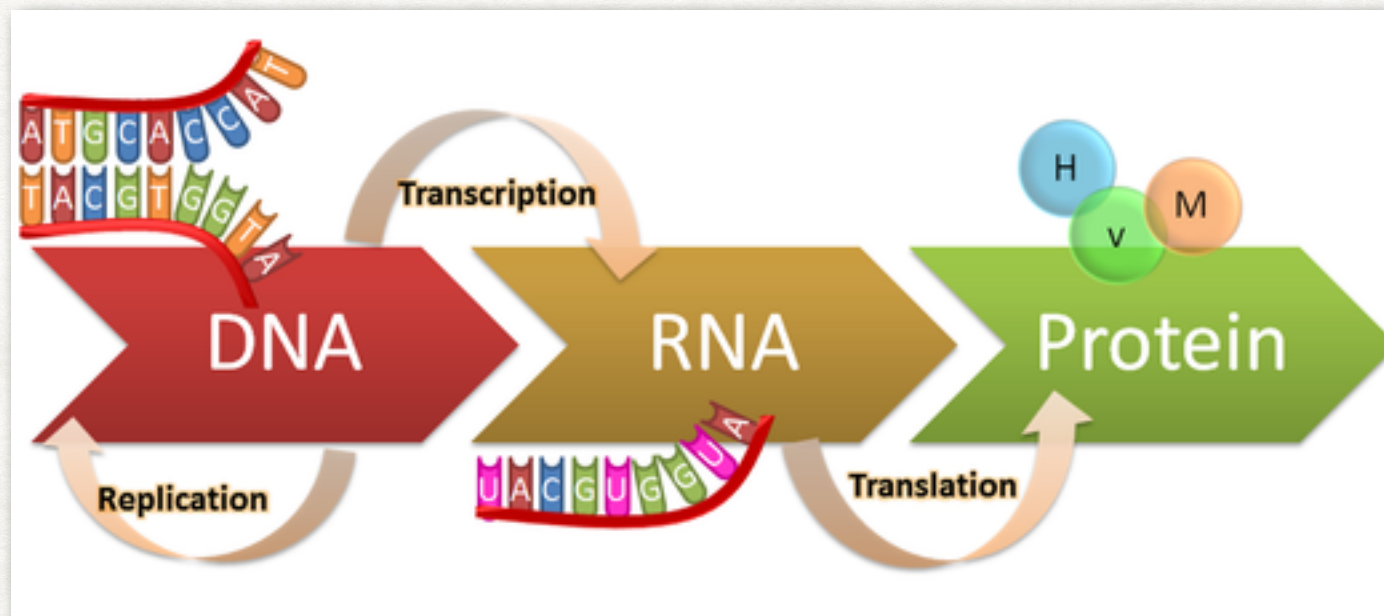


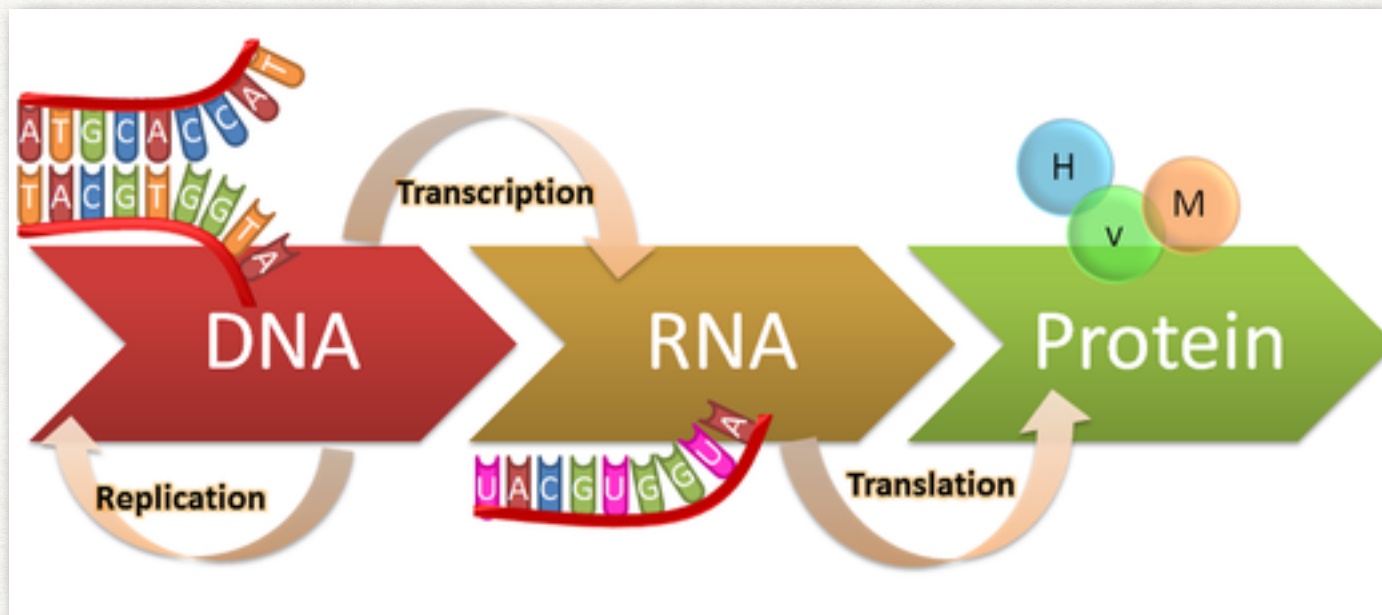
Predictive, diagnostic and prognostic markers

The central dogma



Predictive, diagnostic and prognostic markers

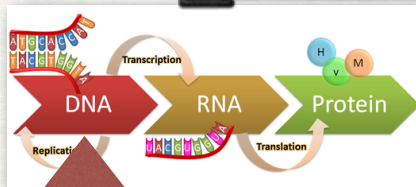
The central dogma



In-situ hybridization
Molecular methods (PCR, SEQ)

Immunohistochemistry

Predictive, diagnostic and prognostic markers



How do oncogenes and tumor suppressors work?

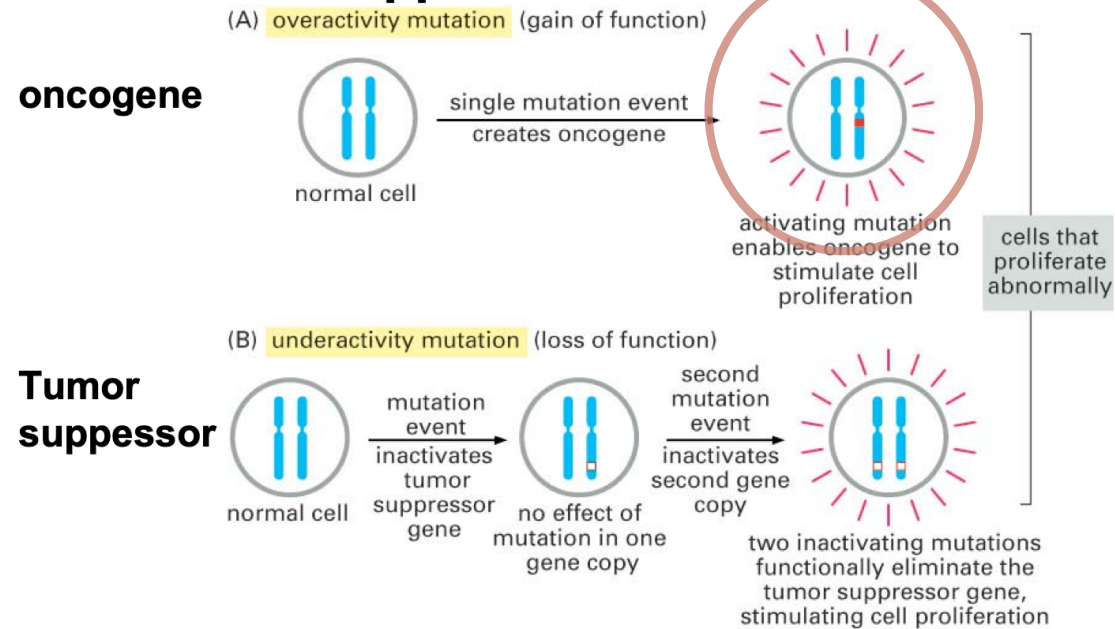
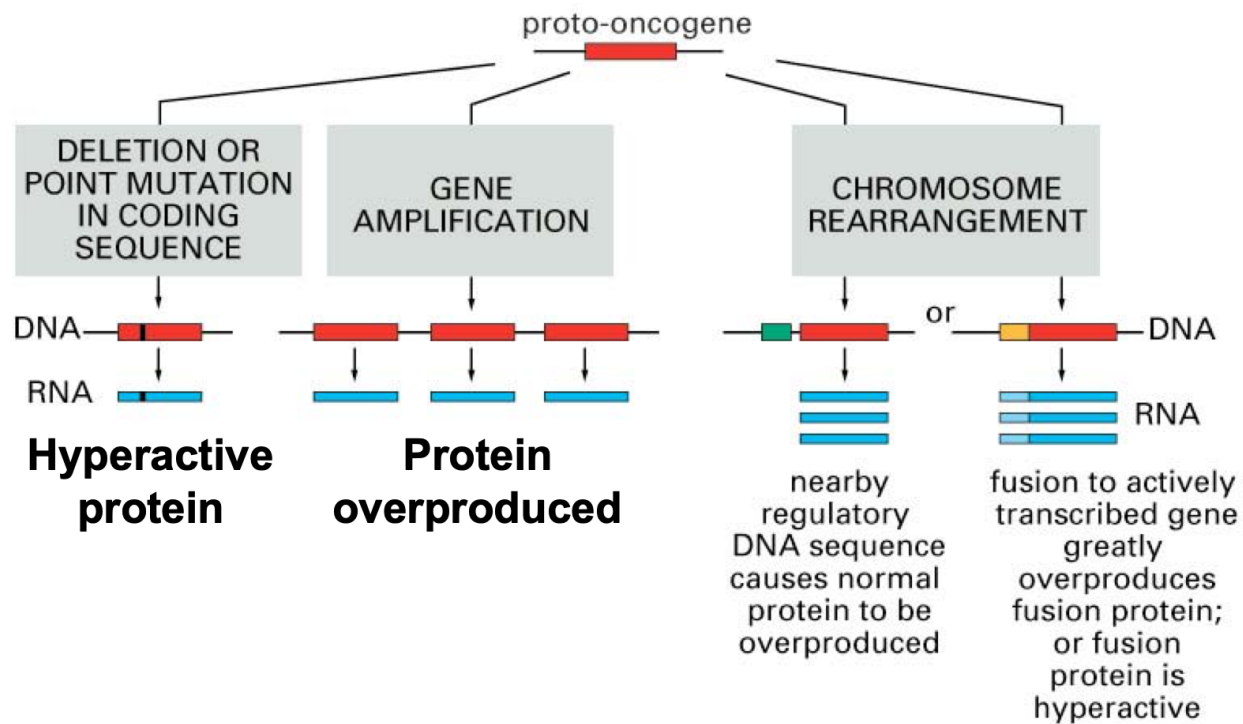
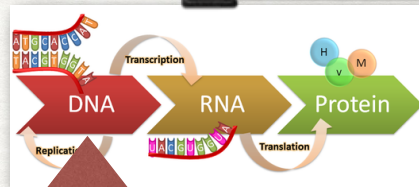
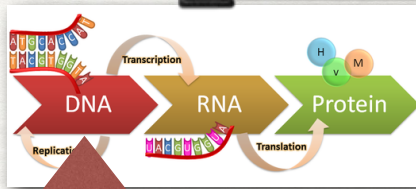


Figure 23–24. Molecular Biology of the Cell, 4th Edition.

Predictive, diagnostic and prognostic markers



Predictive, diagnostic and prognostic markers



How do oncogenes and tumor suppressors work?

