Molecular mechanisms involved into cancer development

Genetic alterations

- Oncogenes
- Tumor suppressor genes
- DNS repair genes
- Telomer and telomerase

Epigenetic alterations

- DNA-methylation
- Micro-RNS expression

Molecular mechanisms involved into cancer development

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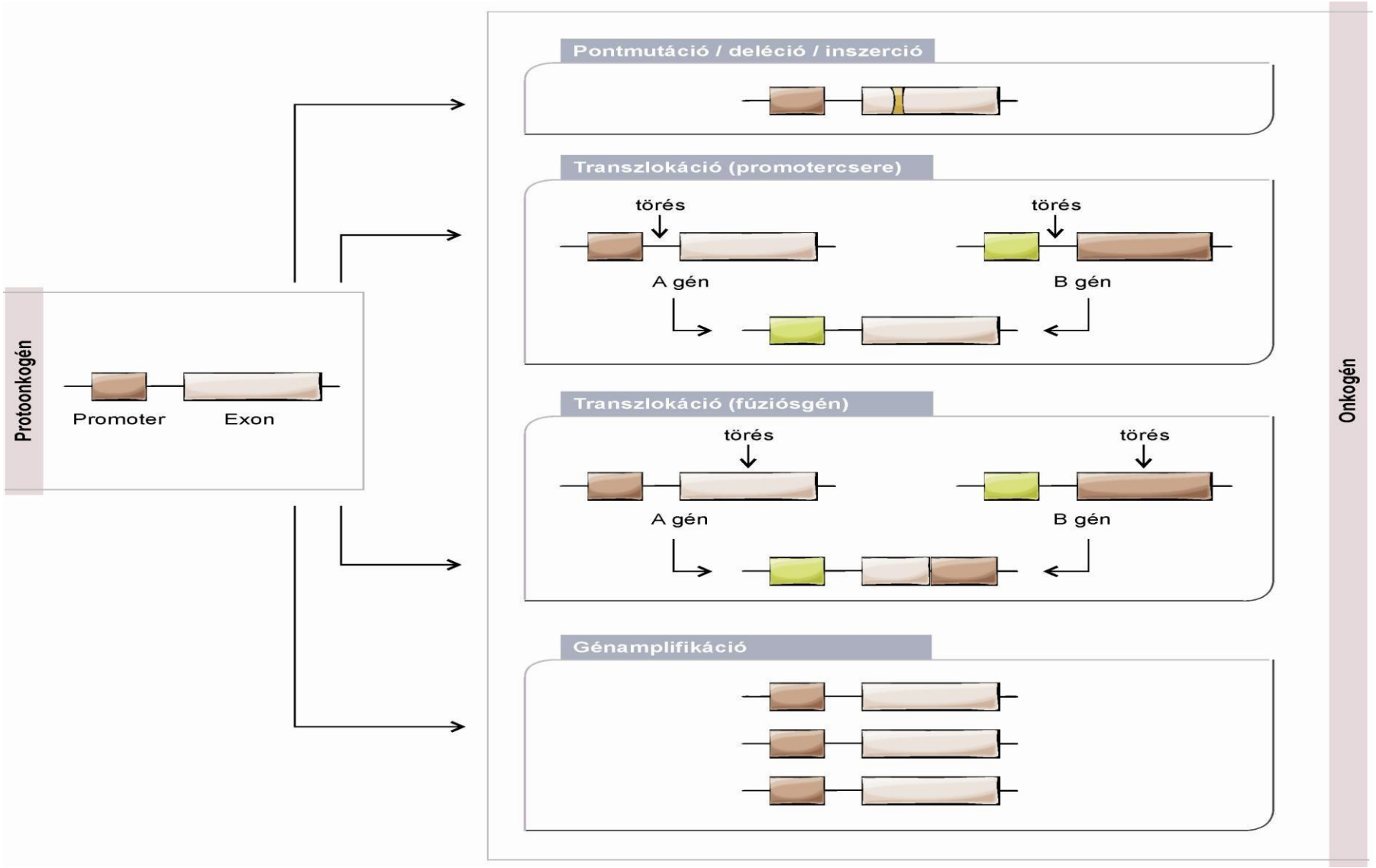
Mechanisms of protooncogene – oncogene transformation



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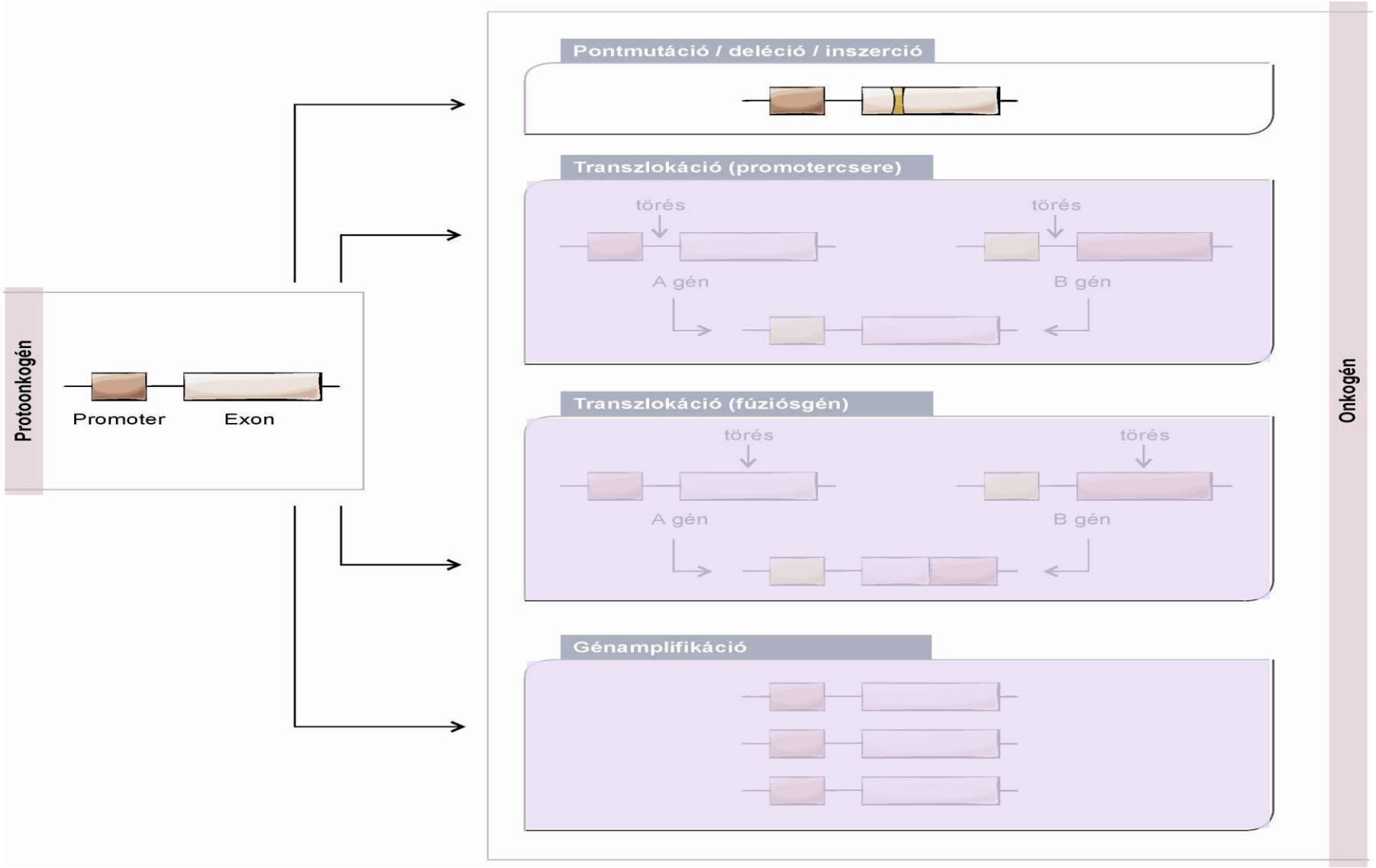
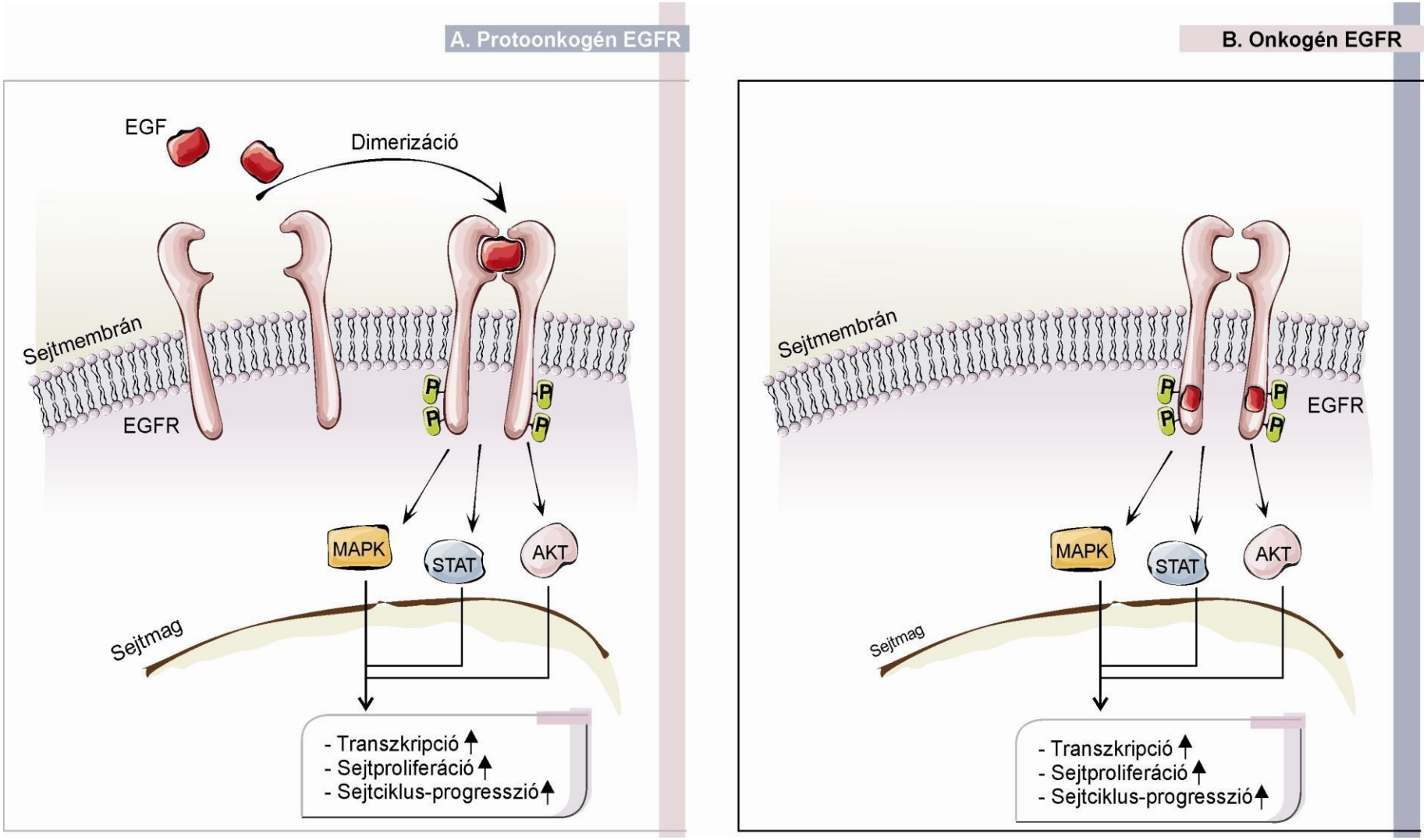
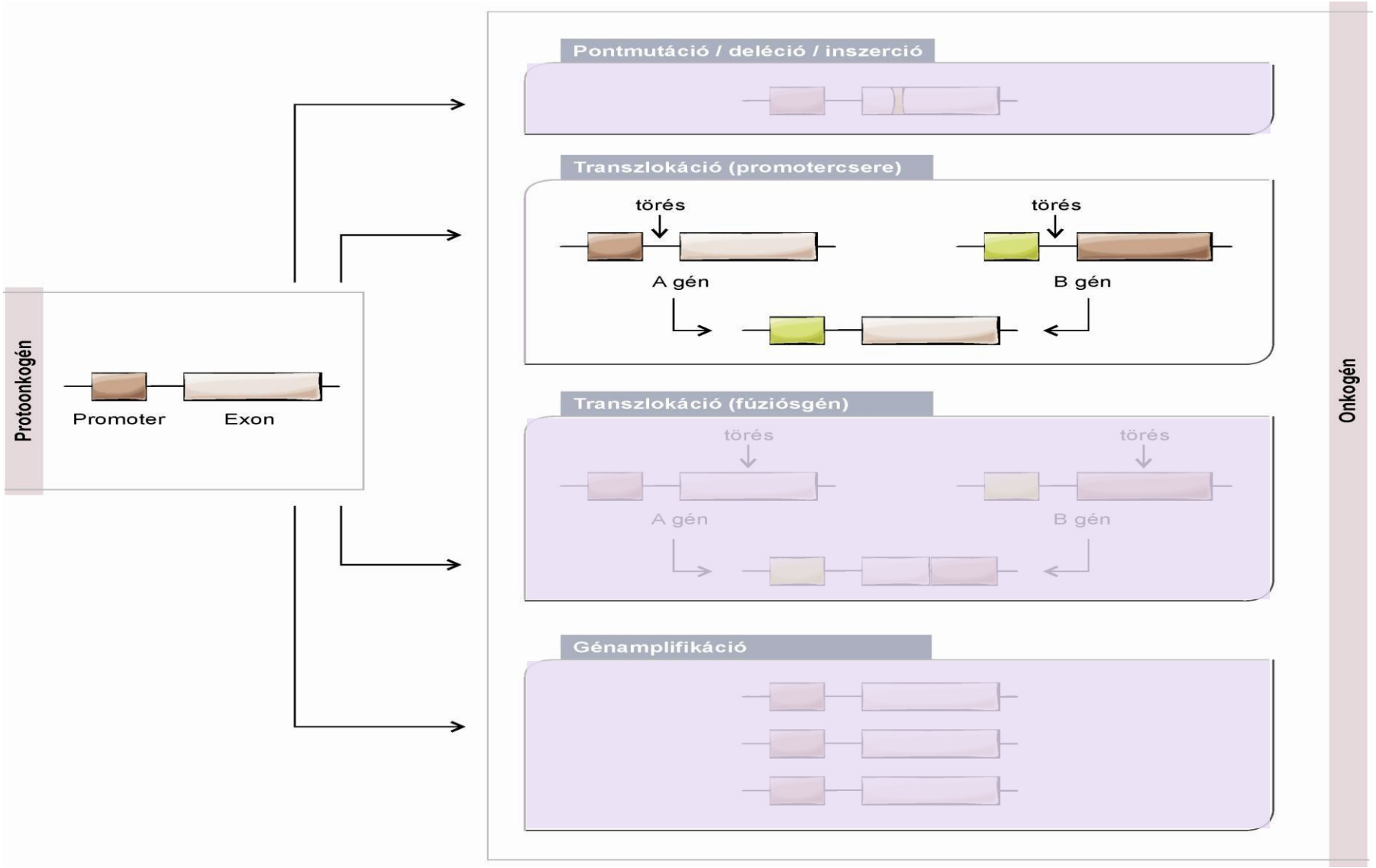


