EVROPSKÁ UNIE
Evropské strukturální a investiční fondy
Operační program Výzkum, vývoj a vzdělávání

Zpráva o řešení projektu reg. č.: CZ.02.2.69/0.0/0.0/16_015/0002362 za období 052020 - 072020

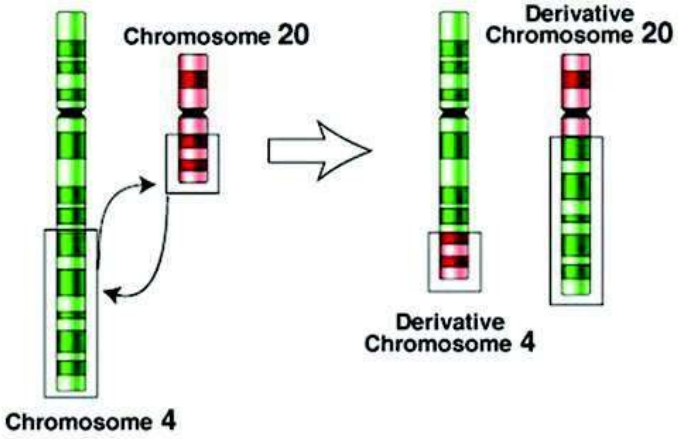
Autor: kolektiv autorů pod vedením prof. MUDr. Petra Zacha, CSc. z Ústavu Anatomie 3. LF UK

Příloha 1

Pracovní sešit
kurz 4

Obrázky a tabulky v tomto pracovním sešitu pochází z:

Norman, Anthony W.; Henry, Helen L.. Hormones (Kindle Location 12035). Elsevier Science. Kindle Edition.



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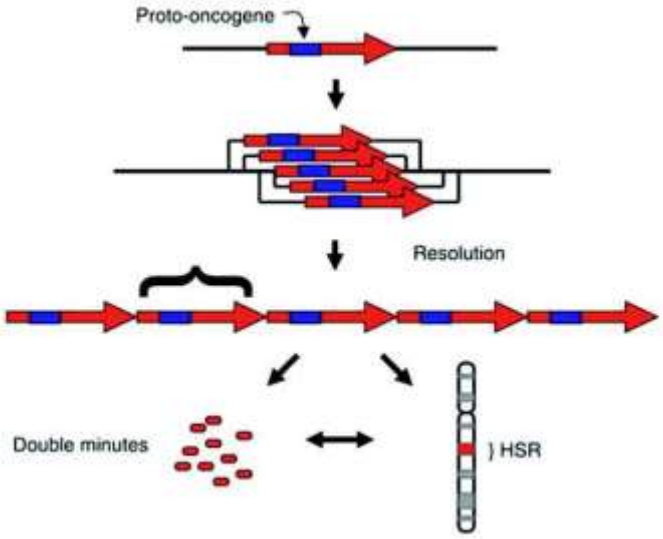
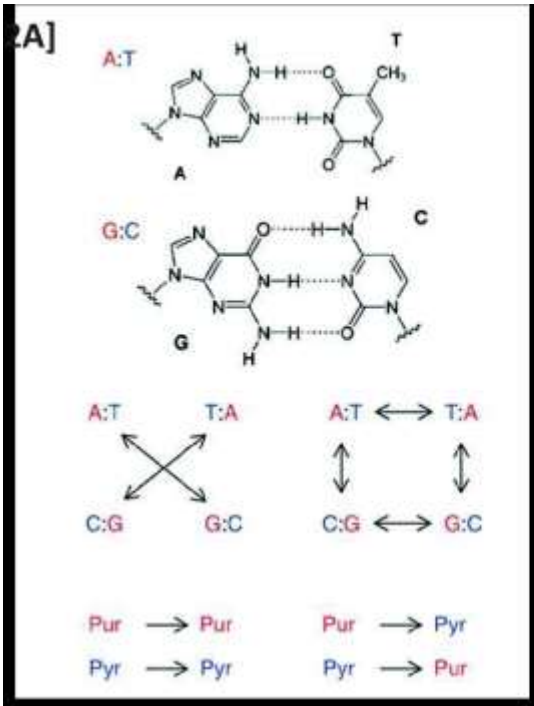
5′-aat agt aaa aag acg ttg Cga gaa gtt gga agt gtg-3′
   N   S   K   K   T   L   R   E   V   G   S   V

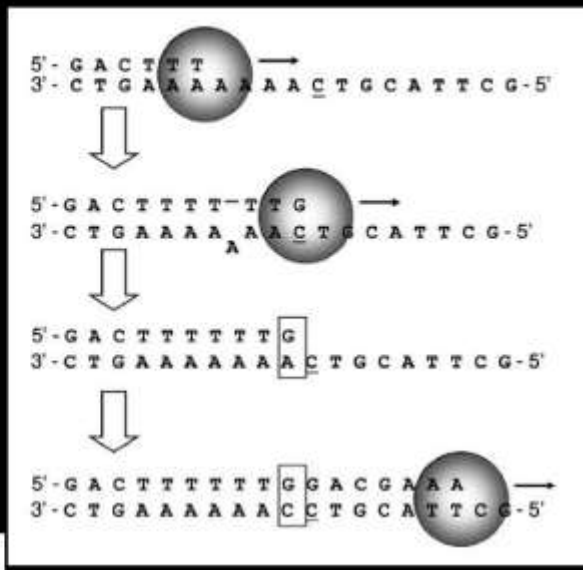
5′-aat agt aaa aag acg ttg Tga gaa gtt gga agt gtg-3′
   N   S   K   K   T   L   STOP
```

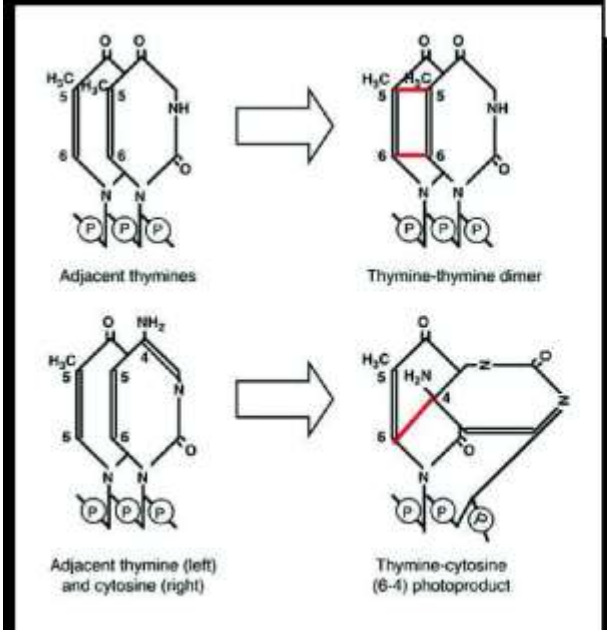
```
5′-gaa ata aaa gaa AAg att gga act agg tca-3′
   E   I   K   E   K   I   G   T   R   S

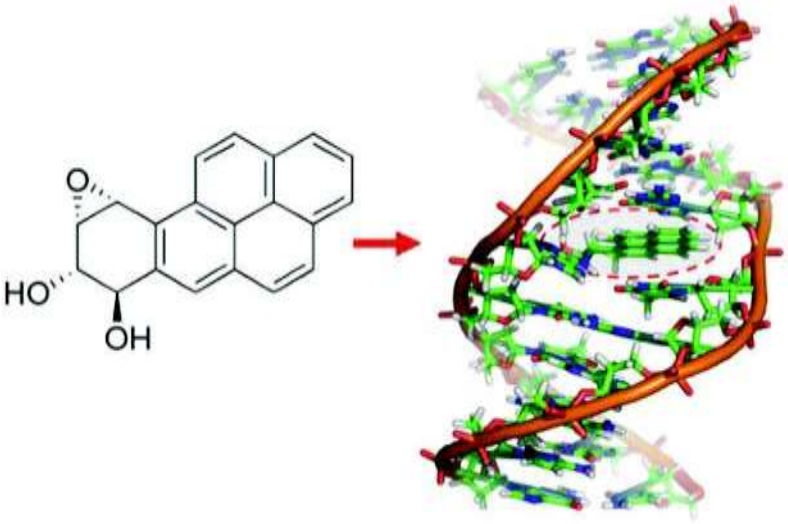
5′-gaa ata aaa gaa gat tgg aac tag gtc a-3′
   E   I   K   E   D   W   N   STOP