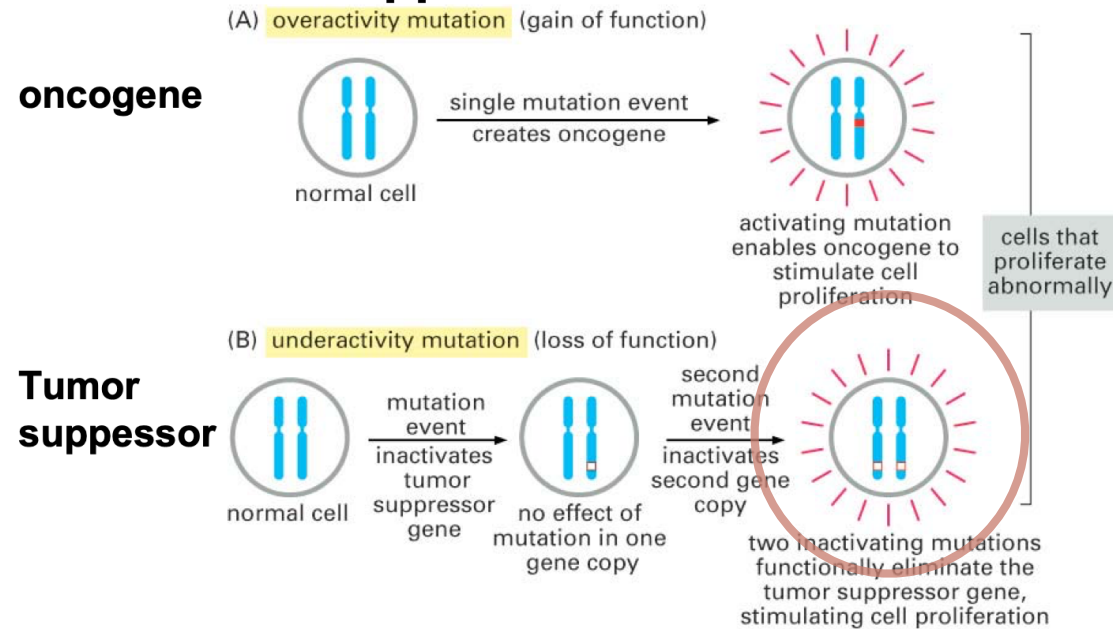
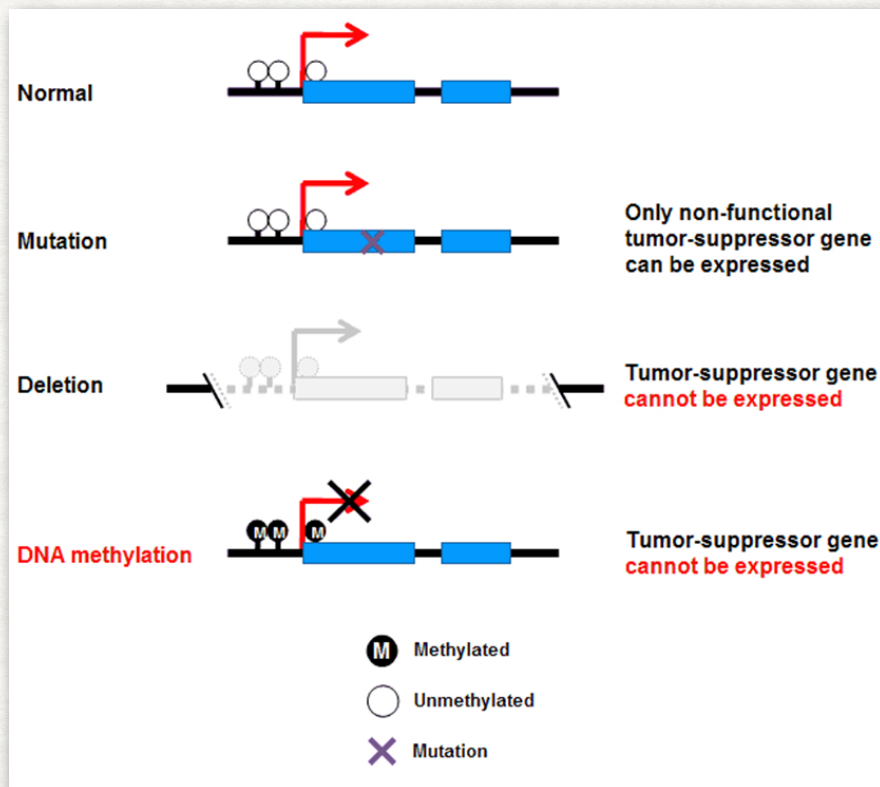
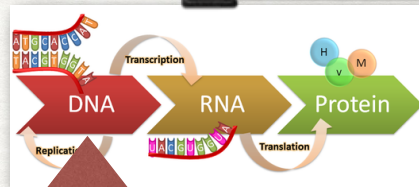
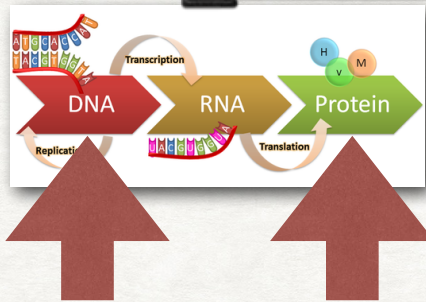


Figure 23–24. Molecular Biology of the Cell, 4th Edition.

Predictive, diagnostic and prognostic markers



Predictive, diagnostic and prognostic markers



Mutation

Translocation

Deletion

Amplification

Methylation

Changed protein

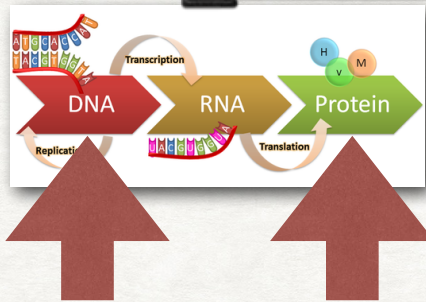
Absence of protein

Abnormal localisation

Over expression

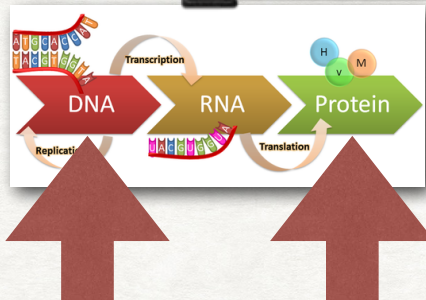
Fusion protein

Predictive, diagnostic and prognostic markers



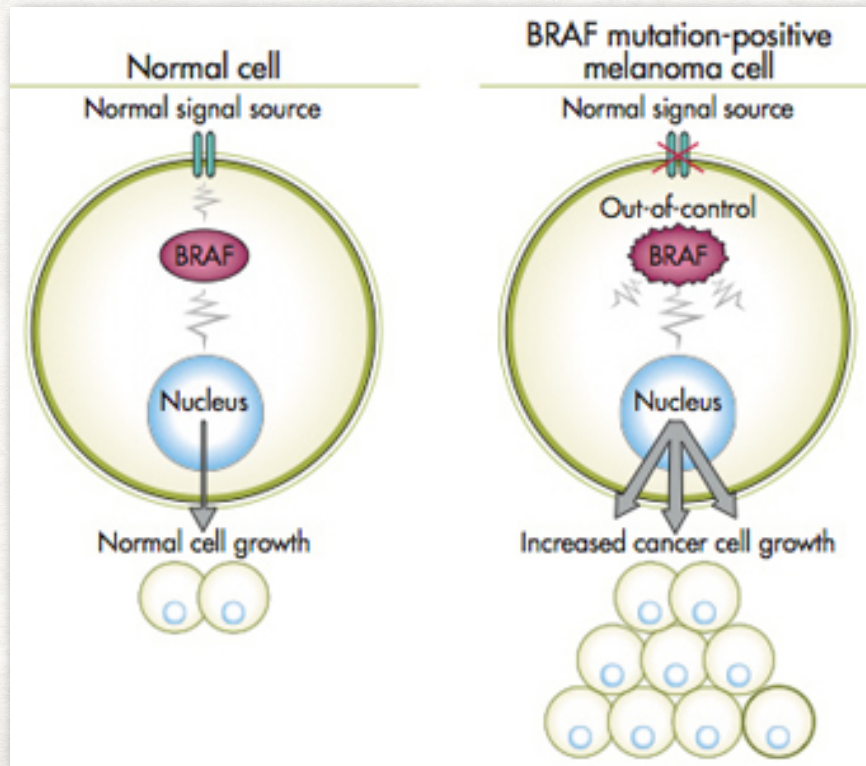
Mutation	→	Changed protein
Translocation		Absence of protein
Deletion		Abnormal localisation
Amplification		Over expression
Methylation		Fussion protein

Predictive, diagnostic and prognostic markers

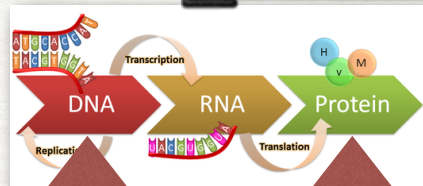


Mutated protein (auto activated)

Melanoma BRAF mutation

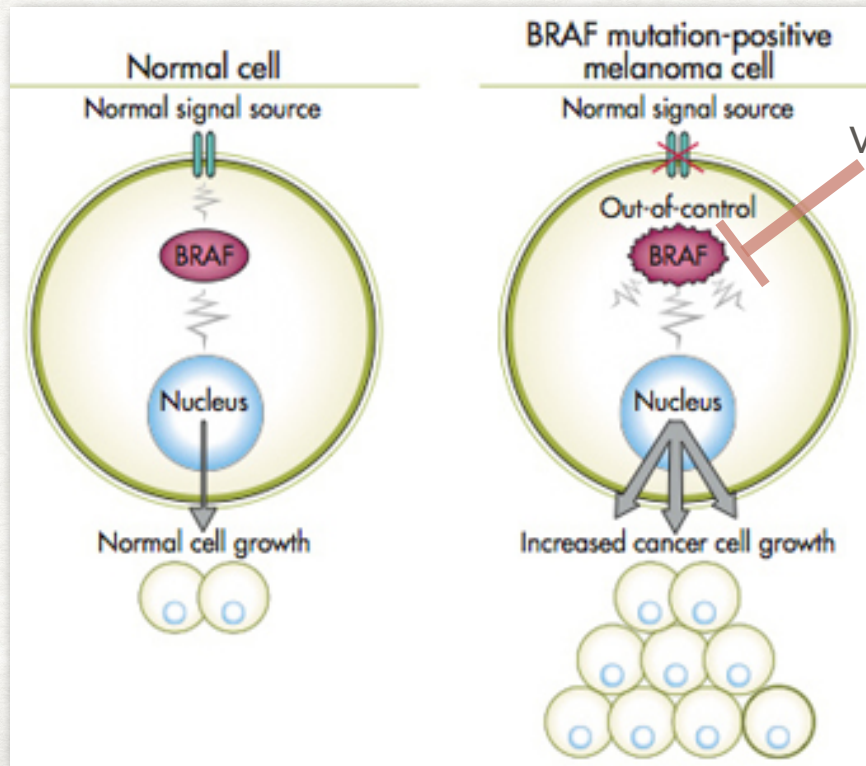


Predictive, diagnostic and prognostic markers

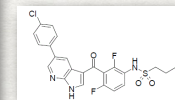


Mutated protein (auto activated)

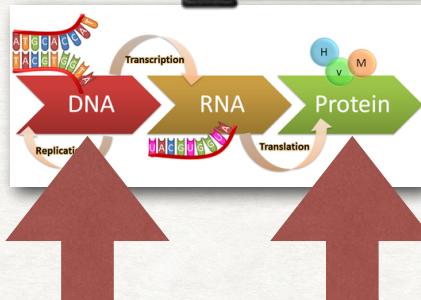
Melanoma BRAF mutation



Vemurafinib

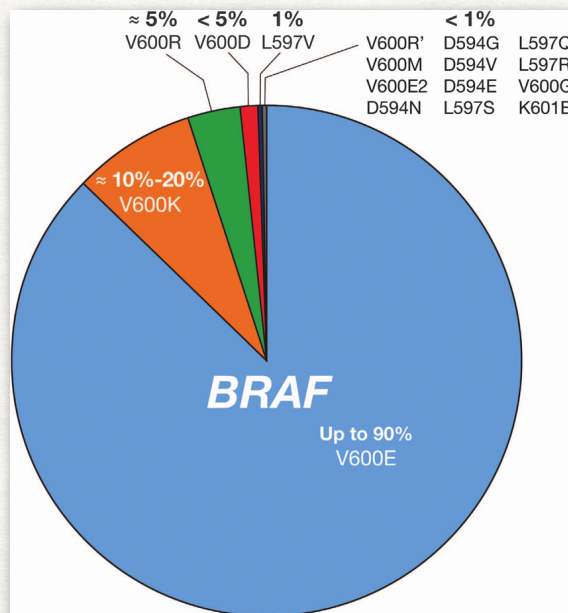


Predictive, diagnostic and prognostic markers



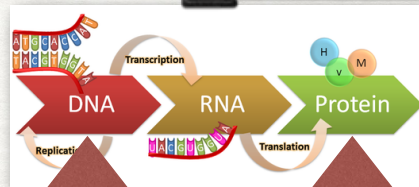
Mutated protein (auto activated)

Melanoma BRAF mutation



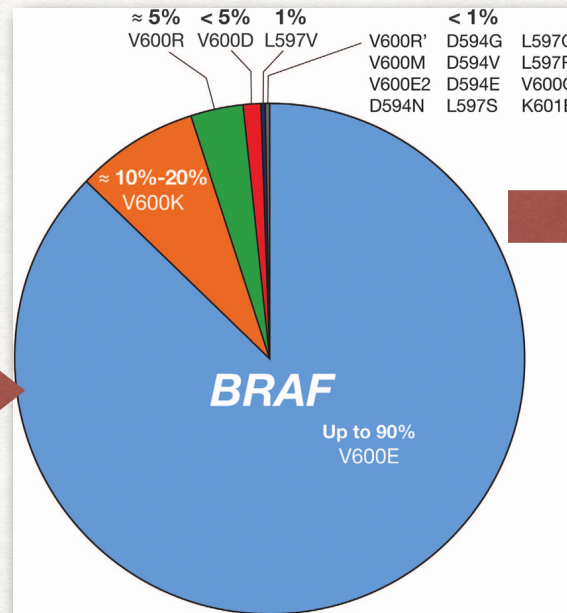
WT: GTG (valin)
V600E: GAG (glutamat)
V600K: AAG (lysin)
V600R: AGG (Arginin)