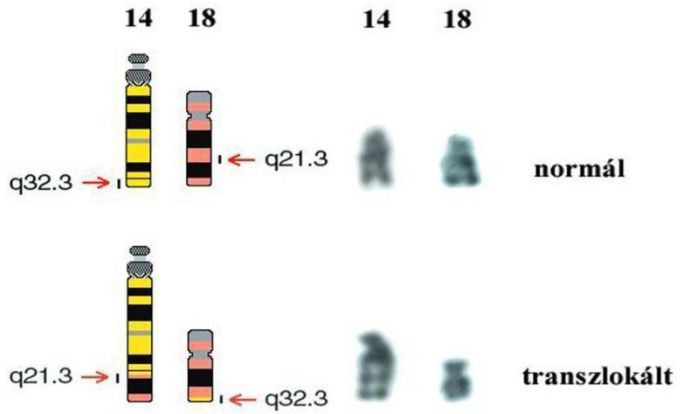
EGFR protooncogene – oncogene transformation (point mutation)

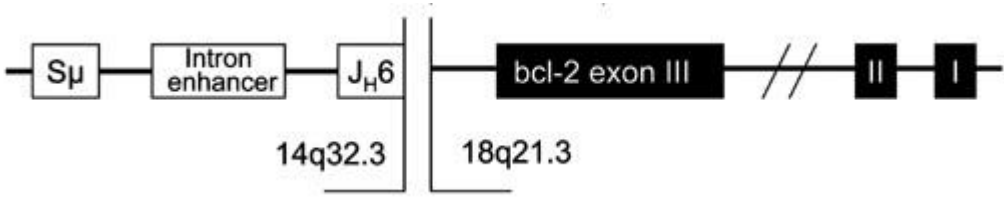


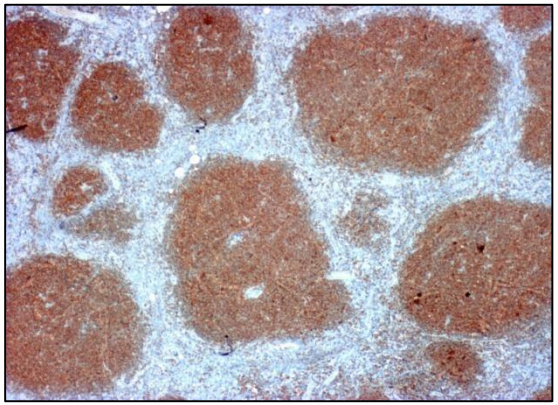
Mechanisms of protooncogene – oncogene transformation

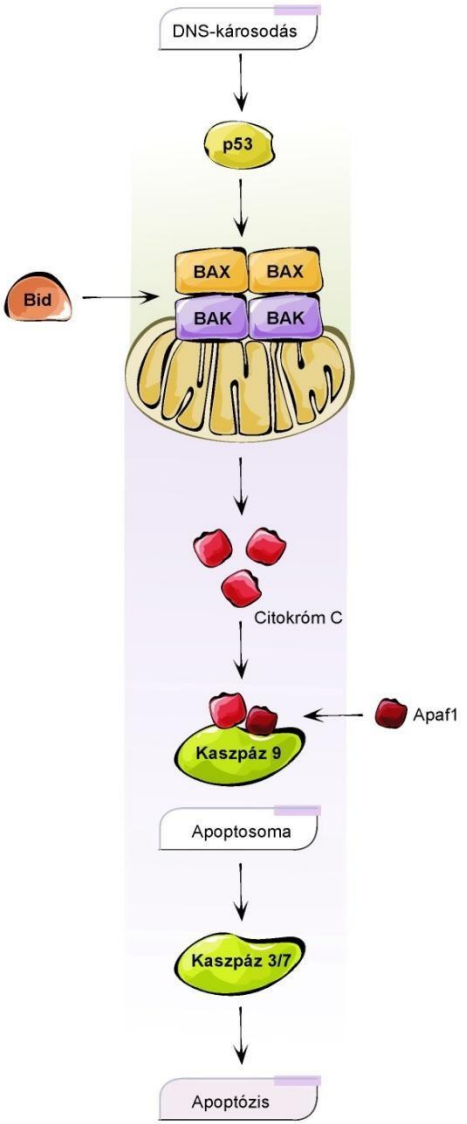


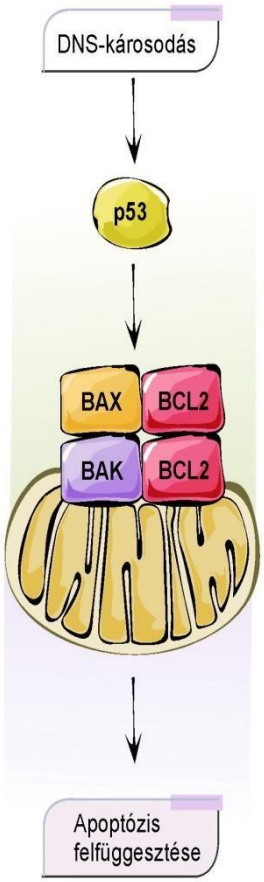
BCL2 protooncogene – oncogene transformation (translocation – promoter exchange)



