

Early microscope

Cytology i moderne patologi

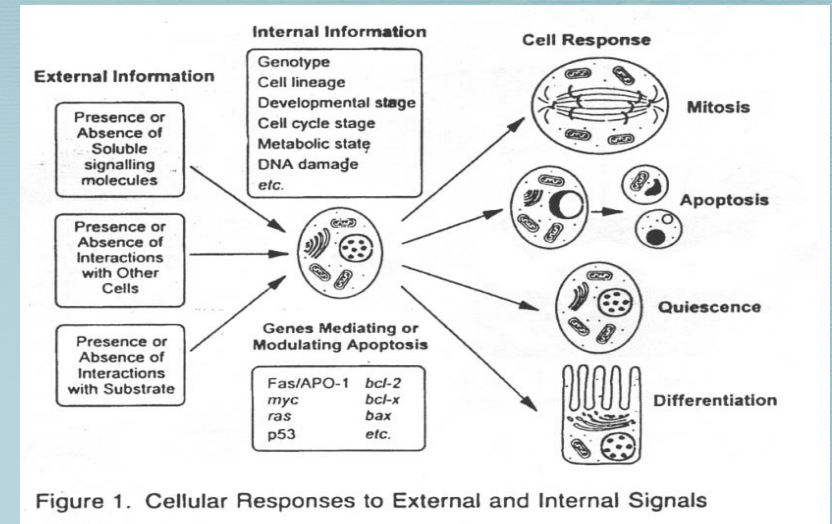
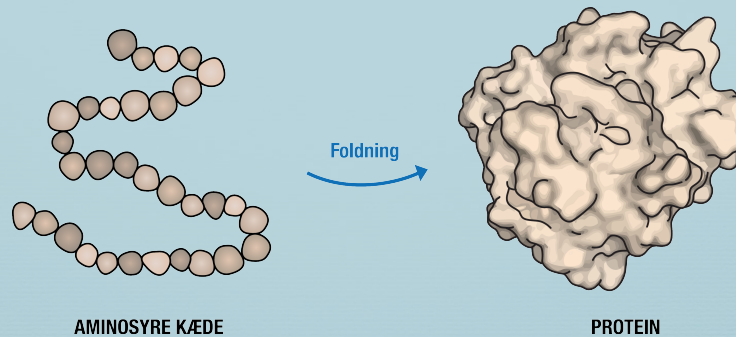
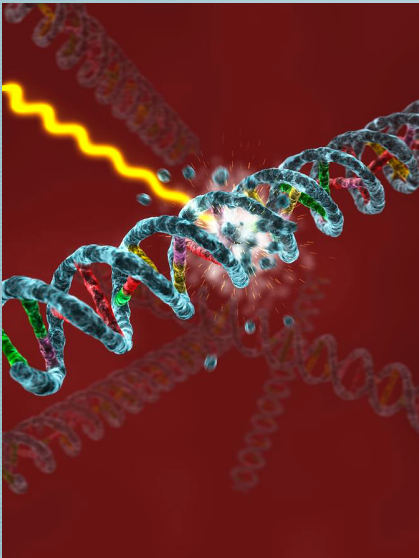
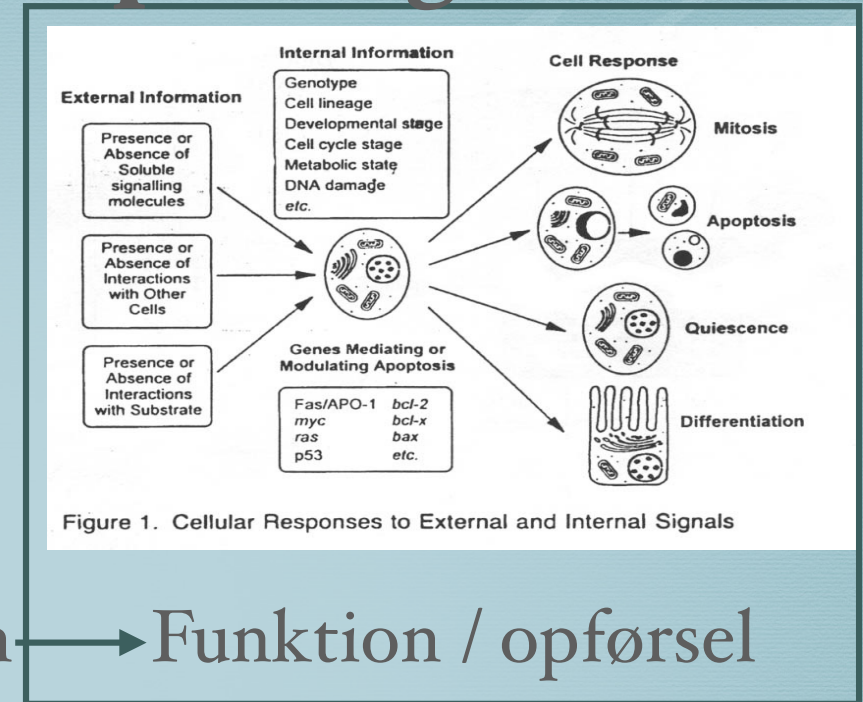


Figure 1. Cellular Responses to External and Internal Signals

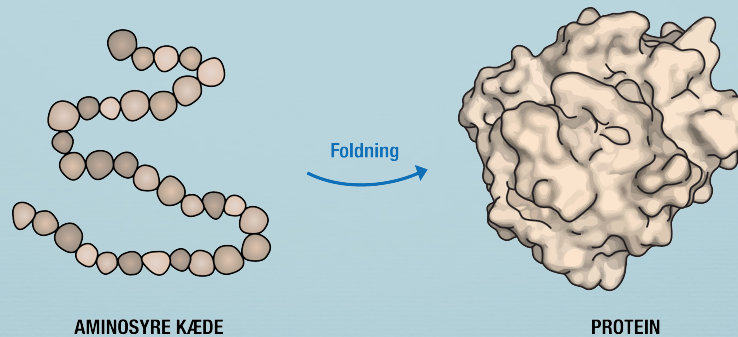
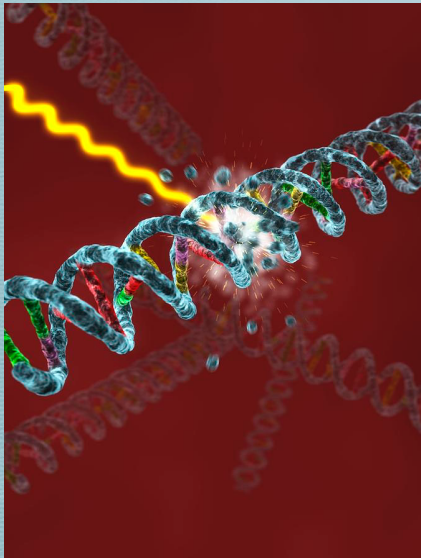
DNA → RNA → Protein → Funktion / opførsel



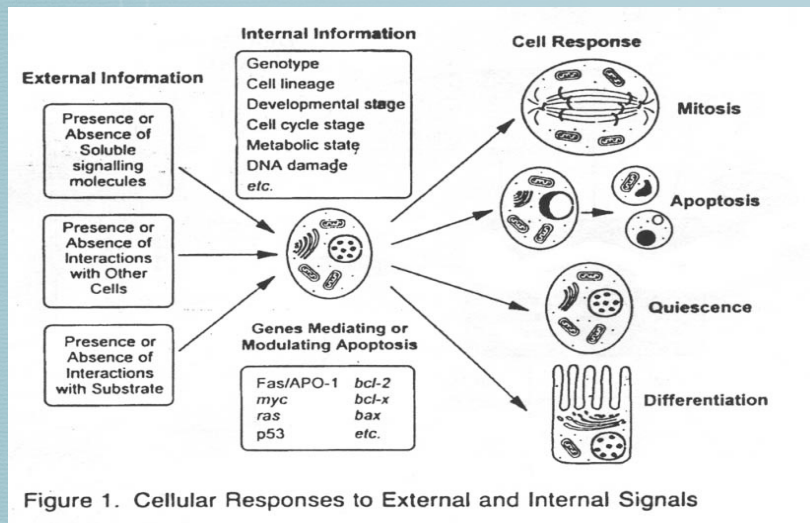
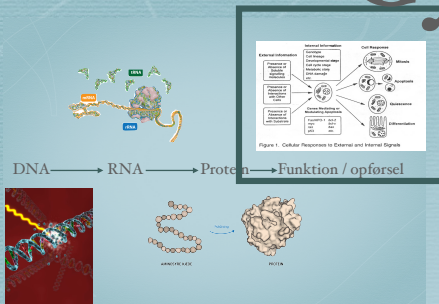
Cytology i moderne patologi



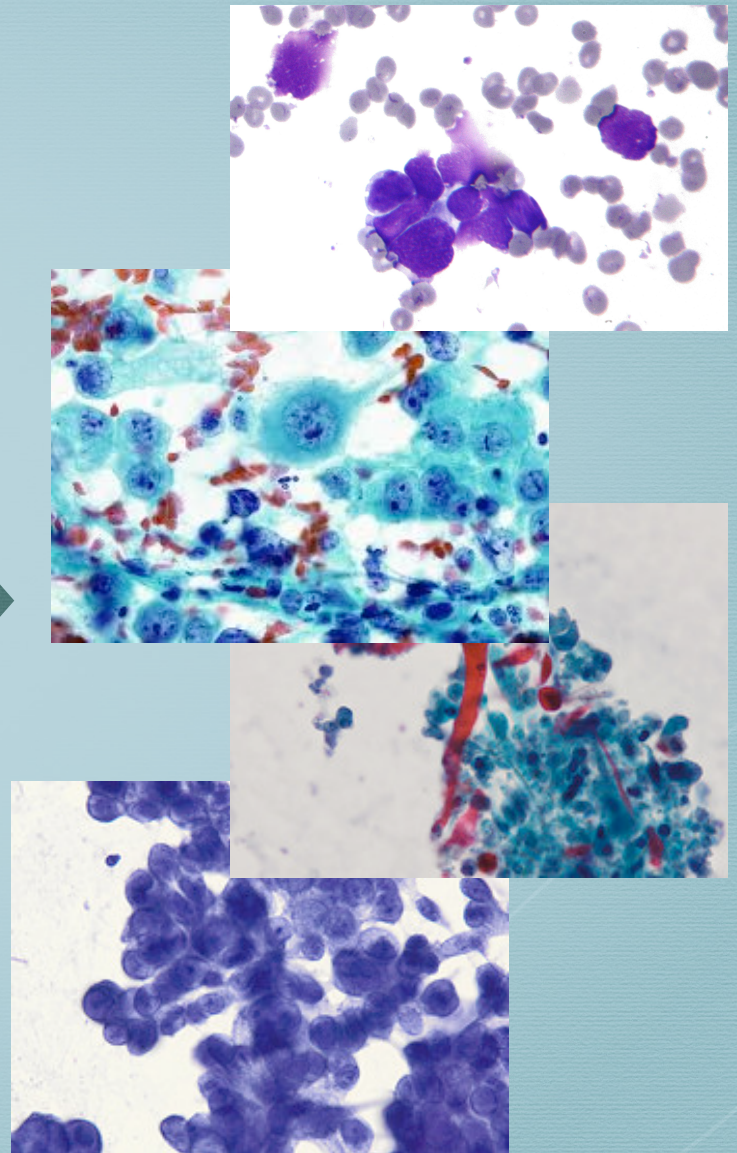
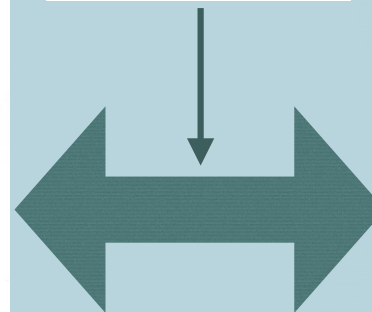
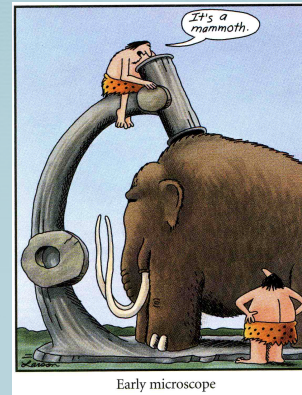
DNA → RNA → Protein → Funktion / opførsel



Cytology i moderne patologi



Funktion / opførsel



morfologi

Cytology i moderne patologi

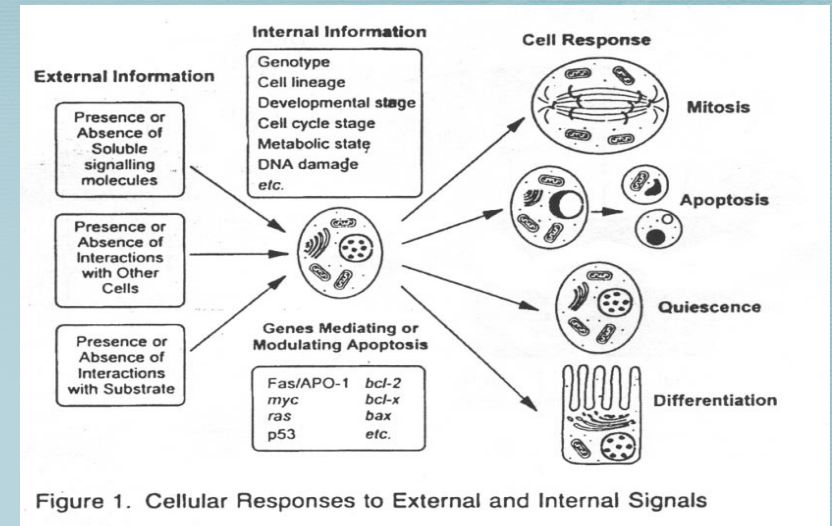
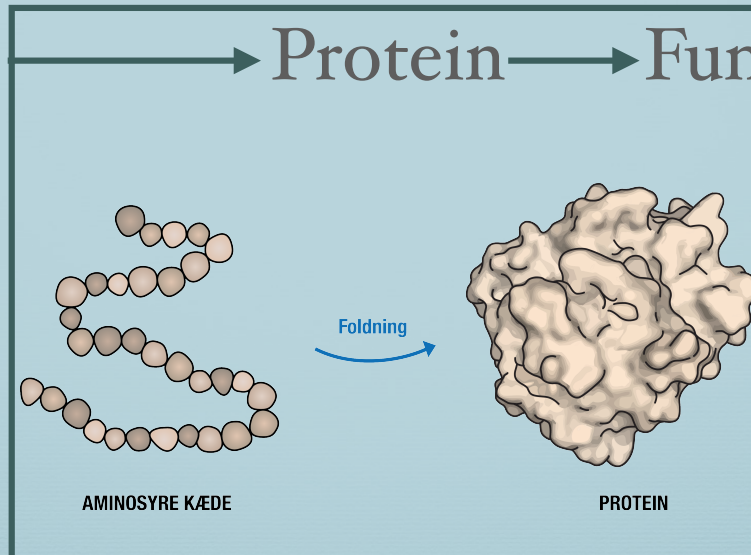
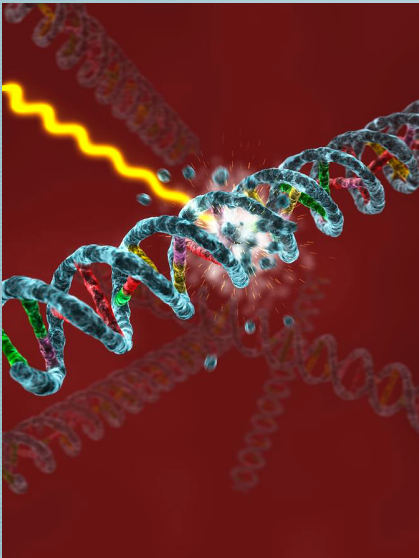
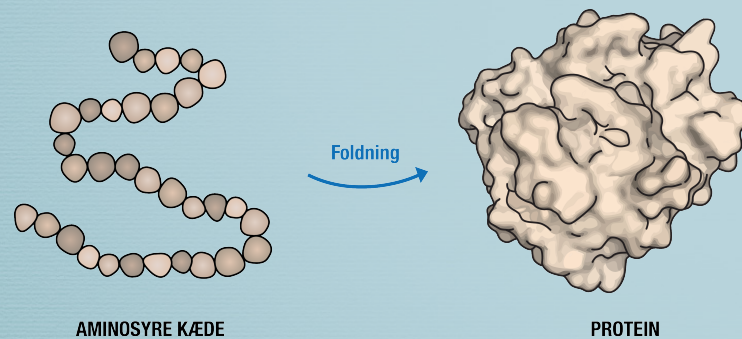
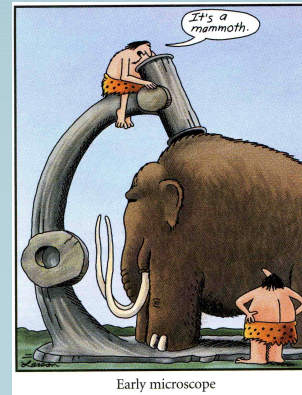
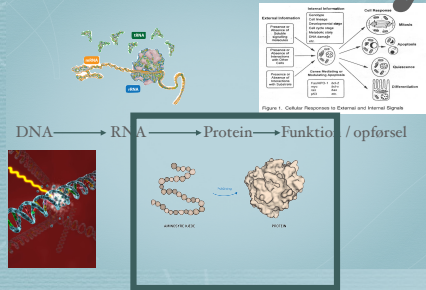