Predictive, diagnostic and prognostic markers



Mutated protein (auto activated)

Melanoma BRAF mutation



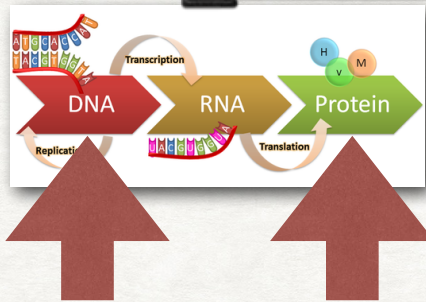
WT: GTG (valin)

V600E: GAG (glutamat)

V600K: AAG (lysin)

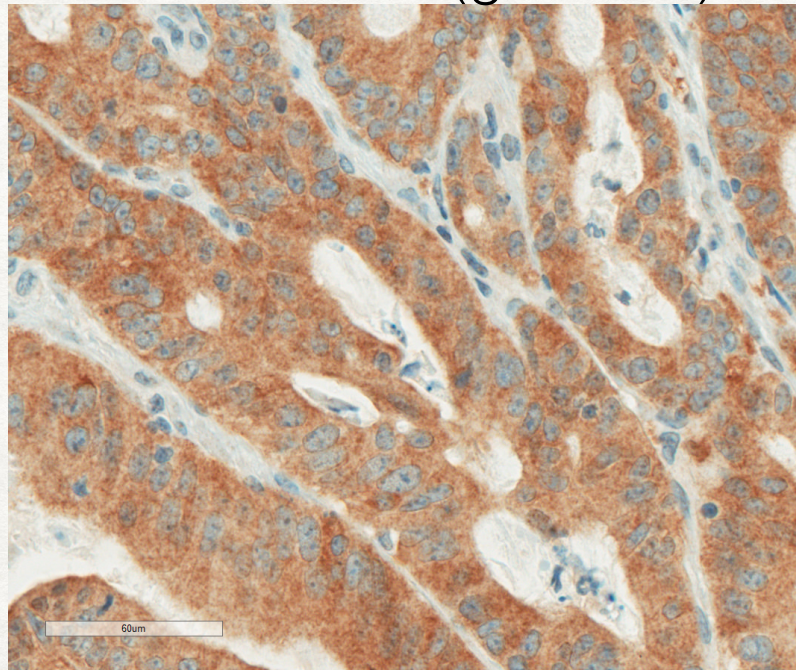
V600R: AGG (Arginin)

Predictive, diagnostic and prognostic markers



Mutated protein (auto activated)

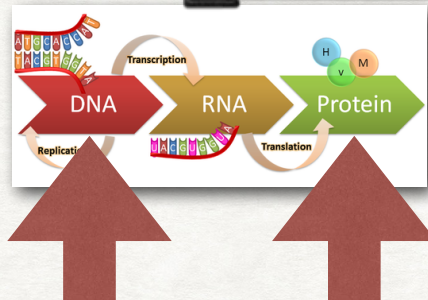
V600E: GAG (glutamat)



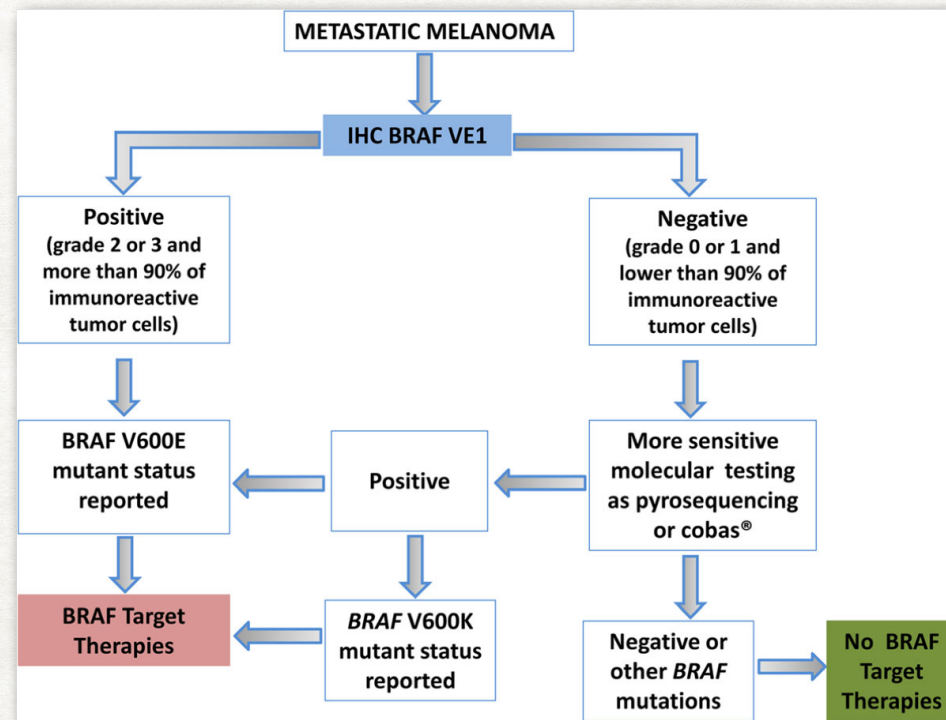
BRAF V600E (VE1)
Mouse Monoclonal Primary Antibody



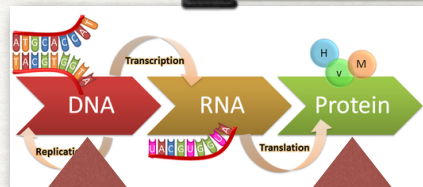
Predictive, diagnostic and prognostic markers



Mutated protein (auto activated)



Predictive, diagnostic and prognostic markers



Mutated protein (auto activated)

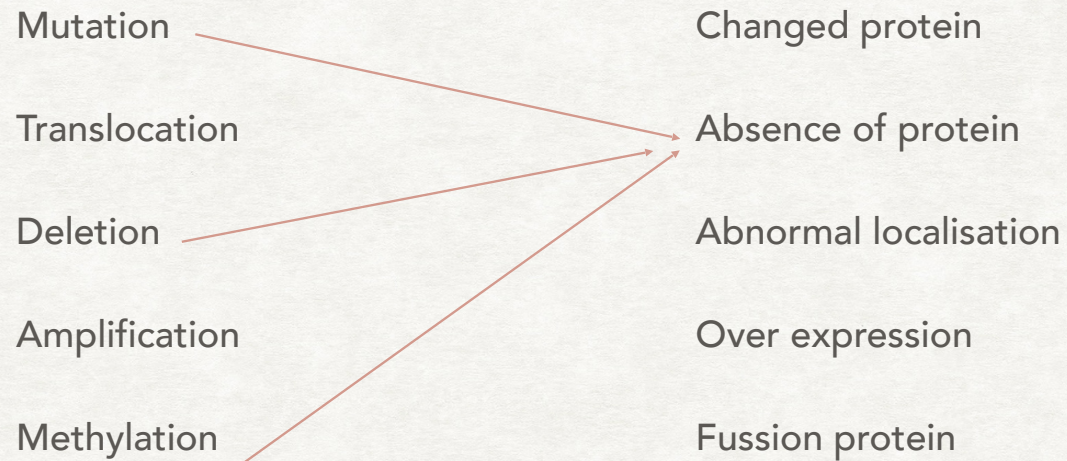
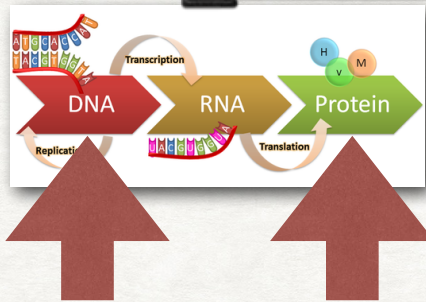


Immunohistochemistry
BRAF V600E

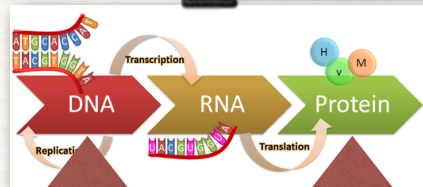


Mutation analysis of BRAF gene

Predictive, diagnostic and prognostic markers



Predictive, diagnostic and prognostic markers



Often combination of
Deletion
Mutation
Methylation

How do oncogenes and tumor suppressors work?

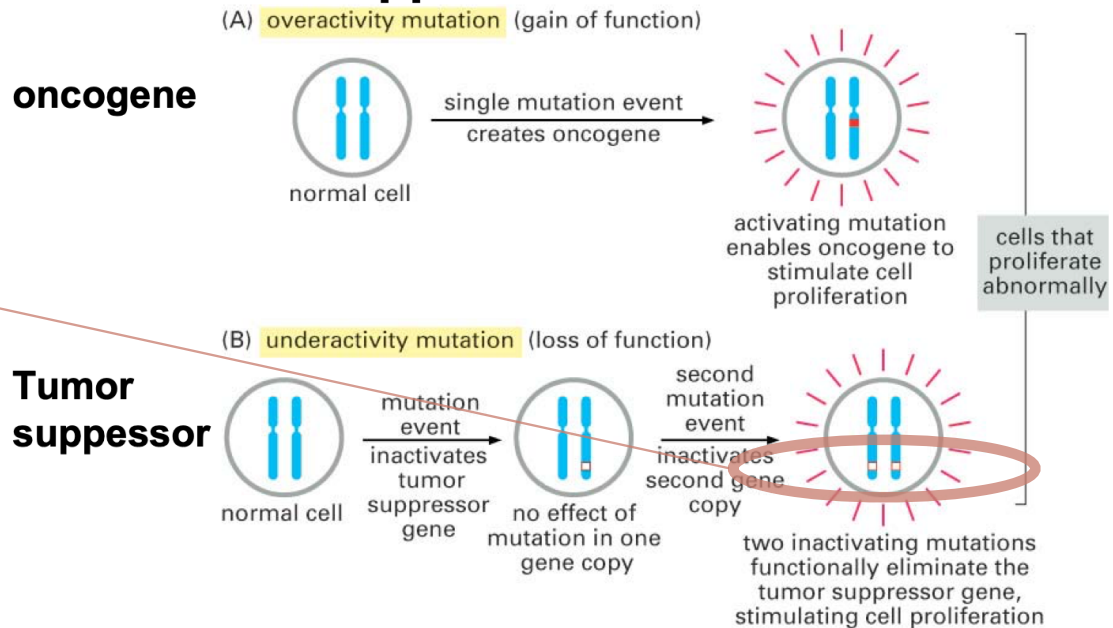
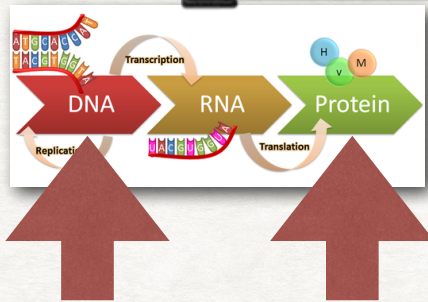
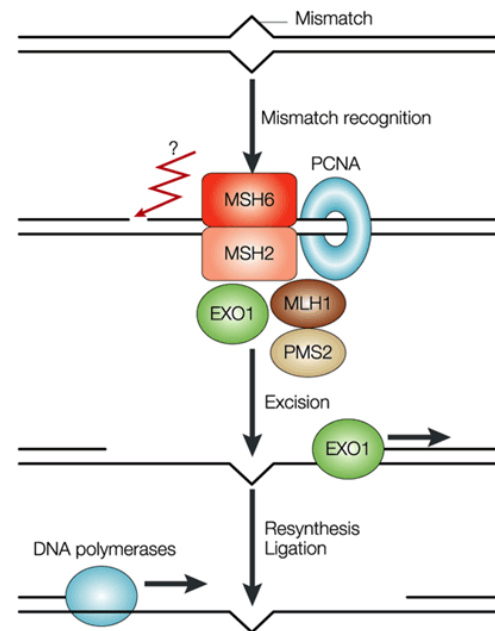


Figure 23-24. Molecular Biology of the Cell, 4th Edition.