```

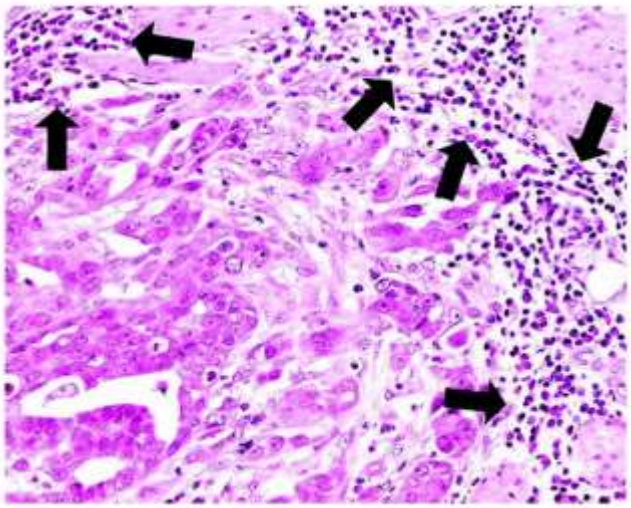


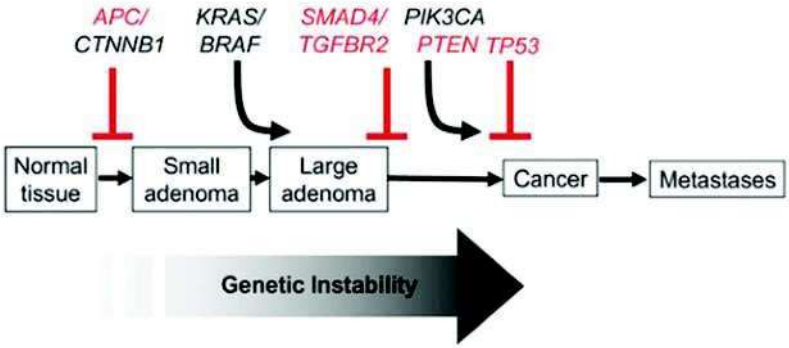

A:T
T
A
G:C
C
G
A:T T:A
C:G G:C
A:T ⟷ T:A
C:G ⟷ G:C
Pur → Pur
Pyr → Pyr
Pur → Pyr
Pyr → Pur

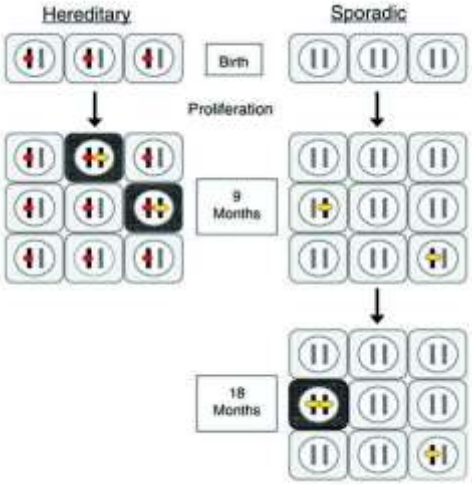

5'-GACTTT
3'-CTGAAAAAACTGCATTCG-5'
5'-GACTTTTTTG
3'-CTGAAAAAACTGCATTCG-5'
5'-GACTTTTTTTG
3'-CTGAAAAAAACTGCATTCG-5'
5'-GACTTTTTTTGGACGAAA
3'-CTGAAAAAAACCTGCATTCG-5'

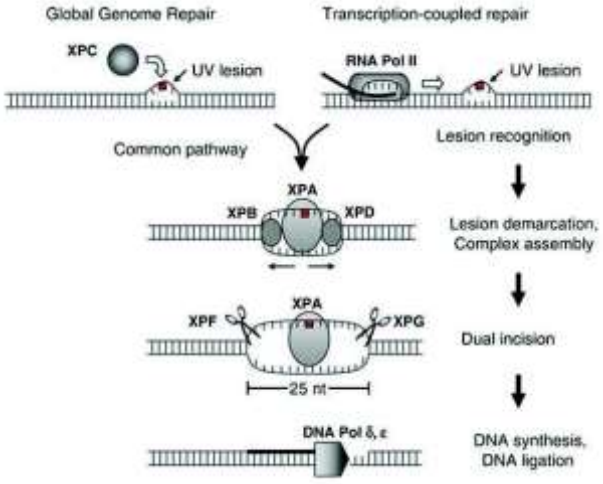

Adjacent thymines
Thymine-thymine dimer
Adjacent thymine (left) and cytosine (right)
Thymine-cytosine (6-4) photoproduct


O
HO
OH



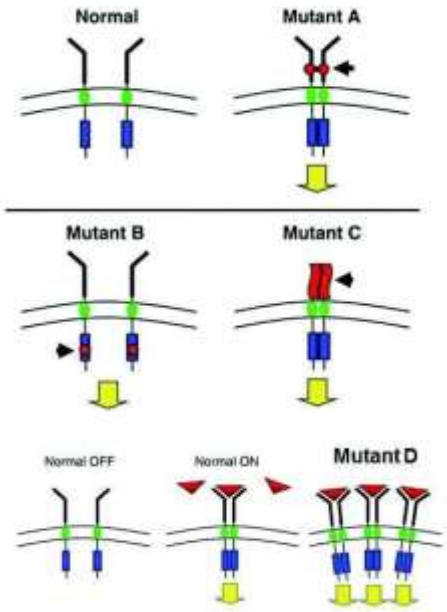

APC/
CTNNB1
KRAS/
BRAF
SMAD4/
TGFBR2
PIK3CA
PTEN
TP53
Normal tissue
Small adenoma
Large adenoma
Cancer
Metastases
Genetic Instability

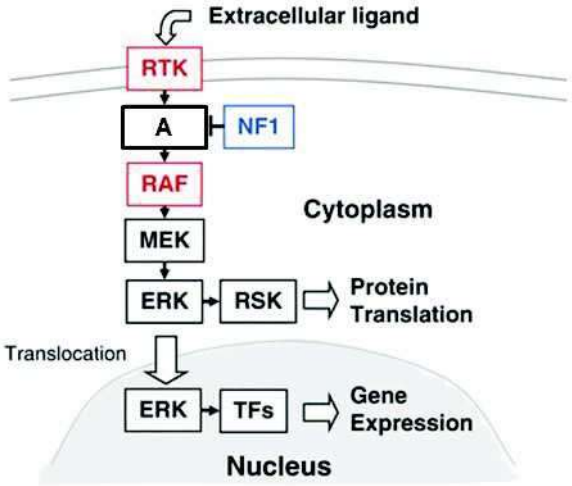


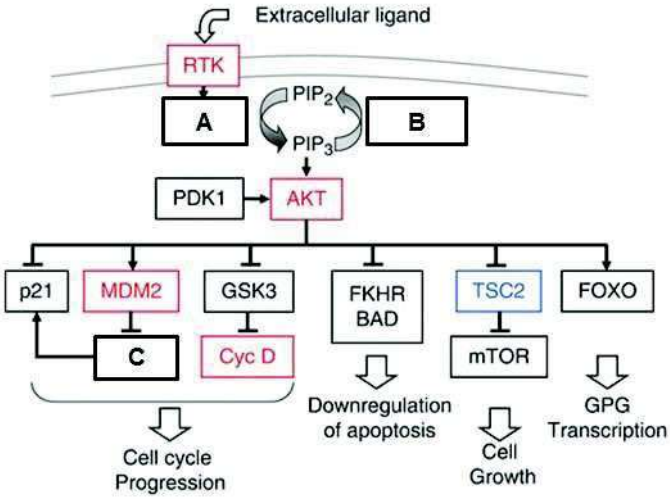


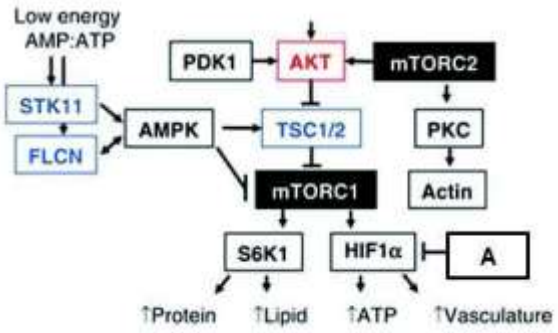
Zděděný zmutovaný gen	*Syndrom*	*Typ rakoviny*
RB1		
APC		
TP53		
BRCA		
	Familial Multiple Mole and Melanoma (FAMMM)	
	Cowdenův syndrom	

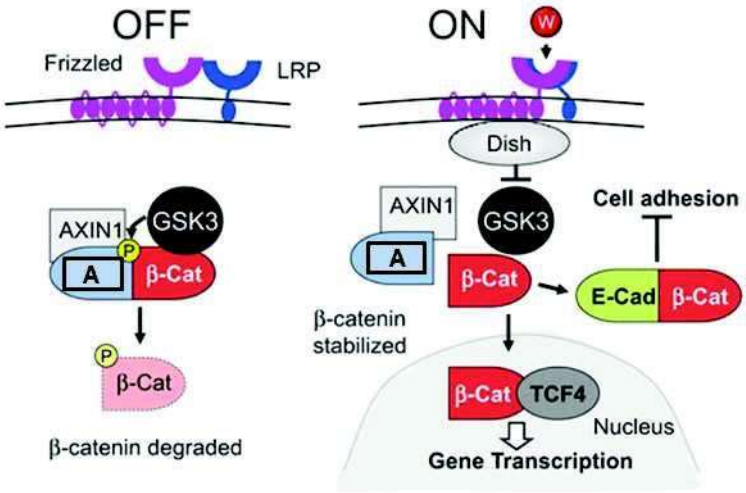
Zděděný zmutovaný gen	*Syndrom*	*Typ rakoviny*
	Juvenilní polypózní syndrom	