Figure 1. Cellular Responses to External and Internal Signals

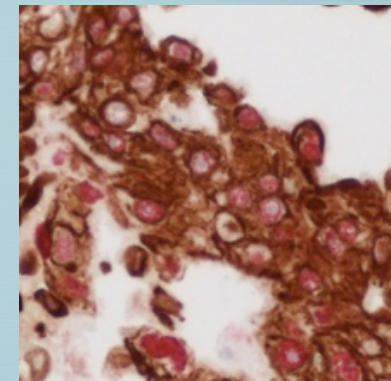
DNA → RNA → Protein → Funktion / opførsel



Cytology i moderne patologi



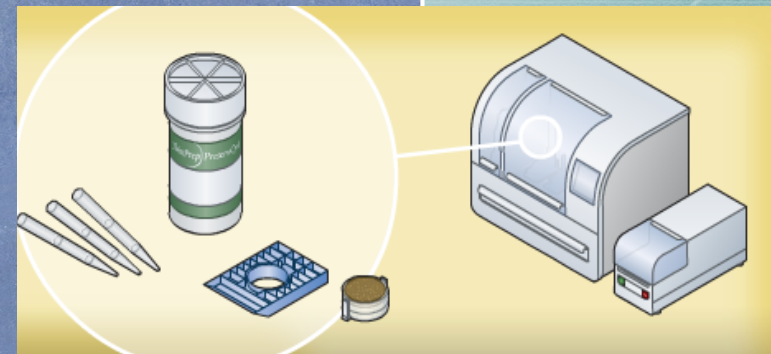
Proteinindhold



Immunocytochemistry
needle biopsy

Cytology i moderne patologi

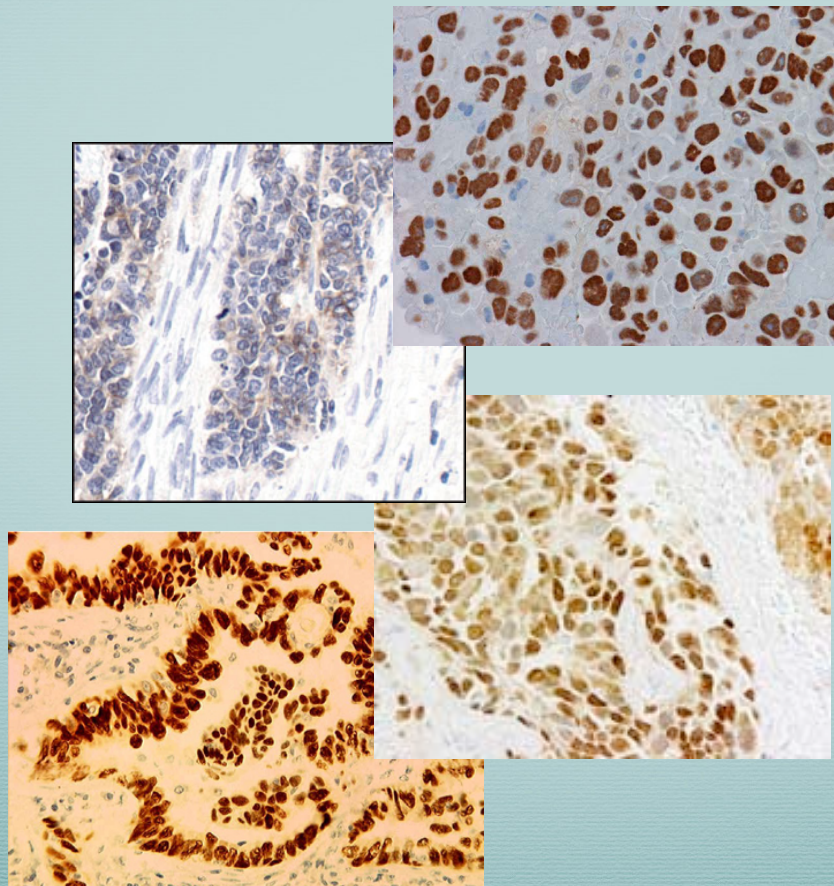
1. Centrifuger materialet 10 min. ved 3000 omdr./min.
2. Hæld supernatanten fra.
3. Tilsæt 3 dråber humant plasma.
4. Opslem, med pipetten, forsigtigt bundfaldet i plasmaen.
5. Tilsæt 2 dråber thrombin. Dannes der ikke et koagel indenfor 1 minut; tilsæt 1 dråbe BT.
6. Tilsæt 4% neutralt bufferet formaldehyd.
7. Åben en gazepose, træk den over reagensglasset.
8. Hæld koaglet i gazeposen.
9. Læg posen i en kapsel med mikroskopi-nummeret.
10. Dryp et par dråber hæmatein på koaglet.
11. Læg kapslen i en bølge med 4% neutralt bufferet formaldehyd.



Cytology i moderne patologi

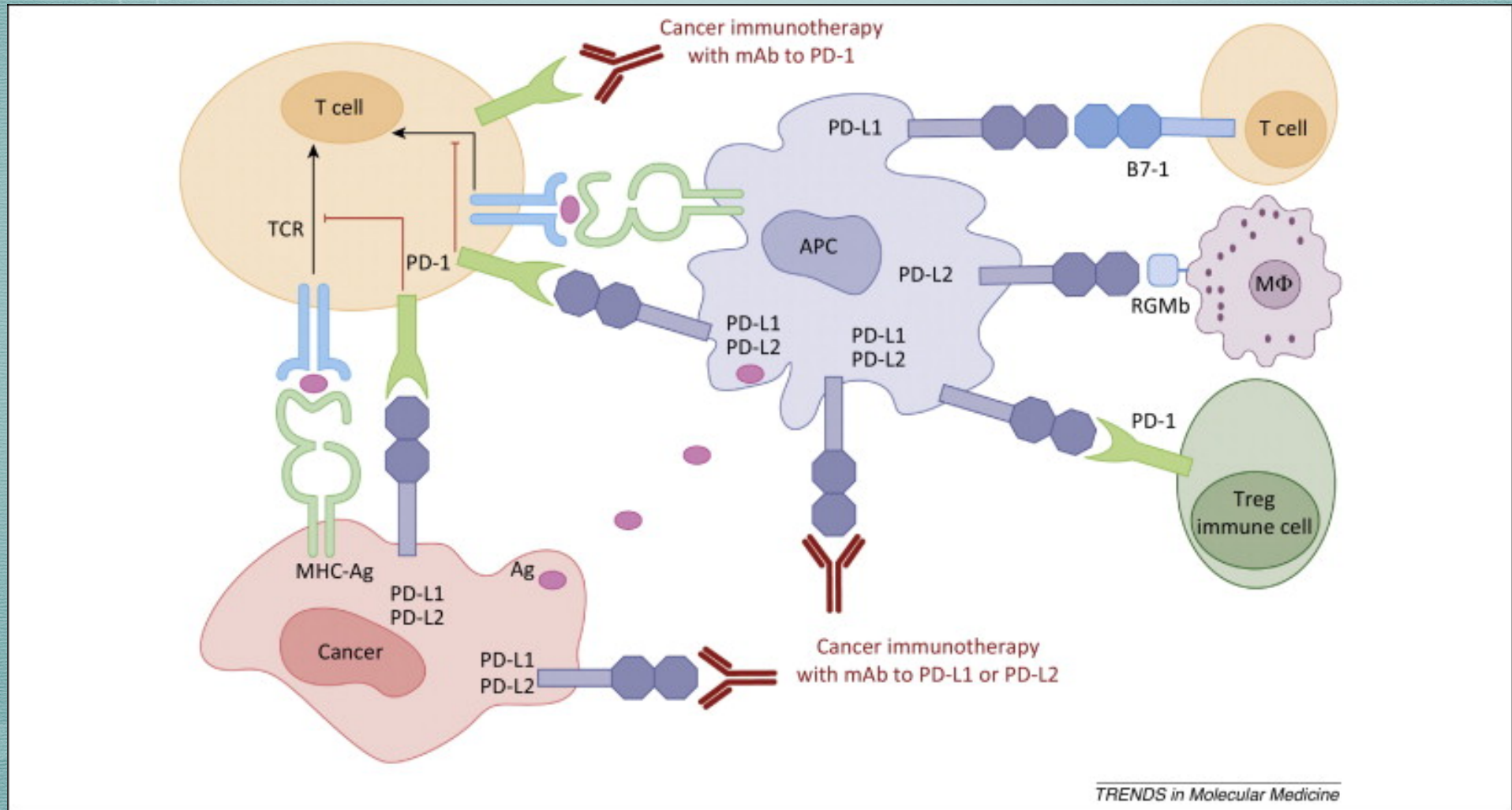
- Mikroskopisk klassifikation, diagnose

Immuncytology



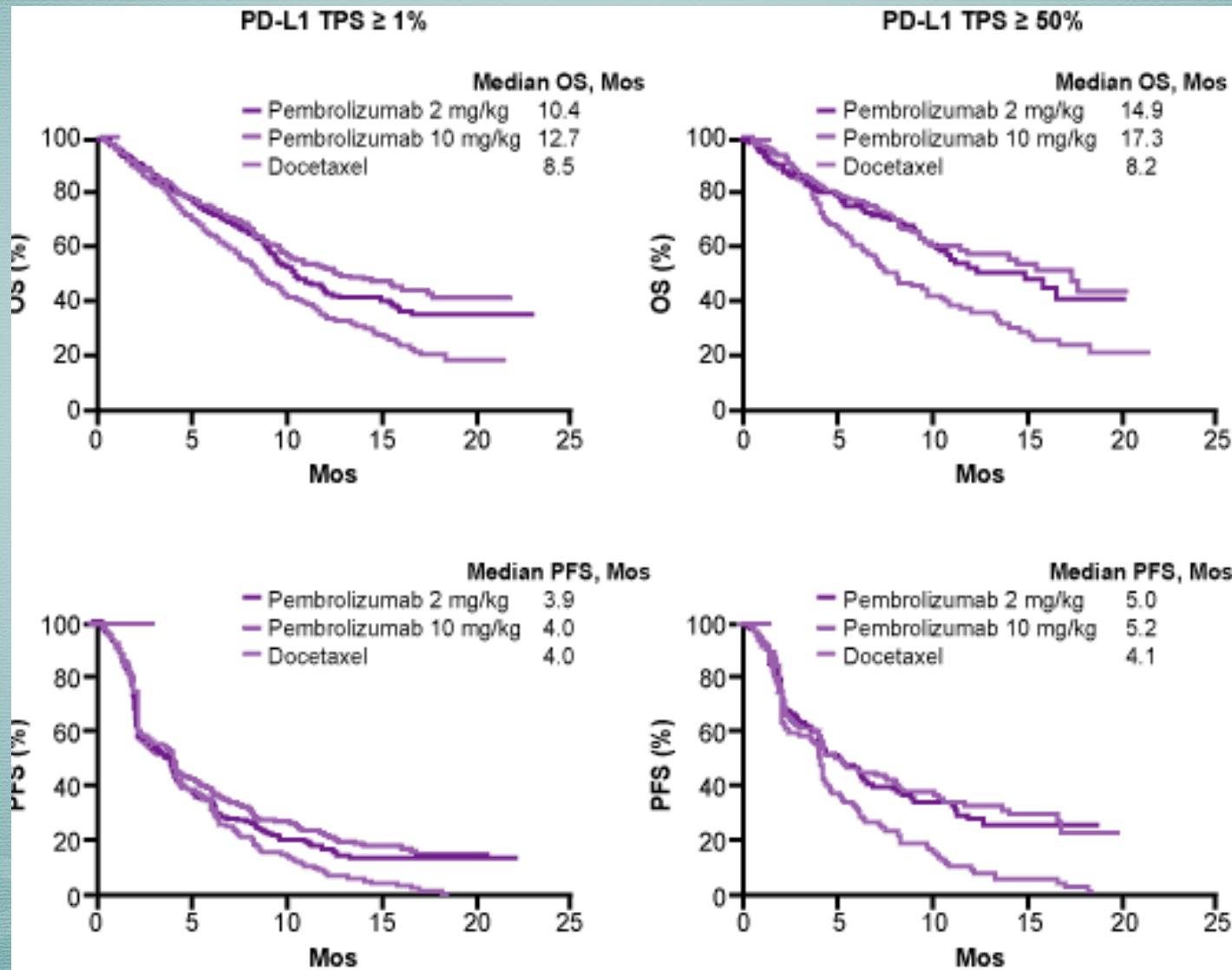
Cytology i moderne patologi

- Prædiktion



Cytology i moderne patologi

- Prædiktion

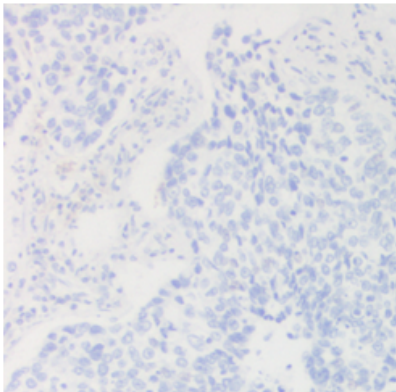


Cytology i moderne patologi

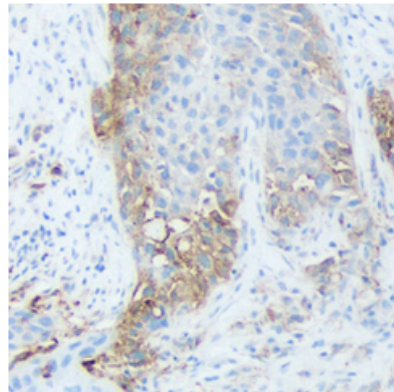
- Prædiktion

Examples of PD-L1 IHC Staining of NSCLC Samples Using the Clinical Trial Assay

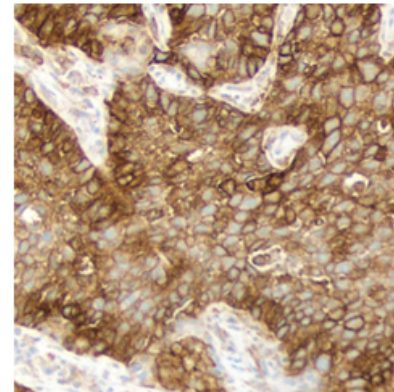
PS <1%



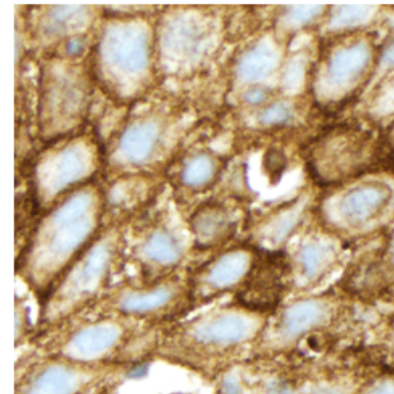
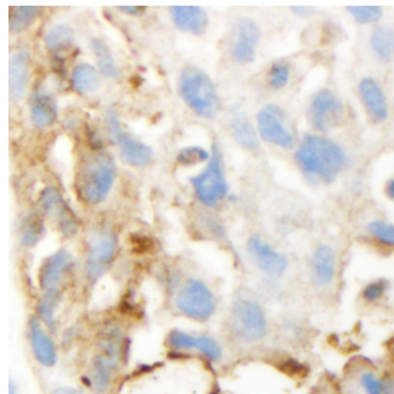
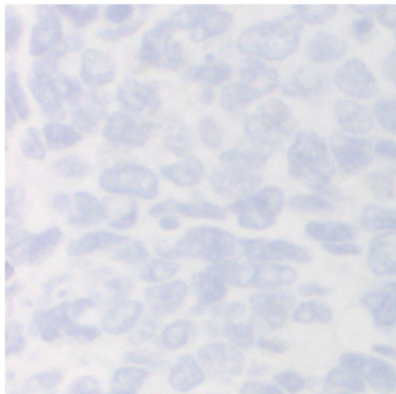
PS 1-49%



