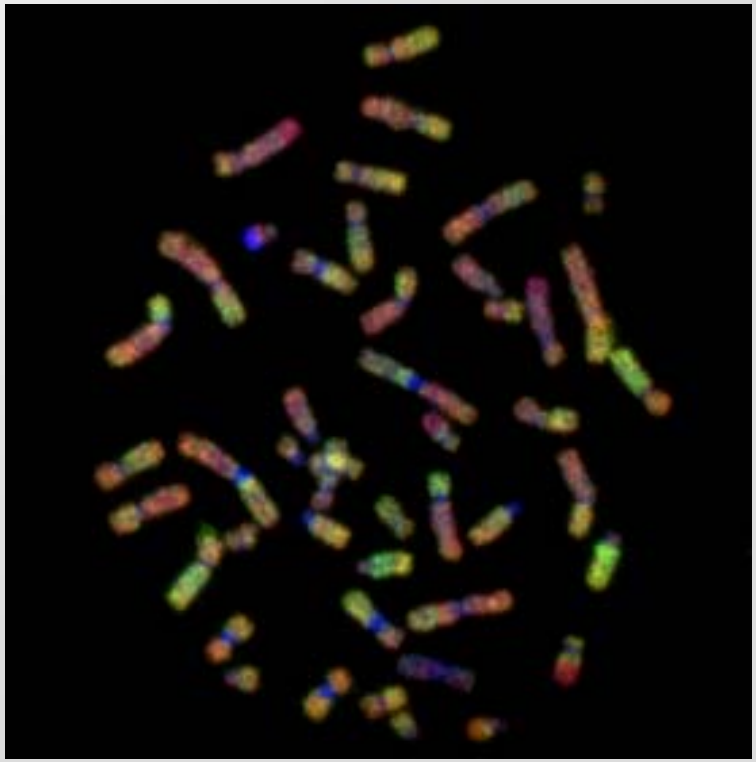


Sattler *et al*., Prostate 39, 1999

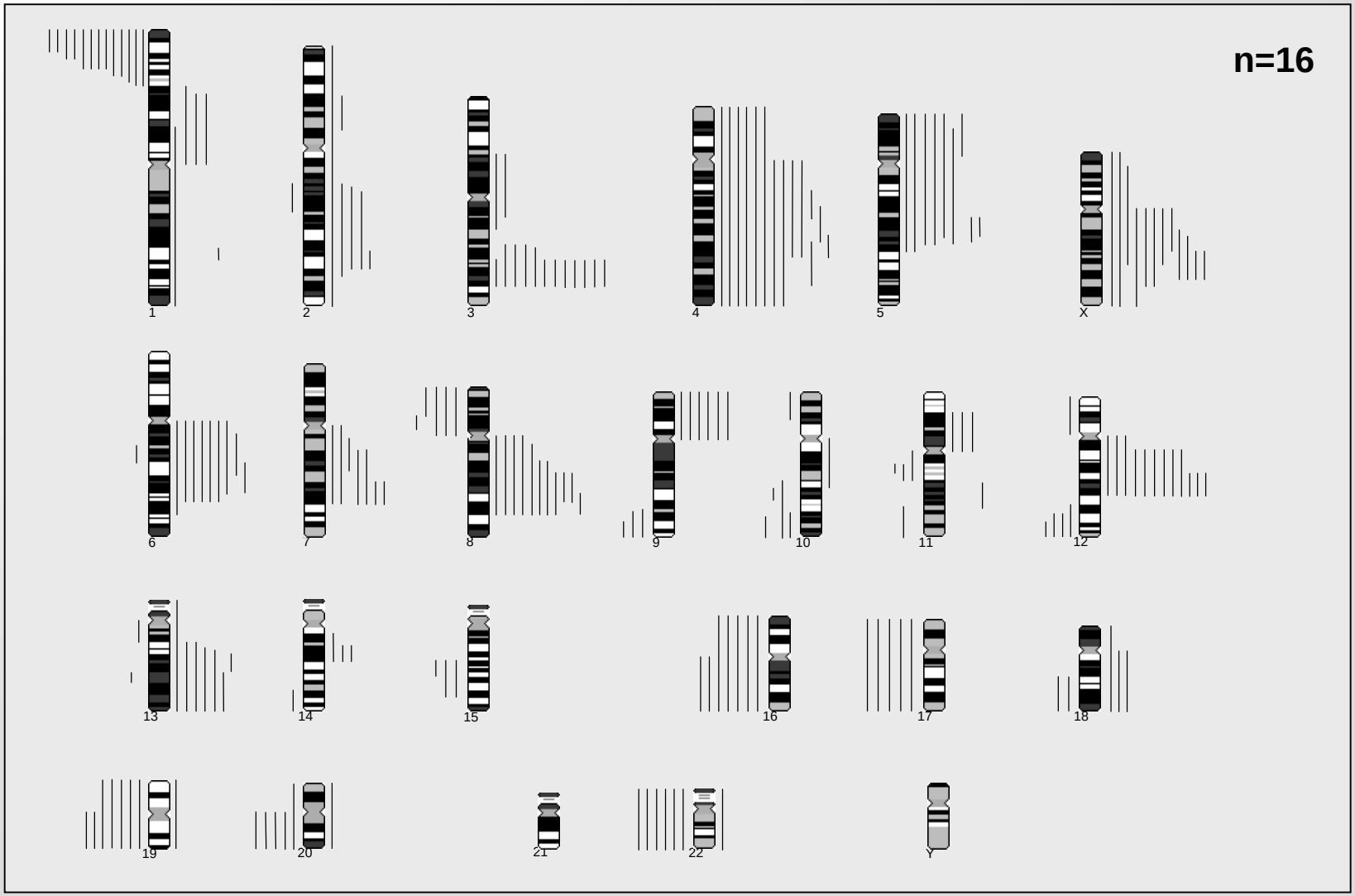
Comparative Genomic Hybridization (CGH)