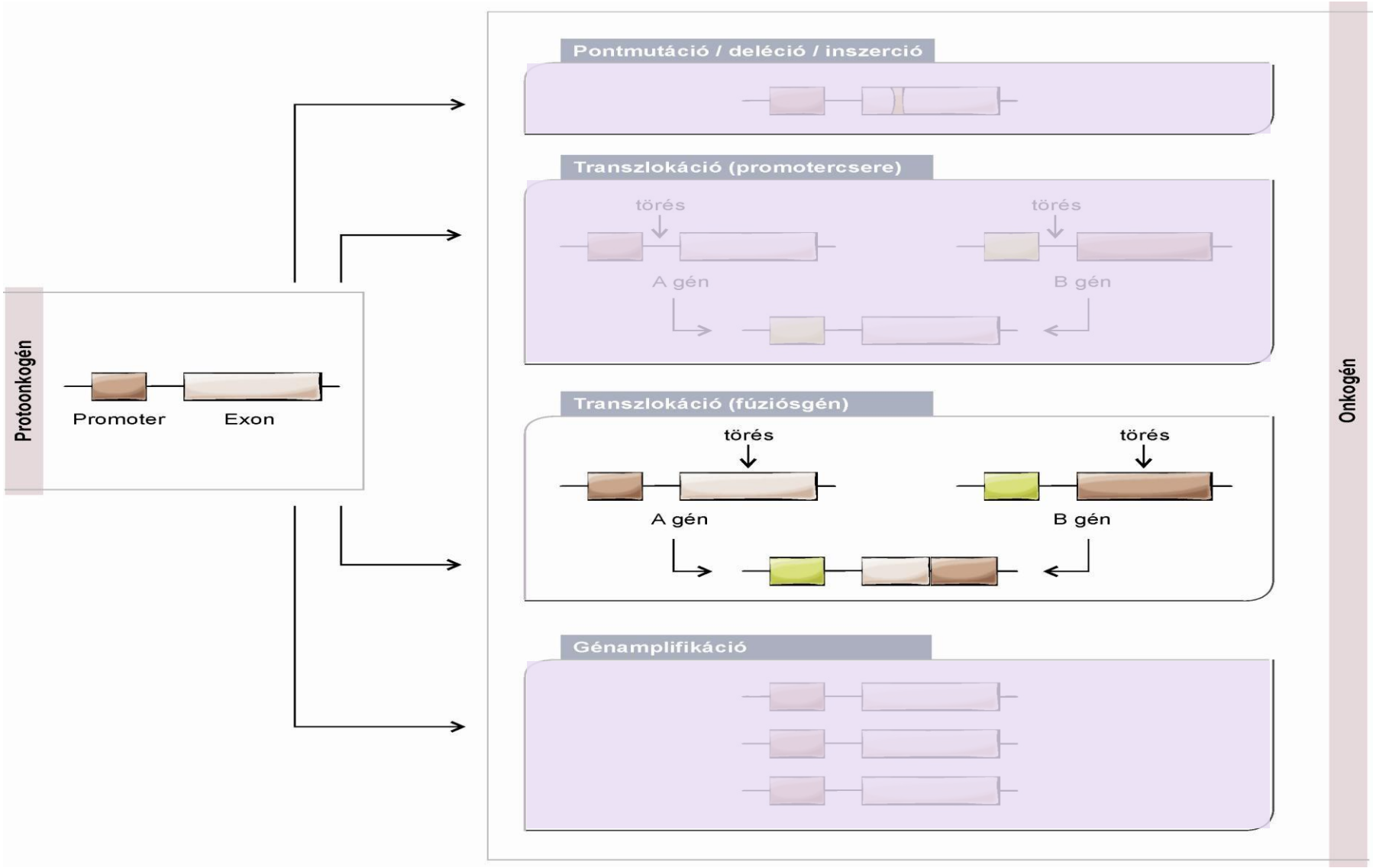




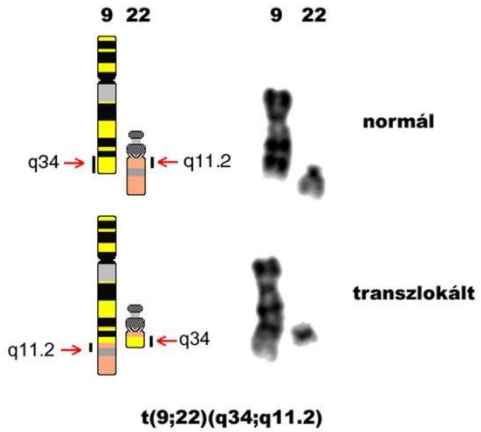


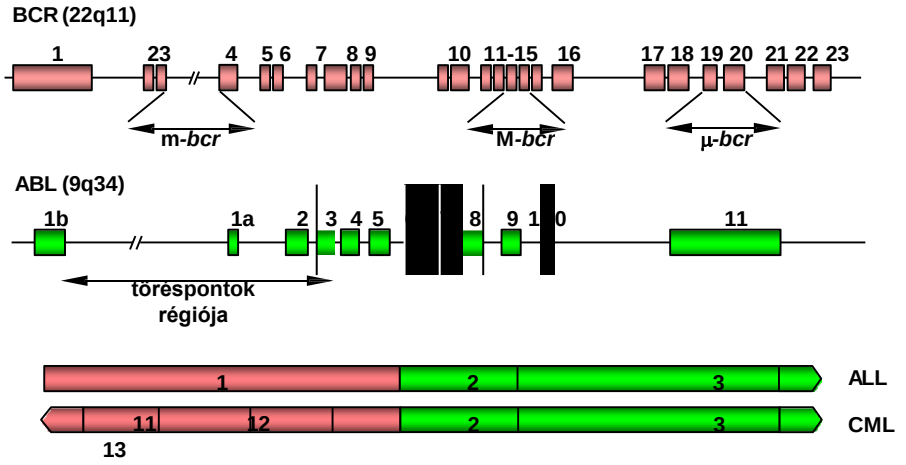


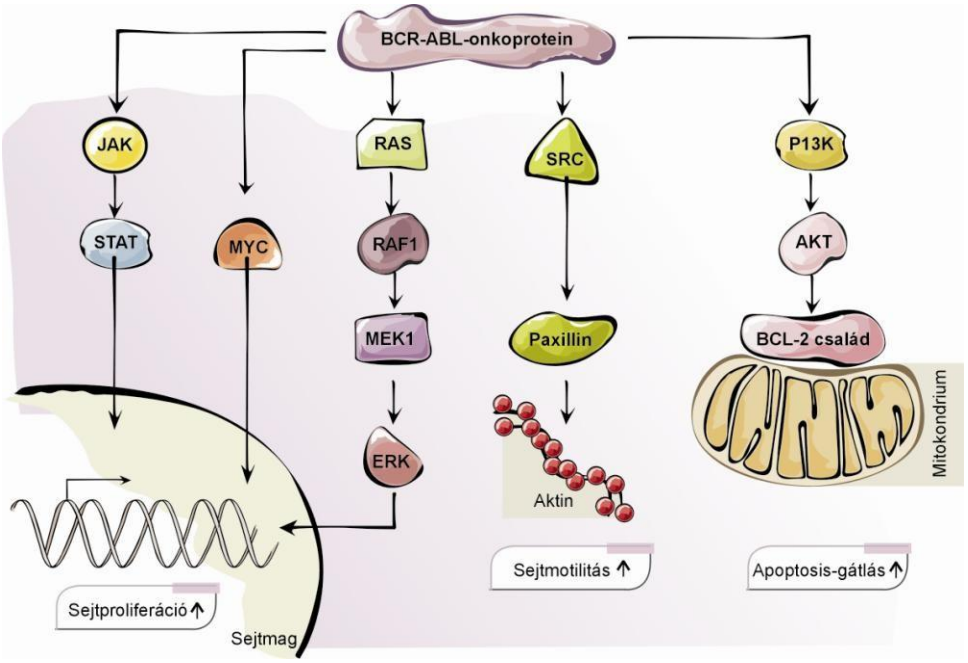
Mechanisms of protooncogene – oncogene transformation



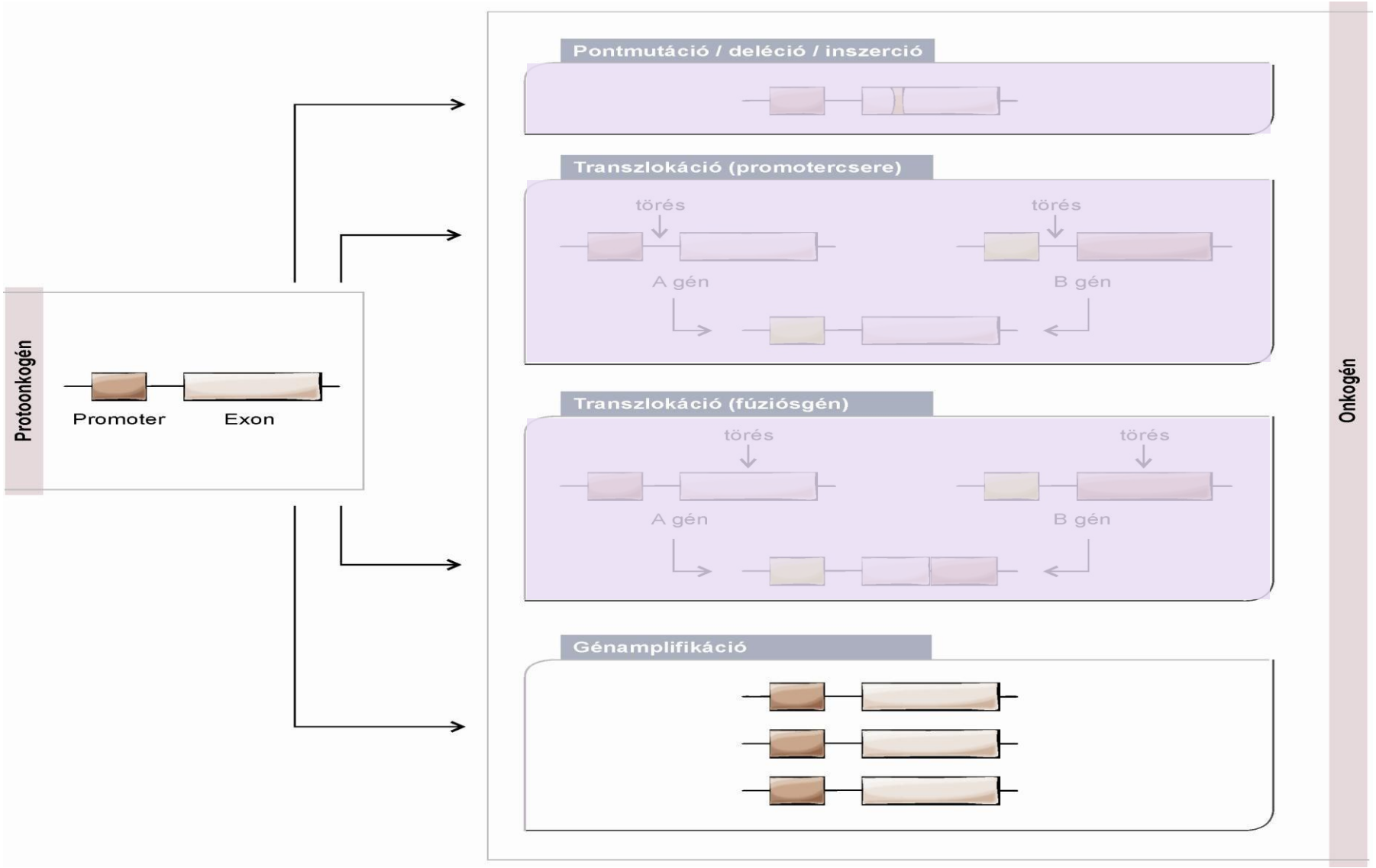
Protooncogene – oncogene transformation (translocation – gene fusion)



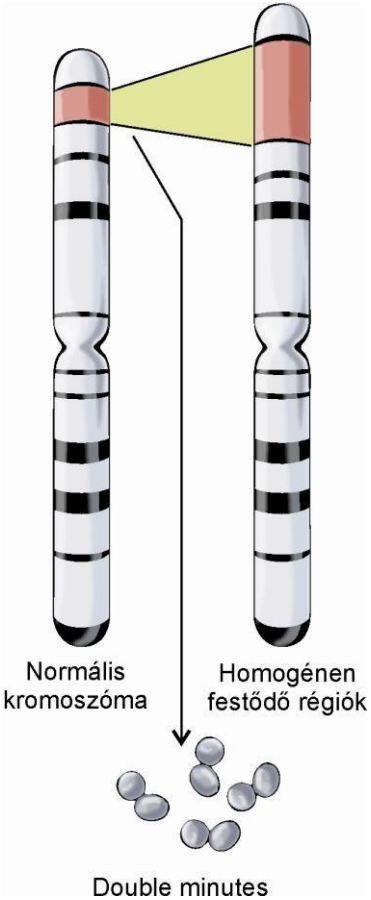


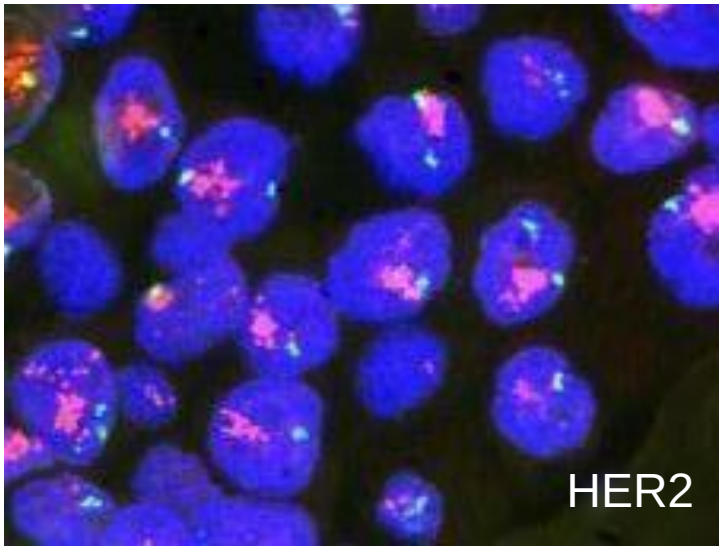


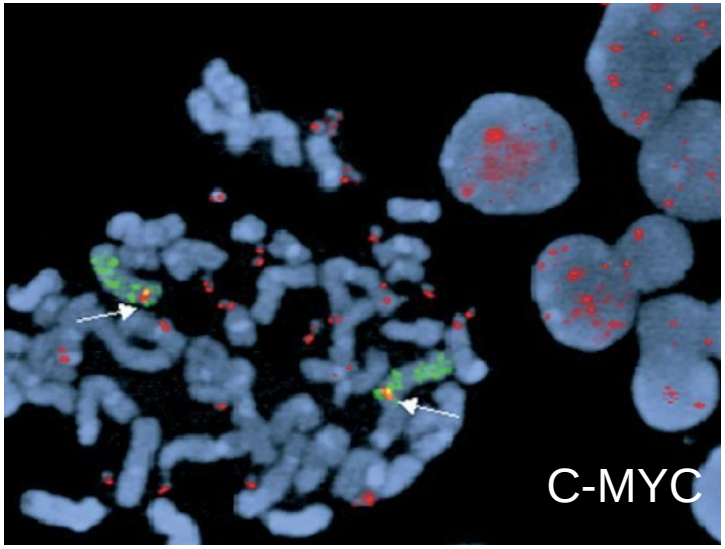
Mechanisms of protooncogene – oncogene transformation



Protooncogene – oncogene transformation (gene amplification)







Protooncogene activations involved in human cancer development

ONCOPROTEIN FUNCTION	PROTO-ONCOGENE	TYPE OF ACTIVATION	NEOPLASM
Growth factor	*SIS* *FGF-3* *HST*	Increased expression Amplification Increased expression	Astrocytoma, osteosarcoma Melanoma, breast-, bladder cancer Stomach cancer, Kaposi-sarcoma
Growth factor receptor	*EGFR* *FLT3* *RET* *KIT* *MET*	Increased expression Amplification Point mutation Point mutation Point mutation	Lung planocellular carcinoma, glioma Breast-, ovarium cancer MEN 2A, 2B, medullary carcinoma GIST Papillary renal cell carcinoma
GTP-binding proteins	*KRAS* *HRAS* *NRAS*	Point mutation Point mutation Point mutation	Lung-, colon-, pancreas cancer Kidney-, bladder cancer Melanoma, AML
Non-receptor thirosine kinase	*ABL* *JAK2*	Translocation Point mutation	CML, ALL PV, ET, MF
Nuclear transcription factor	*C-MYC* *N-MYC* *L-MYC* *C-JUN*	Translocation Amplification Amplification Increased expression	Burkitt lymphoma Neuroblastoma, SCLC SCLC Lung-, colon cancer
Ciklin and ciklin dependent kinase	*Ciklin D* *Ciklin E* *CDK4*	Translocation Amplification Increased expression Point mutation	Mantle cell lymphoma Breast-, oesophagus cancer Breast cancer Melanoma, glioblastoma
Antiapoptotic protein	*BCL2*	Translocation	Follicular lymphoma