NF1		
	Gorlinův syndrom	
VHL		
	Turcotův syndrom	
	Mnohočetná endokrinní neoplazie	
	Lynchův syndrom	

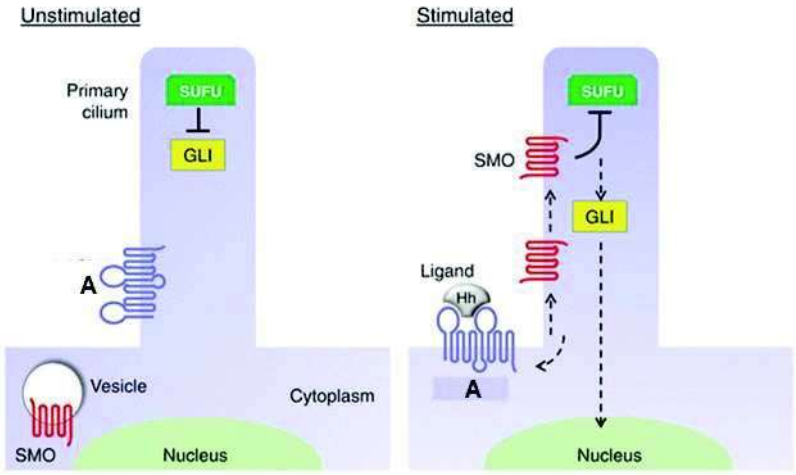

Normal
Mutant A
Mutant B
Mutant C
Normal OFF
Normal ON
Mutant D

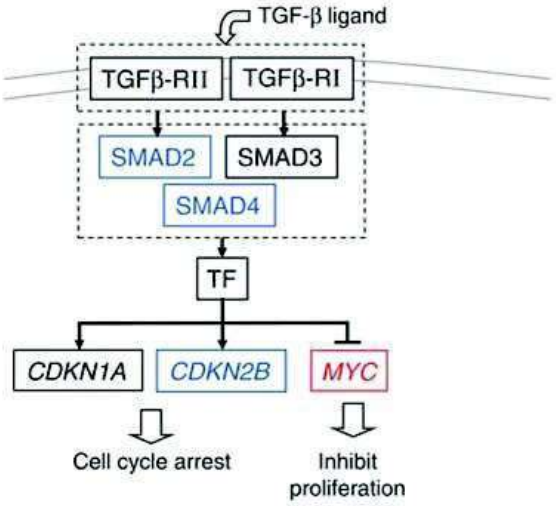

Extracellular ligand
RTK
A
NF1
RAF
MEK
Cytoplasm
ERK
RSK
Protein Translation
Translocation
ERK
TFs
Gene Expression
Nucleus

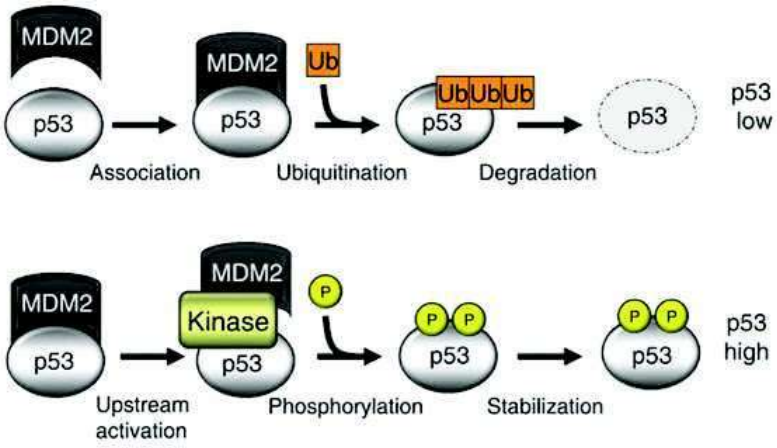

Extracellular ligand
RTK
A
PIP2
PIP3
B
PDK1
AKT
p21
MDM2
GSK3
FKHR BAD
TSC2
FOXO
C
Cyc D
mTOR
Downregulation of apoptosis
GPG Transcription
Cell cycle Progression
Cell Growth

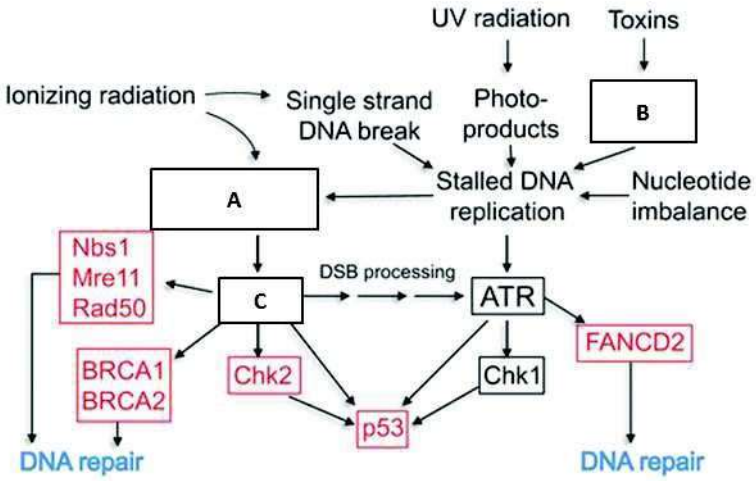

Low energy
AMP:ATP
PDK1
AKT
mTORC2
STK11
AMPK
TSC1/2
PKC
FLCN
mTORC1
Actin
S6K1
HIF1α
A
↑Protein
↑Lipid
↑ATP
↑Vasculature

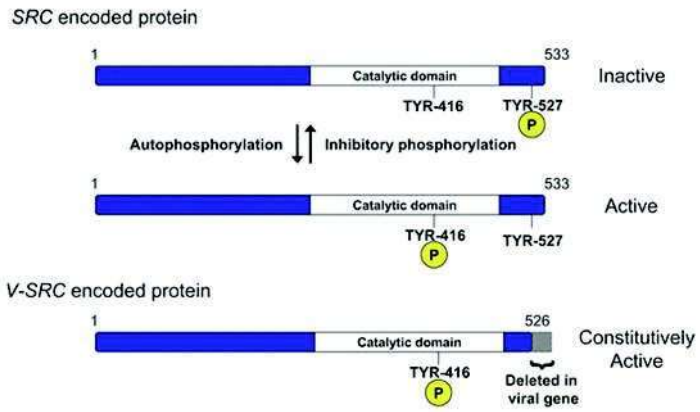

OFF
Frizzled
LRP
AXIN1
GSK3
P
A
β-Cat
P
β-Cat
β-catenin degraded
ON
W
Dish
AXIN1
GSK3
A
Cell adhesion
β-Cat
E-Cad
β-Cat
β-catenin
stabilized
β-Cat
TCF4
Nucleus
Gene Transcription

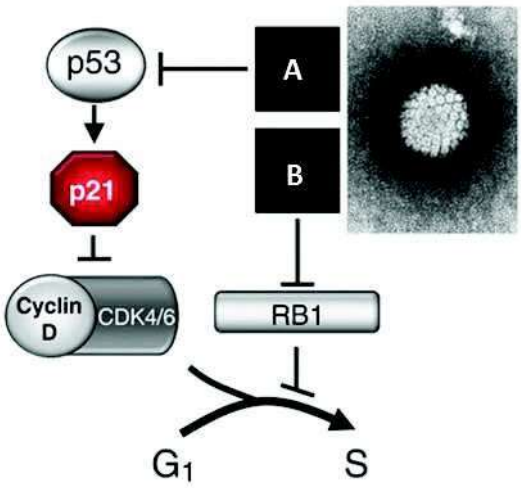

Unstimulated
Primary
cilium
SUFU
GLI
A
Vesicle
Cytoplasm
SMO
Nucleus
Stimulated
SUFU
SMO
GLI
Ligand
Hh
A
Nucleus