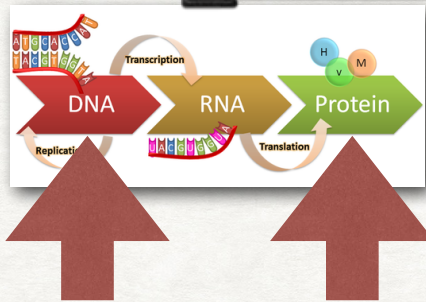
Predictive, diagnostic and prognostic markers



Absence of protein



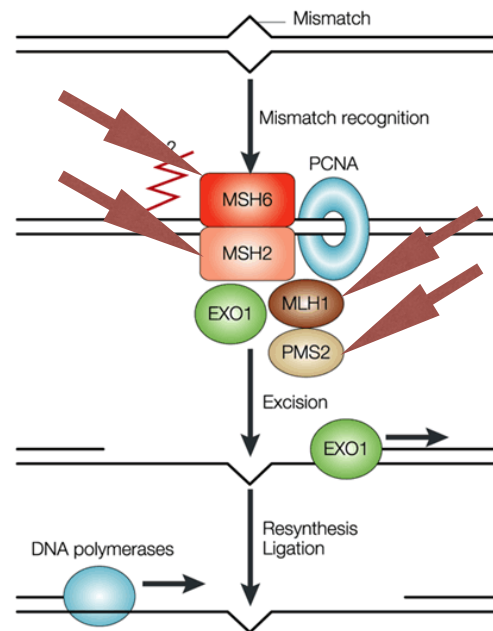
Predictive, diagnostic and prognostic markers



Absence of protein

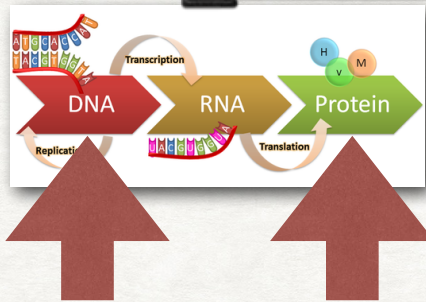
→
Mutation
(Methylation)

Mismatch Repair deficiency
Microsatellite instability



Nature Reviews | Immunology

Predictive, diagnostic and prognostic markers

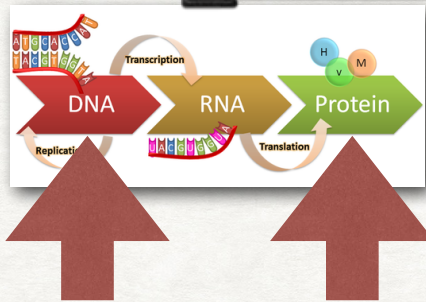


Absence of protein

Identify colon cancer patients with inherited colon cancer (Lynch syndrome)

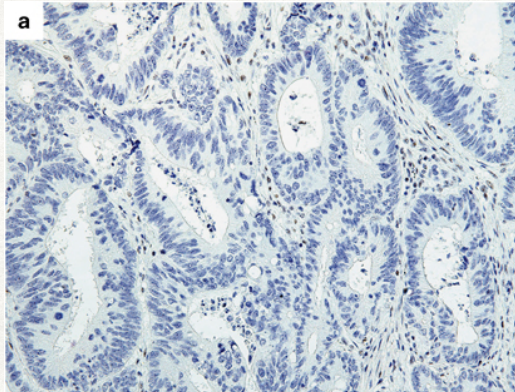
Identify patients with sporadic MSI colon cancers

Predictive, diagnostic and prognostic markers

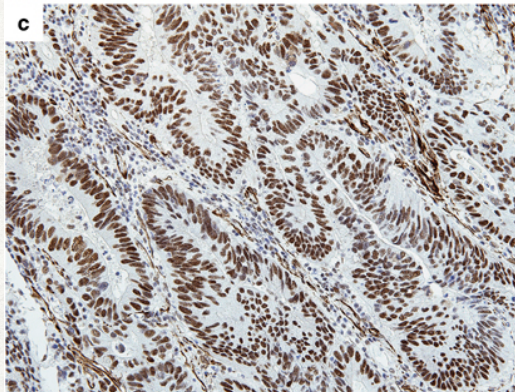
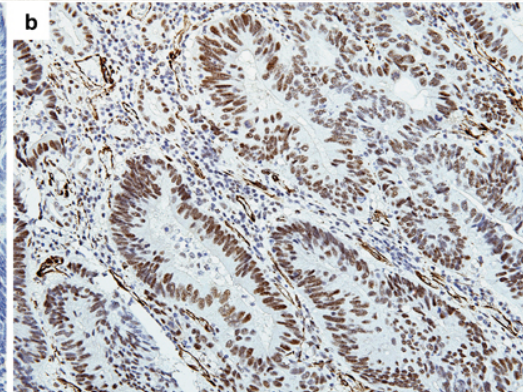


Absence of protein

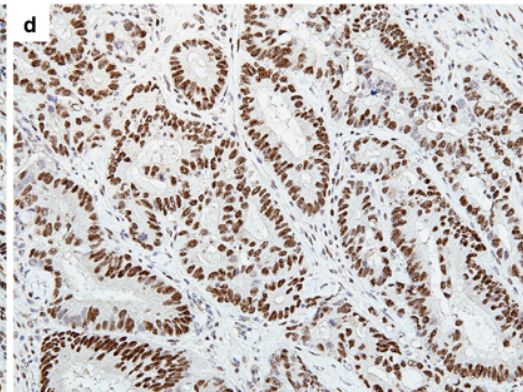
MLH1



MLH6

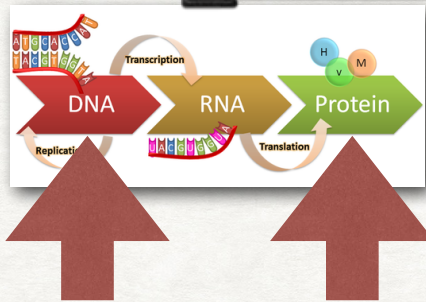


PMS2



MSH6

Predictive, diagnostic and prognostic markers

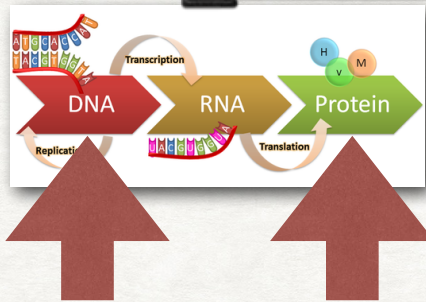


Immunohistochemistry
of MLH1, PMS2, MLH6 and MSH2



Mutation of MLH1, PMS2, MLH6 and MSH2 genes
Measurement of length of Microsatellites

Predictive, diagnostic and prognostic markers



Mutation

Translocation

Deletion

Amplification

Methylation

Changed protein

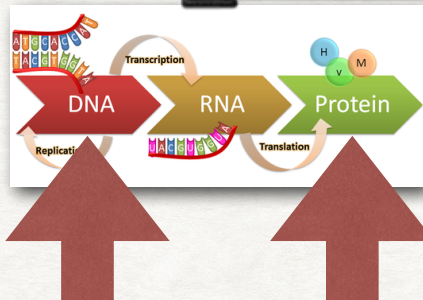
Absence of protein

Abnormal localisation

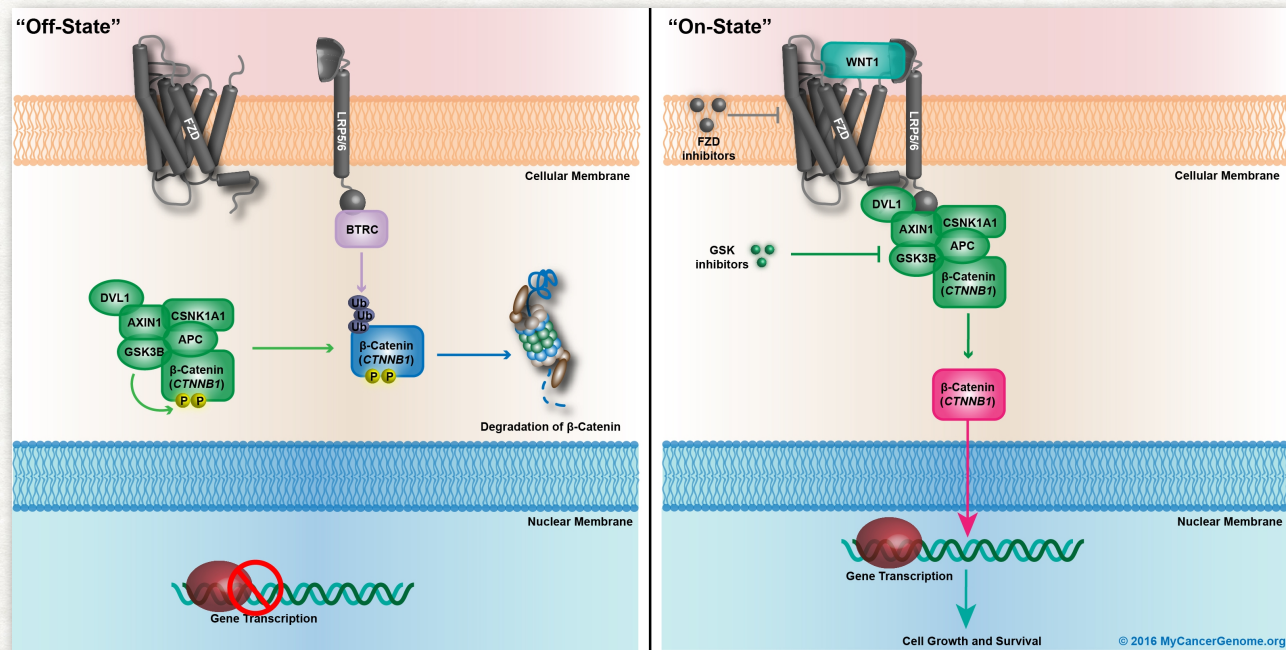
Over expression

Fusion protein

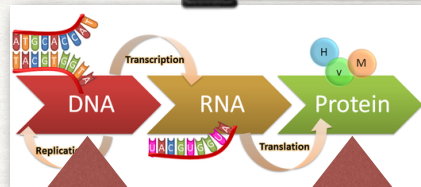
Predictive, diagnostic and prognostic markers