Method for detecting and assigning genomic imbalances (resolution ~ 5Mb)





CGH: prostate cancer



Sattler *et al*., Prostate 39, 1999

pT2b, Gleason 7

#70

losses: 3

gains: 0

pT2b, Gleason 7

#133

losses: 1

gains: 11

pT3b, Gleason 7

#47

losses: 3

gains: 2

pT3b, Gleason 7

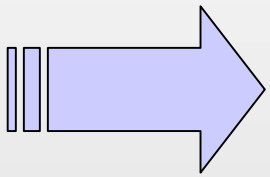
#169

losses: 4

gains: 11

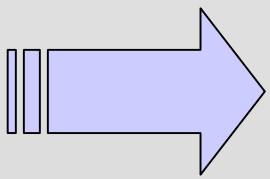
Major directions

Analysis of the complexity of genomic changes



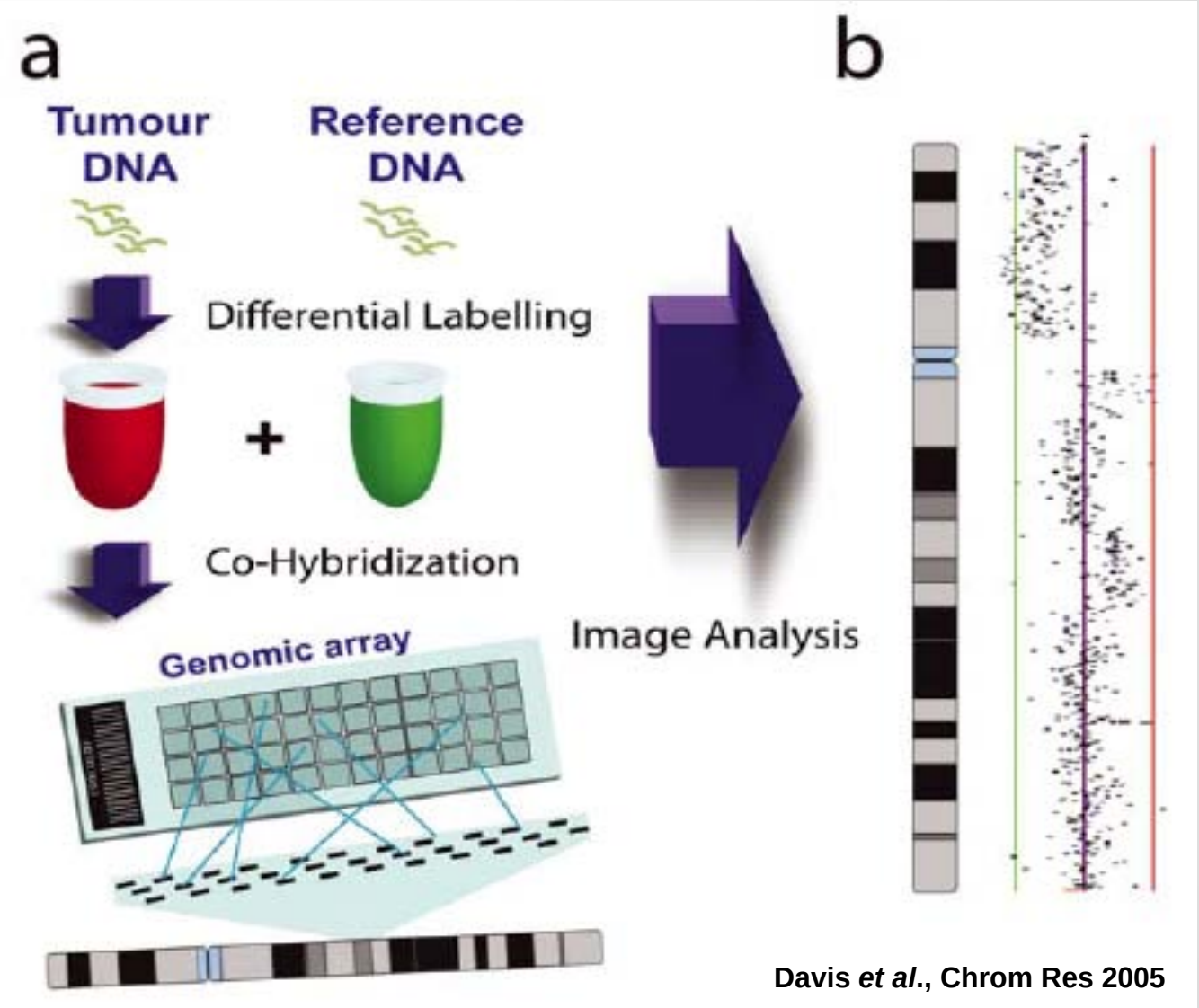
Genetic progression scores

Analysis of single locus-changes



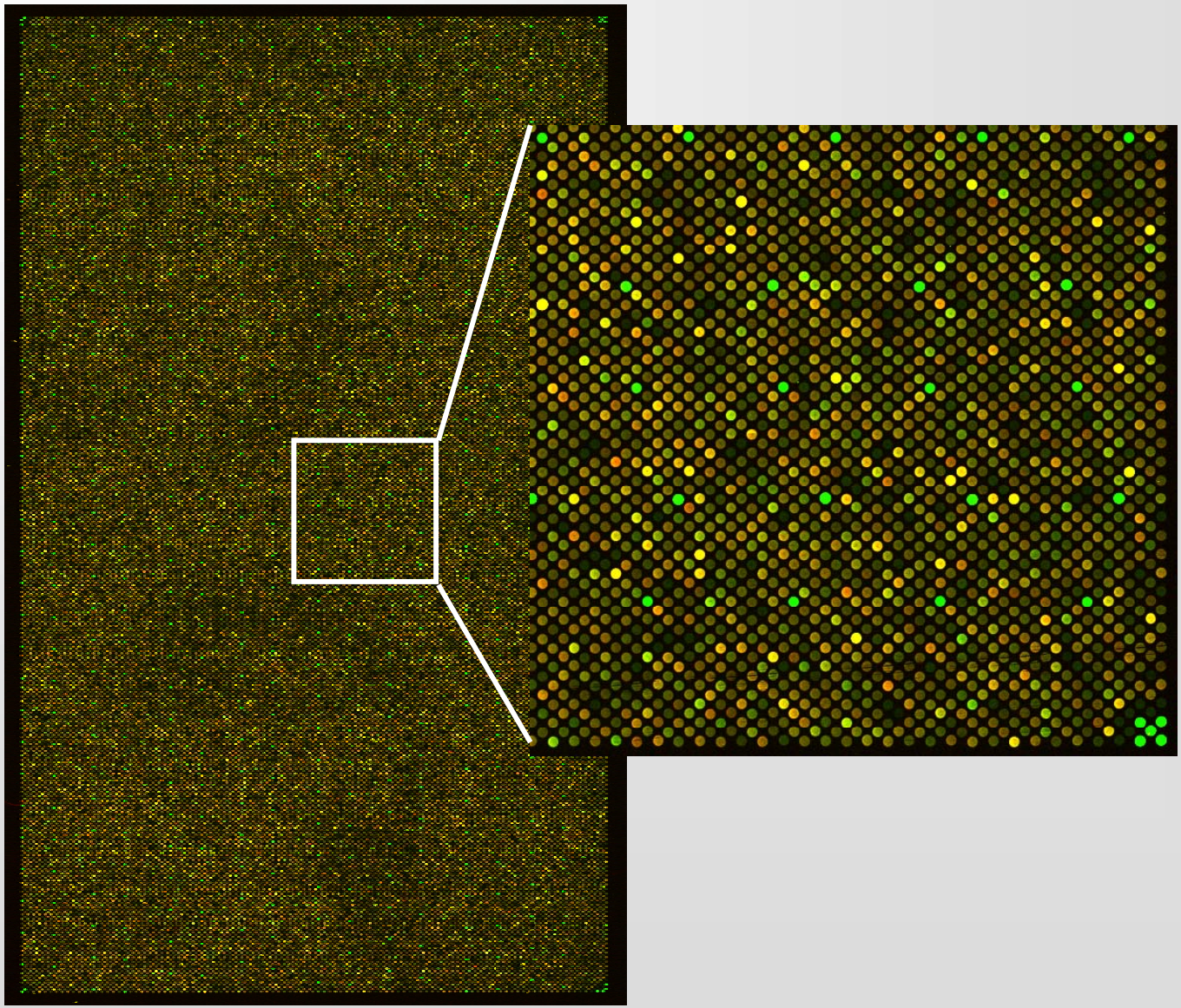
Search for novel target genes

Microarray-based CGH