Molecular mechanisms involved into cancer development

Genetic alterations

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Epigenetic alterations

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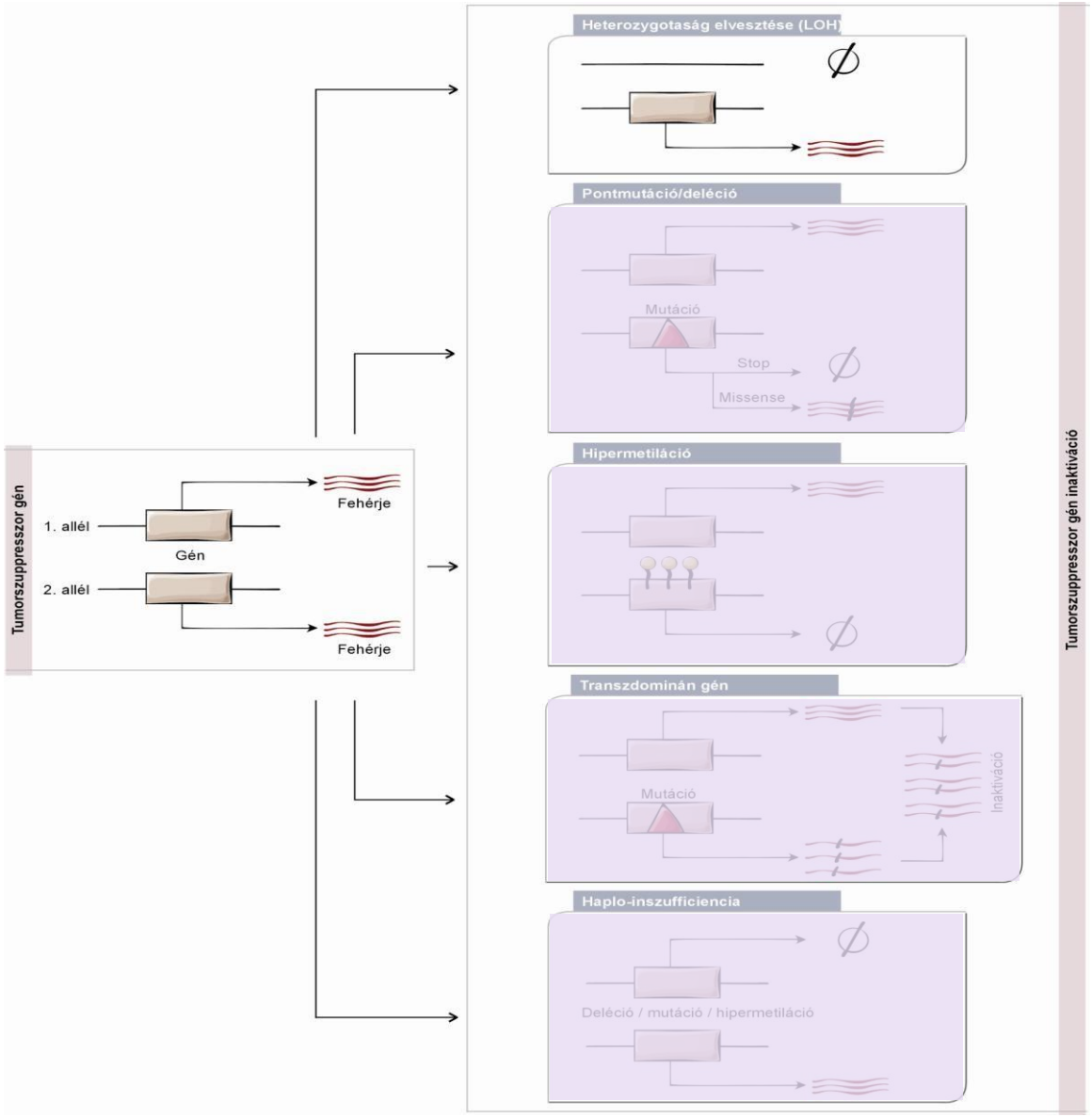
- Micro-RNS expression

Mechanisms of tumor suppressor gén inactivations



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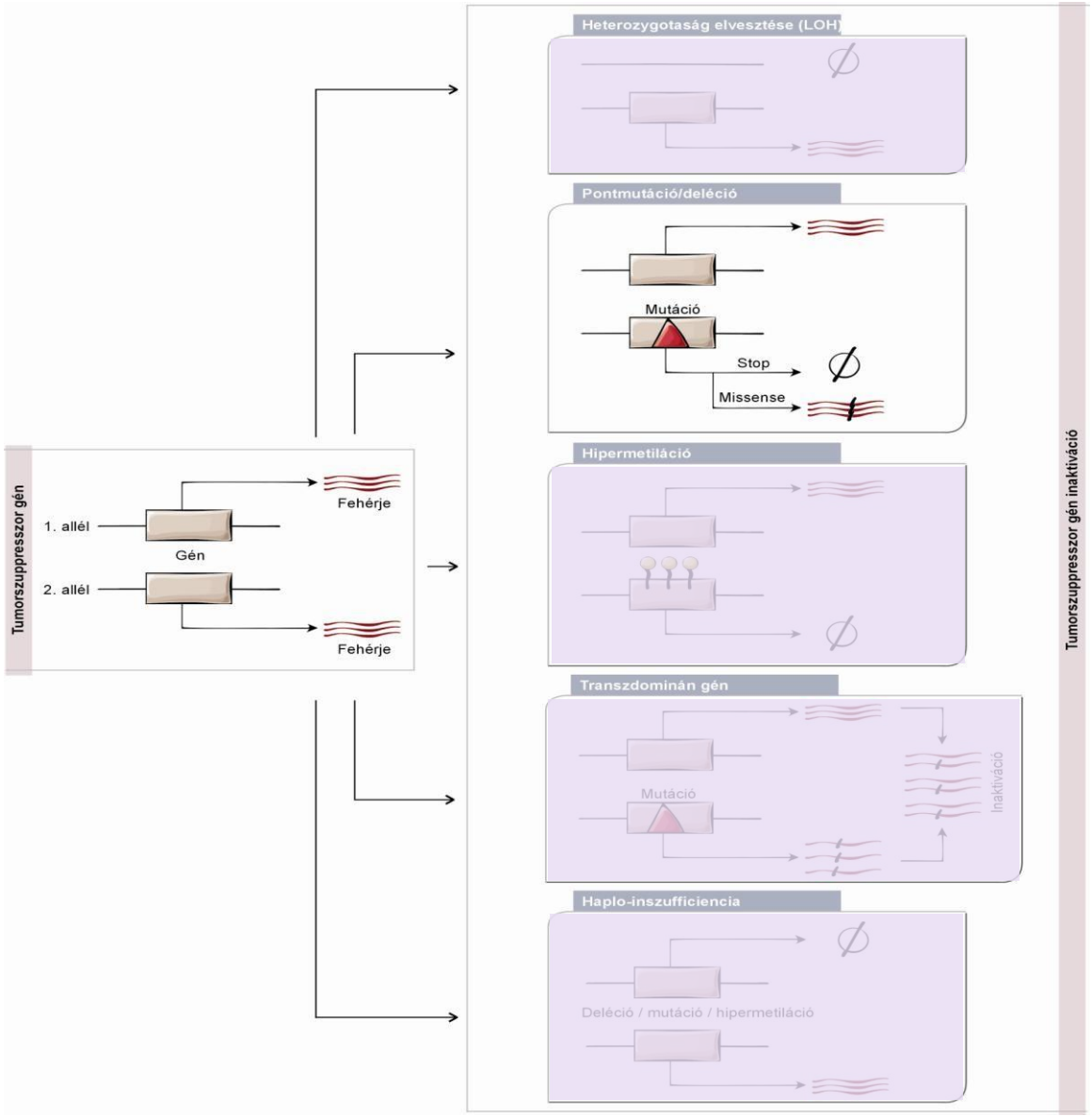

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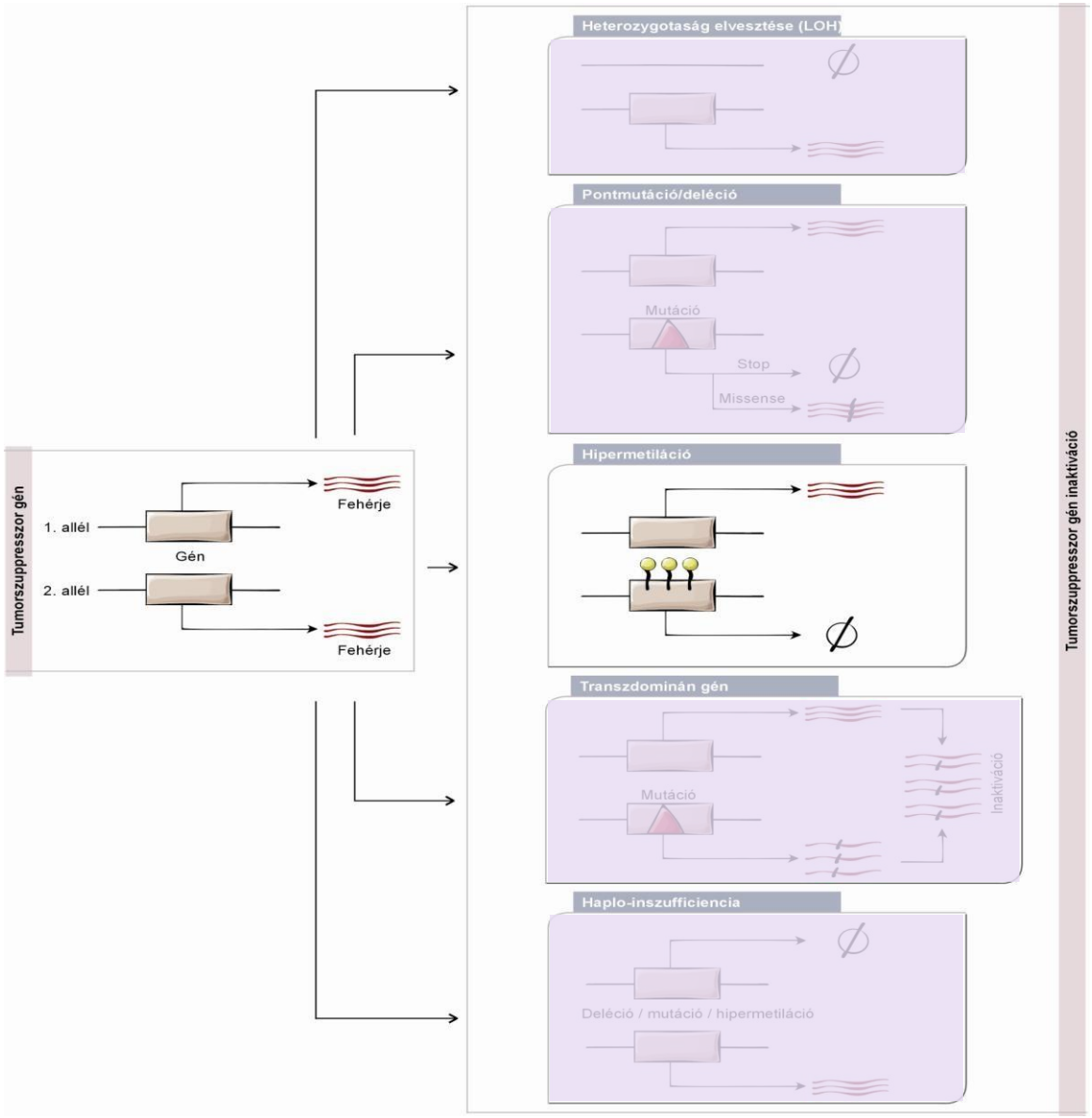

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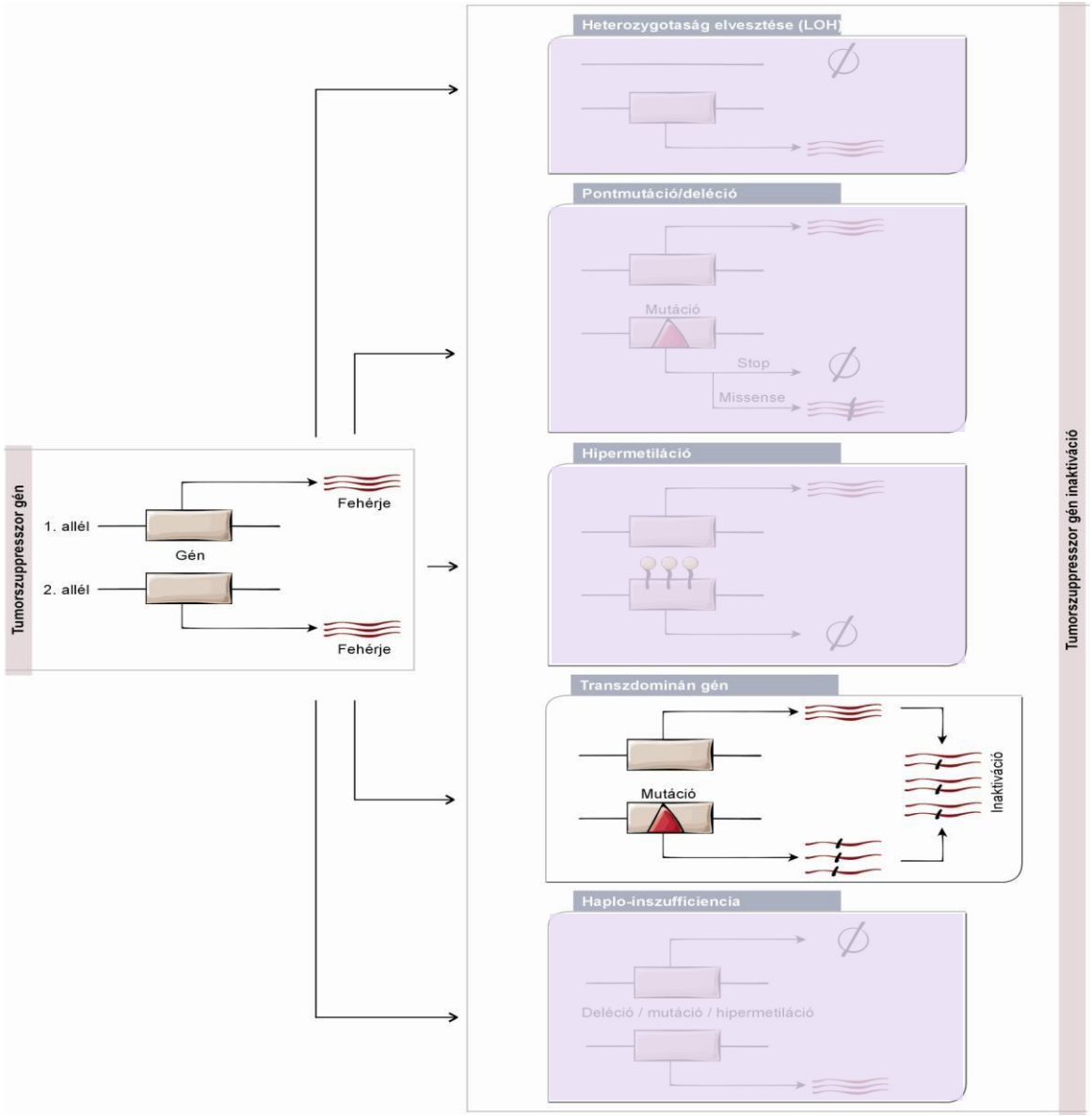