Abnormal localisation

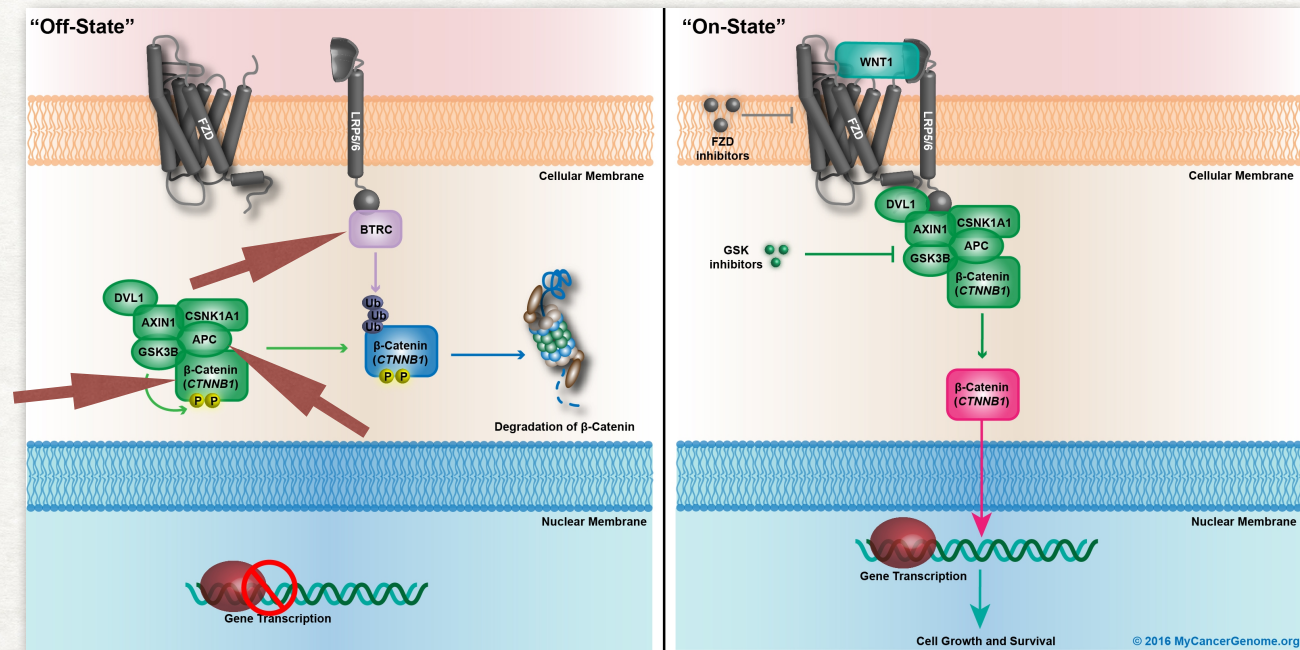


Predictive, diagnostic and prognostic markers

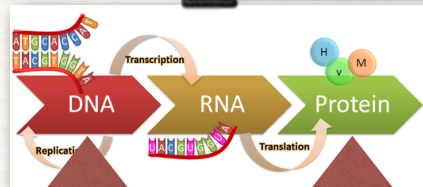


Abnormal localisation

Mutations

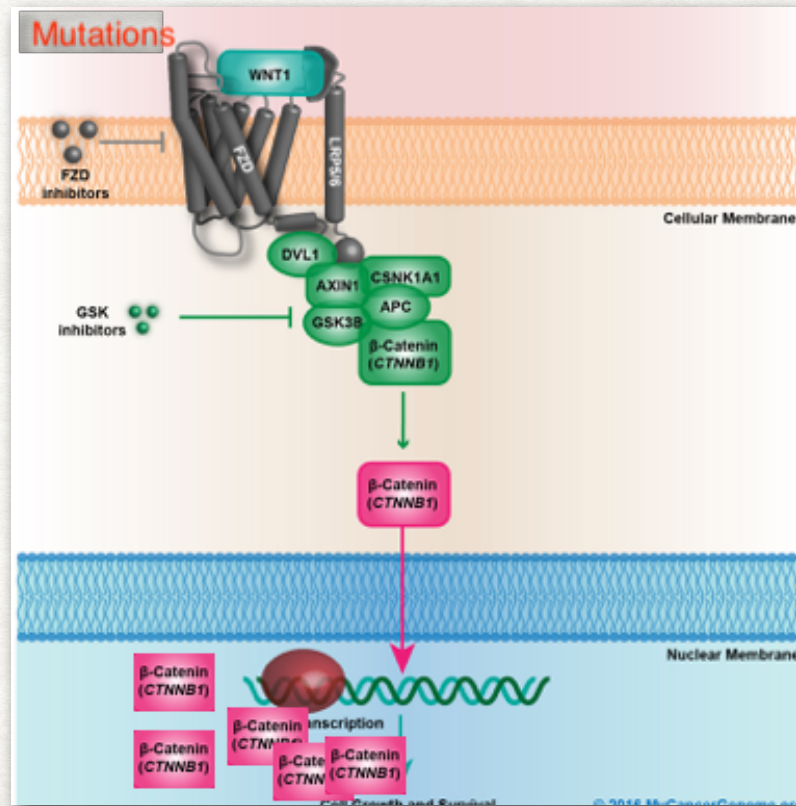


Predictive, diagnostic and prognostic markers

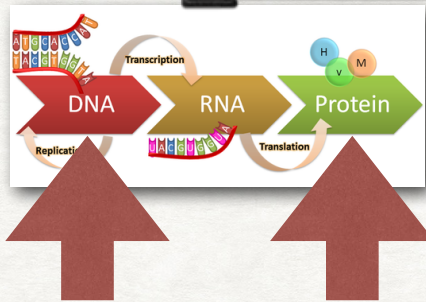


Abnormal localisation

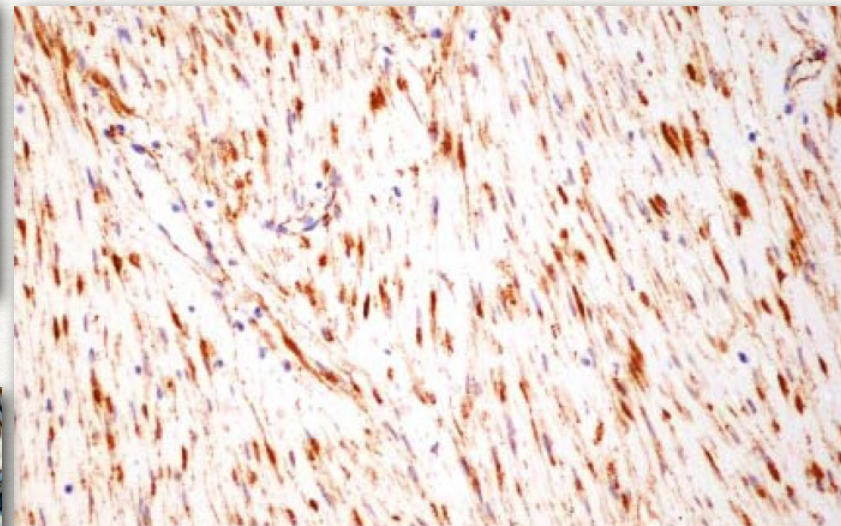
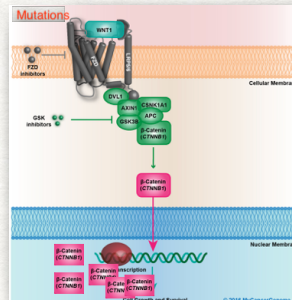
→
Mutations



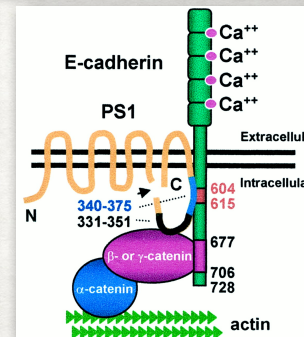
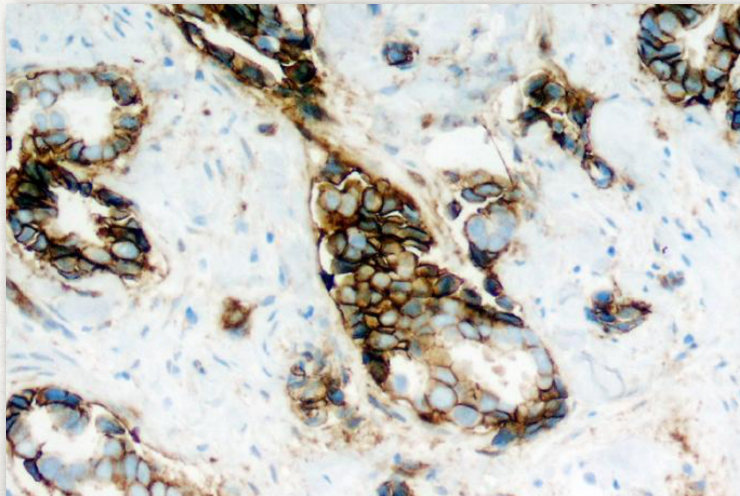
Predictive, diagnostic and prognostic markers



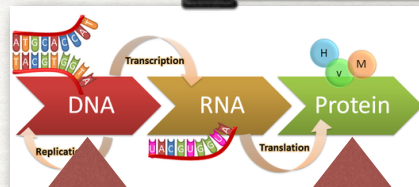
Abnormal localisation



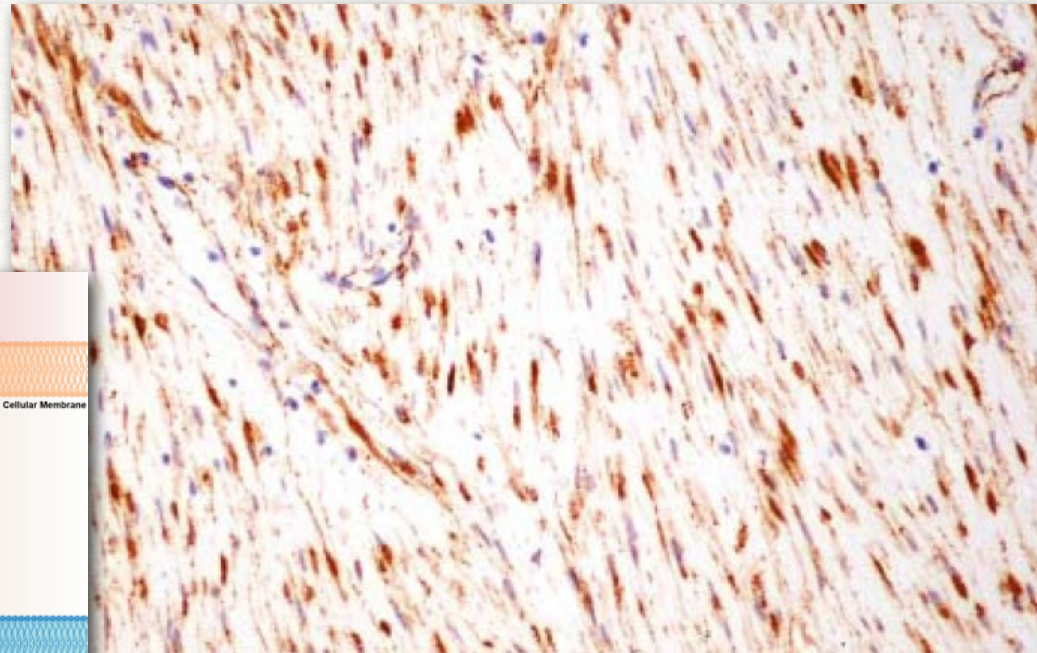
Normal lokalisation



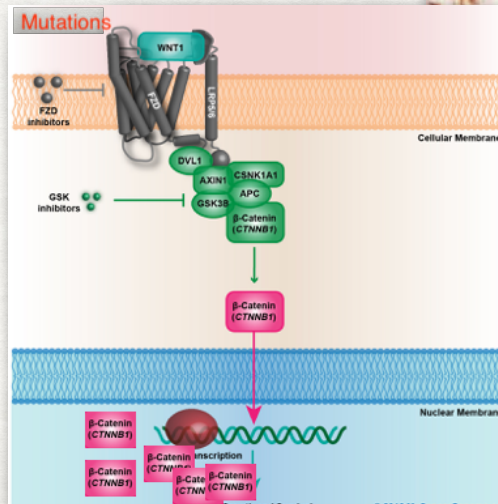
Predictive, diagnostic and prognostic markers



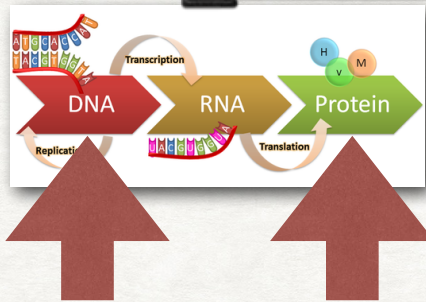
Abnormal localisation



Aggressive fibromatosis



Predictive, diagnostic and prognostic markers

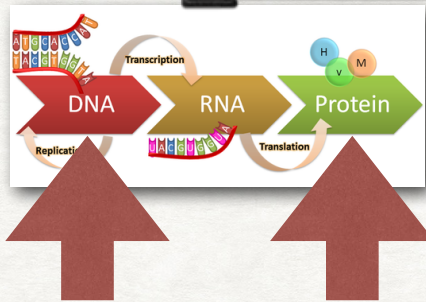


Immunohistochemistry
of B-catenin



Mutations of B-catenin, APC og BTRC

Predictive, diagnostic and prognostic markers



Mutation

Translocation

Deletion

Amplification

Methylation

Changed protein

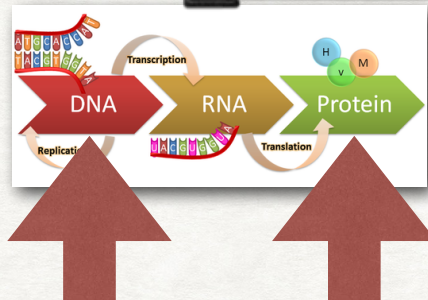
Absence of protein

Abnormal localisation

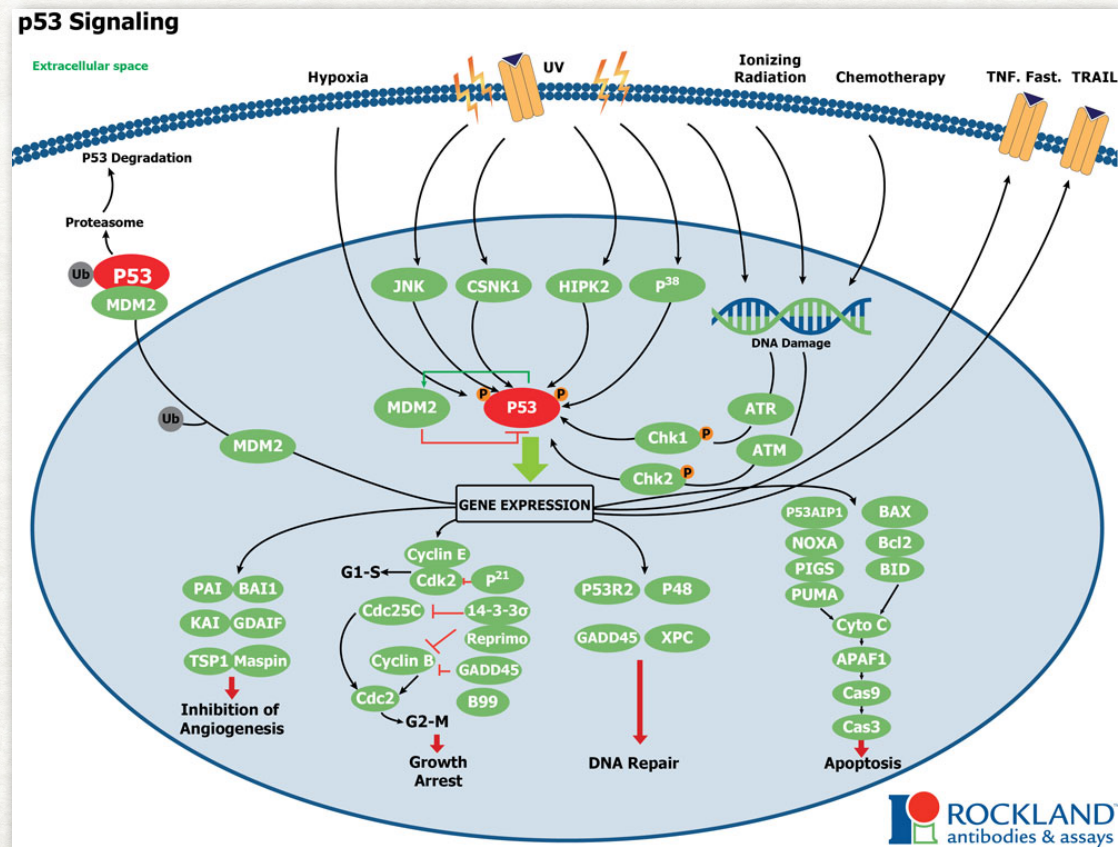
Over expression

Fusion protein

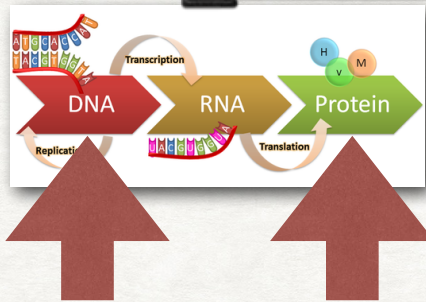
Predictive, diagnostic and prognostic markers