TGF-β ligand
TGFβ-RII
TGFβ-RI
SMAD2
SMAD3
SMAD4
TF
CDKN1A
CDKN2B
MYC
Cell cycle arrest
Inhibit proliferation


MDM2
p53
Association
Ub
Ubiquitination
Ub Ub Ub
Degradation
p53 low
Kinase
P
Upstream activation
Phosphorylation
Stabilization
p53 high

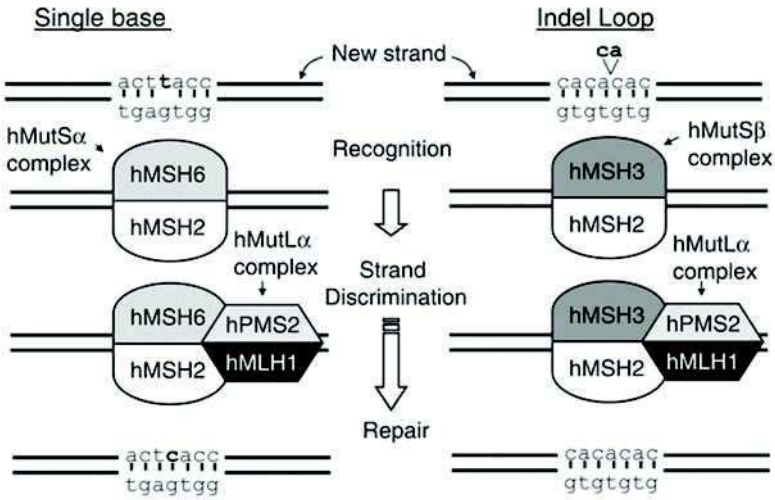

UV radiation
Toxins
Ionizing radiation
Single strand DNA break
Photo-products
B
A
Stalled DNA replication
Nucleotide imbalance
Nbs1
Mre11
Rad50
C
DSB processing
ATR
FANCD2
BRCA1
BRCA2
Chk2
Chk1
p53
DNA repair
DNA repair





Infekční agens	Typ	Zánětlivá choroba	Rakovina
Hepatitis B virus Hepatitis C virus	DNA virus	hepatitis	
	bakterie	gastritis	rakovina žaludku
Epstein-Barr virus	DNA virus	mononukleóza	
	DNA virus	cervicitis	rakovina děložního čípku
Schistosoma haematobium	motolice	cystitis	
Opisthorchis viverrini	motolice	cholangitis	

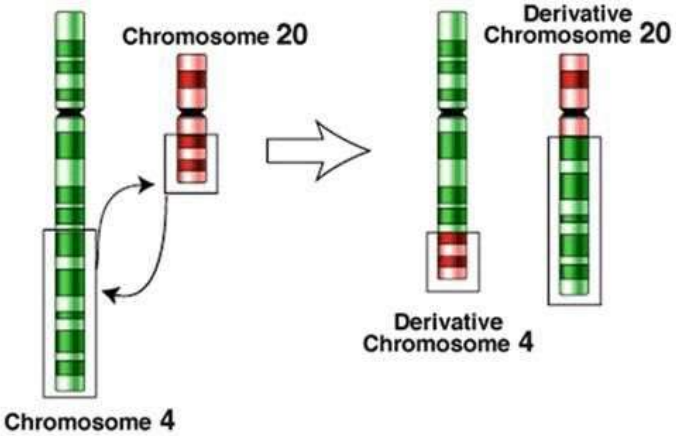
gen	protein
sis	
	FGF-4
erbB	
	HGFR
trkA	



Workbook course 4

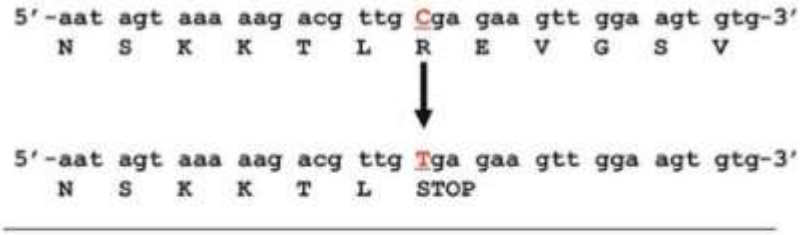
The pictures and tables in this workbook are from:

Norman, Anthony W.; Henry, Helen L.. Hormones (Kindle Location 12035). Elsevier Science. Kindle Edition.