PS ≥50%



5x
magnification



40x
magnification

Brown chromogen: PD-L1 staining.
Blue color: hematoxylin counterstain.

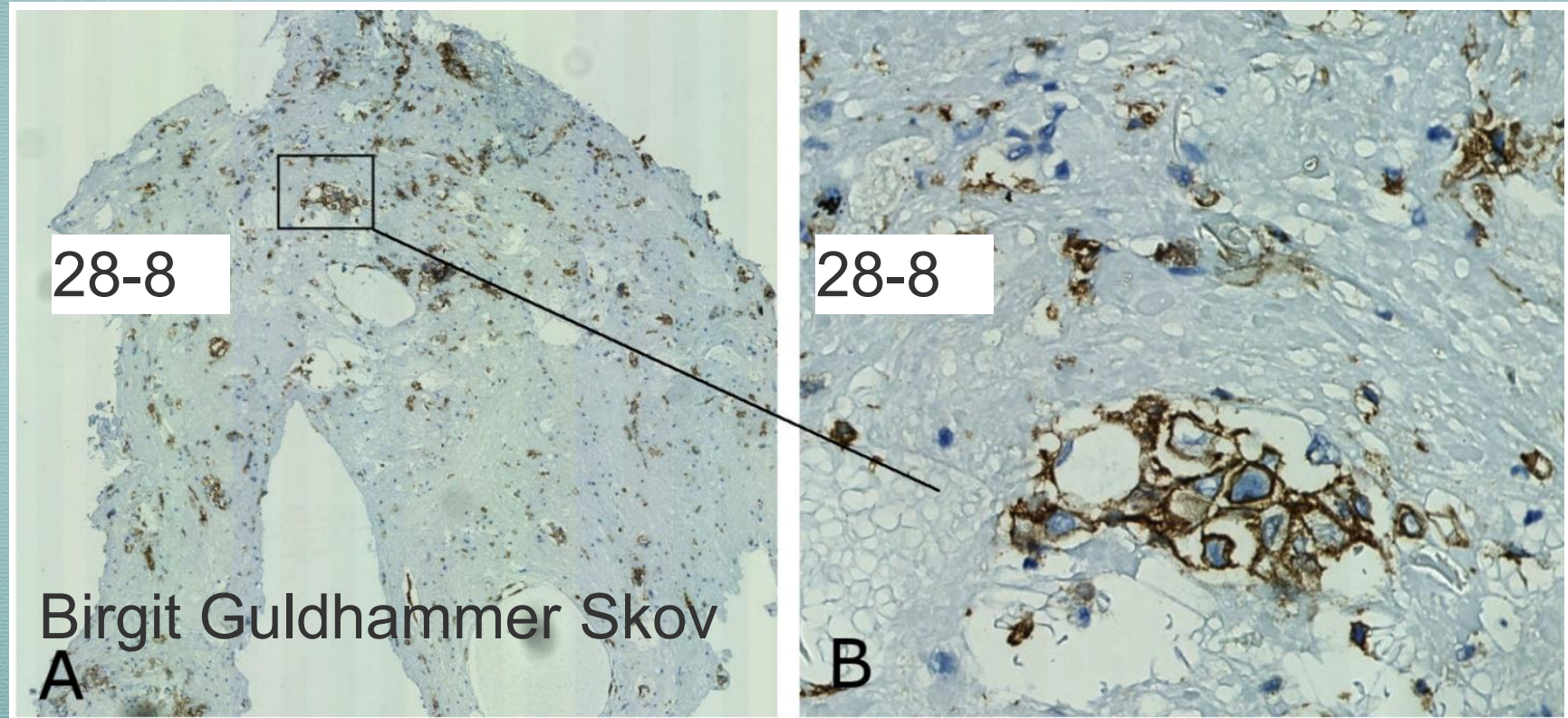
Cytology i moderne patologi

- Prædiktion

PD-L1 IHC 28-8 pharmDx			
	Cutoff ≥ 1% positive cells	Cutoff ≥ 5% positive cells	Cutoff ≥ 10 % positive cells
Overall agreement	87 (80 – 94)	95 (91 – 99)	90 (83 – 95)
Average Positive Agreement	86 (77 – 94)	94 (86 – 99)	84 (71 – 93)
Average Negative Agreement	88 (80 – 94)	96 (92 – 99)	92 (87 – 97)
Positive Percent Agreement	81 (69 – 92)	91 (79 – 100)	79 (63 – 93)
Negative Percent Agreement (NPA)	93 (85 – 100)	98 (94 – 100)	95 (88 – 100)
Pearson R ² of PD-L1 scores	0.89		

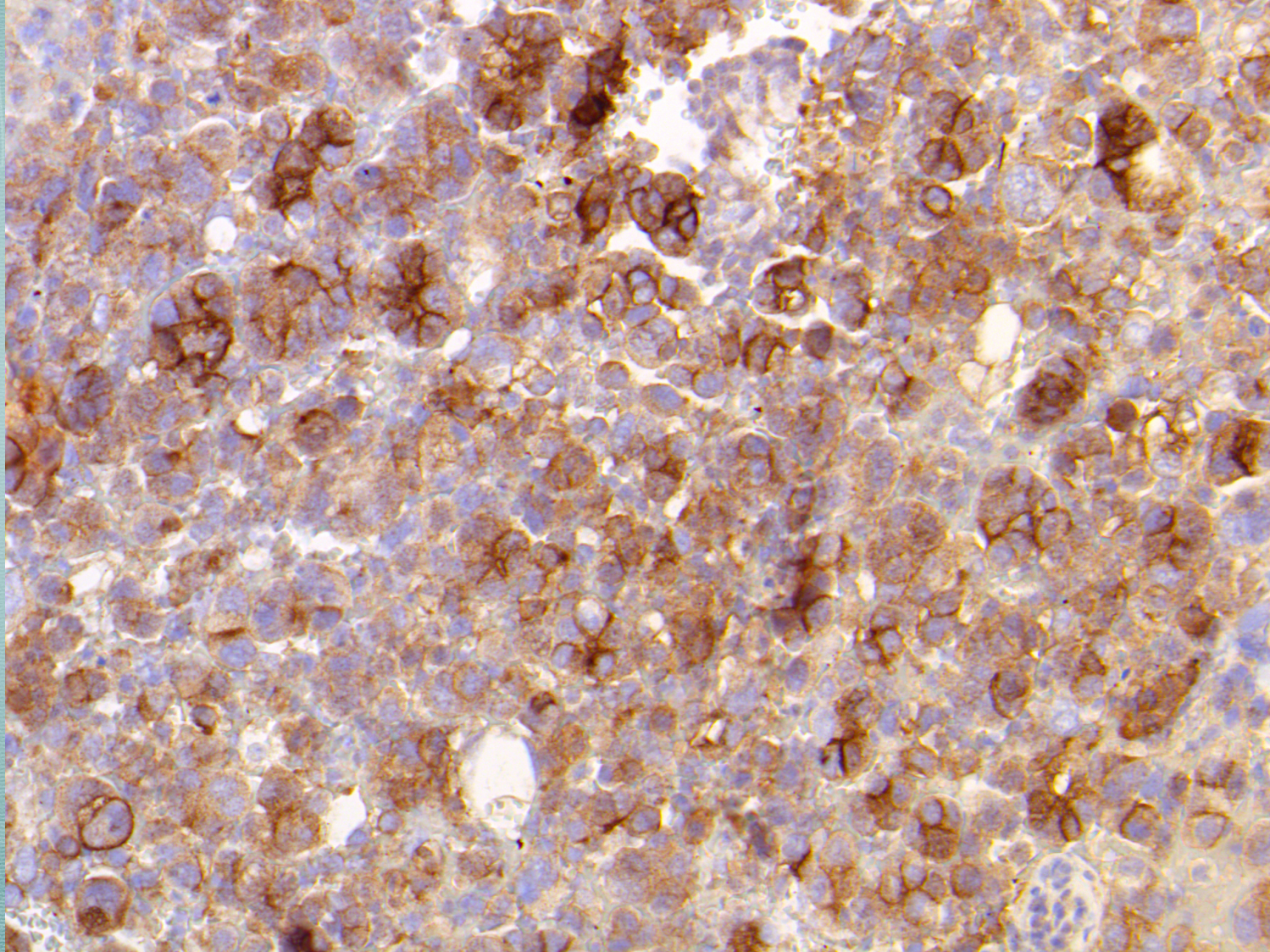
Cytology i moderne patologi

- Prædiktion



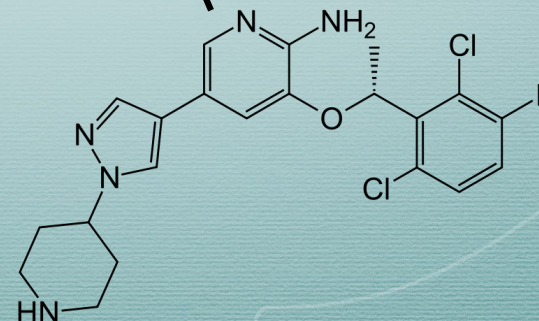
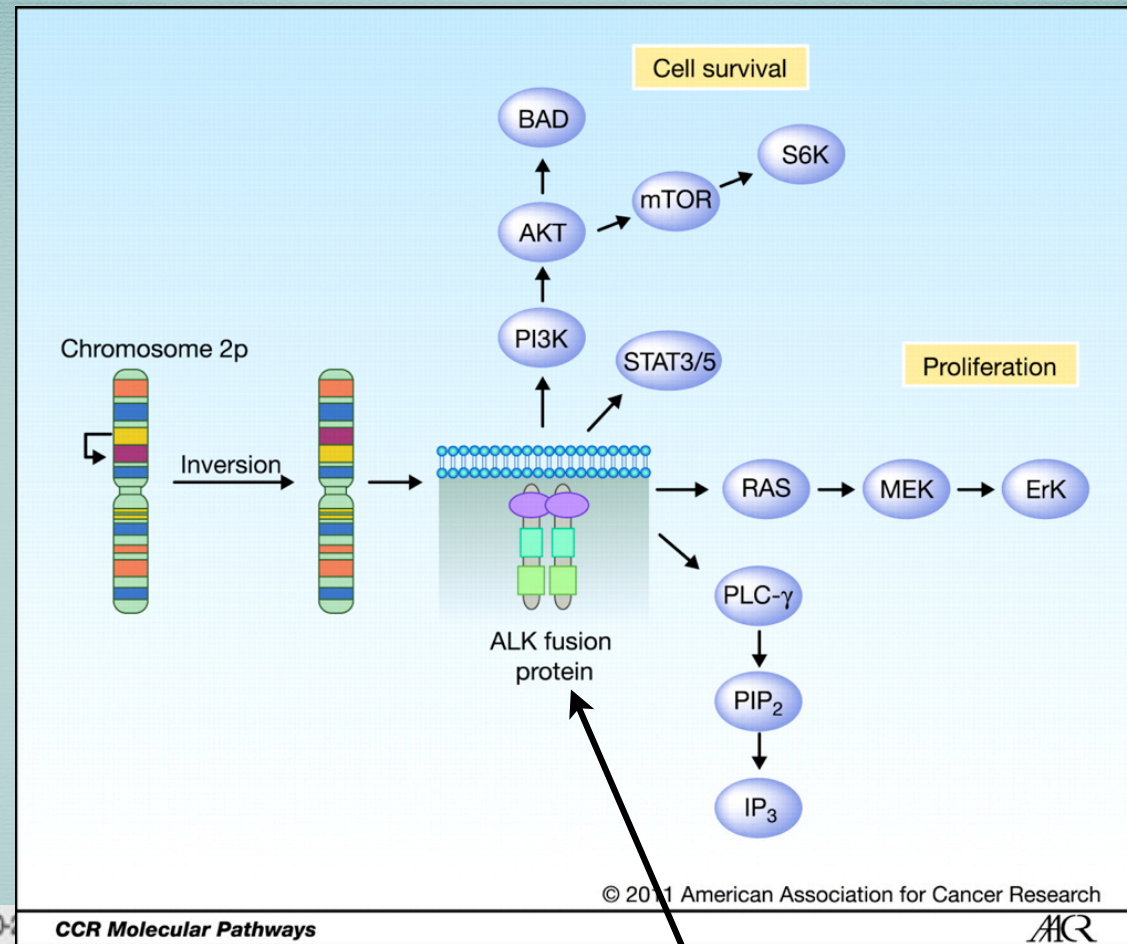
Cytology i moderne patologi