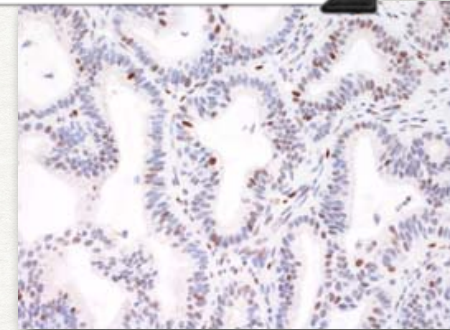
Over ekspression



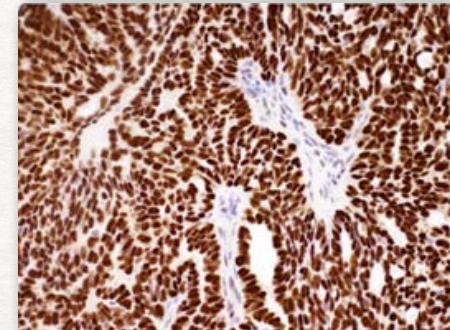
Predictive, diagnostic and prognostic markers



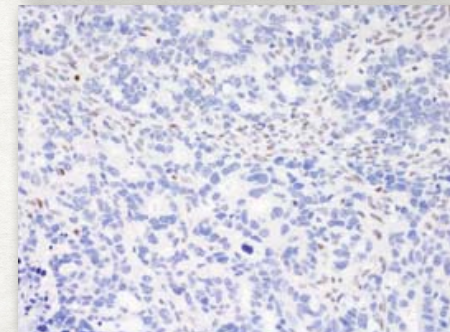
Normal expression



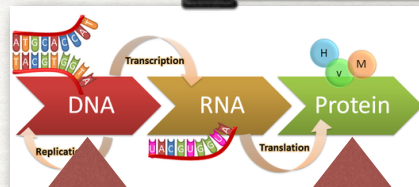
Some mutations cause (besides inactivation) that the P53 protein does not degrade and accumulates in the nucleus



Large deletions cause lack of protein expression



Predictive, diagnostic and prognostic markers



Journal of Pathology

J Pathol 2010; **222**: 191–198

Published online 13 July 2010 in Wiley Online Library

(wileyonlinelibrary.com) DOI: 10.1002/path.2744

ORIGINAL PAPER

The biological and clinical value of p53 expression in pelvic high-grade serous carcinomas

Martin Köbel,¹ Alexander Reuss,² Andreas du Bois,³ Stefan Kommoss,³ Friedrich Kommoss,³ Dongxia Gao,⁴ Steve E Kalloger,⁴ David G Huntsman⁴ and C Blake Gilks^{1*}

¹ Department of Pathology and Laboratory Medicine, Calgary Laboratory Services/Alberta Health Services and University of Calgary, Canada

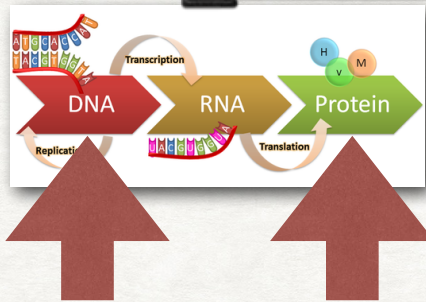
² Coordinating Centre for Clinical Trials (KKS), University Marburg (AGO-OVAR Statistical Centre), Germany

³ Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe (AGO-OVAR), Germany

⁴ Genetic Pathology Evaluation Centre of the Prostate Research Centre, Department of Pathology, Vancouver General Hospital and British Columbia Cancer Agency, Vancouver, BC, Canada

stage, residual tumour, and stratification by cohort. The association of complete absence of p53 expression with unfavourable outcome suggests functional differences of *TP53* mutations underlying overexpression, compared to those underlying complete absence of expression.

Predictive, diagnostic and prognostic markers

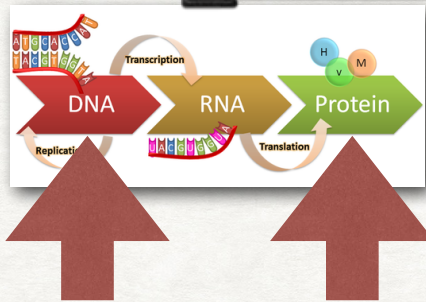


Immunohistochemistry
of p53



NGS of the p53 gene

Predictive, diagnostic and prognostic markers



Mutation

Translocation

Deletion

Amplification

Methylation

Changed protein

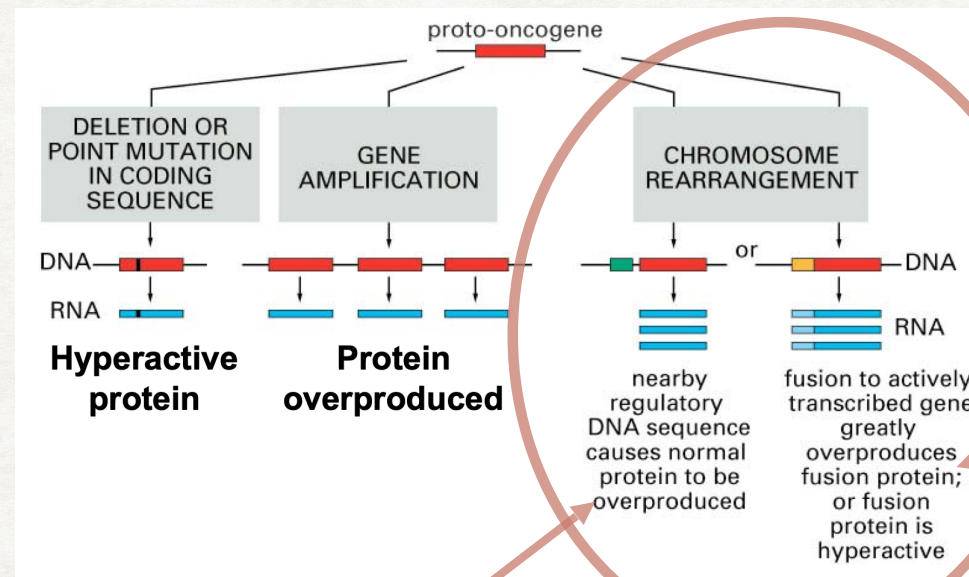
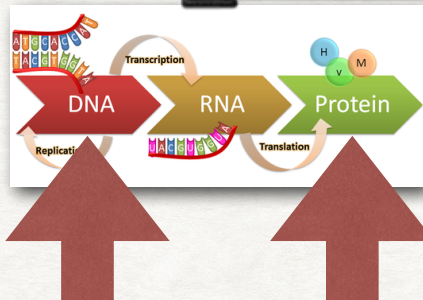
Absence of protein

Abnormal localisation

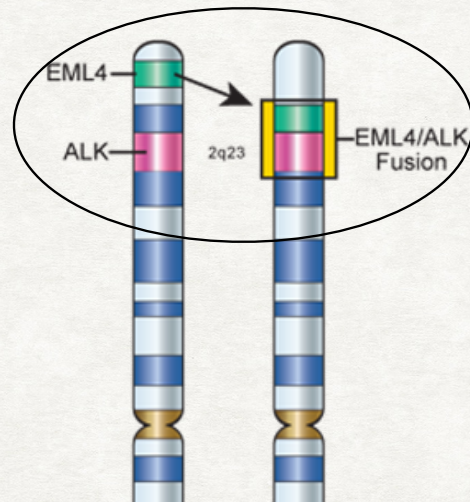
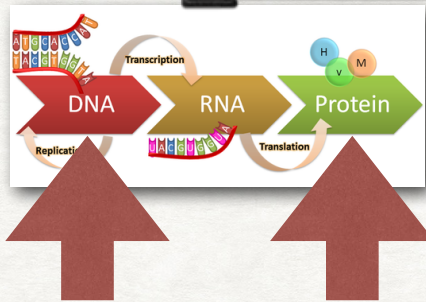
Over expression

Fusion protein

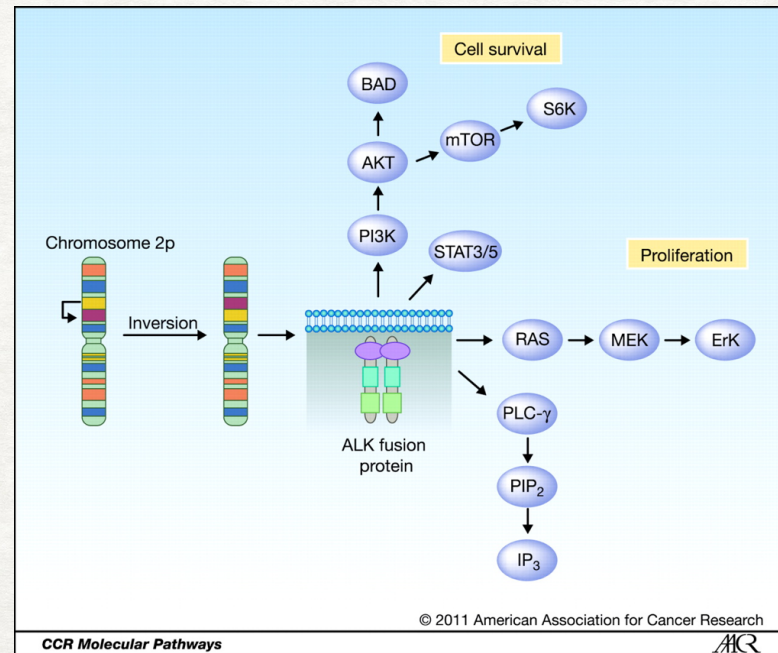
Predictive, diagnostic and prognostic markers



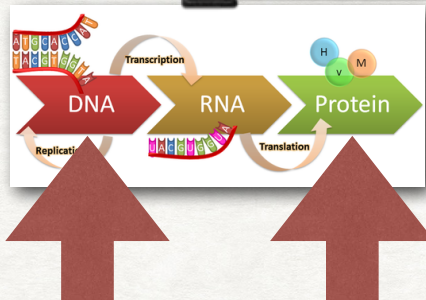
Predictive, diagnostic and prognostic markers



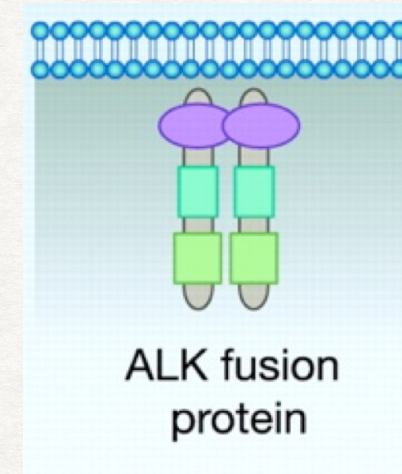
Lunge adenocarcinomer



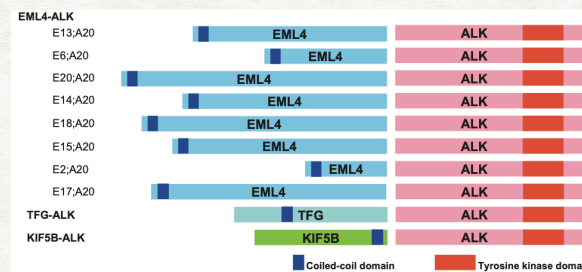
Predictive, diagnostic and prognostic markers