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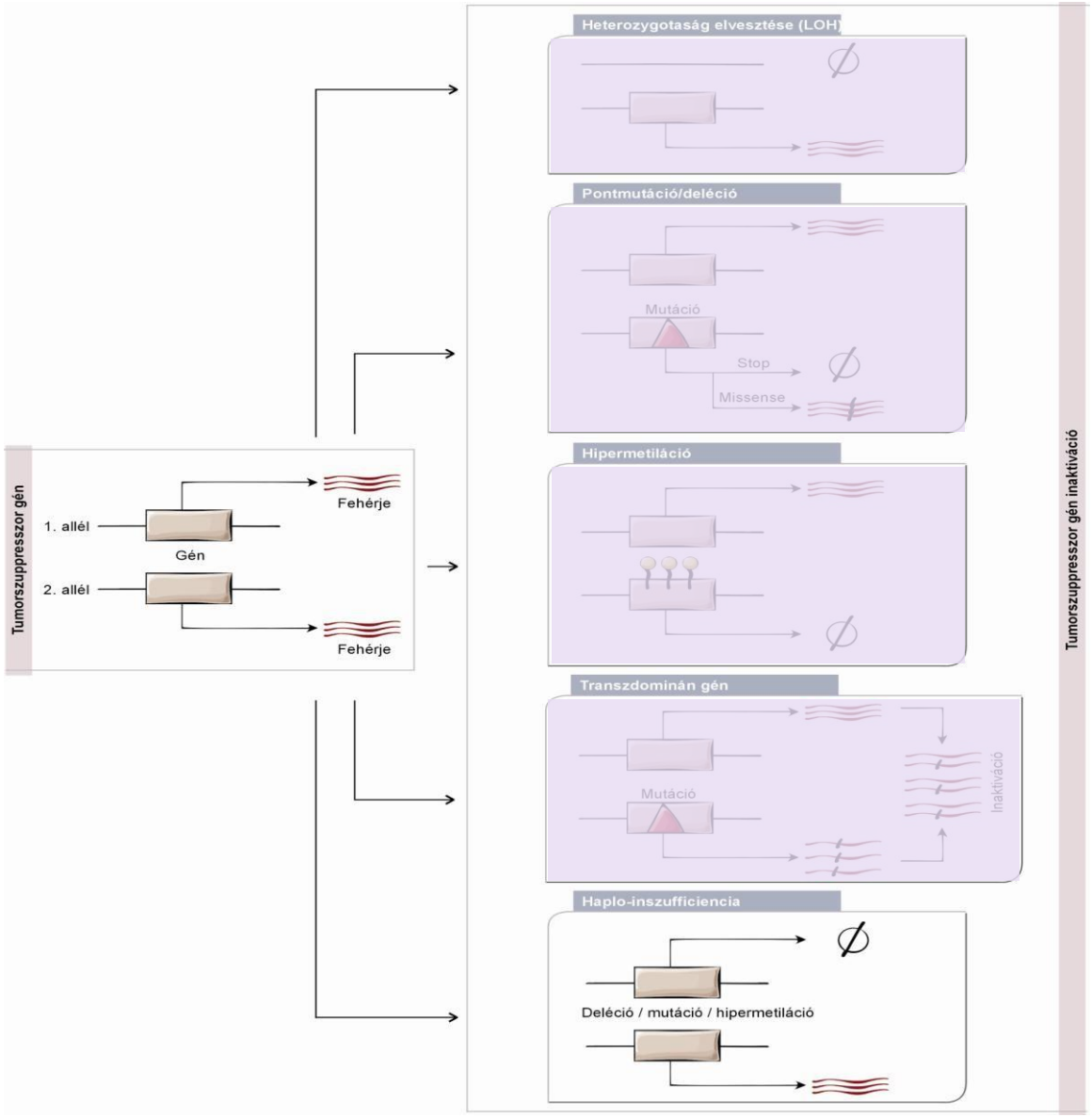
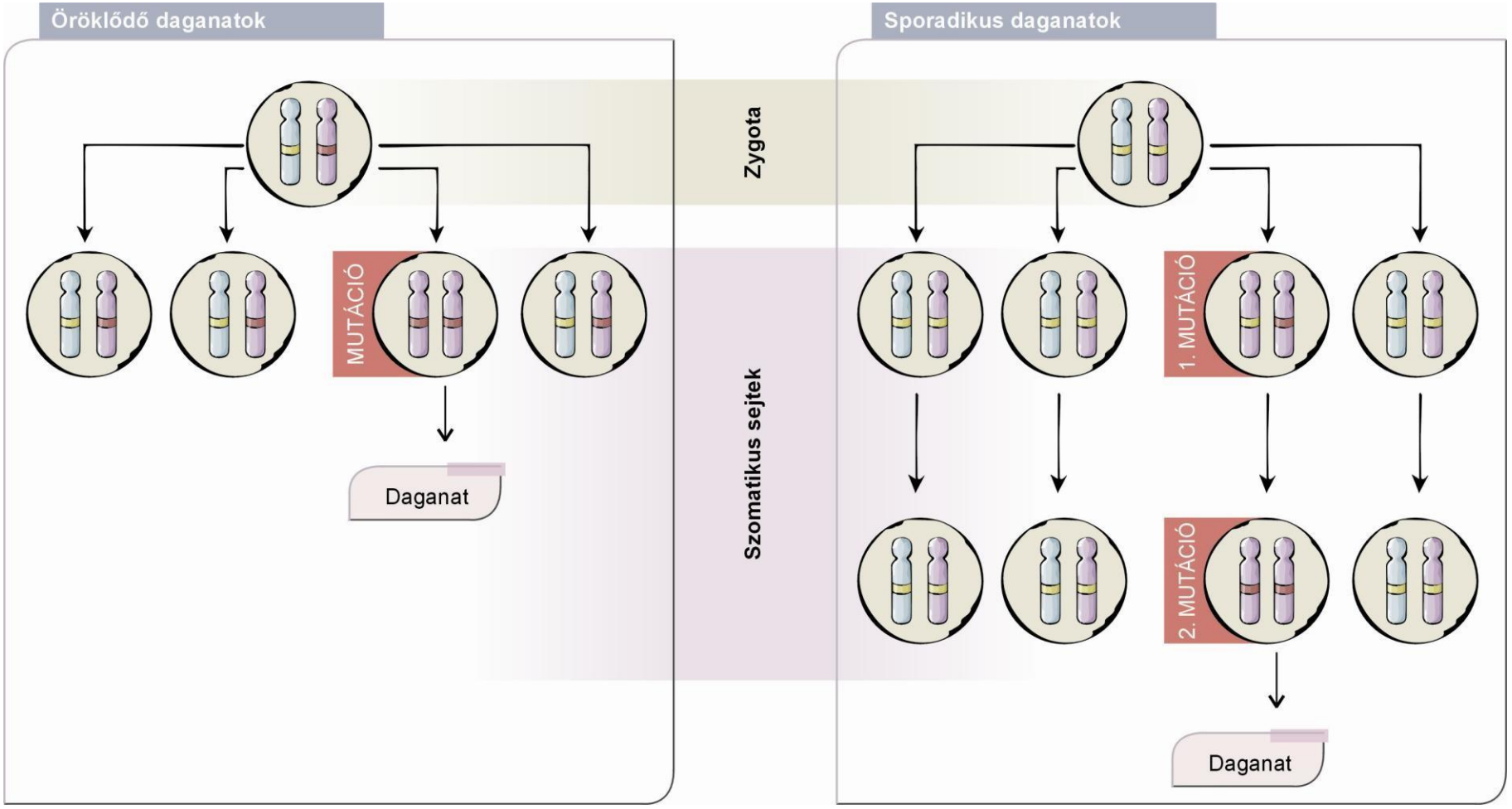


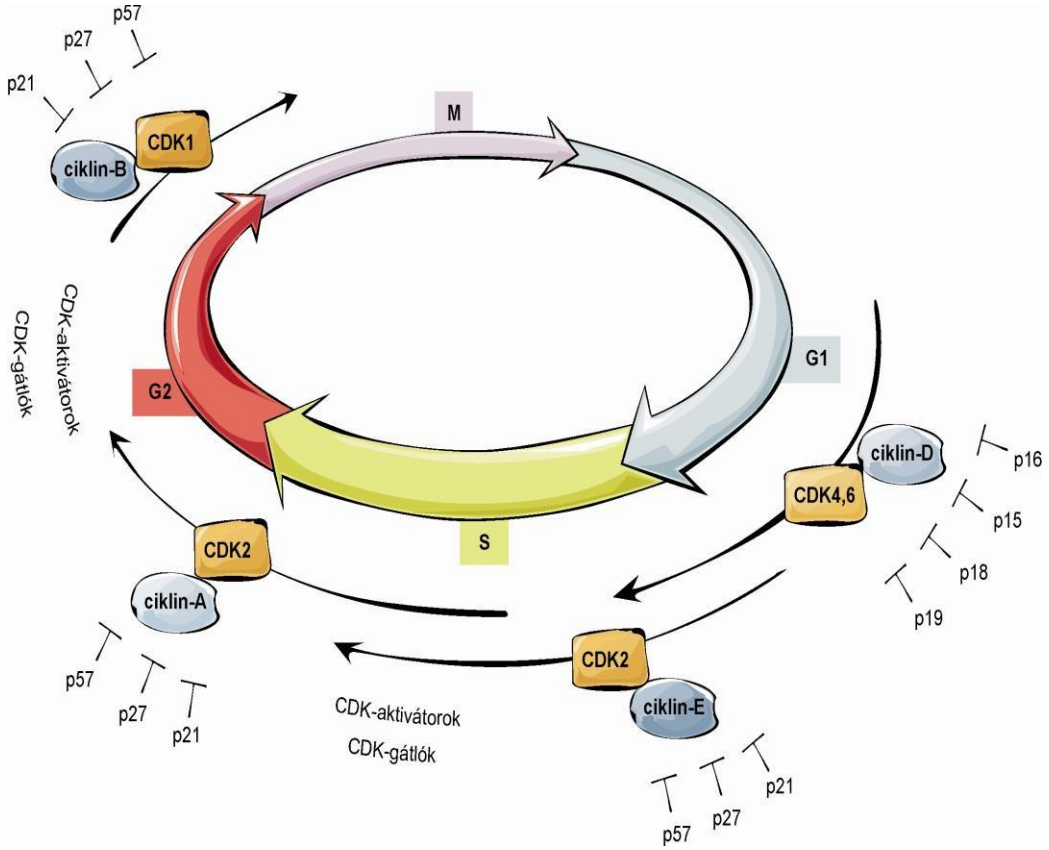
Tumorsuppressor gene inactivation in hereditary and sporadic cancers