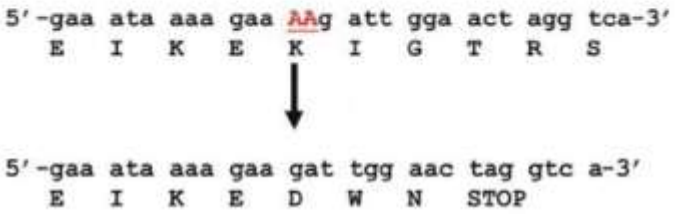


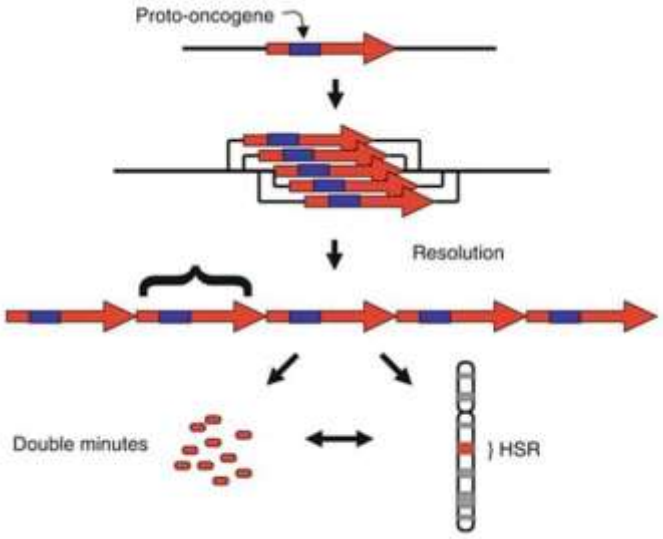
[1A]

[1B]



[1C]





[1D]

[1A]

1. Write the name of the type of mutation in the picture.
2. What kind of damage has to happen to DNA to make this mutation possible?
3. Which environmental factor can cause this kind of DNA damage?
4. This type of mutation leads preferably to one kind of cancer. Which one?
5. How can this mutation influence the expression of proteins?

[1B]

1. What is the name of the mutation in picture B?

2. How will the final protein look?

3. How can this mutation influence the function of the final protein?

[1C]

1. What is the name of the mutation in picture C?

2. When you consider reading the genetic information, what has happened?

3. How will the final protein look?

4. How can this mutation influence the function of the final protein?

[1D]

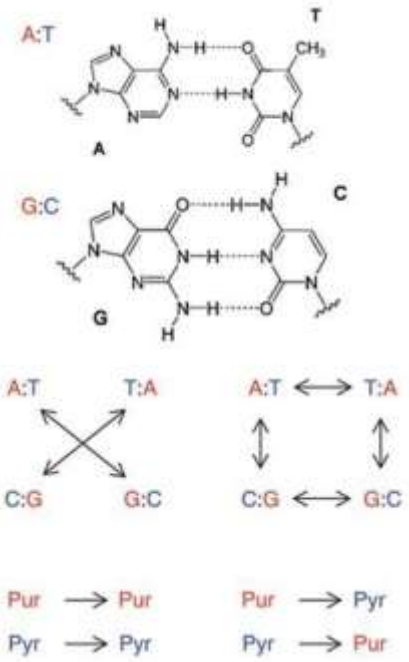
1. Write the name of the type of mutation in the picture.

2. Does this mutation matter in oncogenes or tumor suppressor genes?

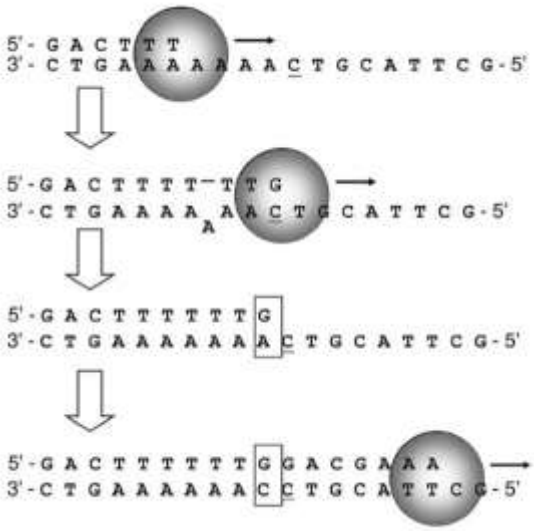
3. How can such mutation happen?

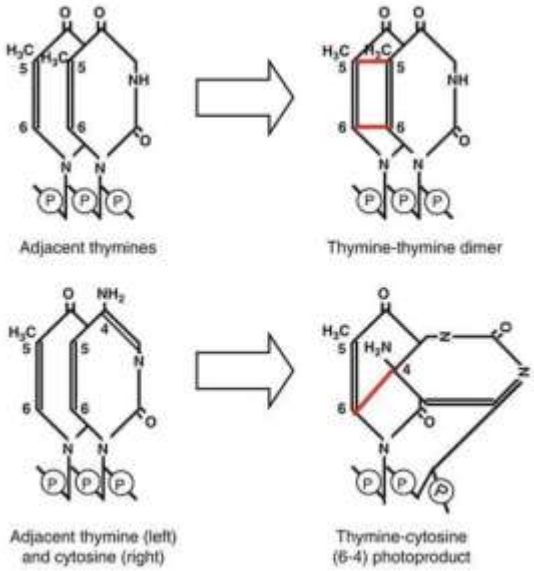
4. Write down some genes that are often mutated in this way in various types of cancer.

[2A]


A:T
T
A
G:C
C
G
A:T
T:A
C:G
G:C
A:T ⟷ T:A
C:G ⟷ G:C
Pur → Pur
Pyr → Pyr
Pur → Pyr
Pyr → Pur

[2B]


5'-GACTTT
3'-CTGAAAAAACTGCATTCG-5'
5'-GACTTTT-TTG
3'-CTGAAAA A AACTGCATTCG-5'
5'-GACTTTTTTTG
3'-CTGAAAAAAAACTGCATTCG-5'
5'-GACTTTTTTTGGACGAAA
3'-CTGAAAAAAACCTGCATTCG-5'


Adjacent thymines
Thymine-thymine dimer
Adjacent thymine (left) and cytosine (right)
Thymine-cytosine (6-4) photoproduct

[2C]

[2A]

1. What is transition?

2. What is transversion?

3. Which one of these types of mutations can happen due to enzyme activity?

4. Which types of substitutions are most common?

[2B]

1. Describe what is happening in the picture.

2. What type of mutation has happened there?

[2C]