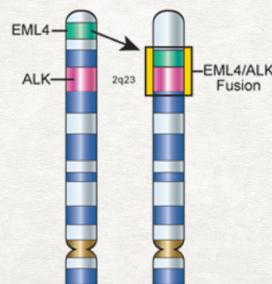
Detektion af fusion protein



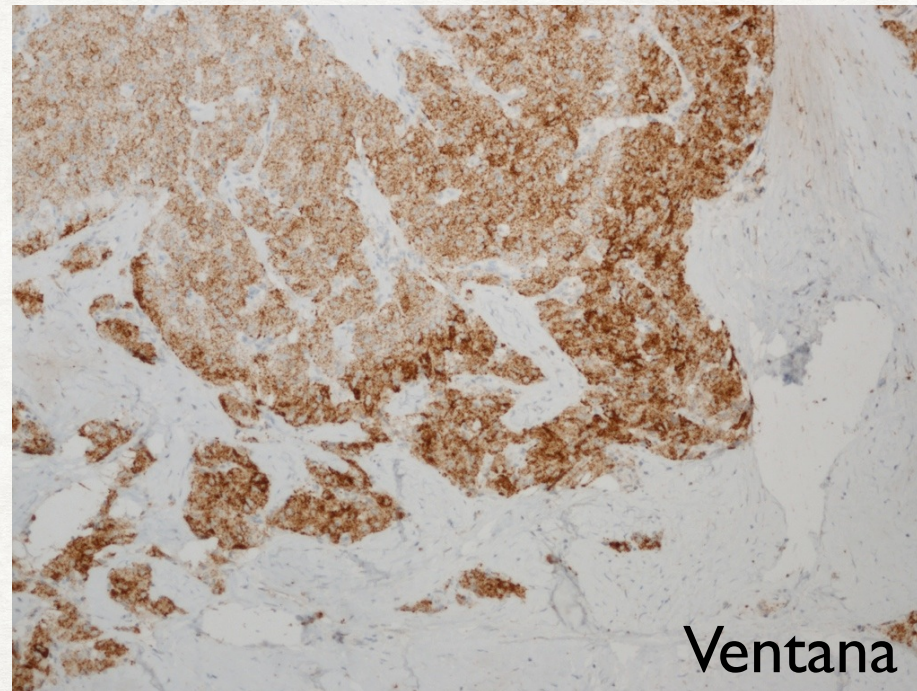
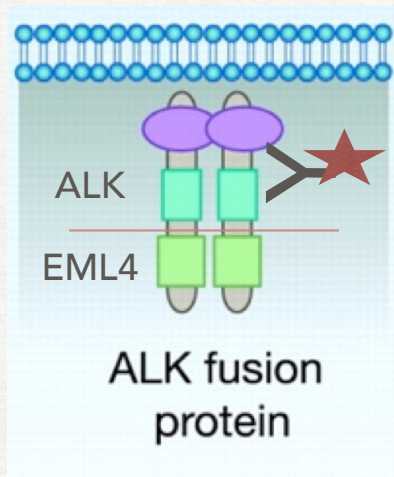
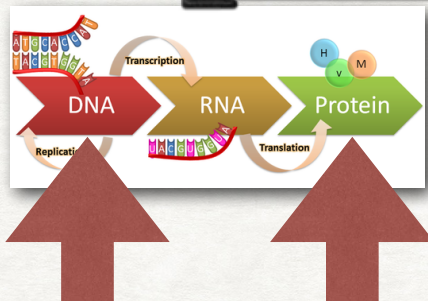
Detektion af fusions RNA



Detektion af chromosomale Forandringer



Predictive, diagnostic and prognostic markers



Ventana

Detects ALK independent of fusion partner

Predictive, diagnostic and prognostic markers

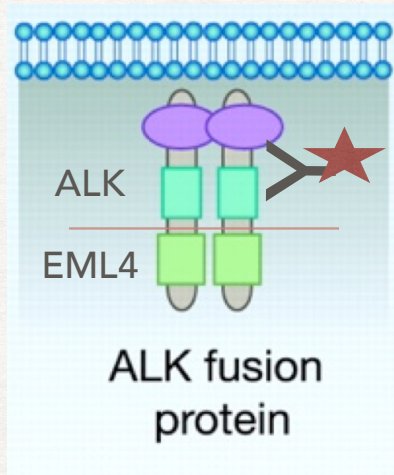
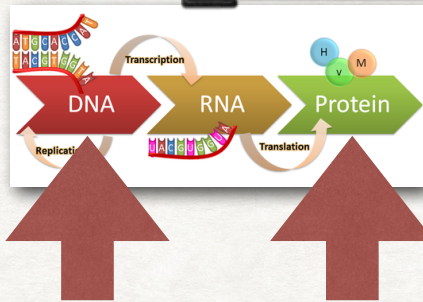
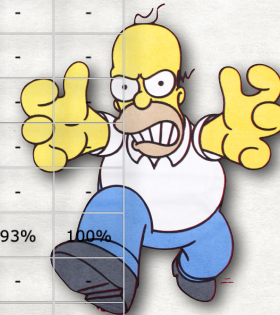


Table 1. Antibodies and assessment marks for lu-ALK, run 51

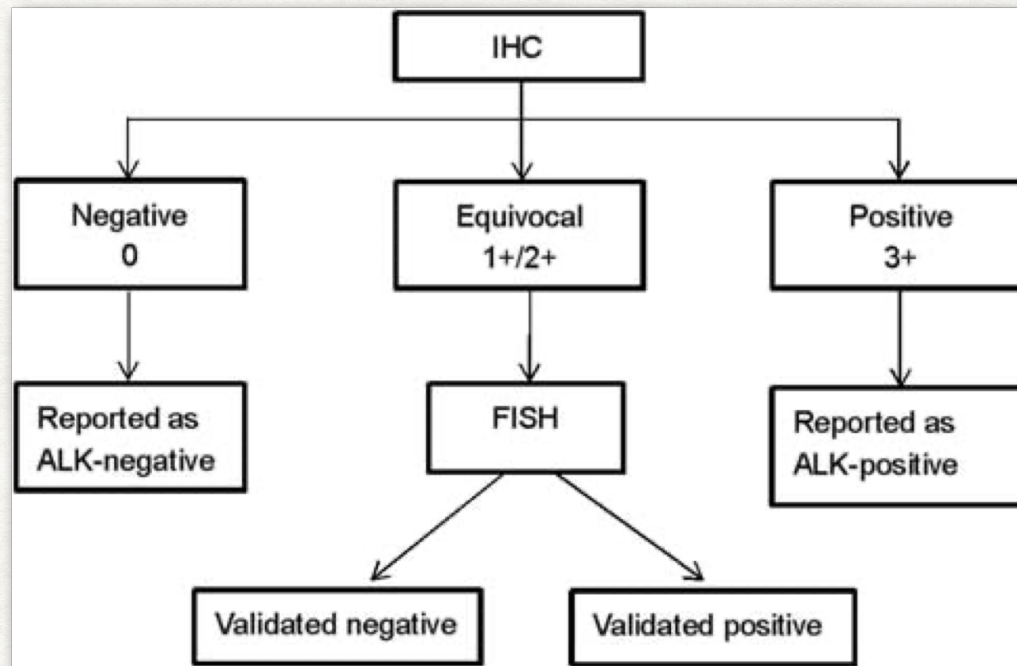
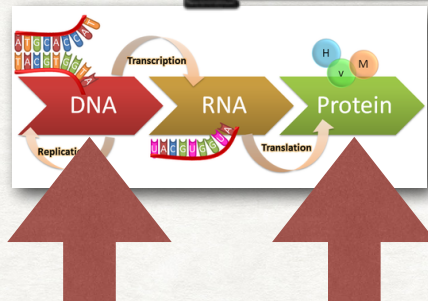
Concentrated antibodies	n	Vendor	Optimal	Good	Borderline	Poor	Suff. ¹	Suff. OPS ²
mAb clone 5A4	43	Leica/Novocastra						
	1	Abcam						
	1	Biocare						
	1	Monosan						
mAb clone ALK1	2	Dako						
	1	Cell Marque						
rmAb clone D5F3	23	Cell Signaling						
mAb clone OTI1A4	13	ORIGENE						
Ready-To-Use antibodies								
mAb clone 5A4 PA0306	6	Leica/Novocastra						
mAb clone 5A4 MAB-0281	1	Maixin						
mAb 5A4 MAD-001720QD	1	Master Diagnostica						
mAb clone 5A4 MS-1104-R7	1	ThermoFisher						
mAb ALK1 IR641	9	Dako						
mAb clone ALK1 GA641	4	Dako						
mAb clone ALK1 790/800-2918	7	Ventana						
rmAb clone SP8 AN770	1	BioGenex						
rmAb clone D5F3 790-4796	70	Ventana						
rmAb clone D5F3 790-4796³	2	Ventana						
mAb clone OTI1A4 8344-C010	1	Sakura Finetek						
Total	189							
Proportion								

1) Proportion of sufficient stains (optimal or good).

2) Proportion of sufficient stains with optimal protocol settings only, see below. . 3) RTU system developed for the Ventana BenchMark systems (Ultra/XT) but used by laboratories on different platforms (e.g Dako Autostainer)



Predictive, diagnostic and prognostic markers

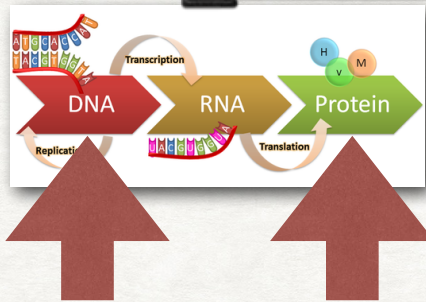


Improving Selection Criteria for ALK Inhibitor Therapy in Non-Small Cell Lung Cancer

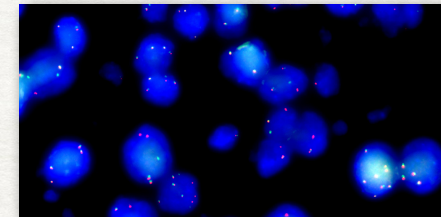
A Pooled-Data Analysis on Diagnostic Operating Characteristics of Immunohistochemistry

Long Jiang, MD, PhD,*† Haihong Yang, MD, PhD,‡ Ping He, MD, PhD,§ Wenhua Liang, MD, PhD,‡ Jianrong Zhang, MD,*† Jingpei Li, MD,*† Yang Liu, MD,*† and Jianxing He, MD, PhD, FACS*†

Predictive, diagnostic and prognostic markers

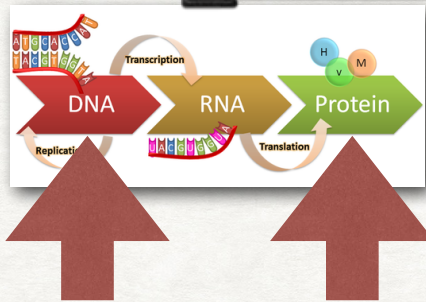


Immunohistochemistry
of ALK



Fusions RNA analysis (PCR), NGS
or FISH

Predictive, diagnostic and prognostic markers



Mutation

Changed protein

Translocation

Absence of protein

Deletion

Abnormal localisation

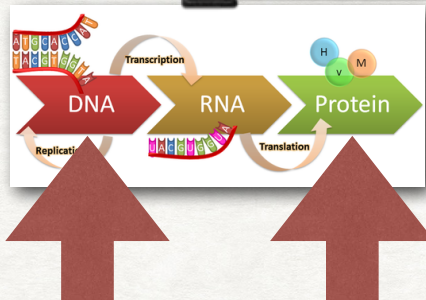
Amplification

Over expression

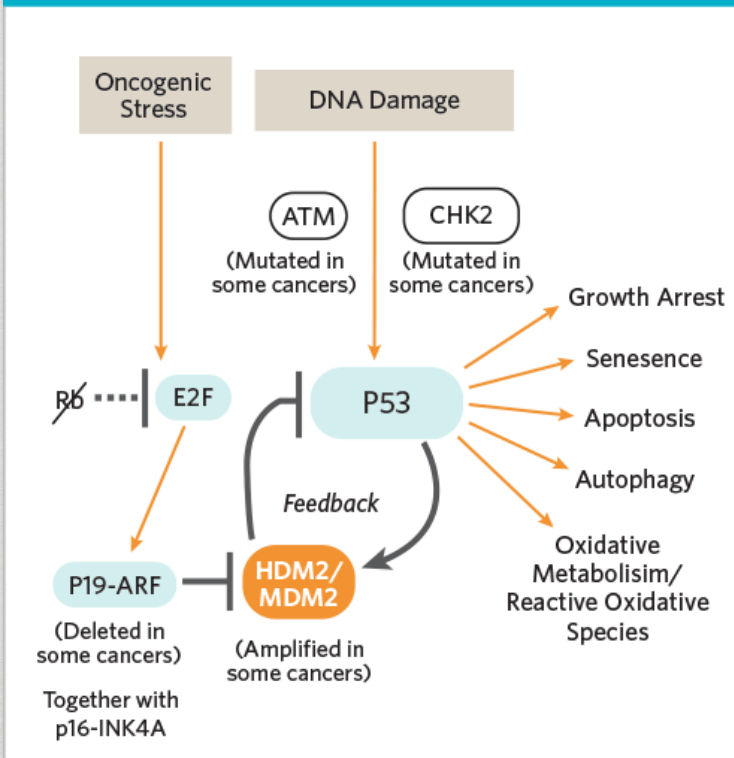
Methylation

Fusion protein

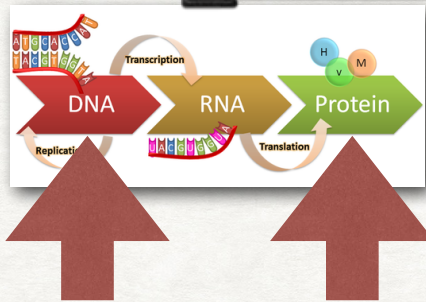
Predictive, diagnostic and prognostic markers