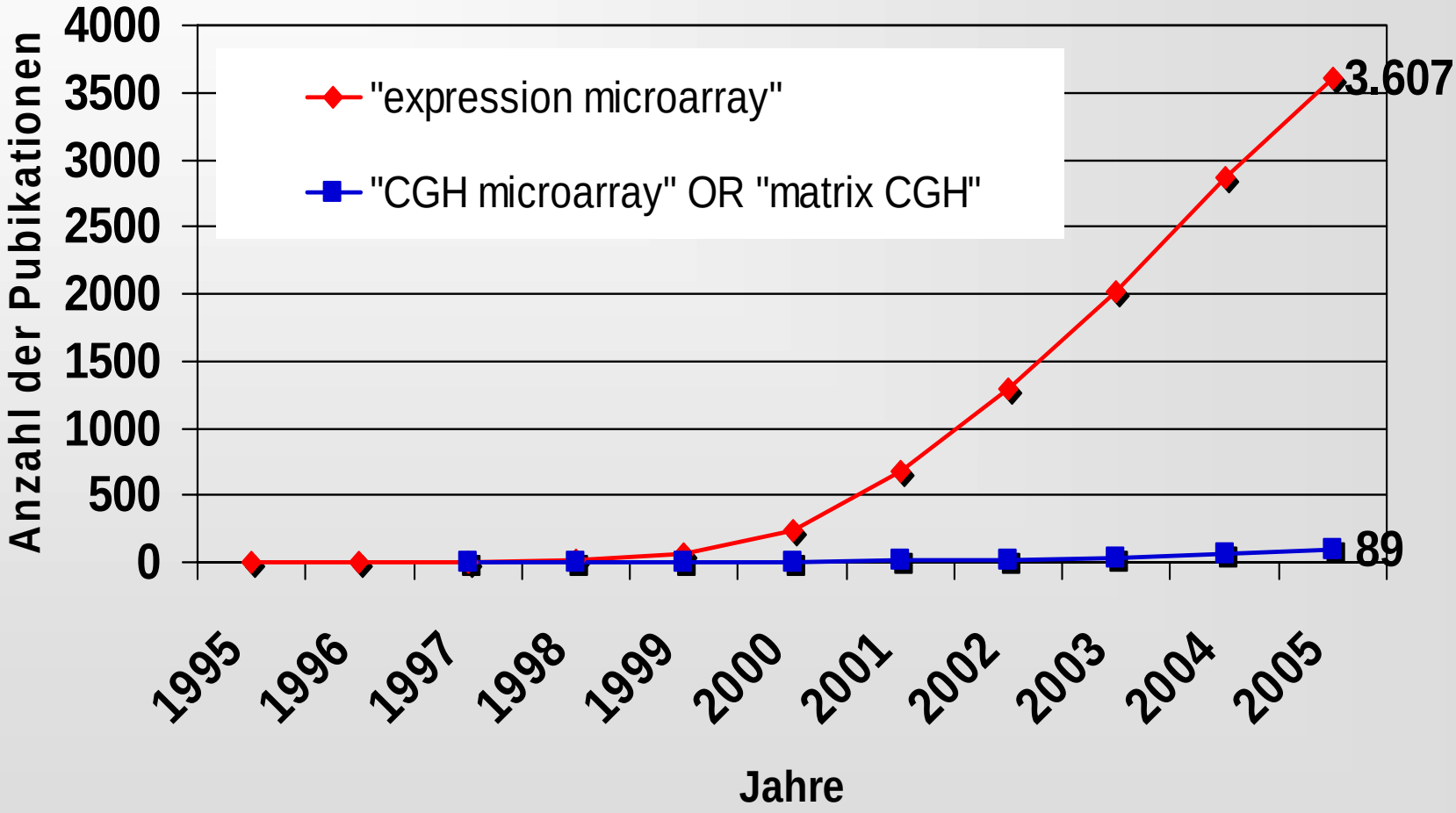


Davis *et al*., Chrom Res 2005

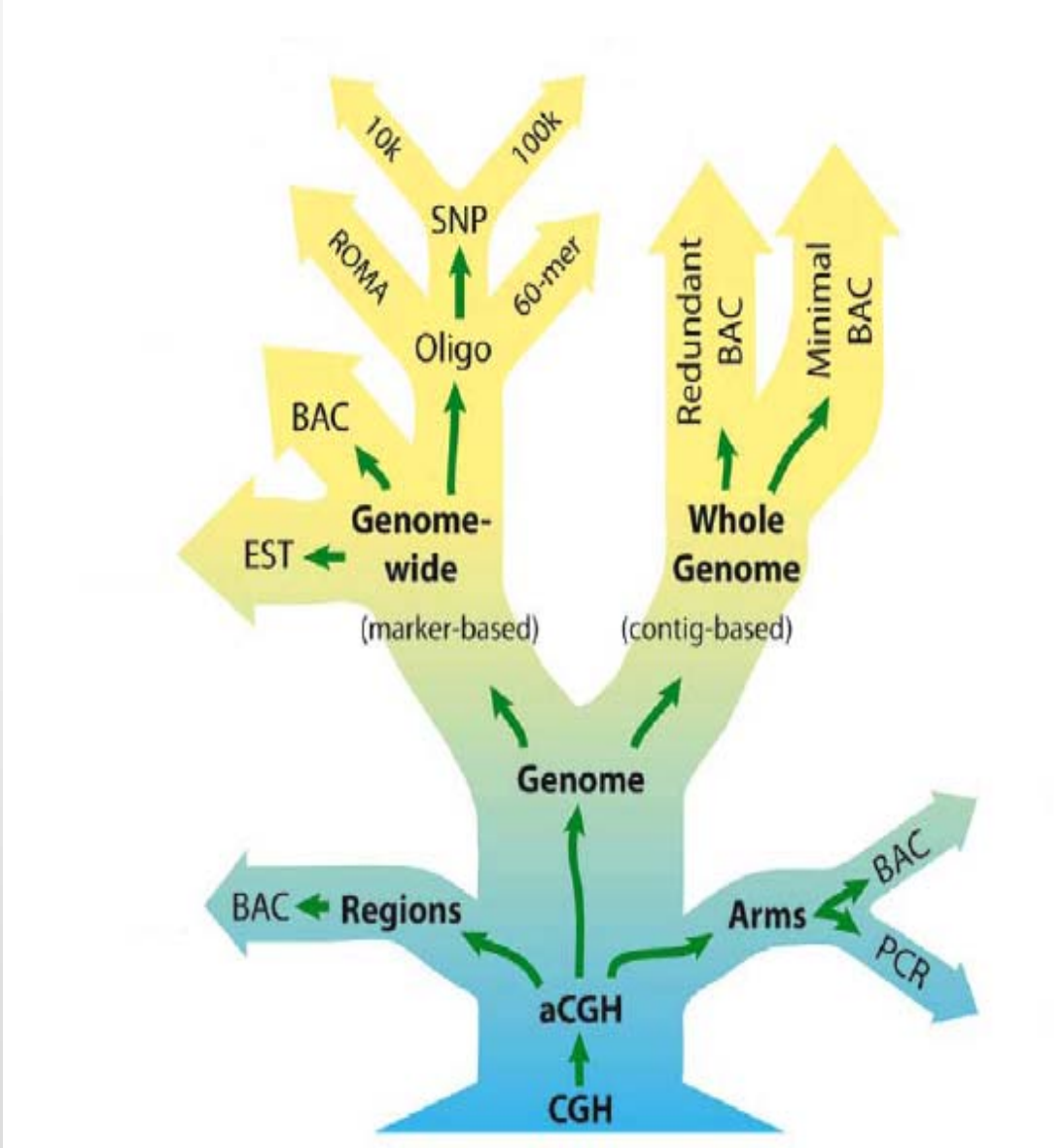
Microarray-based CGH



PubMed search



Evolutionary tree of array platforms

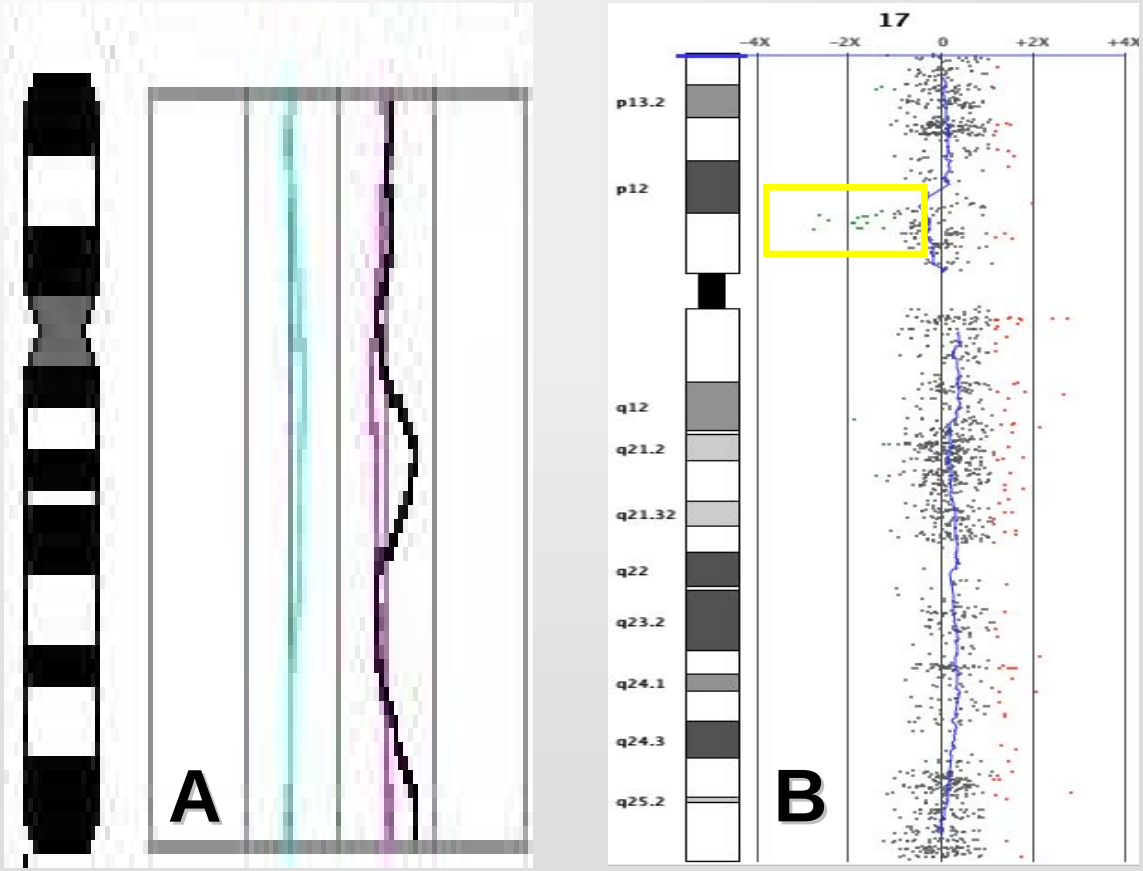


Davis *et al*., Chrom Res 2005

CGH *vs.* arrayCGH

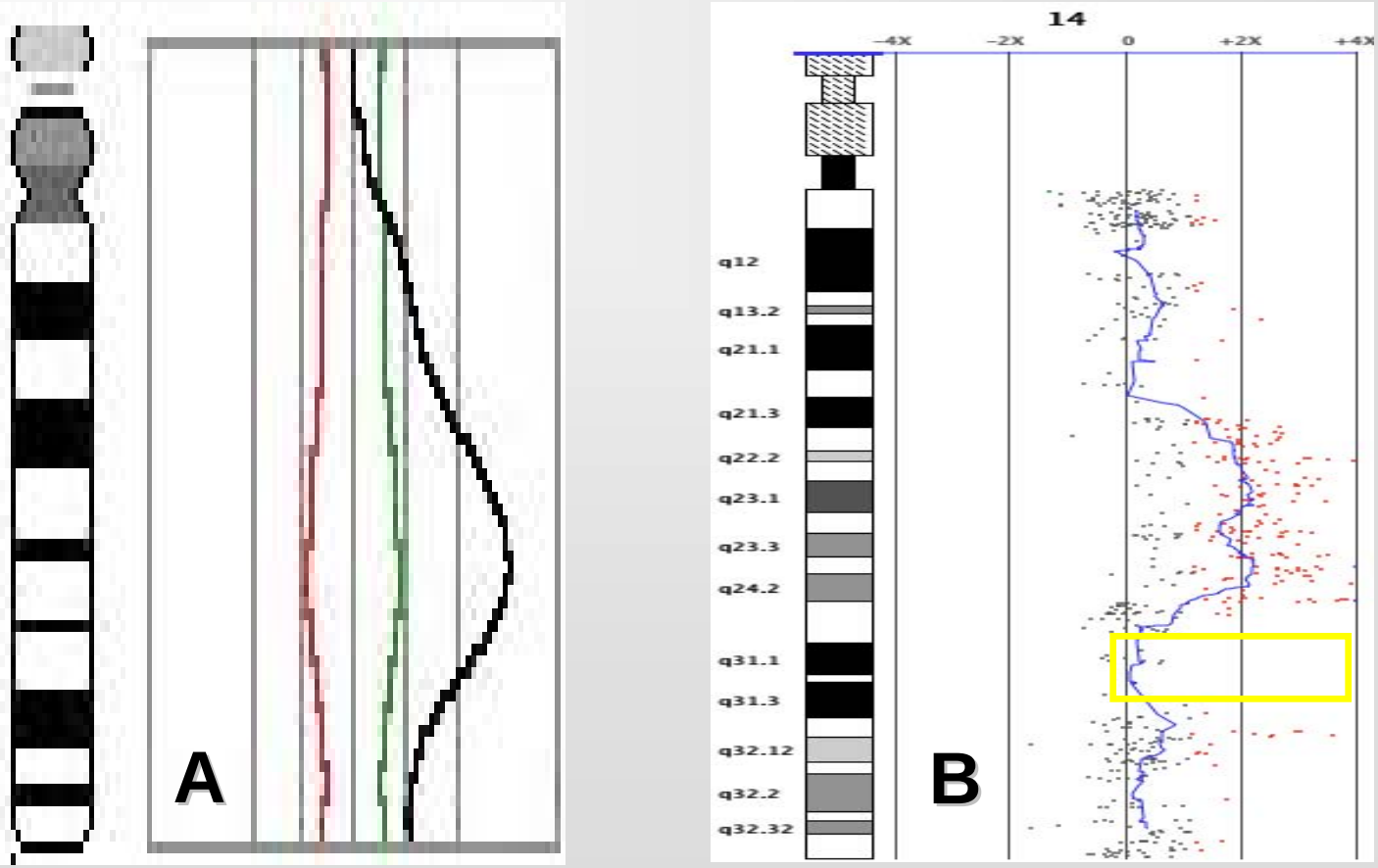
Cell line	Chromosomal aberrations		
	no. found with both techniques	found **only** in arrayCGH	found **only** in CGH
PC3	14	-1q, -3q, -5q, -12p, +12p, -17q	+7, +11q, +12q, -X
PC3-N	8	+1q, -1q, -9p, -13q, -17q	+2q, +7p, +9q, +14, +20q, -X
PC3-125L	8	-1q, -5q, +Xp	-4q, +7, +11q, +12q, -19q, +17q, +20
LNCaP	4	-1p, -2, +3p, -11q, -13q, -19q	-X
LNCaP-CN4-2	9	-1p, -10q, -11q, -19q	+1q, +5, -2q, +9p, +3q, -X
DU145	18	-9p, -11p, +12p, -17p	+2p, +7p, +10q, +11q, +12q, +15, +16q, -X, -Y
DU145 MN1	24	-1p, -9p, -11p, +12p, -12p, -14q, -17p, -19q	+1p, +2p, +5q, +10q, +12q, +15, +17, +19q, +20q, +21, -X
CRW22	6	-2p	+8q, +10q, +12, -13
CRW22 RV1	3	-2, -4q, -5q, -10p, +12, -13	

