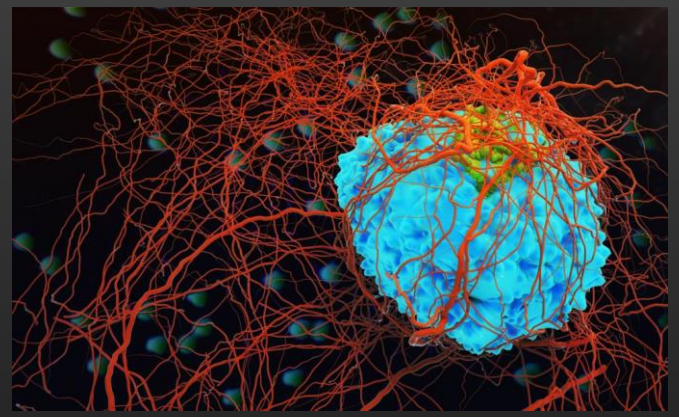
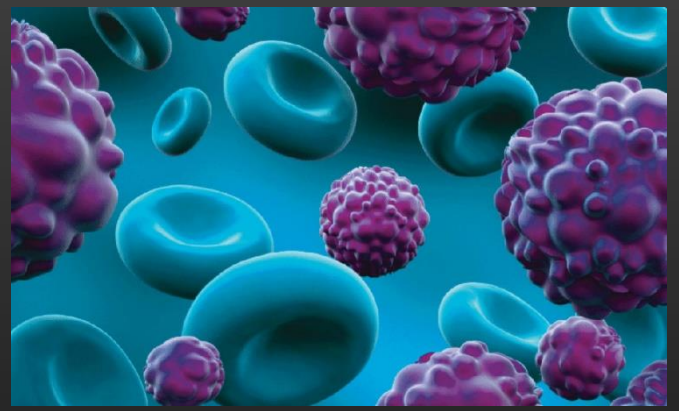
Universitas Indonesia
2019


ONKOLOGI DASAR

MODUL HEMATOLOGI-ONKOLOGI

Narator

dr. Fikri Ichsan Wiguna

Narasumber

Dr. dr. Ikhwan Rinaldi, Sp.PD-KHOM, M. Epid

Tujuan Pembelajaran

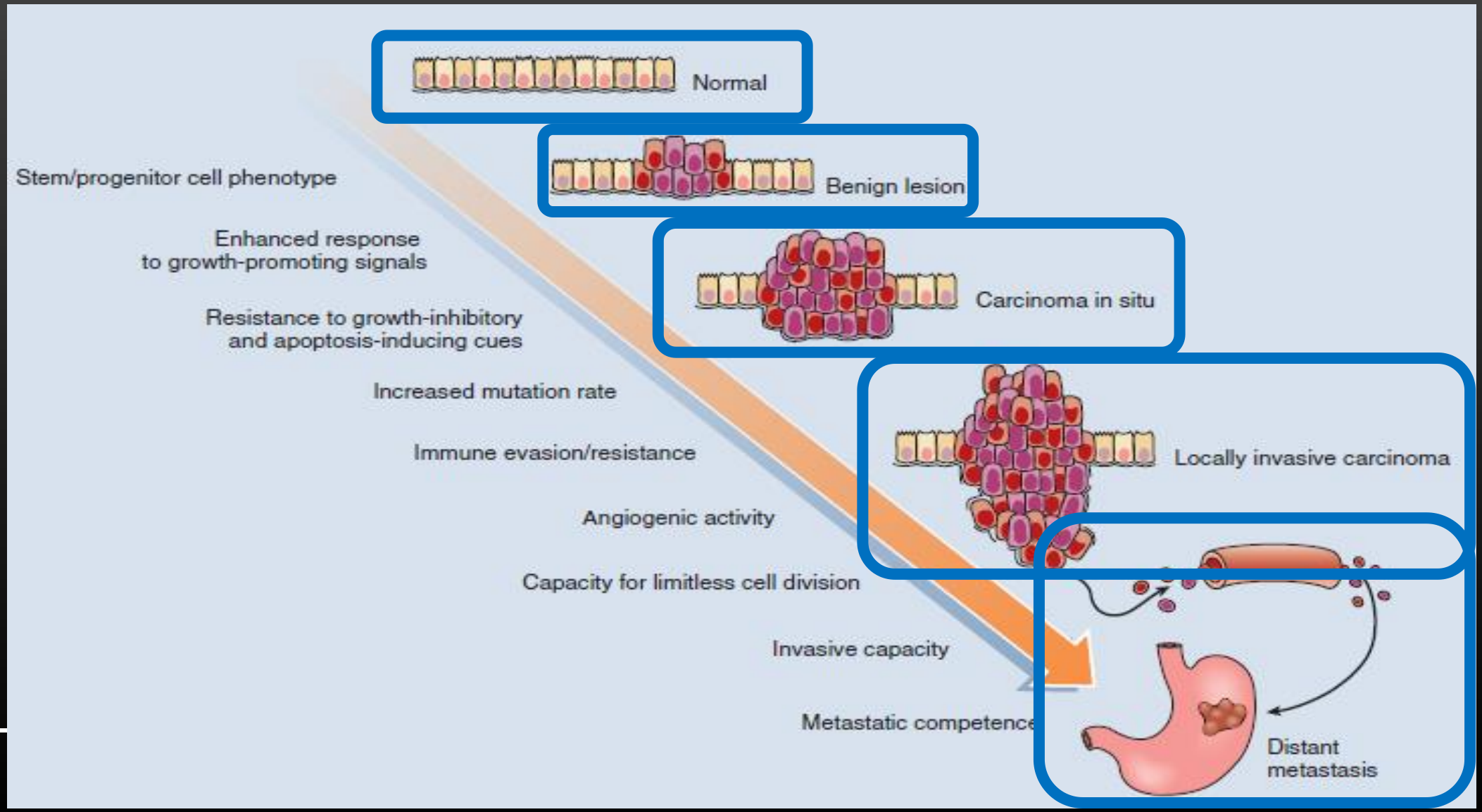
- Mahasiswa mampu menjelaskan patofisiologi terjadinya kanker
- Mahasiswa mampu menjelaskan zat-zat karsinogen beserta faktor risiko kanker
- Mahasiswa mengetahui petanda keganasan