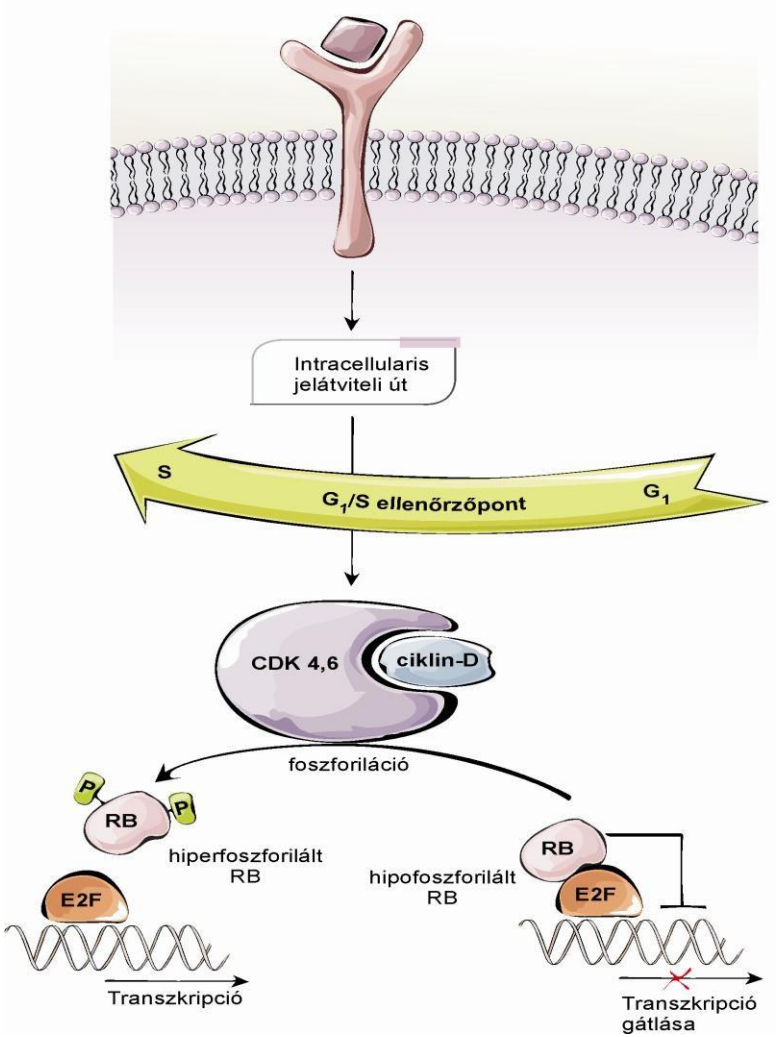


Tumorsuppressor genes involved in human cancer development

GENE	FUNCTION	HEREDITARY NEOPLASMS	SPORADIC NEOPLASMS
RB	Cell cycle regulation	Retinoblastoma, osteosarcoma	Retinoblastoma, osteosarcoma, emlő-, colon-, tüdőcarcinoma
p53	Cell cycle block, apoptosis, cell aging	Li-Fraumeni-syndroma	Most human cancer
APC	β-katenin block	Familiar adenomatosus polyposis, melanoma	Colon-, stomach-, pancreas cancer
WT1	Nuclear transcription	Wilms-tumor	Wilms-tumor
p16/p16	Ciklin dependent kinase inhibitor	Melanoma	Breast-, eosophagus,- prostata-, panceras cancer
BRCA1	DNA-repair	Breast-, ovarium cancer	Breast-, ovarium cancer
BRCA2	DNA-repair	Breast cancer	Stomach cancer
VHL	Elongin inhibitor	vonHippel-Lindau-syndrome	Renal cell carcinoma, haemangioma
NF1	RAS, p21 inhibitor	Neurofibromatosis 1	Neuroblastoma, melanoma
NF2	Citosleketon stability	Neurofibromatosis 2	Schwannoma, meningeoma
PTEN	Tyrosine kinase inhibitor	Cowden-syndrome	Emdometrium-, prostate cancer

The role of inactivation of *RB* tumorsuppressor gene in cancer development





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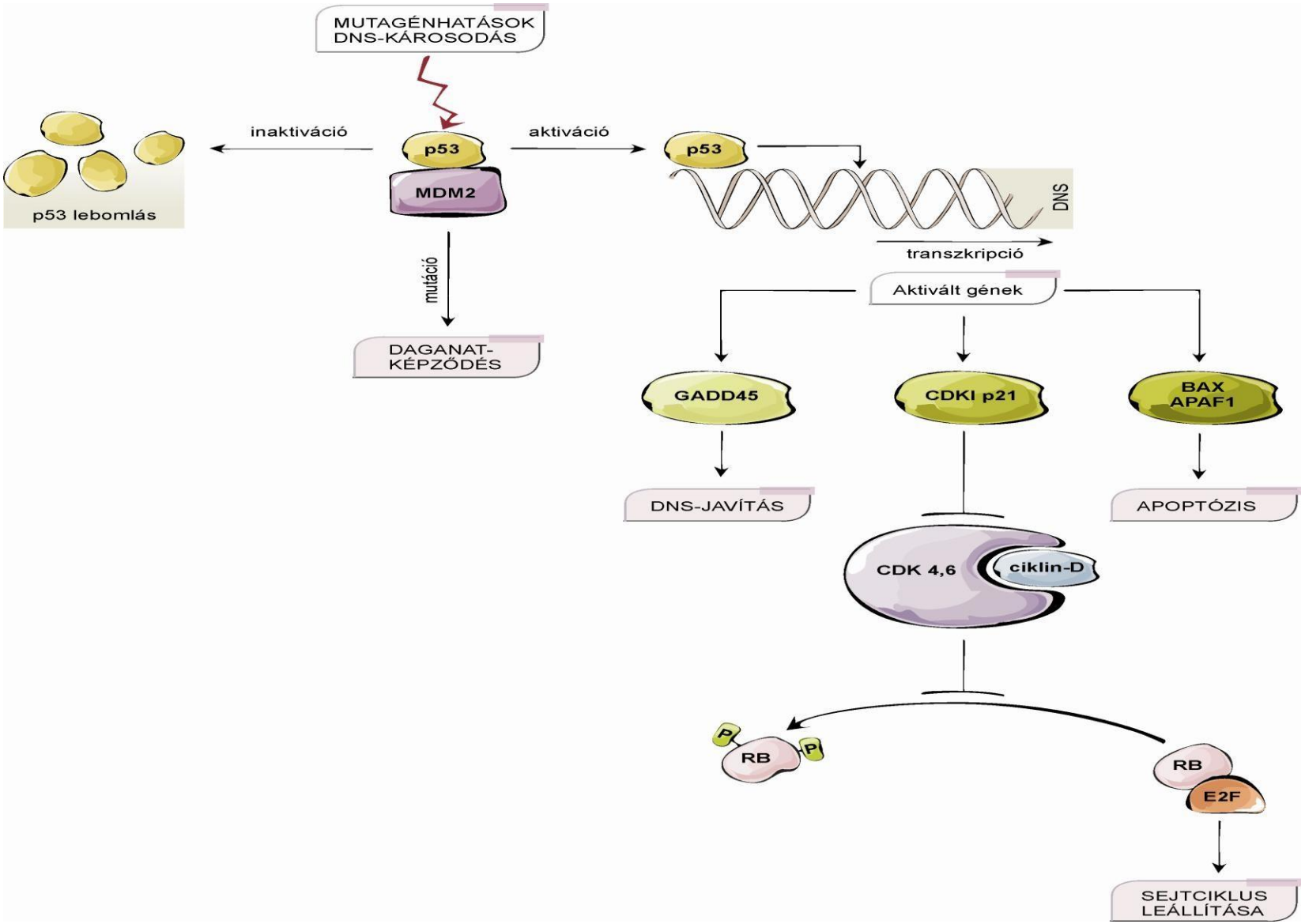
The role of inactivation of *p53* tumorsuppressor gene in cancer development



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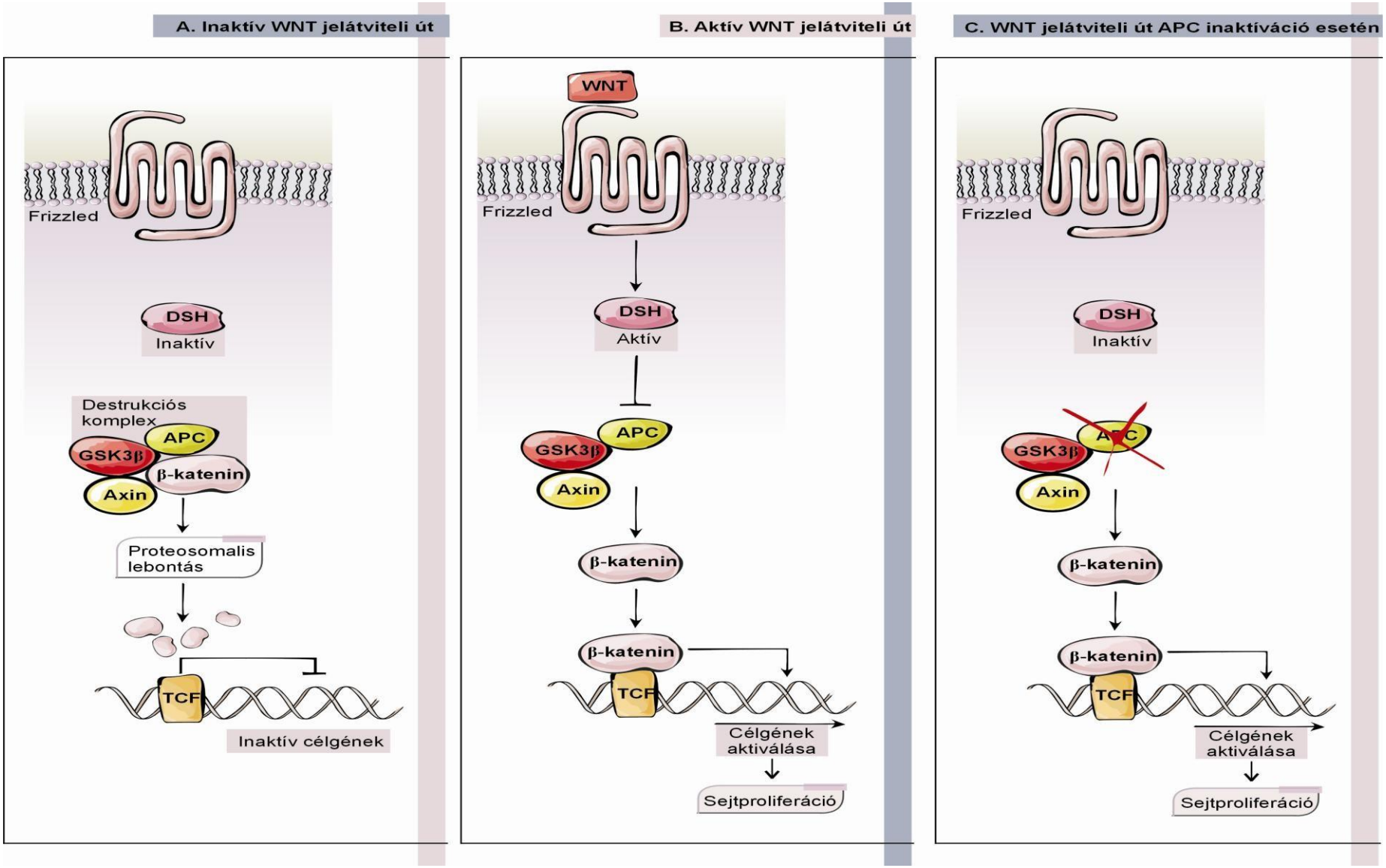
PTEN	Tyrosine kinase inhibitor	Cowden-syndrome	Emdometrium-, prostata carcinoma