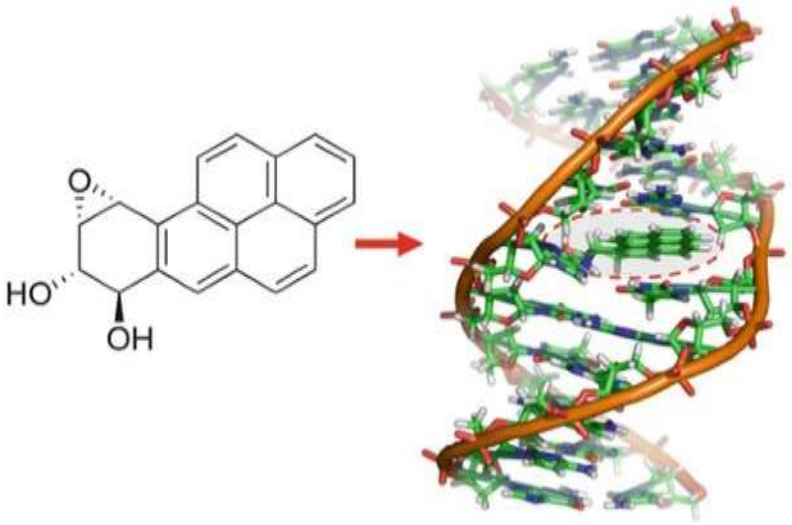
1. Which environmental factor has caused this type of DNA damage?

2. This type of DNA damage causes a specific type of cancer. Which one?

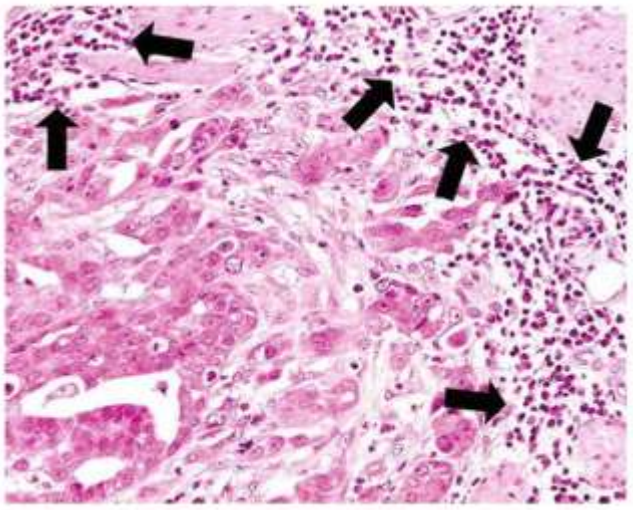
3. Name the mechanism that can repair this type of DNA damage.

4. So-called ionizing irradiation causes a different kind of DNA damage. Which one? Which mechanisms can the cell use to repair that damage?

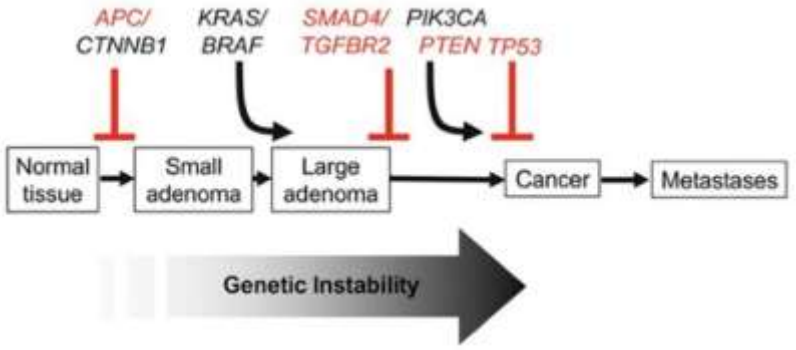
5. Which of the mentioned repair mechanisms is less prone to make a mistake?



[3A]



[3B]



[3C]

[3A]

1. Na obrázku je aktivní metabolit kterého karcinogenu?

2. Které skupině látek ten karcinogen patří?

3. Jak může tato látka vniknout do našeho organismu?

4. Jakým způsobem interaguje s DNA?

5. Jak se nazývá výsledek této interakce?

6. K čemu následně doje při replikaci DNA?

7. Jaký druh rakoviny tato látka způsobuje?

[3B]

1. Jakým způsobem může chronický zánět přispět ke vzniku nádorového bujení?

2. Jakým způsobem může chronický zánět přispět k propagaci nádorového bujení?

[3C]

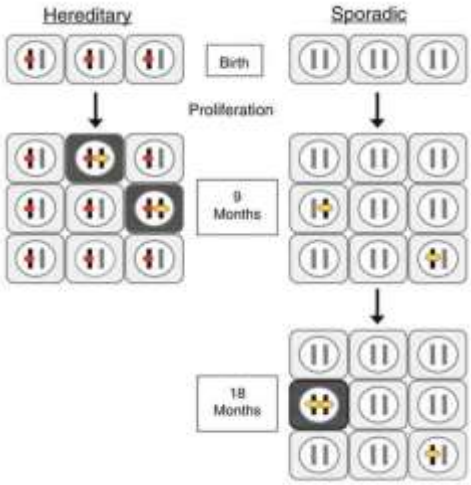
1. Vznik které rakoviny tento obrázek znázorňuje?

2. Kterou barvou jsou vyznačeny onkogeny a kterou tumor supresorové geny?

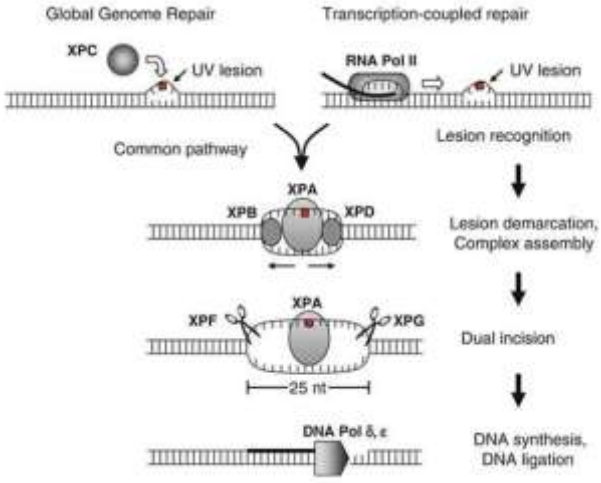
3. Popište funkci jednotlivých onkogenů uvedených na obrázku.

4. Popište funkci jednotlivých tumor supresorových genů uvedených na obrázku.

5. Dělí se rakovinné buňky rychleji než normální buňky?



[4A]



[4B]

[4C]

Zděděný zmutovaný gen	*Syndrom*	*Typ rakoviny*
RB1		
APC		
TP53		
BRCA		
	Familial Multiple Mole and Melanoma (FAMMM)	
	Cowdenův syndrom	

Zděděný zmutovaný gen	*Syndrom*	*Typ rakoviny*
	Juvenilní polypózní syndrom	
NF1		
	Gorlinův syndrom	
VHL		
	Turcotův syndrom	
	Mnohočetná endokrinní neoplazie	
	Lynchův syndrom	

[4A]

1. The picture shows the tumorigenesis of a specific tumor. Which tumor?

2. Which protein gets mutated in the picture?

3. What is the function of the mutated protein in the cell cycle?

4. What happens when the protein loses its function due to mutation?

[4B]

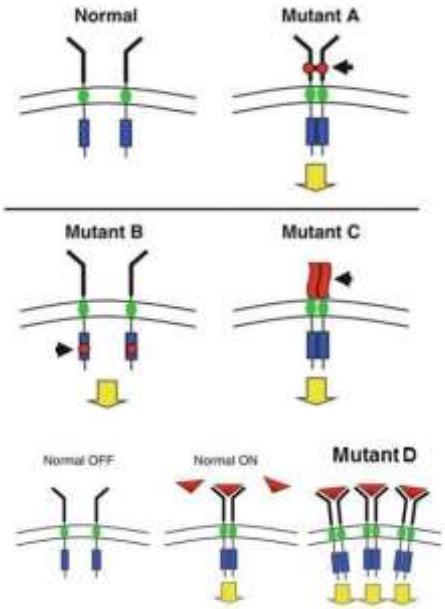
1. What is the name of the process in the picture?