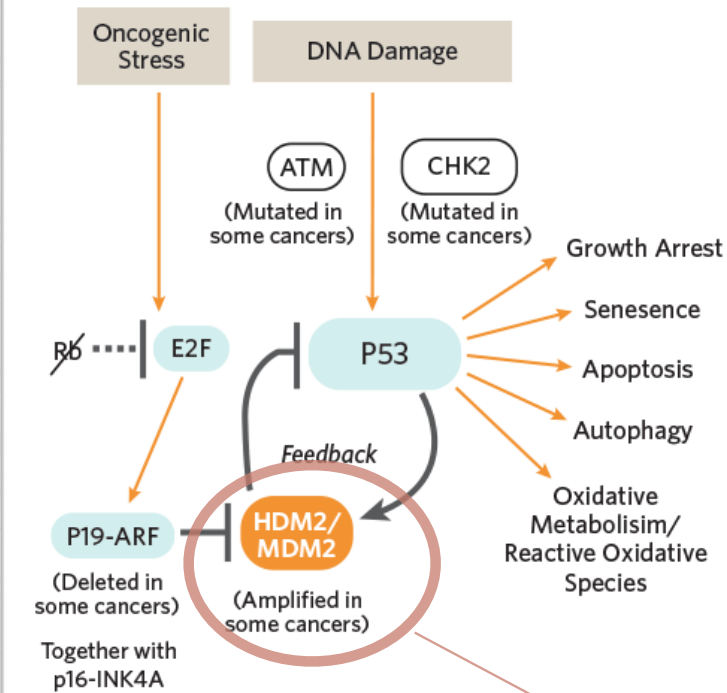
Regulator of the TP53 Tumor Suppressor- HDM2/MDM2



Predictive, diagnostic and prognostic markers

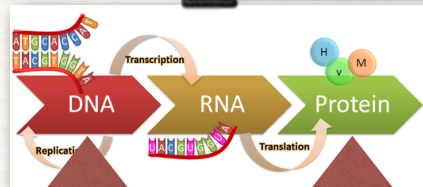


Regulator of the TP53 Tumor Suppressor- HDM2/MDM2

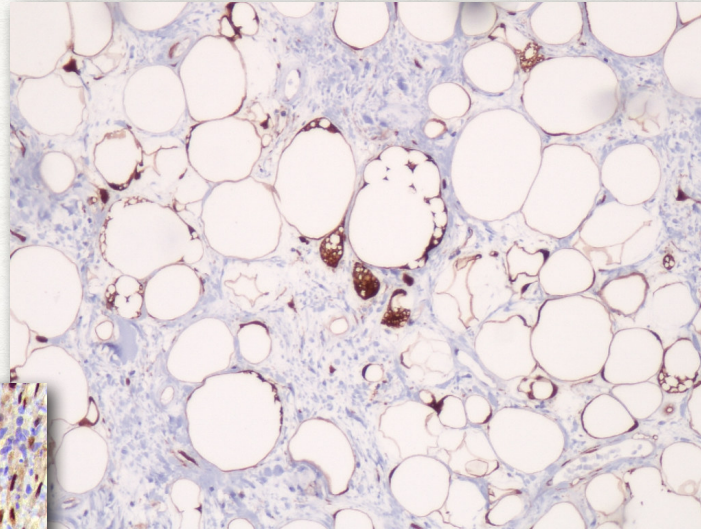


E.g. liposarcoma

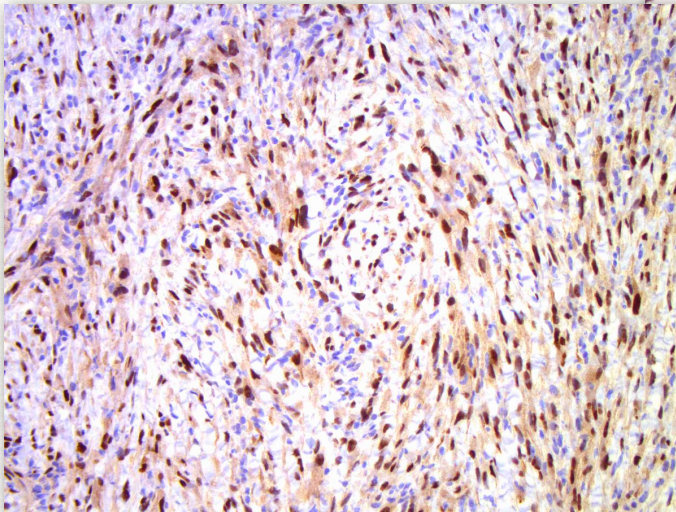
Predictive, diagnostic and prognostic markers



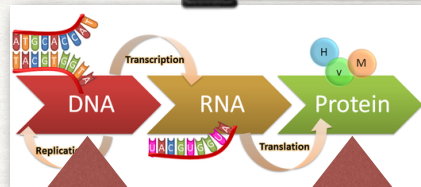
Well differentieret liposarcoma



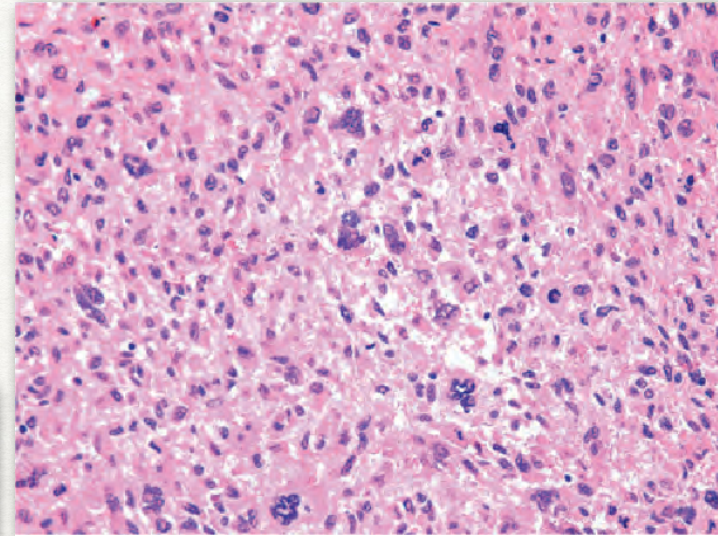
Dedifferentiated liposarcoma



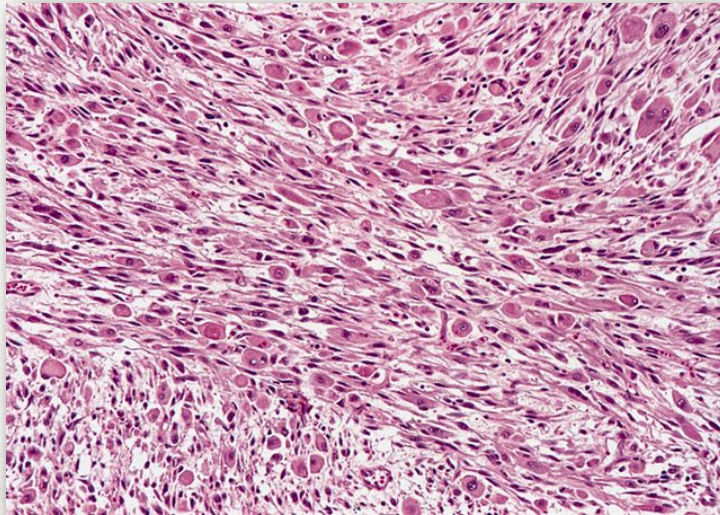
Predictive, diagnostic and prognostic markers



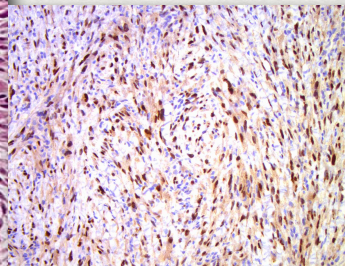
Pleomorph undifferentiated sarcoma



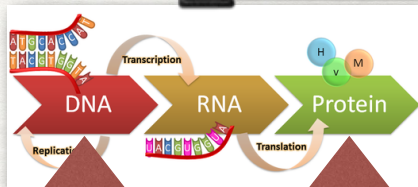
Dedifferentieret liposarcoma



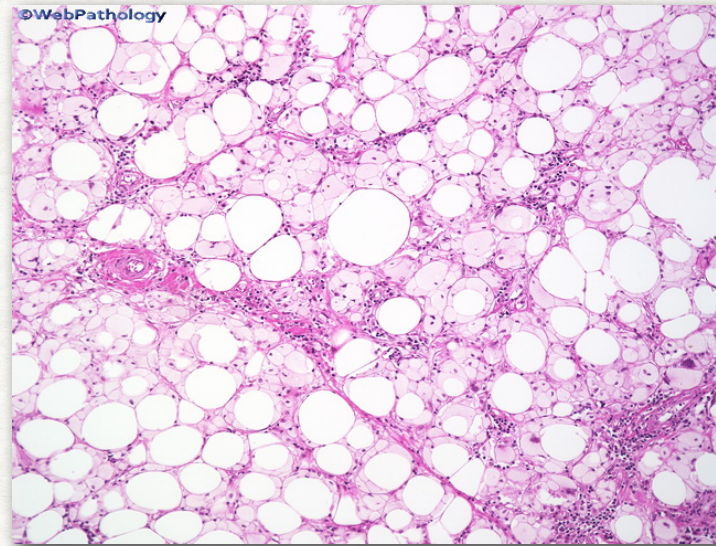
MDM2



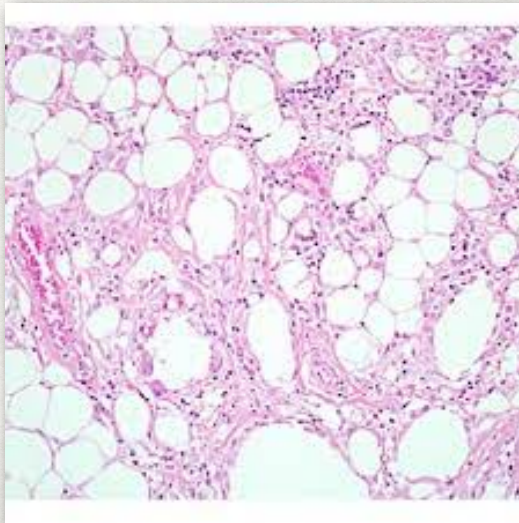
Predictive, diagnostic and prognostic markers



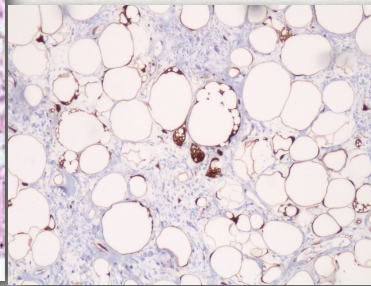
Lipoma



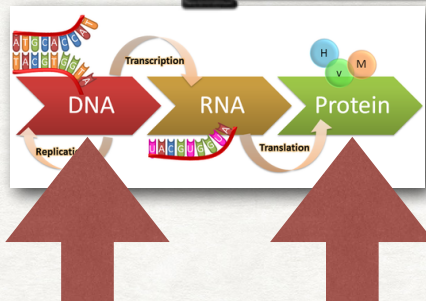
Well differentiated liposarcoma



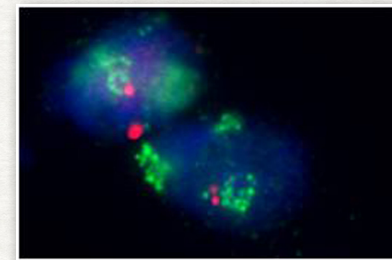
MDM2



Predictive, diagnostic and prognostic markers



Immunohistochemistry
of MDM2



NGS or FISH analysis of amplification
of MDM2 gene.