- Prædiktation



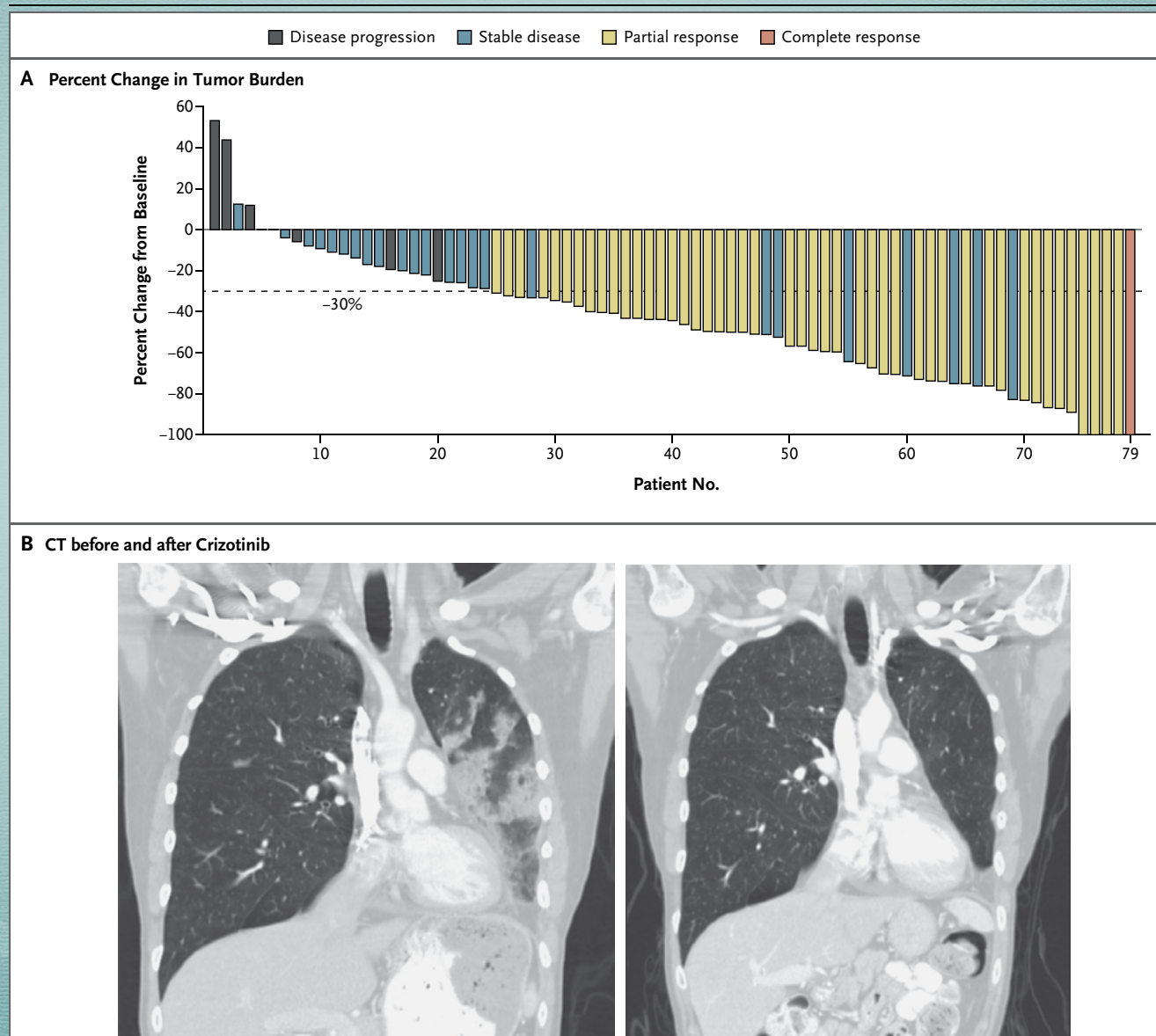
Cytology i moderne patologi

- Prædiktion



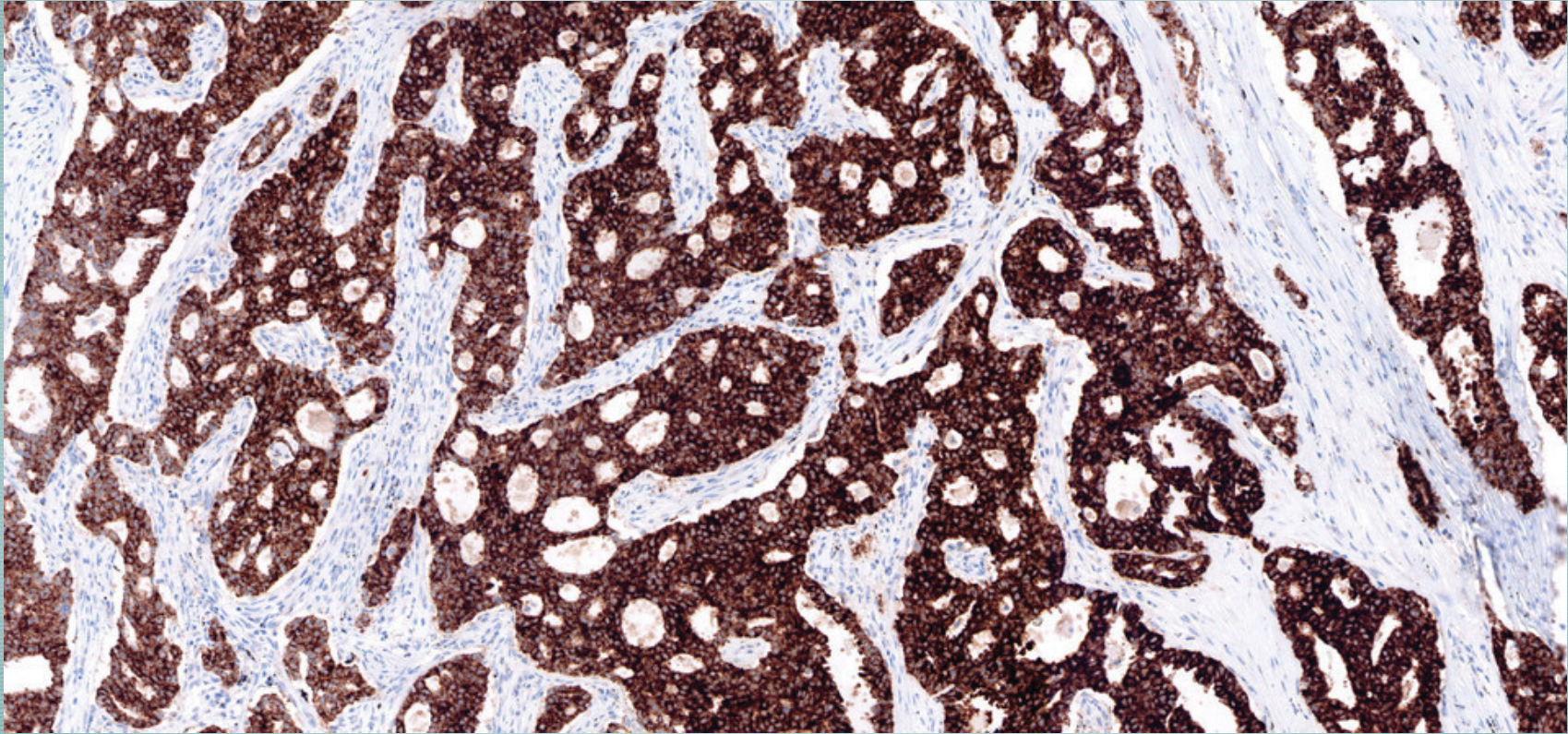
Cytology i moderne patologi

- Prædiktion



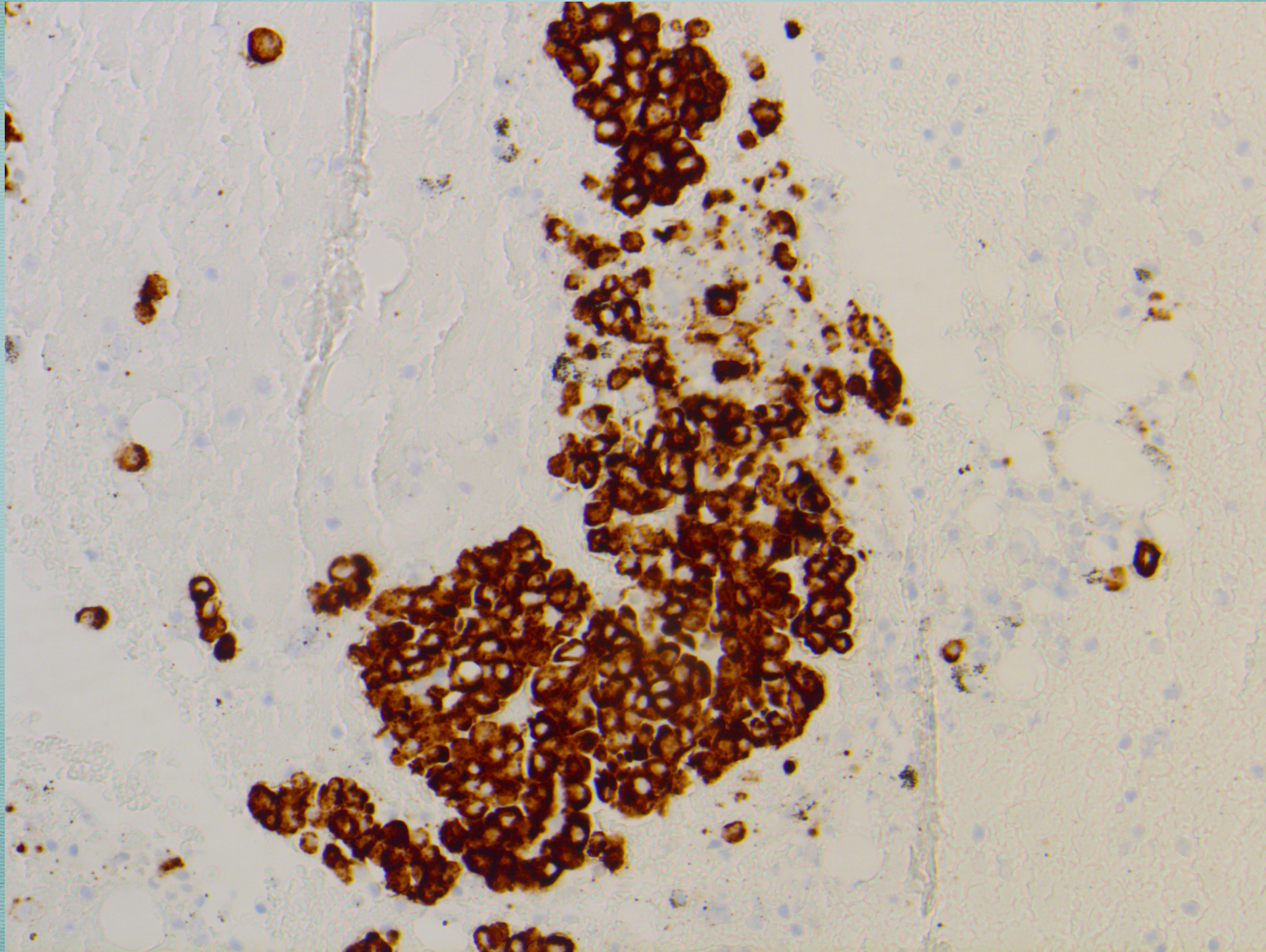
Cytology i moderne patologi

- Prædiktation



Cytology i moderne patologi

- Prædiktion



Cytology i moderne patologi

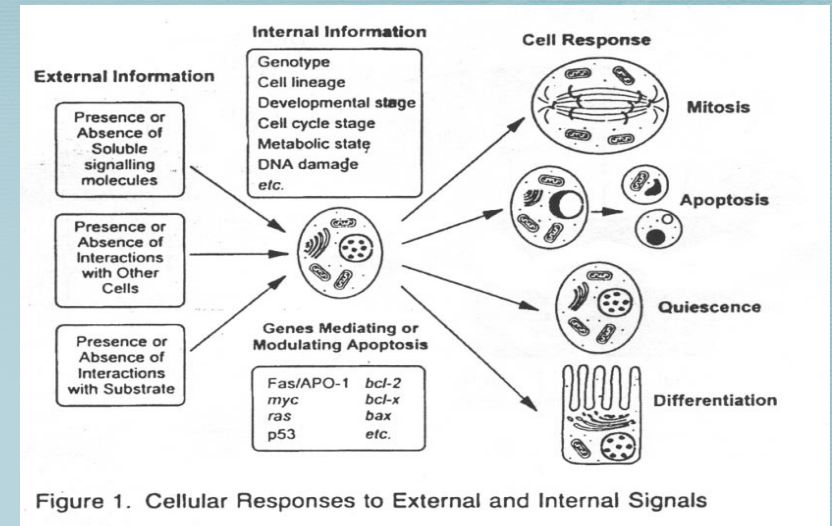
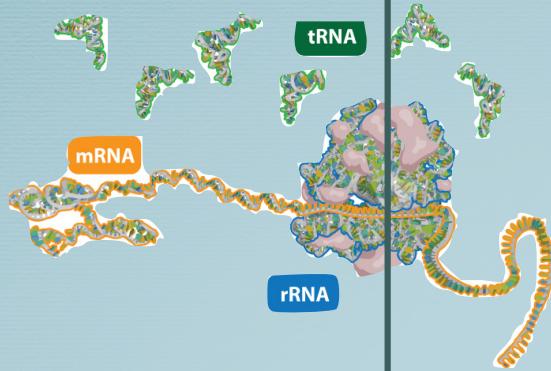
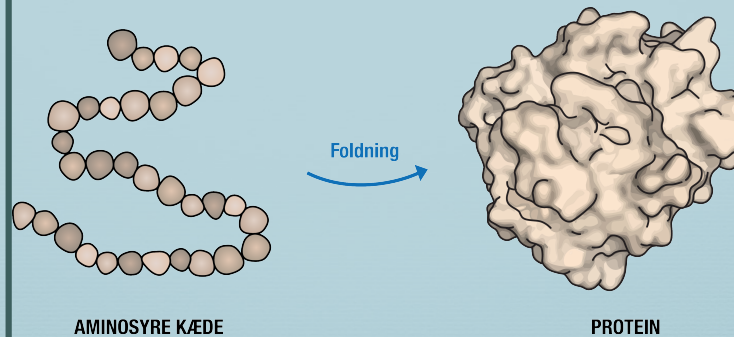
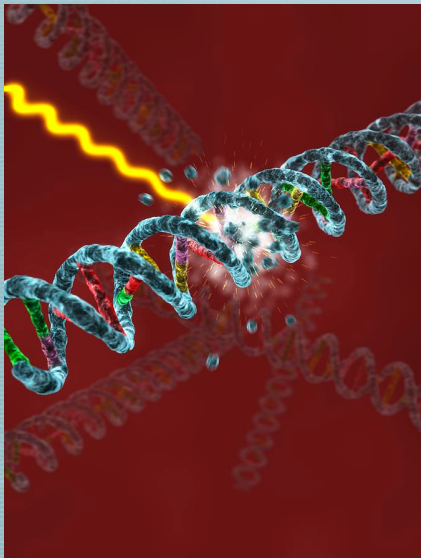


Figure 1. Cellular Responses to External and Internal Signals

DNA → RNA → Protein → Funktion / opførsel



Cytology i moderne patologi

Kan DNA ekstraheres fra cytologisk materiale ?