2. What kind of mutations does this process repair?

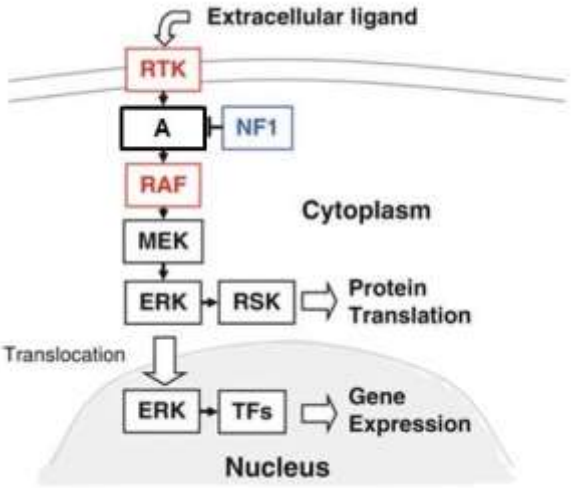
3. What is xenoderma pigmentosum? Describe its symptoms.

[4C]

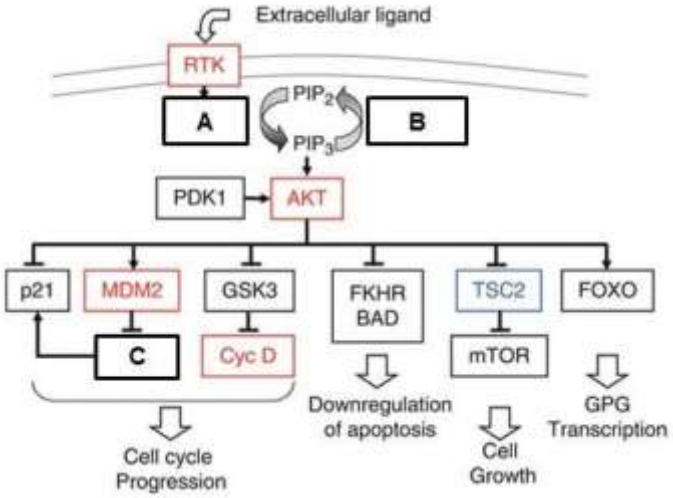
1. Fill in the table.



[5A]



[5B]



[5C]

[5A]

1. Which type of membrane receptors is in the picture?

2. Which types of mutations do you see in the pictures A, B, C a D?

[5B]

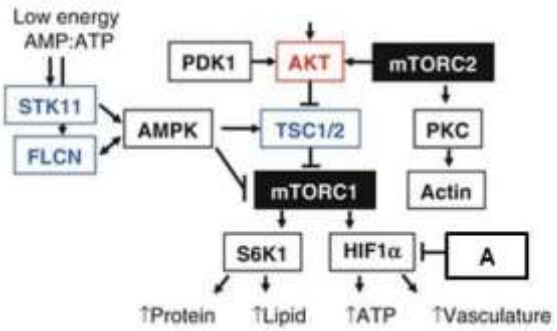
1. What is the name of the molecule „A“?

2. Is „A“ an oncogene or a tumor suppressor gene?

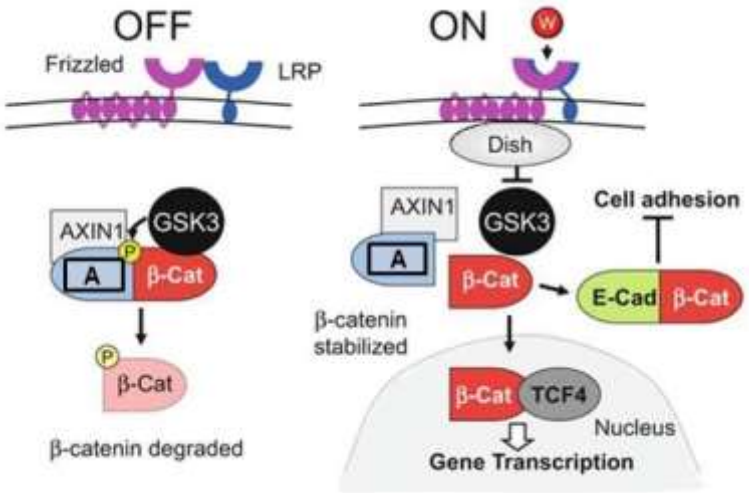
3. What do you know about NF1?

[5C]

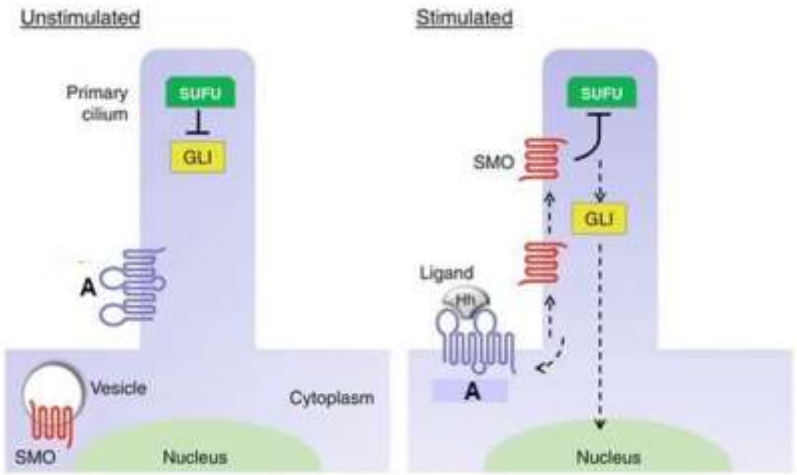
1. What is the name of the molecule „A“?
2. Is the „A“ an oncogene or a tumor suppressor gene?
3. What is the name of the molecule „B“?
4. Is the „B“ an oncogene or a tumor suppressor gene?
5. Hereditary mutation of the „B“ molecule causes a cancer syndrome. Which one?
6. What is the name of the molecule „C“?
7. Is the „C“ an oncogene or a tumor suppressor gene?
8. Hereditary mutation of the „C“ molecule causes a cancer syndrome. Which one?



[6A]



[6B]



[6C]

[6A]

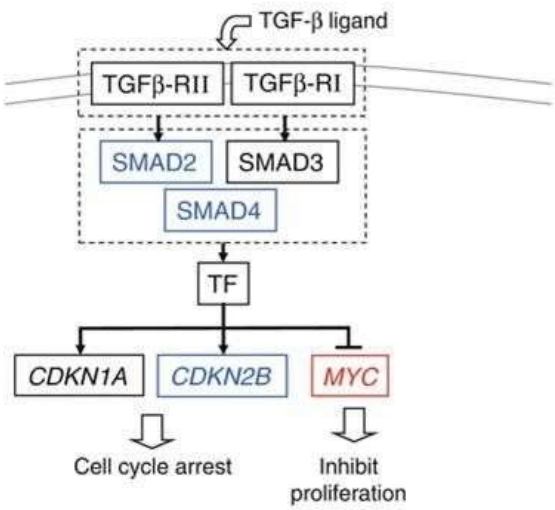
1. What is the main function of the mTOR signaling?
2. What is the name of the „A“?
3. What is the function of the „A“?
4. Is the „A“ an oncogene or a tumor suppressor gene?
5. The hereditary mutation of the „A“ causes a cancer syndrome. Which one?
6. The hereditary mutation of one of the molecules in the picture (not the „A“) causes Birt–Hogg–Dubé syndrome? Which one?