The role of *APC* in the development of adenomatosus polyposis coli



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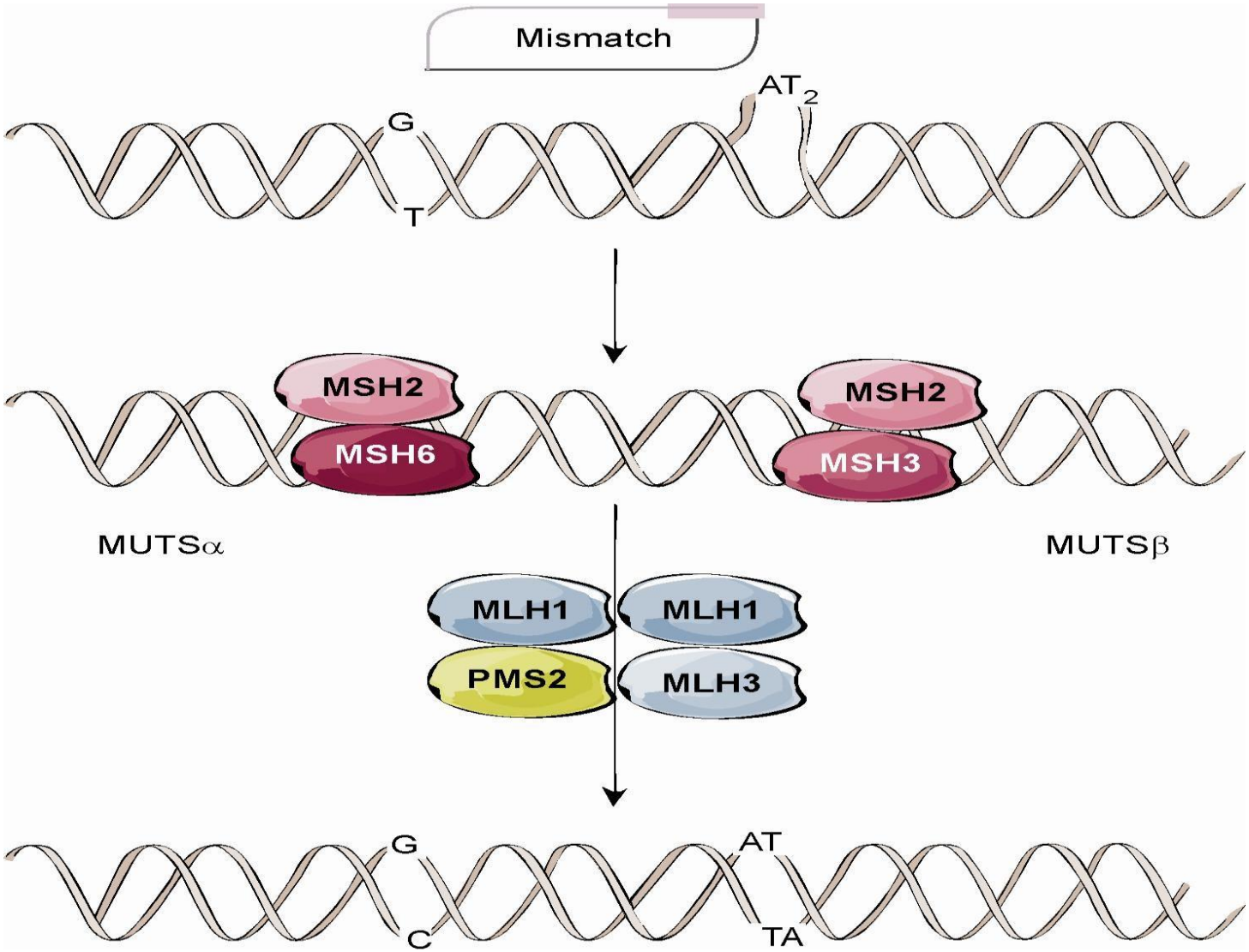
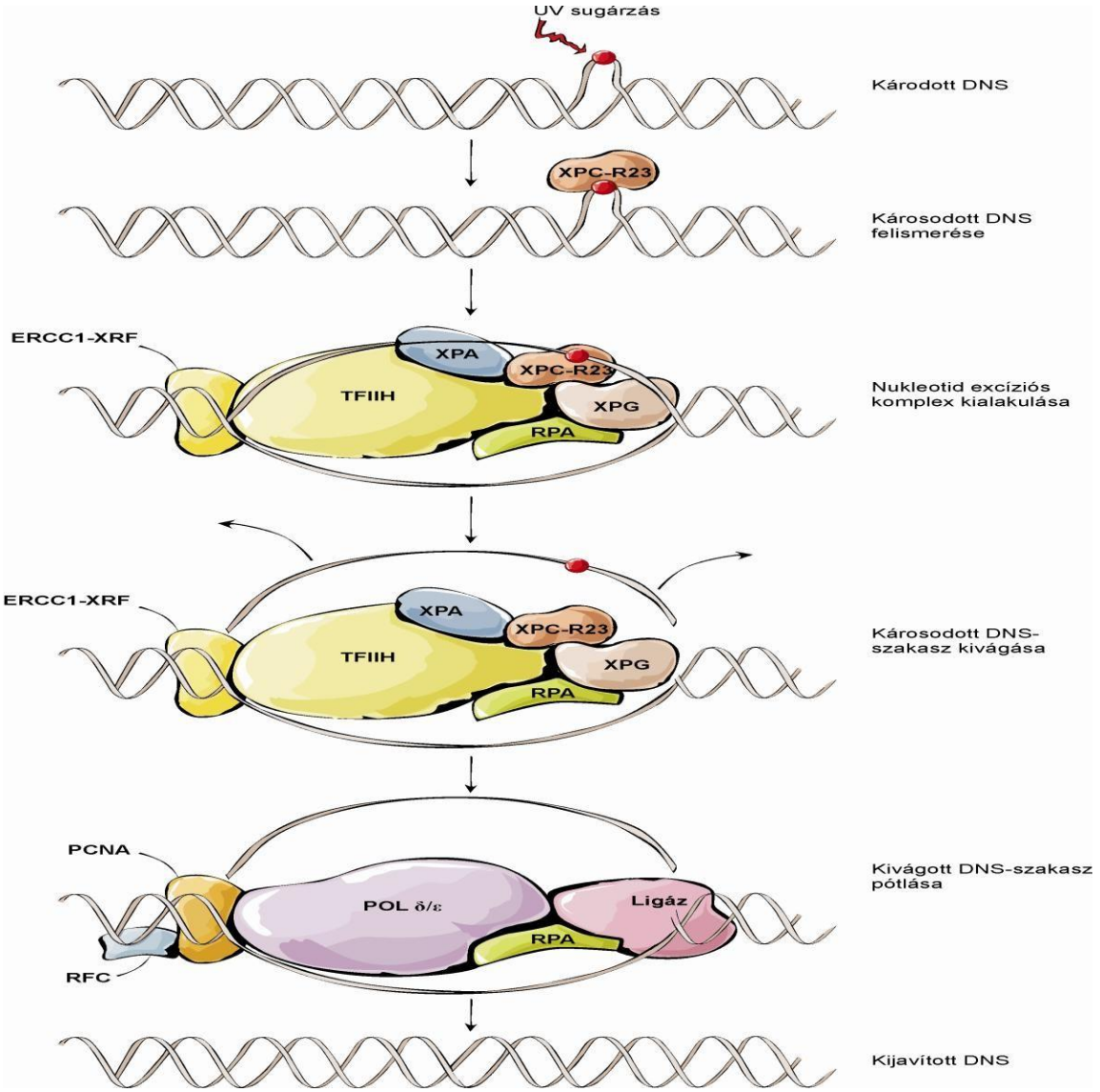
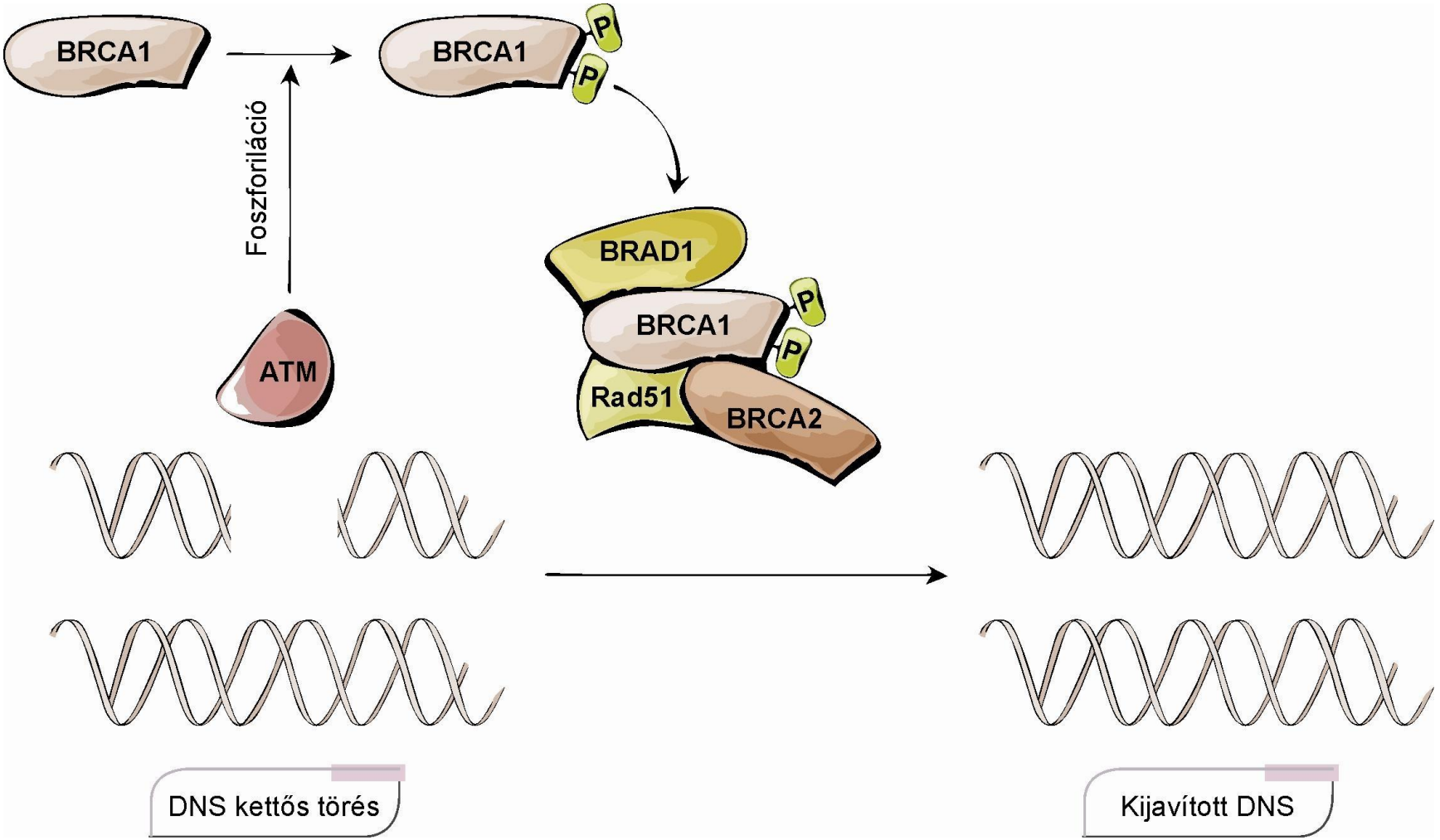
The role of DNA mismatch repair in cancer development



The role of nucleotide excision repair in cancer development



The role of homolgue recombination repair in cancer development



The role of DNA repair gene mutations in cancer development

RPAIR SYSTEM	GENES	NEOPLASM
Mismatch repair	*MSH2* *MLH1* *MSH6*	Colorectal-, ovarium-, endometrium-, stomach cancer
Nucleotide excision repair	*XPA* *XPC* *XPG*	Basocellular-, planocellular carcinoma, melanoma
Homolog recombination repair	*BRCA1* *BRCA2* *ATM*	Breast-, ovarium-, prostata carcinoma Breast-, ovarium-, pancreas, stomach carcinoma, melanoma Ataxia teleangiectasia, breast carcinoma, different sporadic neoplasms