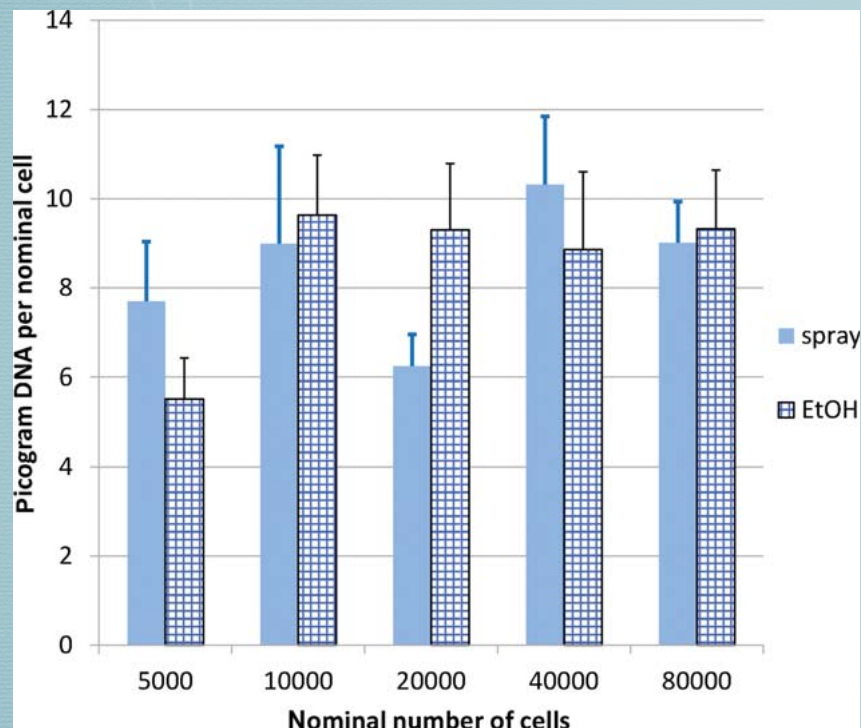


FIGURE 3. Comparison of yields using fixation with isopropanol-based spray (“spray”) or ethanol (EtOH) (90%) is shown. Cells were stained using the Papanicolaou method and EcoMount (Biocare Medical LLC, Concord, Calif) was used as the mounting medium. The means and the standard error of the mean from 2 batches with 3 replicates of each case are shown.

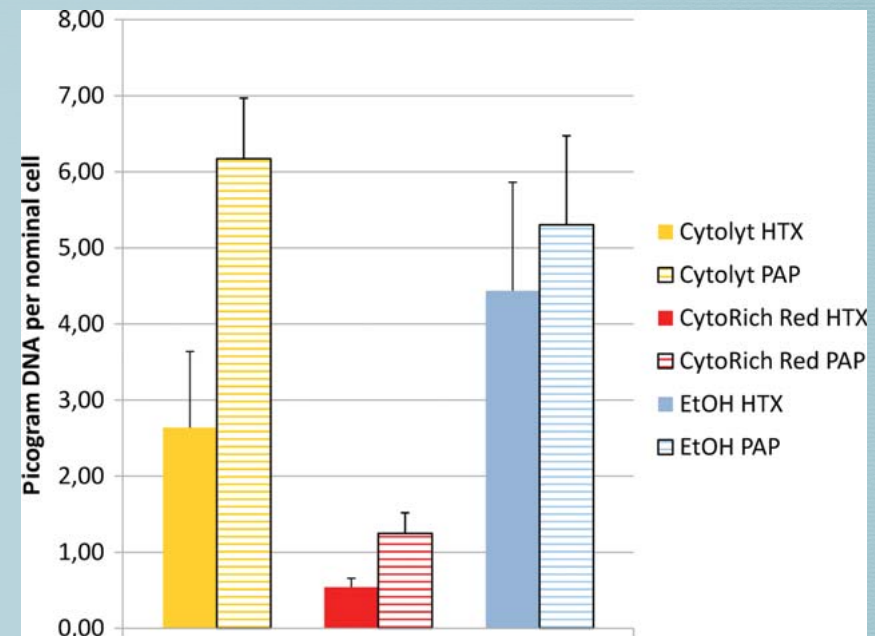


FIGURE 4. Comparison of yields are shown between 2 liquid-based methods and ethanol (EtOH) fixation, each with nominally 40,000 cells, stained with hematoxylin and eosin (HTX) and Papanicolaou (PAP) and with EcoMount (Biocare Medical LLC, Concord, Calif) used as the mounting medium. According to the manufacturer’s instructions, precoated slides were used for cells in CytoRich Red, whereas routine slides were used for the other fixations.

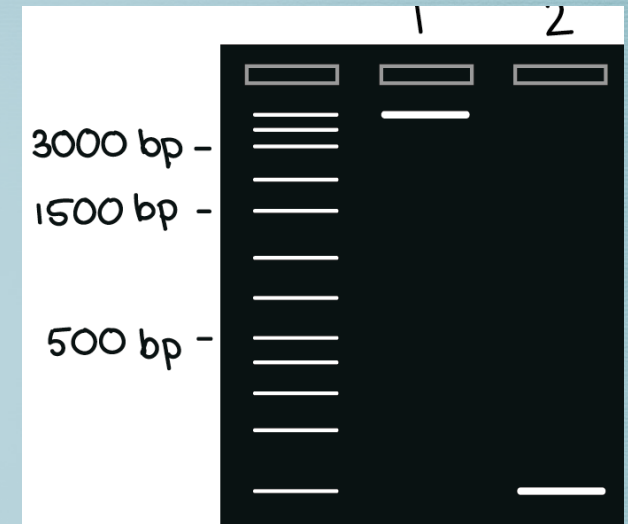
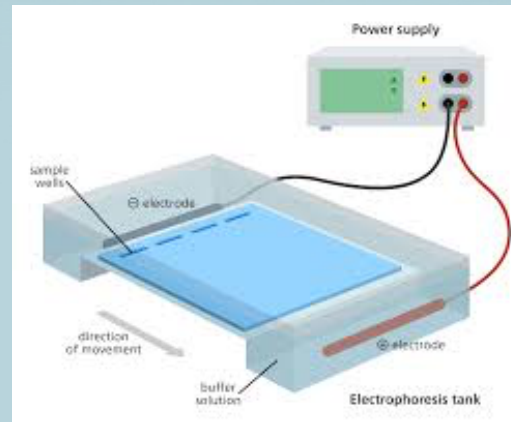
Preparation of DNA From Cytological Material

Effects of Fixation, Staining, and Mounting Medium on DNA Yield and Quality

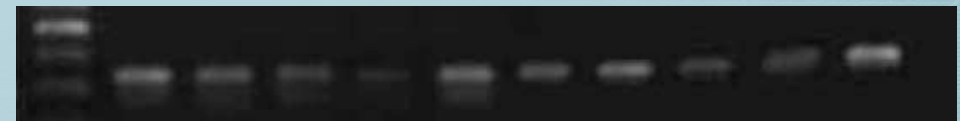
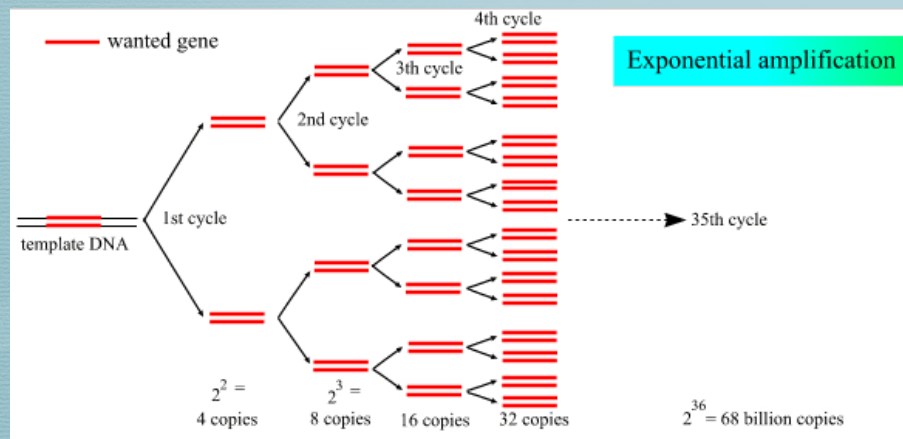
Annika Dejmek, MD, PhD^{1,2}; Nooreldin Zendeherokh, PhD¹;
Malgorzata Tomaszewska, MSc³; and Anders Edsjö, MD, PhD^{1,2,4,5}

Cytology i moderne patologi

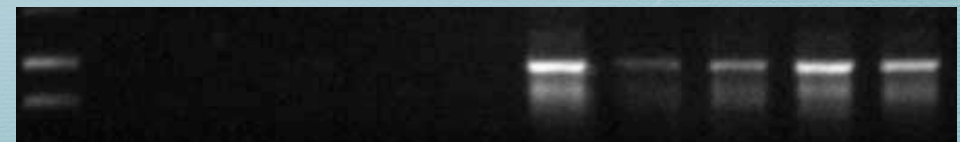
Kan DNA ekstraheres fra cytologisk materiale ?



200 bp



600 bp



Cytology i moderne patologi

Kan DNA ekstraheres fra cytologisk materiale ?

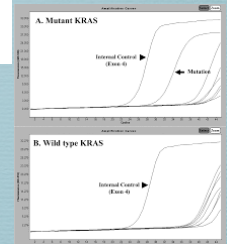
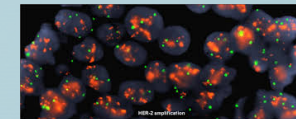
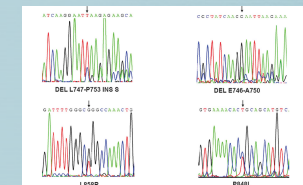
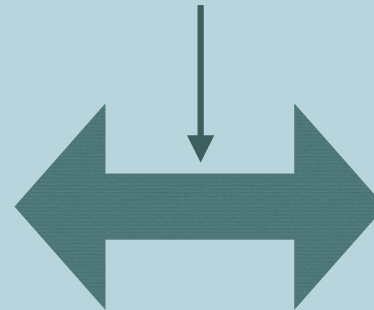
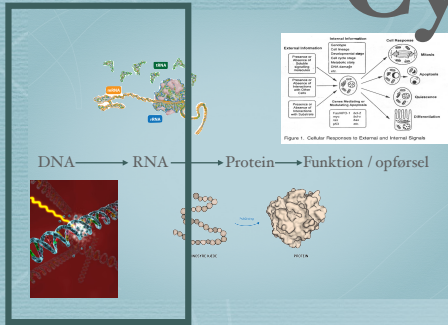
TABLE 2. Presence of Visible Bands of DNA Fragments in Extracts With Different Fixations (Median Value of 2 Batches With 3 Replicates Is Shown)^a

Nominal Cell Count	Air				Spray				CytoRich Red			
	209 bp	388 bp	578 bp	760 bp	209 bp	388 bp	578 bp	760 bp	209 bp	388 bp	578 bp	760 bp
5000	2	1	-1	-1	2	2	1	1	2	2	1	0
10,000	2	1	-1	-1	2	2	1.5	1	2	2	1	.5
20,000	2	1	-1	-1	2	2	2	2	2	2	1.5	.5
40,000	2	1.5	-1	-1	2	2	2	2	2	2	1.5	.5

Abbreviation: bp, base pair.

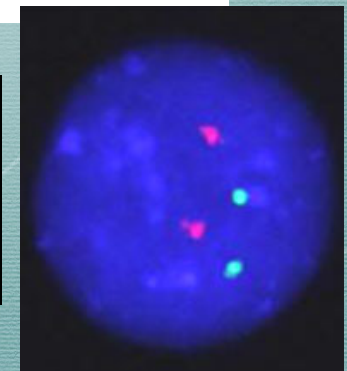
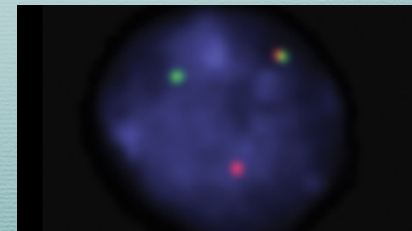
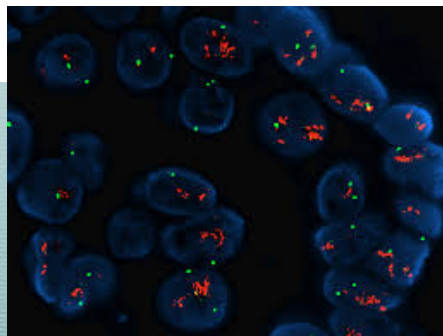
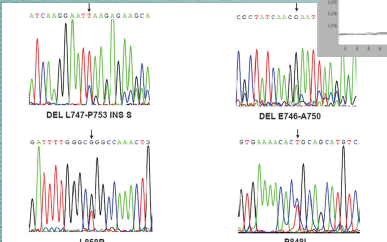
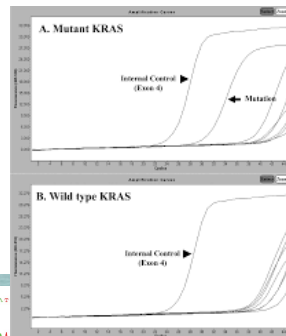
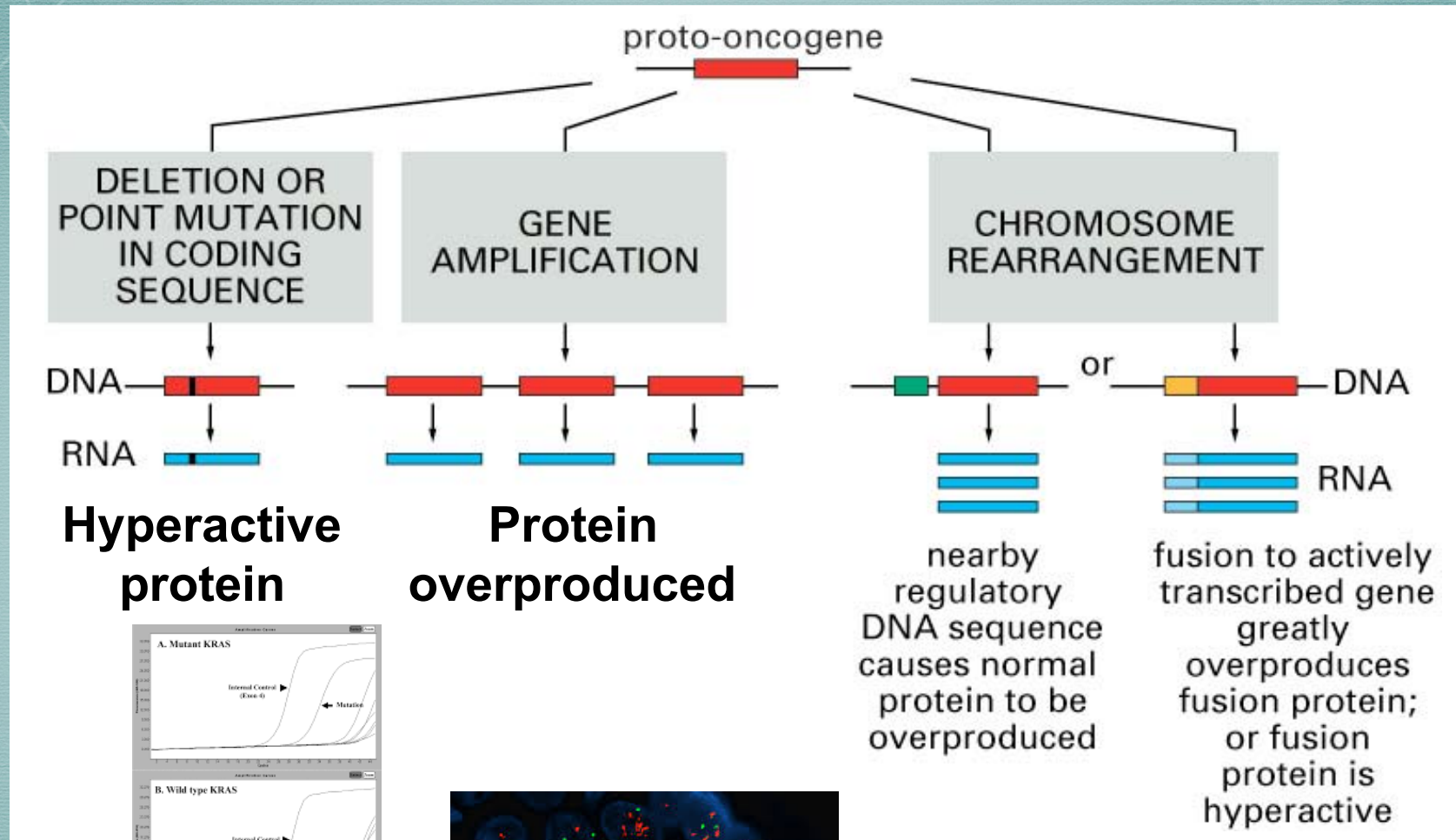
^a Scoring: strong band=2; distinct band=1; indefinite=0; no band=-1.