Daftar Isi

- ❑Gambaran Umum Onkologi
- ❑Patogenesis dan Patofisiologi Kanker
- ❑Faktor risiko
- ❑Tumor Marker

GAMBARAN UMUM ONKOLOGI

Onkologi



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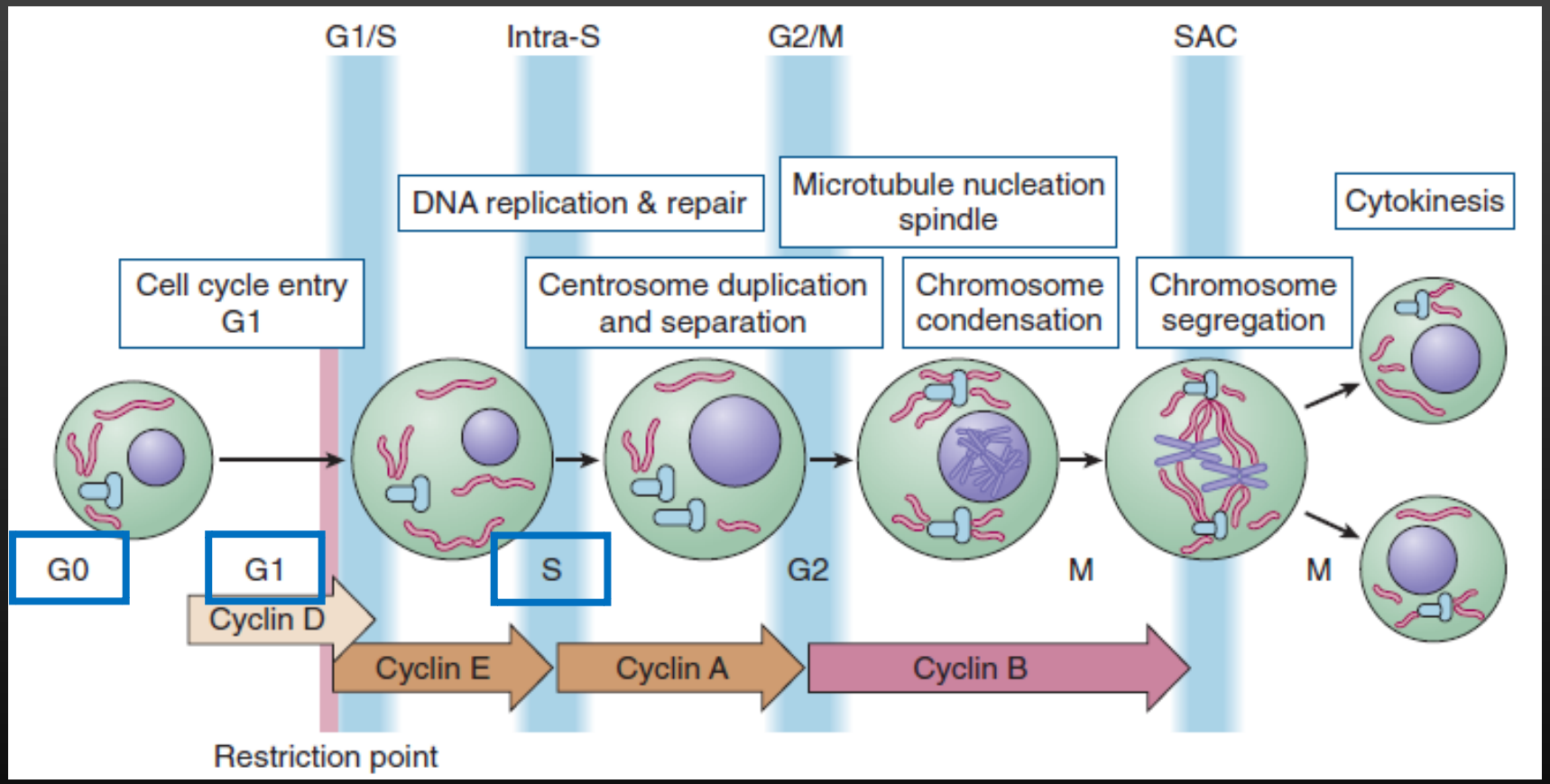