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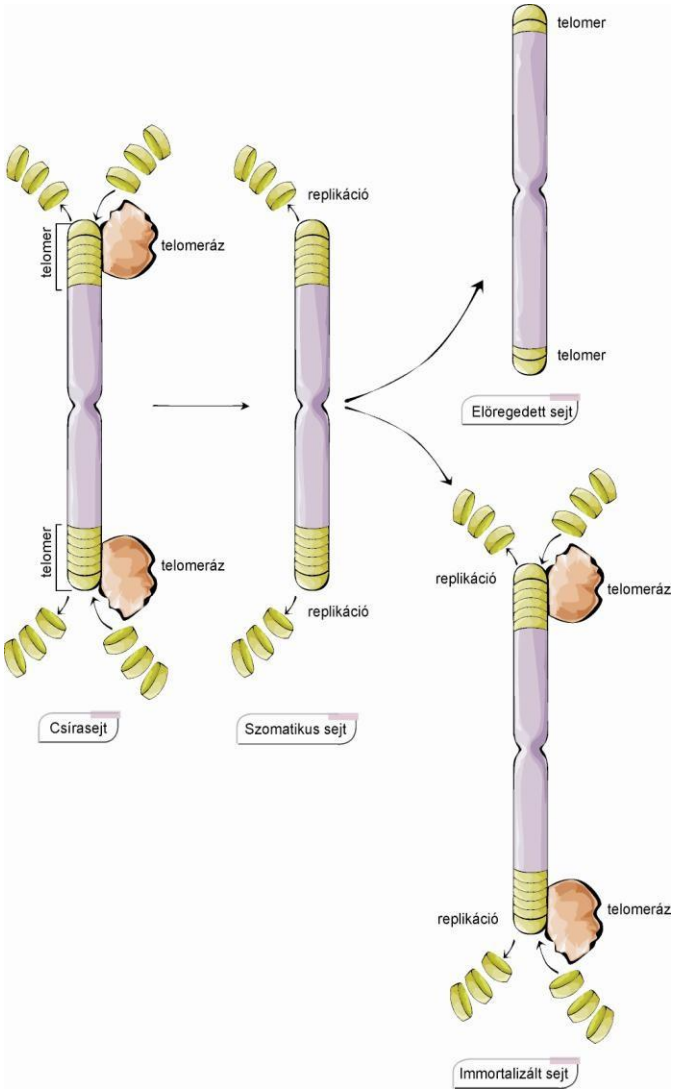
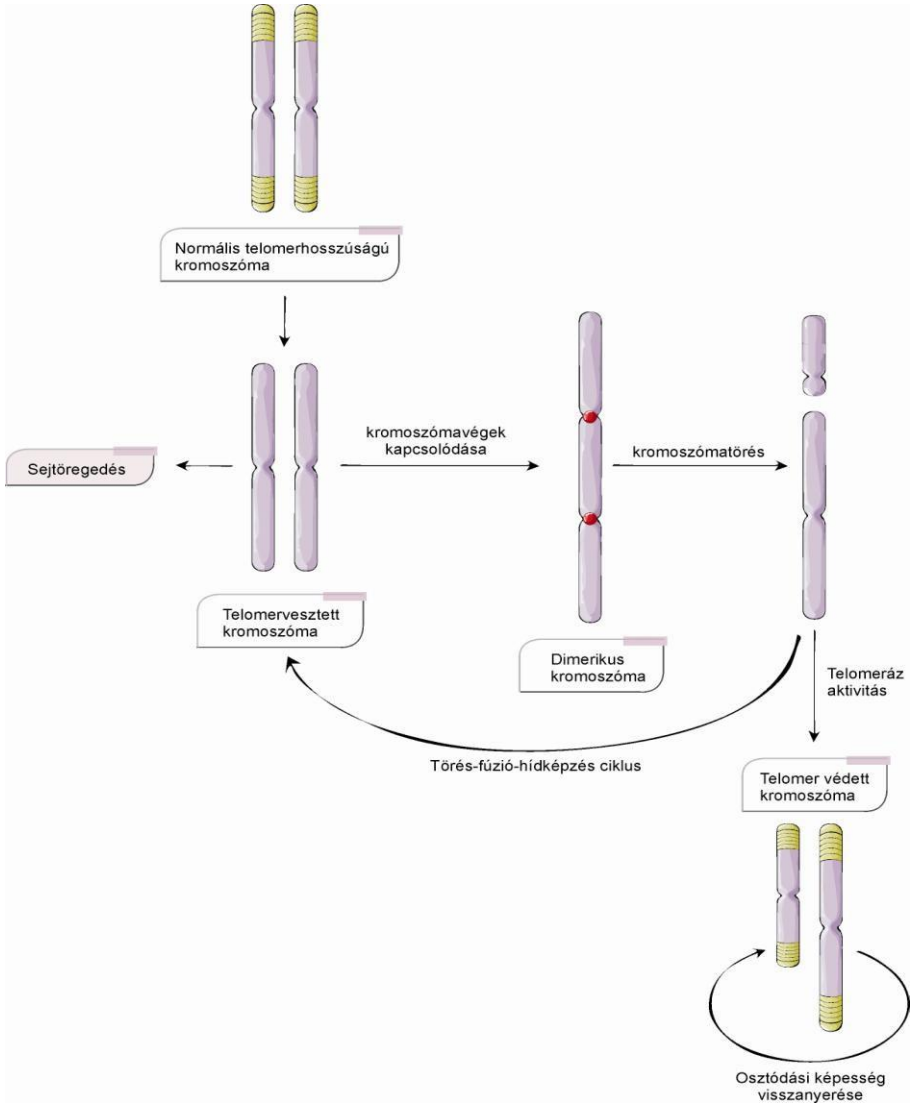
The role of telomer and telomerase in cancer development





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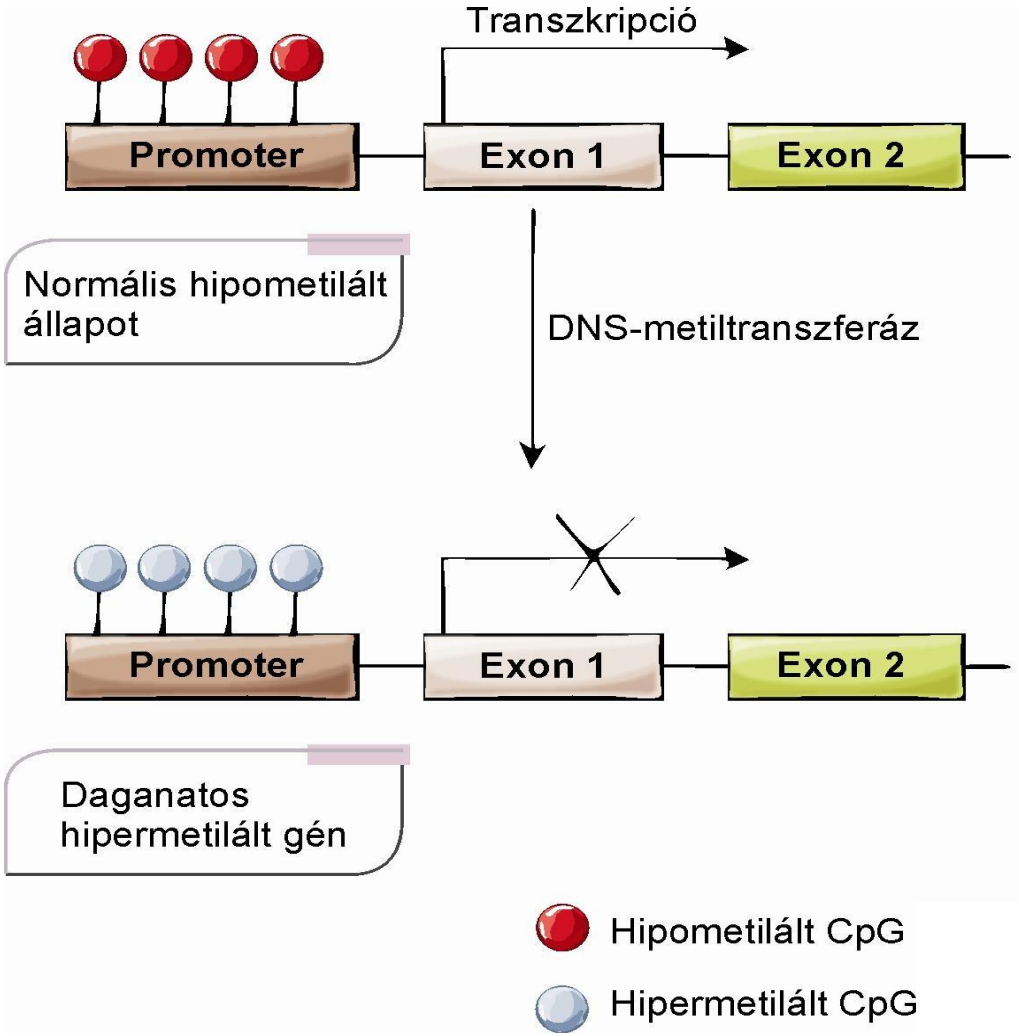
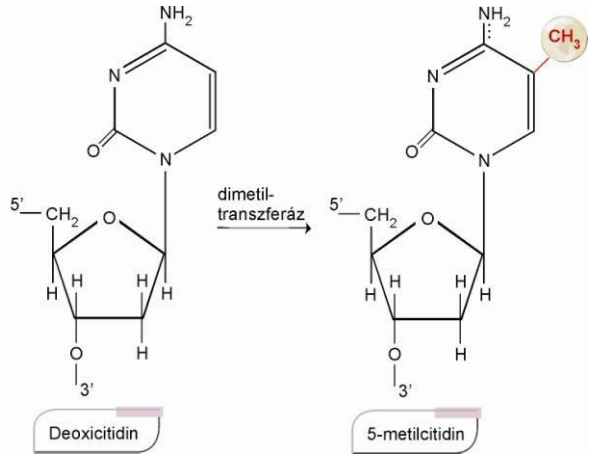
Hipermetiláció szerpe a daganatok kialakulásában





Frequently hypermethylated genes in different cancers

GENE	NEOPLASM
hMLH1	Stomach-, colorectali-, ovarium carcinoma
APC	Colorectal carcinoma
ARF	Colorectal carcinoma
RB	Retinoblastoma
CDKN2B	Leukaemia
CDKN2A	Different neoplasmsípusok
VHL	Renal cell carcinoma
p16INK4A	Colorectal-, urinary bladder-, oesophagus-, lung carcinoma, lymphoma
BRCA1	Breast-, ovarium carcinoma

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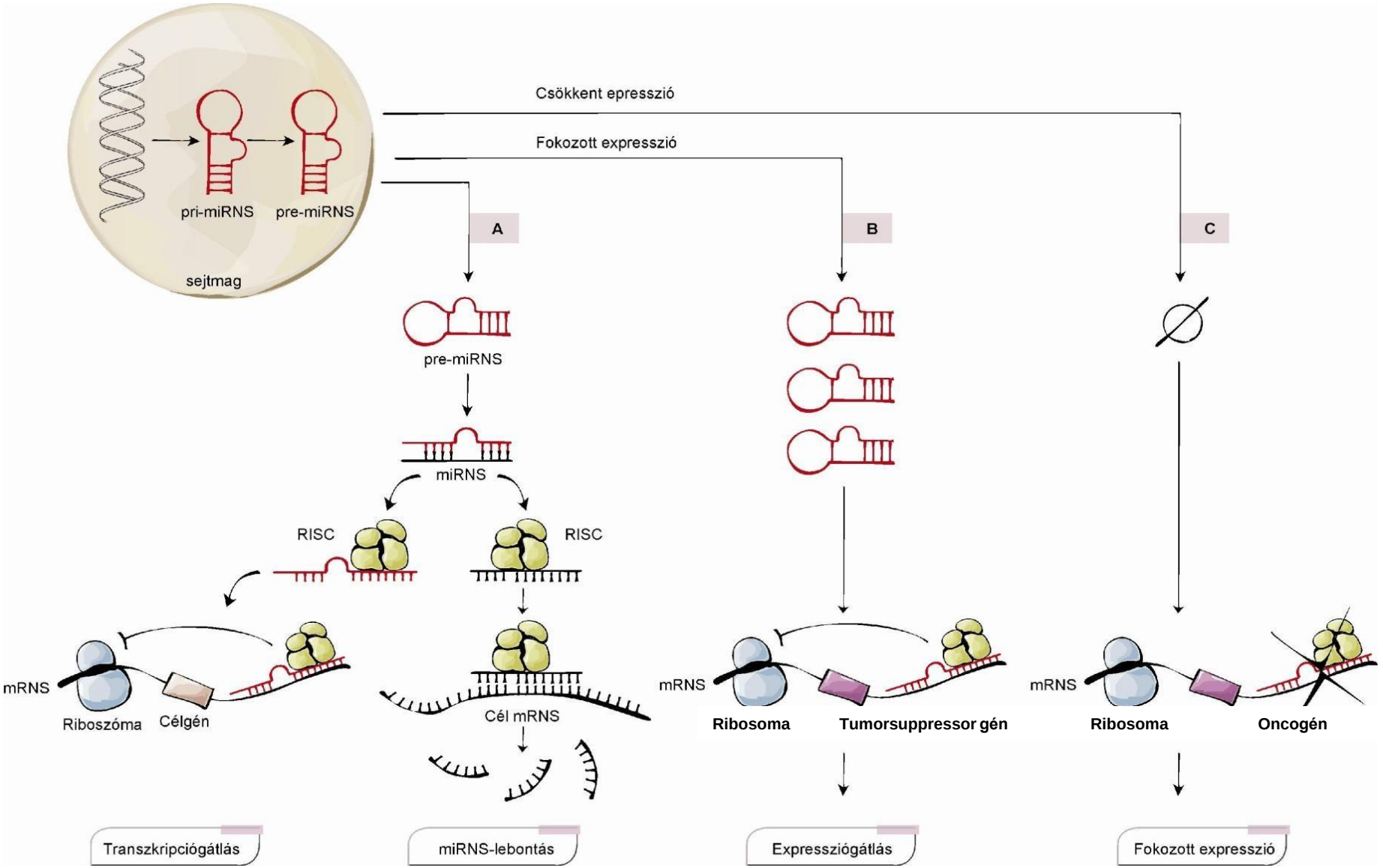
- Micro-RNS expression

The role of miRNS in the development of cancer



The role of miRNS in the development of cancer

miRNA type	miRNA	Neoplasm
Onkogene miRNA	miR-17-92	Lung cancer
	miR-372-373	Testis germinal tumors
	miR-21	Glioblastoma, breast cancer
	miR-155	Breast-, colon-, lung cancer, B-cell lymphoma
	miR-146	Breast-, pancreas-, prostate cancer
	miR-121,122	Papillary thyroid cancer
Tumor suppressor miRNA	miR-127	Urinary bladder-, prostate cancer
	miR-15a	CLL
	miR-145	Colon-, breast cancer
	Let-7	Related to prognosis of lung cancer

Multistep genetic alteration in cancer development