Cytology i moderne patologi



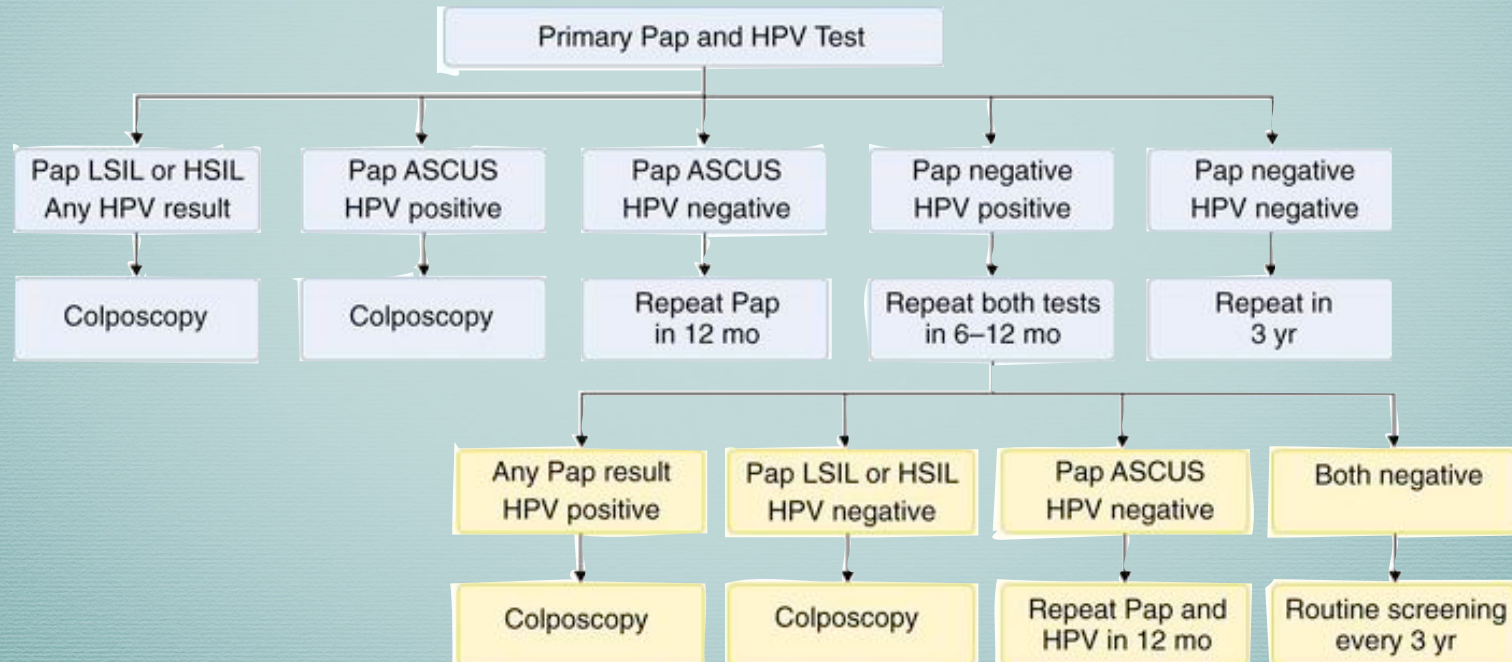
Molekylær patologi

Cytology i moderne patologi



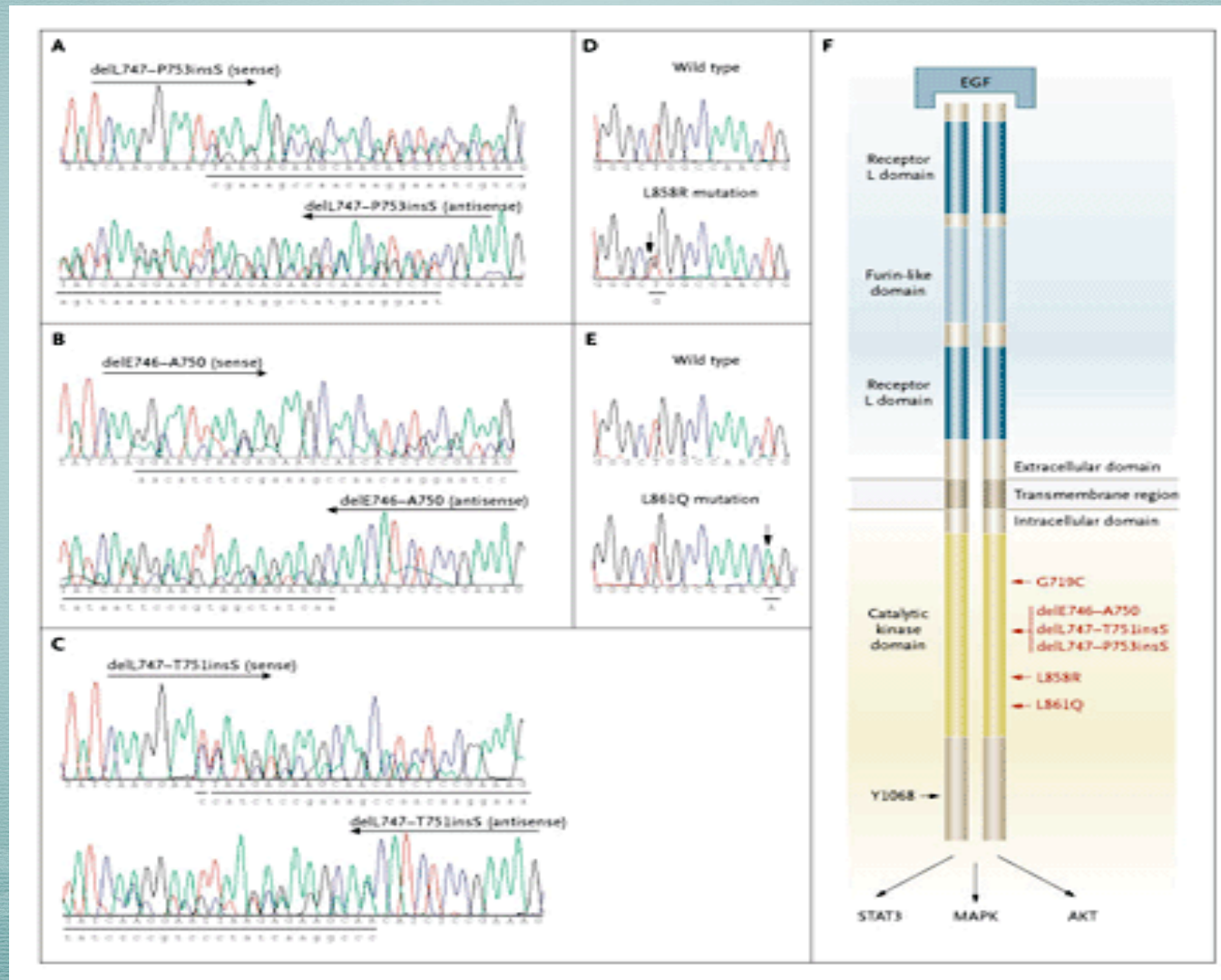
Cytology i moderne patologi

- Prognostisk markør (risiko hos raske)