Detection of small deletions



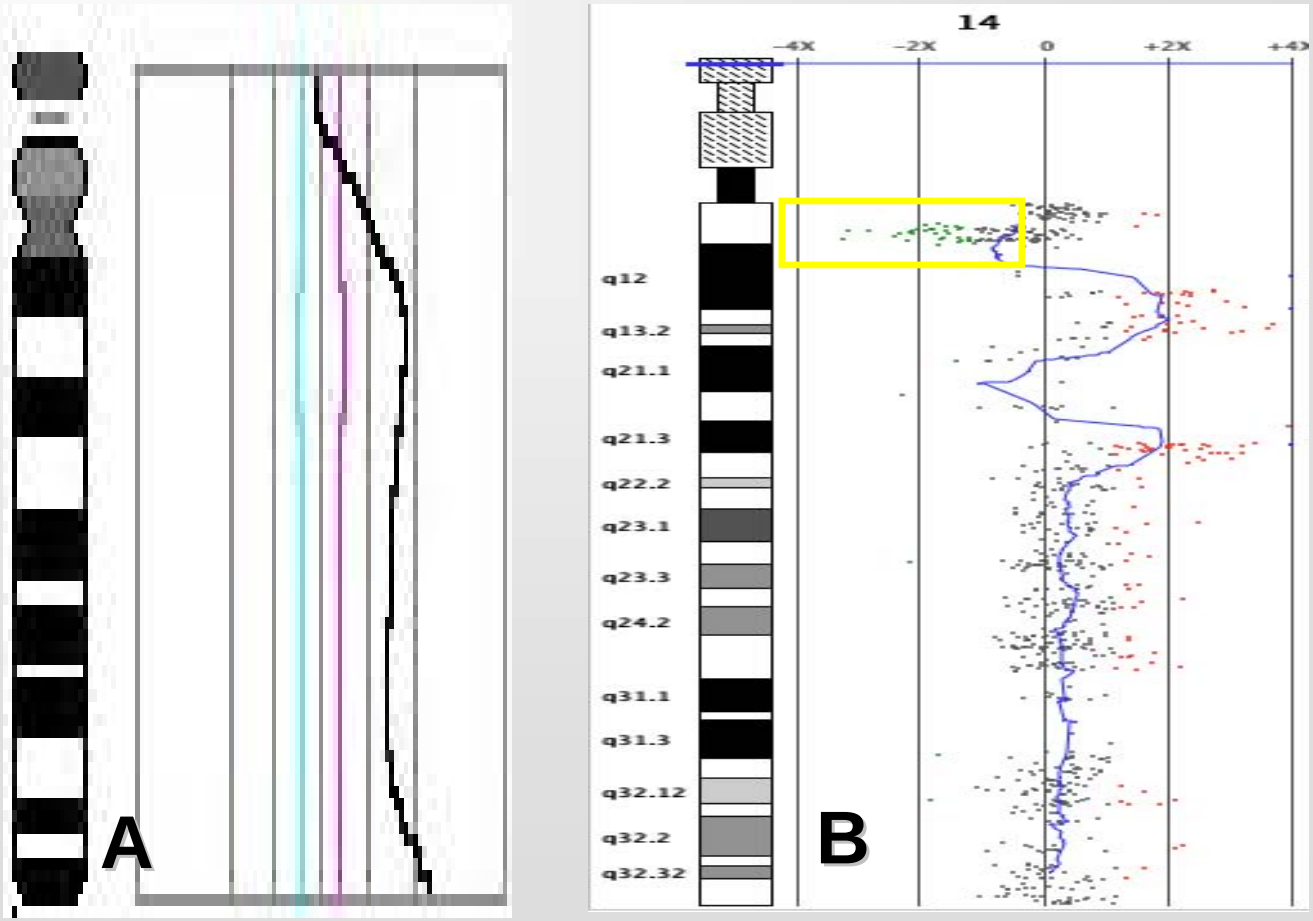
Chromosom 17, LNCaP-CN4-2

High-resolution mapping of amplifications



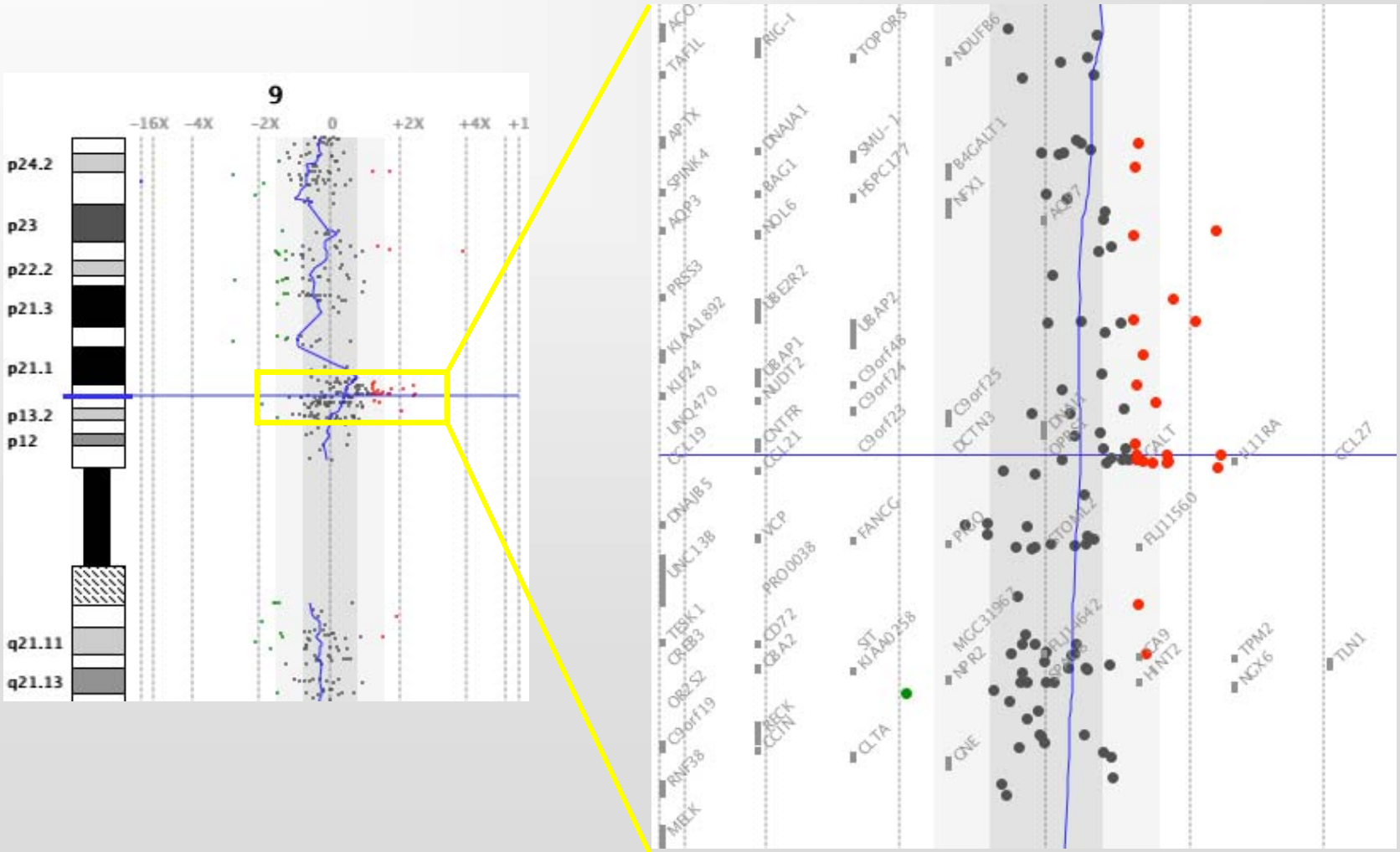
Chromosom 14, PC3

Detection of alterations in pericentromeric regions



Chromosom 14, DU145

Direct identification of amplified genes



Our expectations toward bioinformatics

Processing of the huge amount of raw data resulting in …

- ✓ tumor subclassification
- ✓ biological predictors for the clinical course
- ✓ identification of pathogenetically relevant genes