[6B]

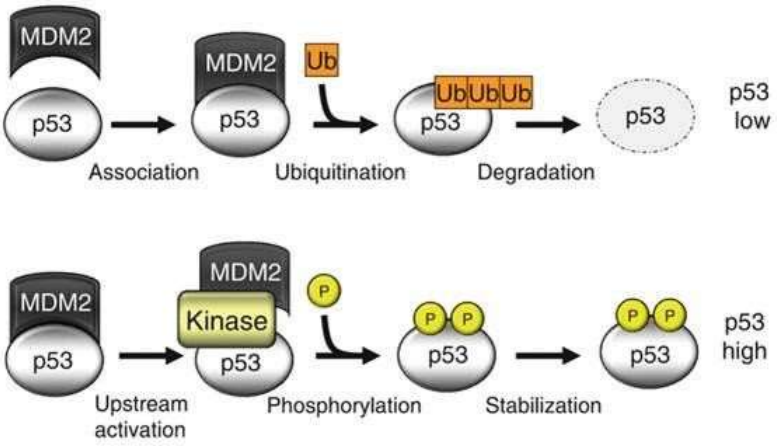
1. What is the name of the ligand, which activates Frizzled and LRP?
2. What is the name of the „A“?
3. Is the „A“ an oncogene or a tumor suppressor gene?
4. The hereditary mutation of the „A“ causes a cancer syndrome. Which one?
5. What is the main function of the β-catenin?
6. Is the β-catenin an oncogene or a tumor suppressor gene?

[6C]

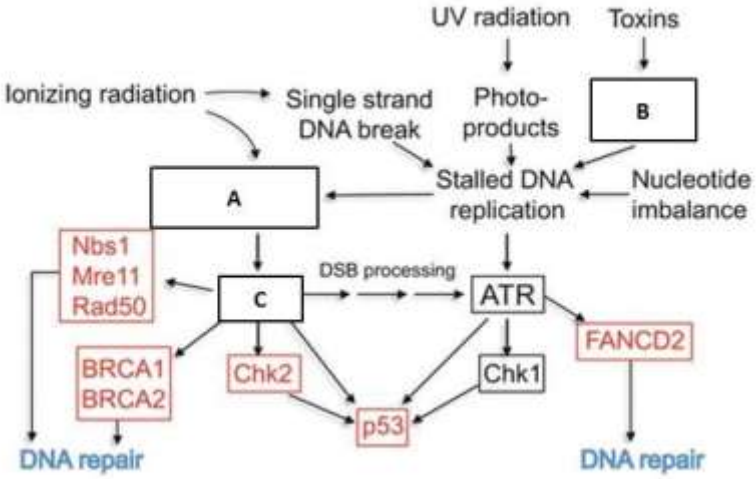
1. Jak se jmenuje molekula je „A“?
2. What is the name of the „A“?
3. What is the function of the „A“?
4. Is the „A“ an oncogene or a tumor suppressor gene?
5. In which type of cells this signaling should not occur?
6. The hereditary mutation of the „A“ causes a cancer syndrome. Which one?



[7A]



[7B]



[7C]

[7A]

1. Which color represents the oncogenes and which the tumor suppressor genes?
2. The gene CDKN2B encodes two proteins. Which ones? What is their function?
3. What is the function of the myc protein?
4. What is the main purpose of the receptor serine-threonine kinases signaling?

[7B]

1. What do you know about the p53 protein?
2. What do you know about the MDM2 protein?

3. Which one of them is the oncogene, and which one is the tumor suppressor gene?

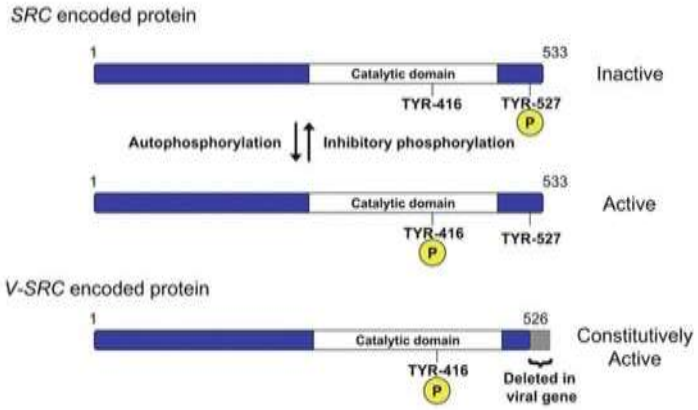
4. Do you know another transcription factor, which, if not activated, is constitutively degraded by the ubiquitination?

[7C]

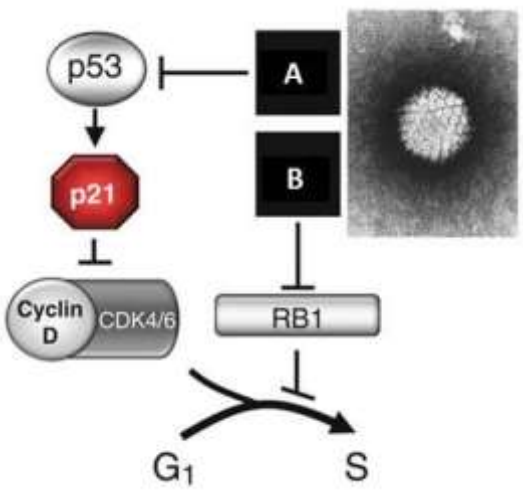
1. How can ionizing radiation affect DNA? Fill in „A“.

2. What can occur when various toxins affect DNA? Fill in „B“.

3. What is the name of the molecule „C“ and what is its function?



[8A]



[8B]

[8C]

Infekční agens	Typ	Zánětlivá choroba	Rakovina
Hepatitis B virus Hepatitis C virus	DNA virus	hepatitis	
	bakterie	gastritis	rakovina žaludku
Epstein-Barr virus	DNA virus	mononukleóza	
	DNA virus	cervicitis	rakovina děložního čípku
Schistosoma haematobium	motolice	cystitis	
Opisthorchis viverrini	motolice	cholangitis	

[8A]

1. What is the function of the src protein?

2. Describe the functional difference between the protein encoded by the gene C-SRC and the protein encoded by the gene V-SRC.

3. Which group of viruses can transmit v-src?

[8B]

1. What is the name of „A“?

2. What is the name of „B“?

3. Name the virus that contains genes for these two proteins.

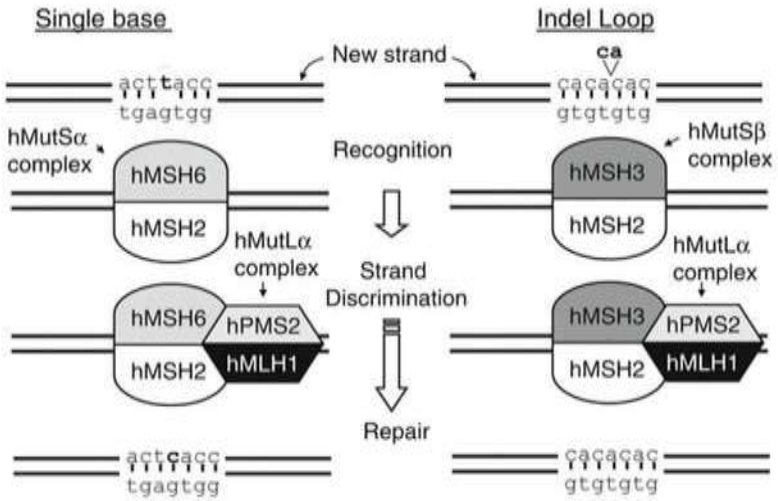
4. Into which group of viruses does that virus belong?

[8C]

1. Fill in the table.

[9A] **[9B]**

gen	protein
sis	
	FGF-4
erbB	
	HGFR
trkA	



[9A]

1. Fill in the table.

[9B]

1. What kind of DNA repair is in the picture?

2. Name at least two syndromes caused by germline mutations of genes that encode protein participating in this type of DNA repair.