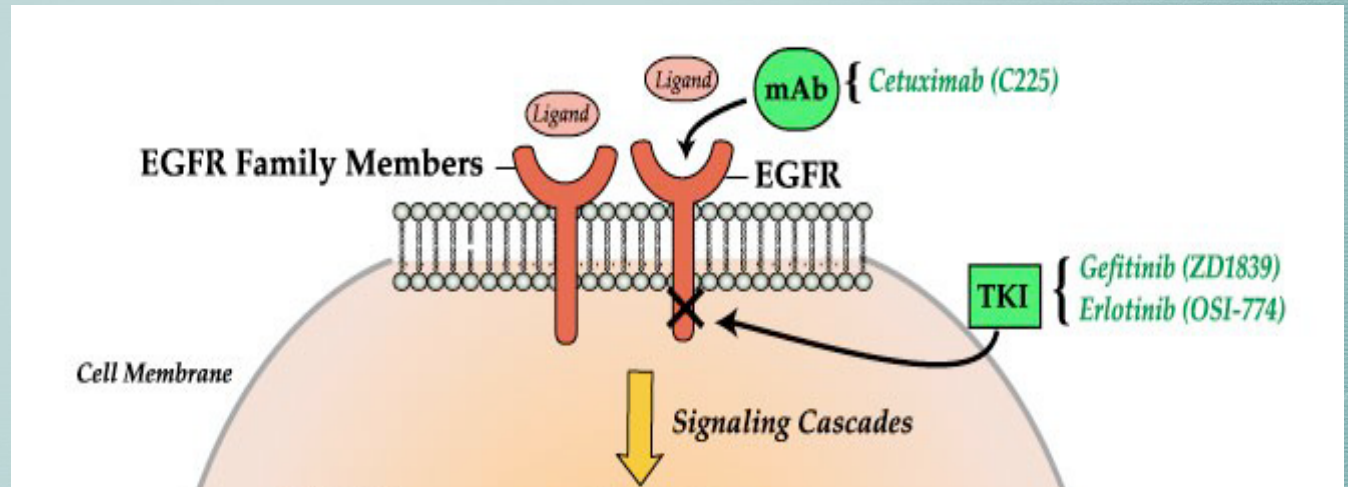
Cytology i moderne patologi

- Prediktiv markør



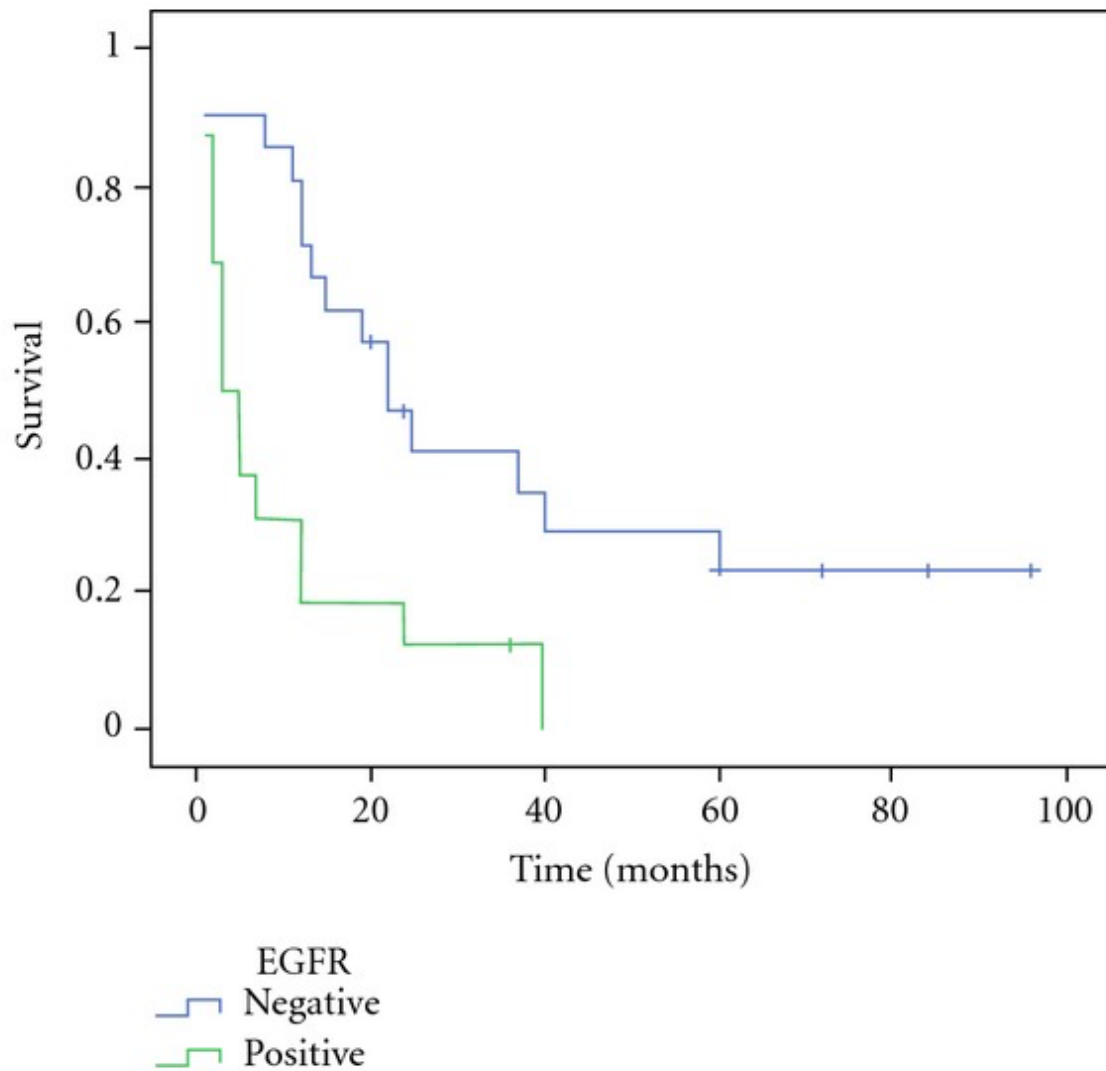
Cytology i moderne patologi

- Prediktiv markør



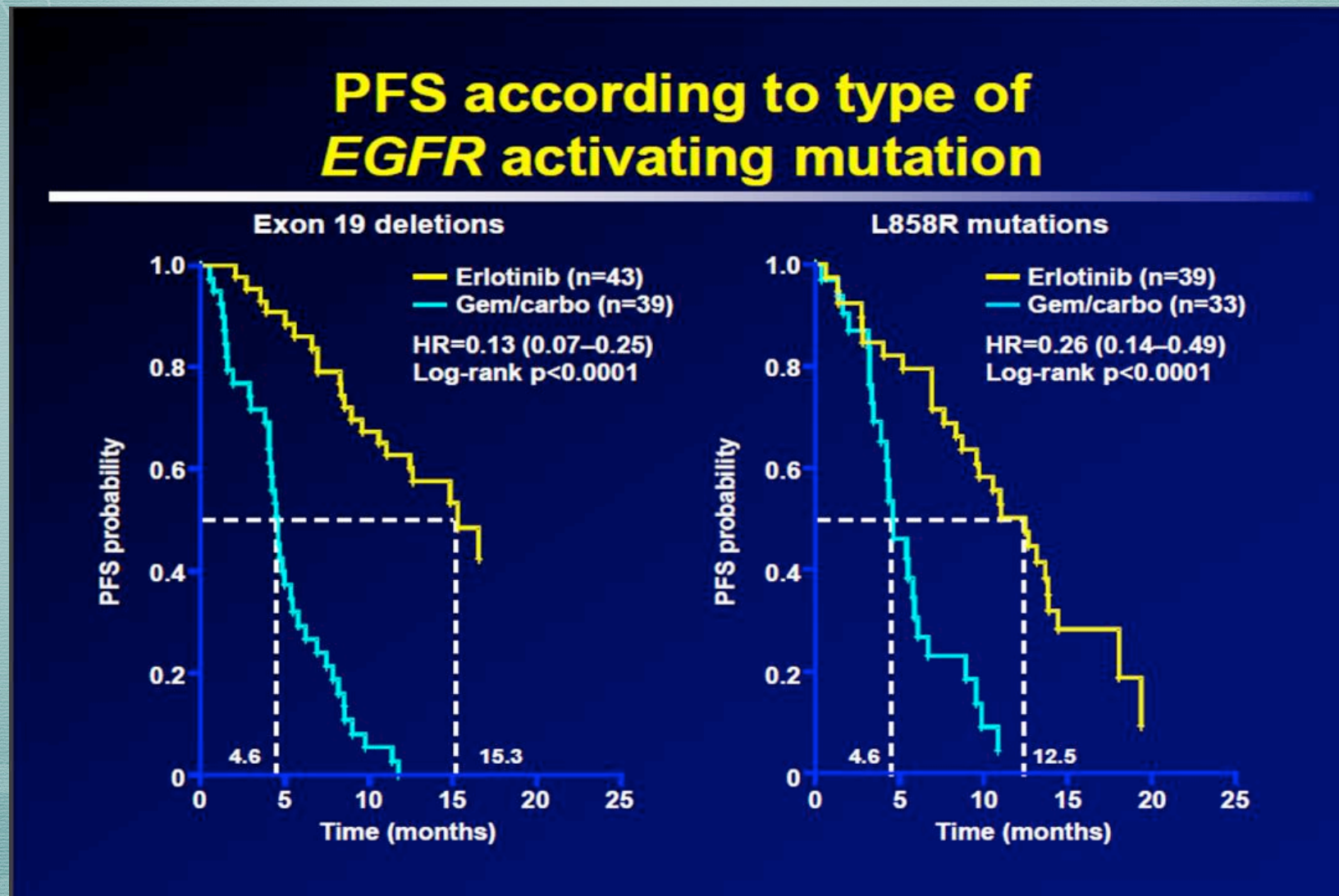
Cytology i moderne patologi

- Prediktiv markør



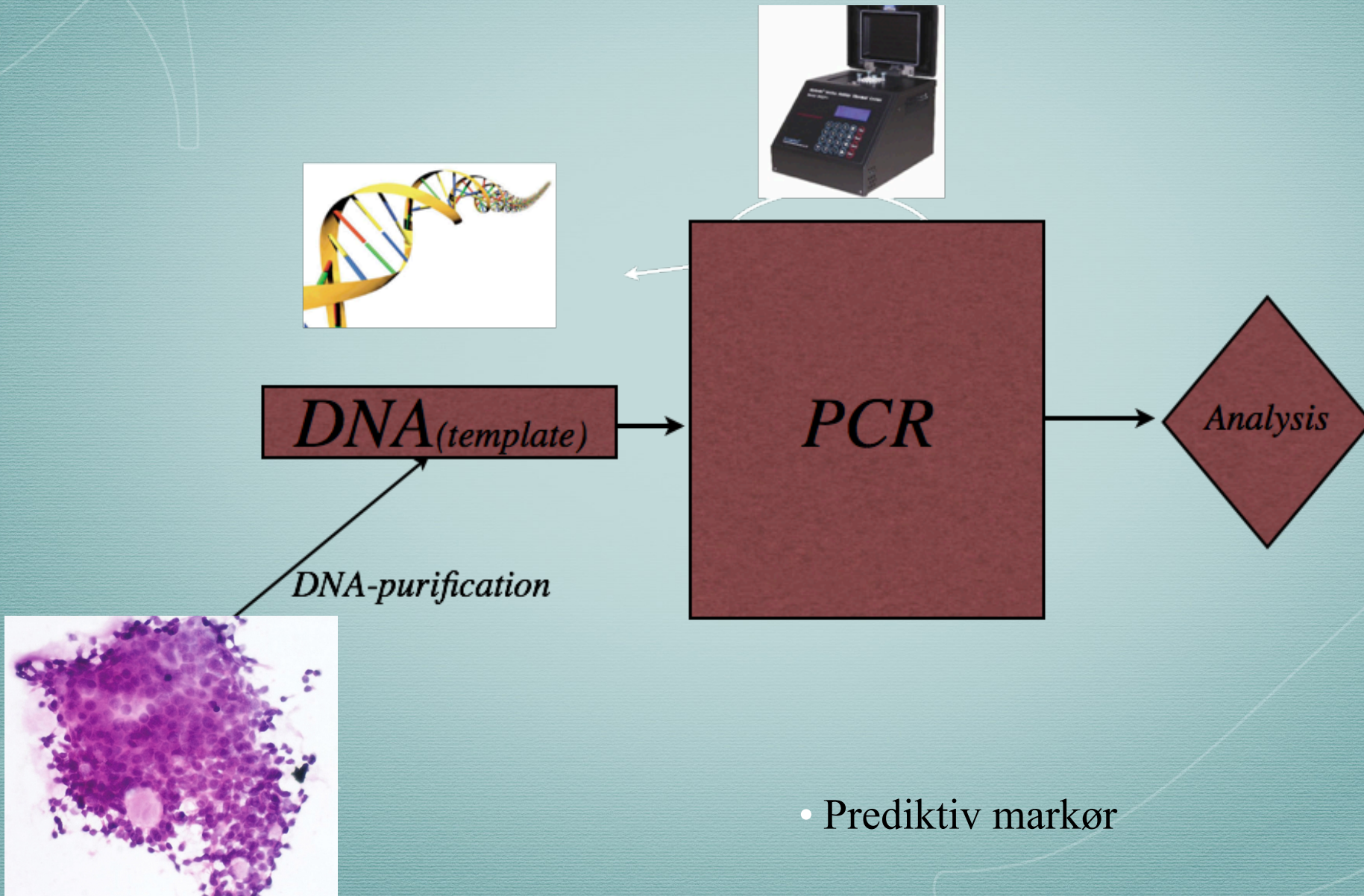
Cytology i moderne patologi

- Prediktiv markør



Cytology i moderne patologi

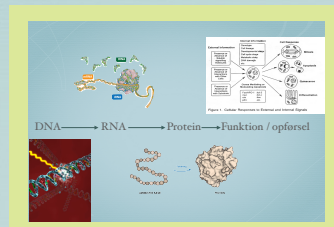
- Prediktiv markør



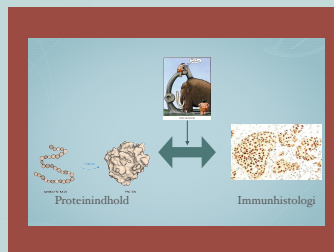
- Prediktiv markør

Cytology i moderne patologi

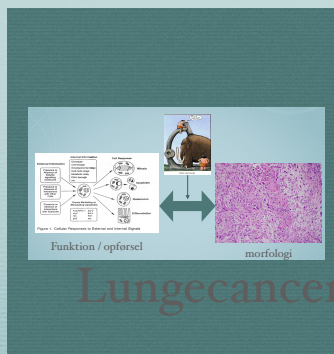
TC
i prøven



EML4-ALK
EGFR



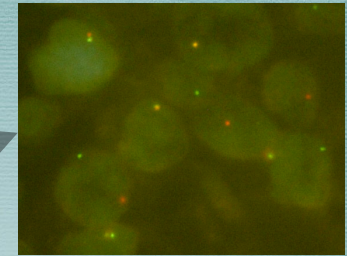
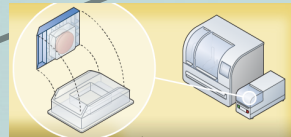
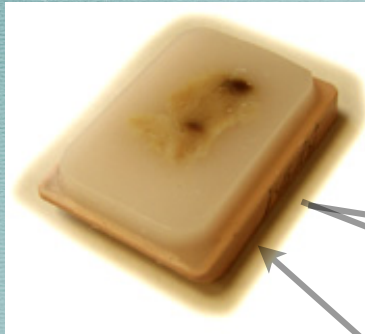
CK7, CK5/6
ttf1, p40
PDL1



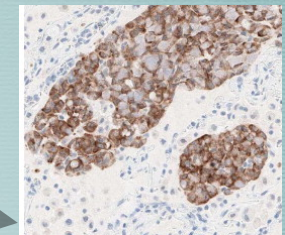
Morfo.

Cytology i moderne patologi

hist



ISH



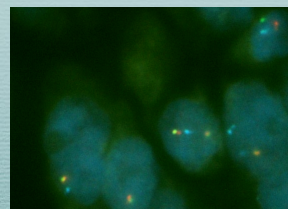
Immunhistologi



Molekylær analyse



Molekylær analyse

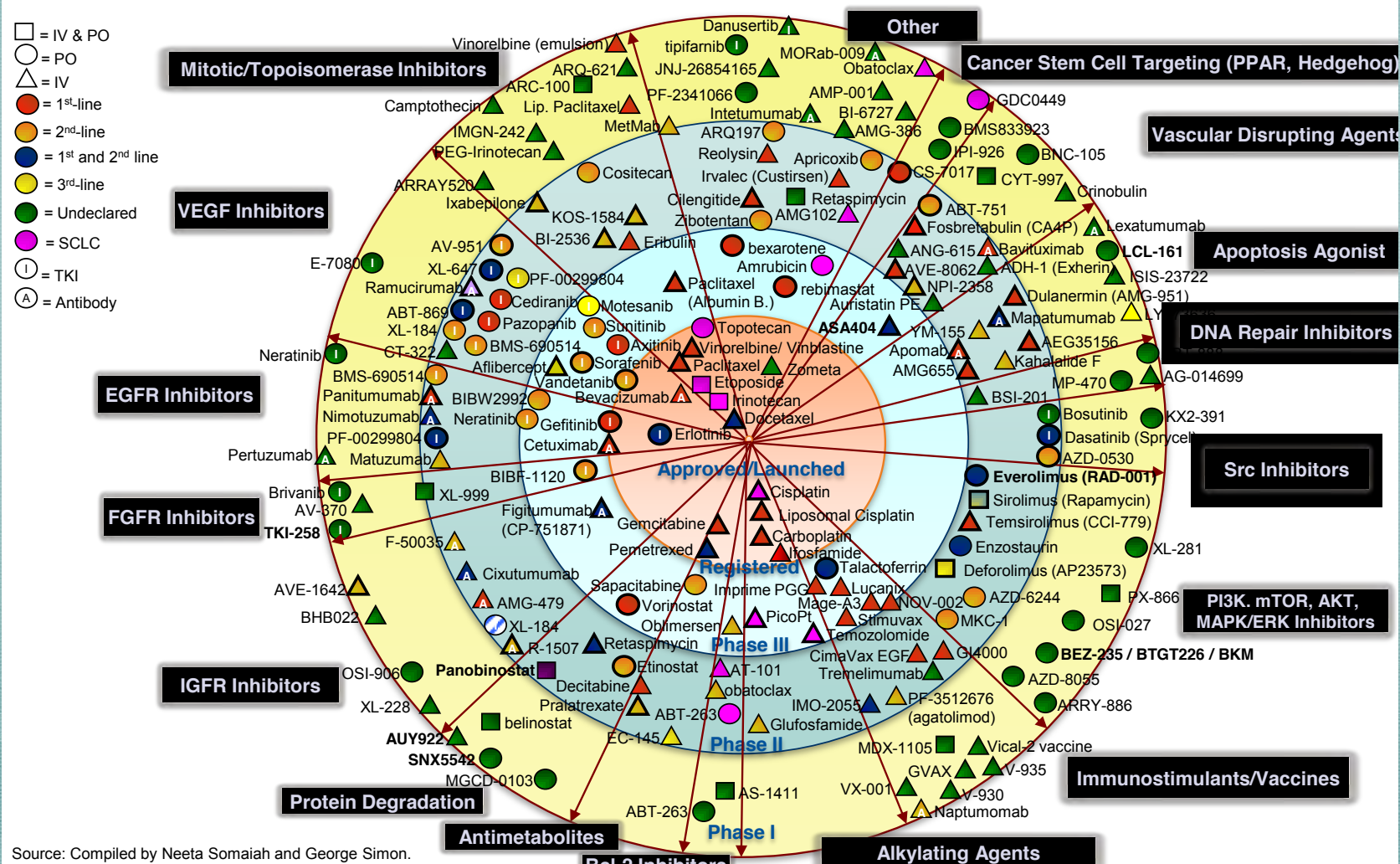


cyt



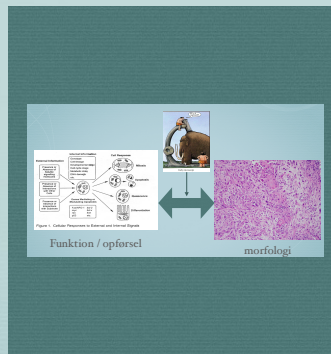
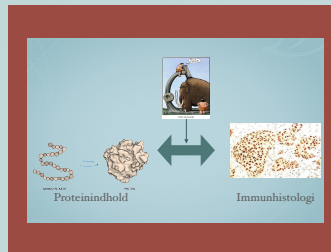
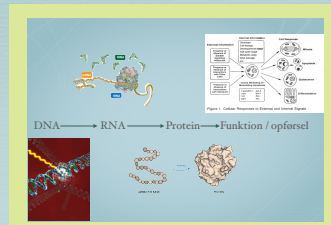
Cytology i moderne patologi

Lung cancer research landscape – MoA group and phase



Cytology i moderne patologi

TC
i prøven



Lungecancer

Multibel biomarkør analyse

CK7, CK5/6
ttf1, p40

PDL1

Er fremtiden molekylær ?

Oncomine Comprehensive Assay* Gene List

Gene list available to customers under CDA only

Hotspot genes, n=73 (hotspot coverage)

ABL1	GNA11	MYD88
AKT1	GNAQ	NFE2L2
ALK	GNAS	NPM1
AR	HNF1A	NRAS
ARAF	HRAS	PAX5
BRAF	IDH1	PDGFRA
BTK	IDH2	PIK3CA
CBL	IFITM1	PPP2R1A
CDK4	IFITM3	PTPN11
CHEK2	JAK1	RAC1
CSF1R	JAK2	RAF1
CTNNB1	JAK3	RET
DDR2	KDR	RHEB
DNMT3A	KIT	RHOA
EGFR	KNSTRN	SF3B1
ERBB2	KRAS	SMO
ERBB3	MAGOH	SPOP
ERBB4	MAP2K1	SRC
ESR1	MAP2K2	STAT3
EZH2	MAPK1	U2AF1
FGFR1	MAX	XPO1
FGFR2	MED12	
FGFR3	MET	
FLT3	MLH1	
FOXL2	MPL	
GATA2	MTOR	

CDS, n=26 (full gene)

APC
ATM
BAP1
BRCA1
BRCA2
CDH1
CDKN2A
FBXW7
GATA3
MSH2
NF1
NF2
NOTCH1
PIK3R1
PTCH1
PTEN
RB1
SMAD4
SMARCB1
STK11
TET2
TP53
TSC1
TSC2
VHL
WT1

Copy gain, n=49

ACVRL1	IGF1R
AKT1	IL6
APEX1	KIT
AR	KRAS
ATP11B	MCL1
BCL2L1	MDM2
BCL9	MDM4
BIRC2	MET
BIRC3	MYC
CCND1	MYCL
CCNE1	MYCN
CD274	MYO18A
CD44	NKX2-1
CDK4	NKX2-8
CDK6	PDCD1LG2
CSNK2A1	PDGFRA
DCUN1D1	PIK3CA
EGFR	PNP
ERBB2	PPARG
FGFR1	RPS6KB1
FGFR2	SOX2
FGFR3	TERT
FGFR4	TIAF1
FLT3	ZNF217
GAS6	

Fusion drivers, n=22 (183 assays)

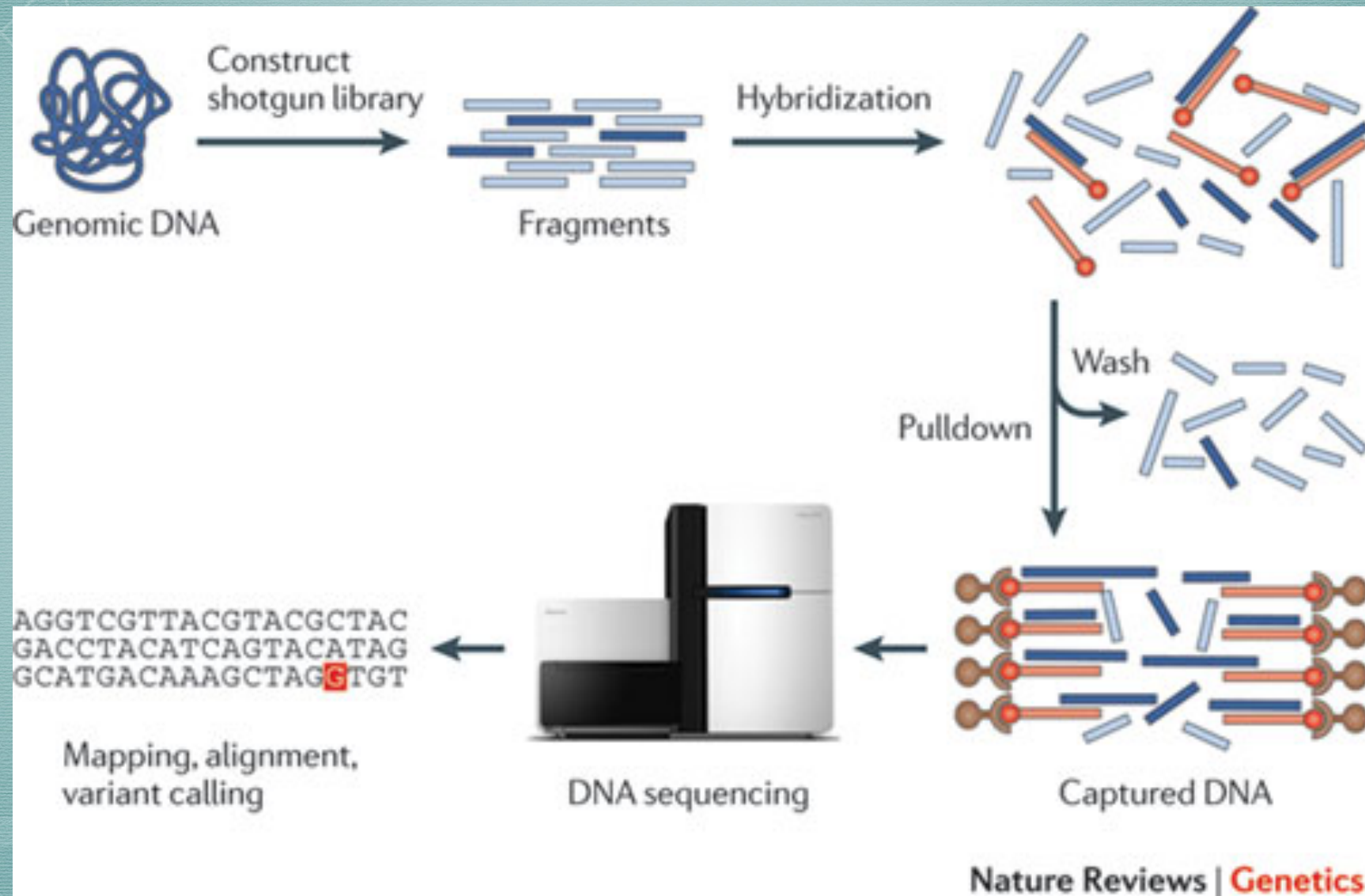
ALK
RET
ROS1
NTRK1
ABL1
AKT3
AXL
BRAF
CDK4
EGFR
ERBB2
ERG
ETV1
ETV4
ETV5
FGFR1
FGFR2
FGFR3
NTRK3
PDGFRA
PPARG
RAF1

DNA Panel

RNA Panel

*For Research Use Only. Not for use in diagnostic procedures.

Er fremtiden molekylær ?



Er fremtiden molekylær ?



Cancer. 2017 Jan 13. doi: 10.1002/cncy.21812. [Epub ahead of print]

Next-generation sequencing of liquid-based cytology non-small cell lung cancer samples.

Reynolds JP¹, Zhou Y¹, Jakubowski MA¹, Wang Z¹, Brainard JA¹, Klein RD¹, Farver CF¹, Almeida FA², Cheng YW¹.

	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6	Run 7	Mean	SE	95% CI
<i>PIK3CA</i> c.1633G>A, p.E545K	1504	1607	1414	1279	1223	1286	1798	1444.43	78.29	1290.99-1597.87
<i>PIK3CA</i> c.3140A>G, p.H1047R	1708	1911	1627	1643	1801	1770	2261	1817.29	82.62	1655.35-1979.22
<i>EGFR</i> c.2155G>A, p.G719S	2188	2592	1962	2149	2017	1619	2563	2155.71	129.30	1902.3-2409.13
<i>BRAF</i> c.1799T>A, p.V600E	1154	1862	1548	1746	1977	1895	2627	1829.86	169.43	1497.79-2161.93
<i>KRAS</i> c.38G>A, p.G13D	1320	2173	1421	1613	2494	2125	2992	2019.71	229.82	1569.27-2470.16
<i>KRAS</i> c.35G>A, p.G12D	1318	2171	1418	1610	2489	2123	2988	2016.71	229.58	1566.75-2466.68

Væv
Væsker



- Mikroskopisk klassifikation, diagnose
- Malignitetsgradering (prognose)
- Tumor udbredning (lokalt)
- Metastasering (Lymfeknude + fjern)

- Prognostisk markør (risiko hos raske)
- Diagnostisks markør
- Prognostisk markør (risiko hos syge)
- Prediktiv markør
- Farmakodynamisk markør



Væv
Væsker

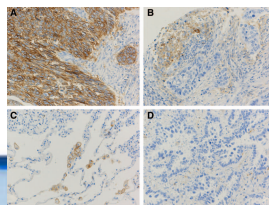


- Mikroskopisk klassifikation, diagnose
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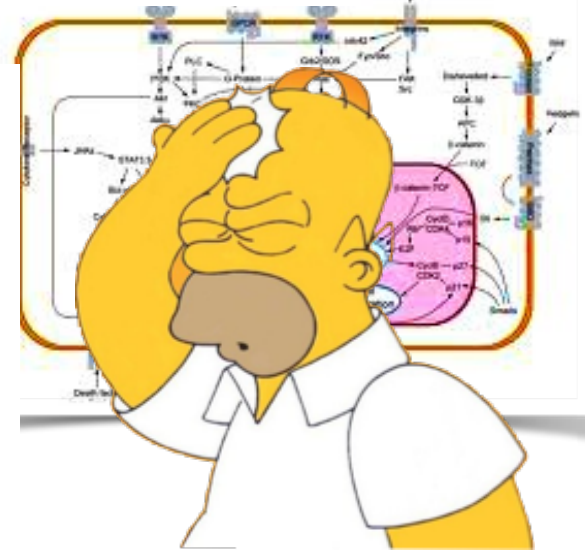
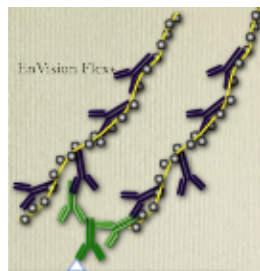
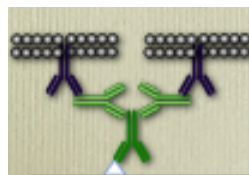
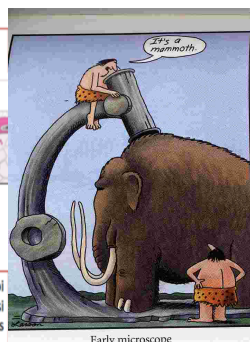
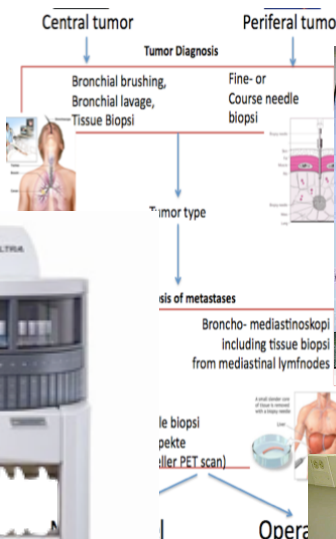
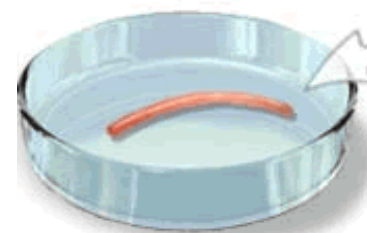
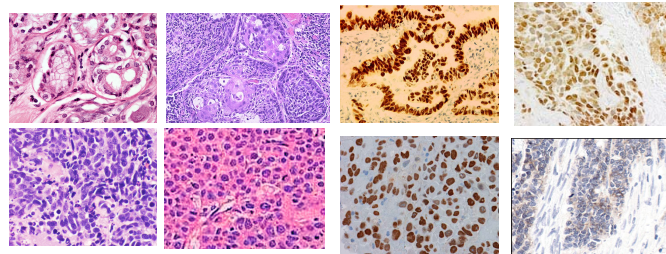
**A fool with a tool
is still a fool!**

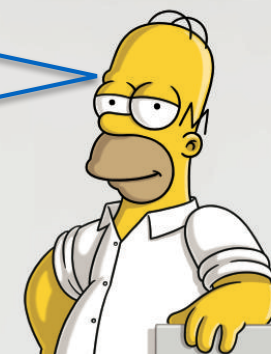
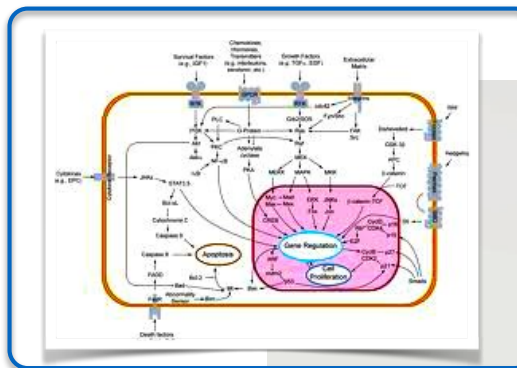
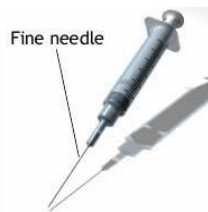
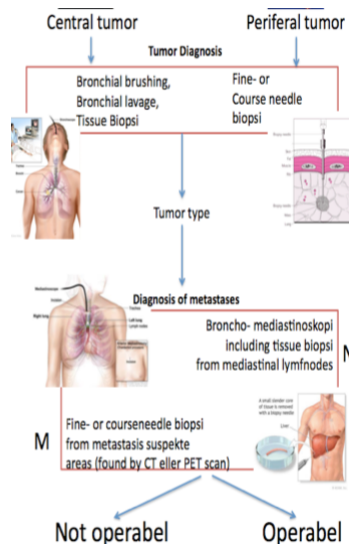




ALK, RET, ROS1, and NTRK1 fusion transcripts, in addition to targets designed to detect 5' and 3' ALK gene expression

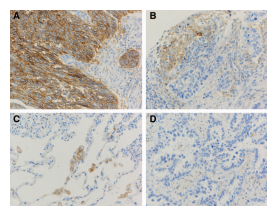
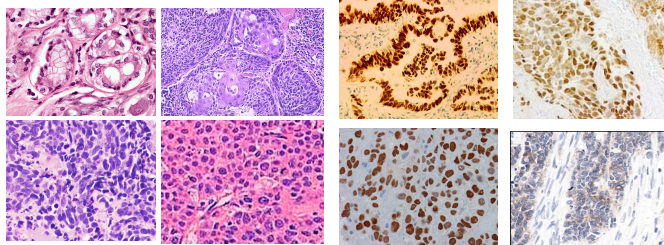
KRAS, EGFR, BRAF, PIK3CA, AKT1, ERBB2, PTEN, NRAS, STK11, MAP2K1, ALK, DDR2, CTNNB1, MET, TP53, SMAD4, FBX7, FGFR3, NOTCH1, ERBB4, FGFR1, FGFR2





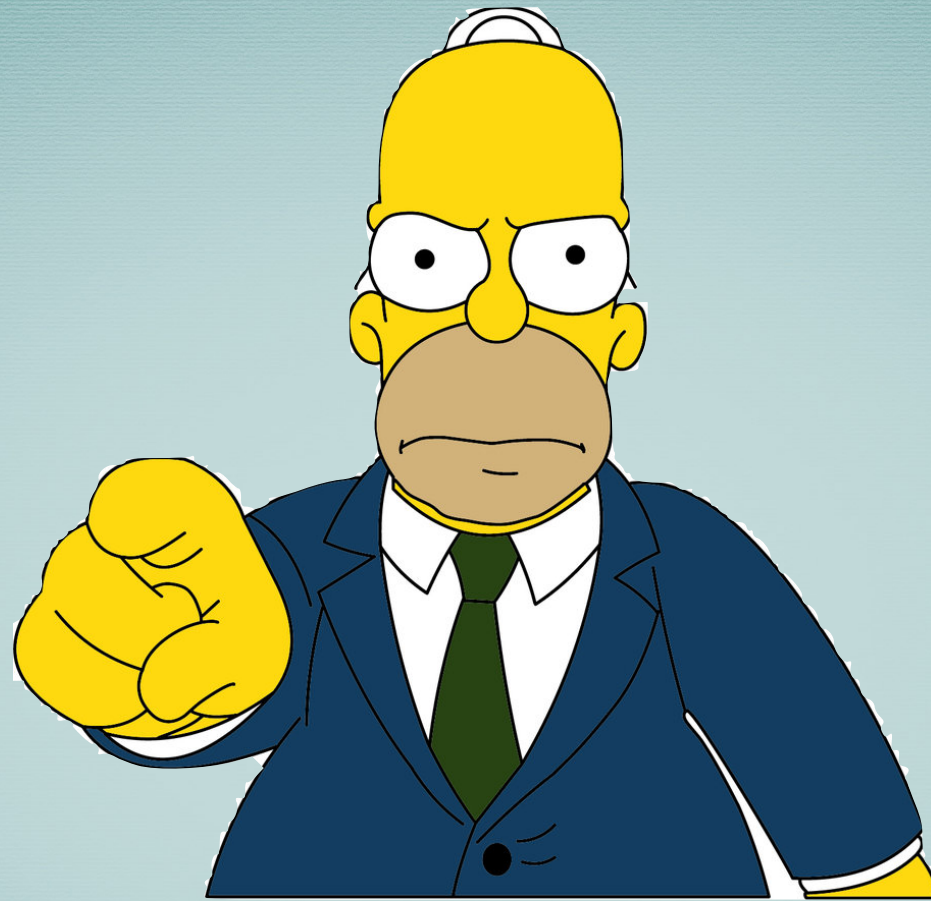
Diagnosis

Prediction



ALK, RET, ROS1, and NTRK1 fusion transcripts, in addition to targets designed to detect 5' and 3' ALK gene expression

KRAS, EGFR, BRAF, PIK3CA, AKT1, ERBB2, PTEN, NRAS, STK11, MAP2K1, ALK, DDR2, CTNNB1, MET, TP53, SMAD4, FBX7, FGFR3, NOTCH1, ERBB4, FGFR1, FGFR2



Take home message



Cytology Rocks