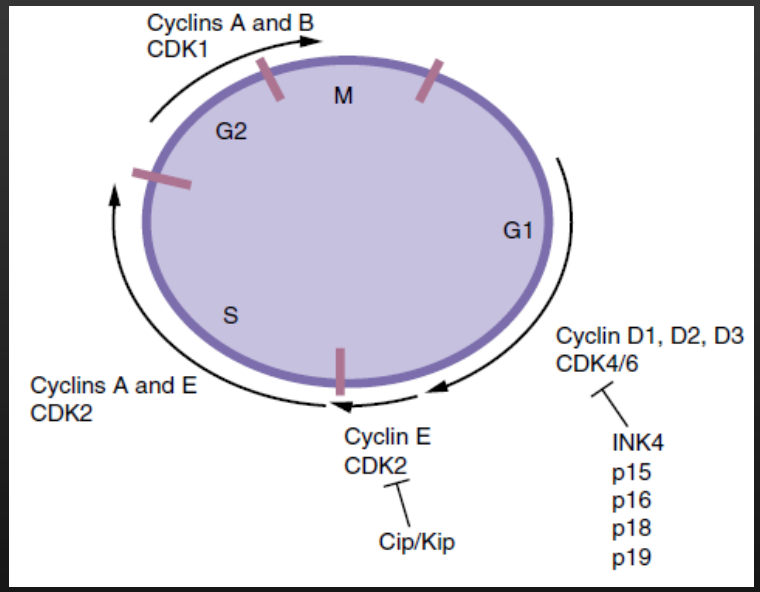

Sumber:

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Siklus Sel

Table 4-1 Molecules Involved in Cell Cycle Regulation

Protein Family/Complex	Representative Members	Function
KINASES		
Cyclin-dependent kinases	Heterodimeric complexes formed of a cyclin (A, B, D, and E types) and a Cdk (Cdk1, Cdk2, Cdk4, Cdk6); Cdk7 functions as a Cdk-activating kinase	Phosphorylation of multiple proteins to drive progression throughout the different phases of the cell cycle
Wee1/Myt1	Wee1, Myt1	Inactivation of Cdks
Aurora A holoenzyme kinases	Aurora A and its non-kinase activator, Tpx2	Spindle dynamics, chromosome segregation and cytokinesis
Chromosome passenger complex	Aurora B (Aurora C?), Incenp, Survivin, Borealin	Chromosome segregation
Polo-like kinases	Plk1–Plk5	Centrosome function, chromosome segregation, and cytokinesis
NIMA-related kinases	Nek1–Nek11	Centrosome function and mitosis
Mastl	Mastl	Inhibition of PP2A phosphatases
CDK INHIBITORS		
INK4 proteins	$p16^{INK4a}$, $p15^{INK4b}$, $p18^{INK4c}$, $p19^{INK4d}$	Inhibition of G1/S progression
Cip/Kip inhibitors	$p21^{Cip1}$, $p27^{Kip1}$, $p57^{Kip2}$	Cdk inhibition and other roles in transcription or the cytoskeleton

Sumber:
1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.

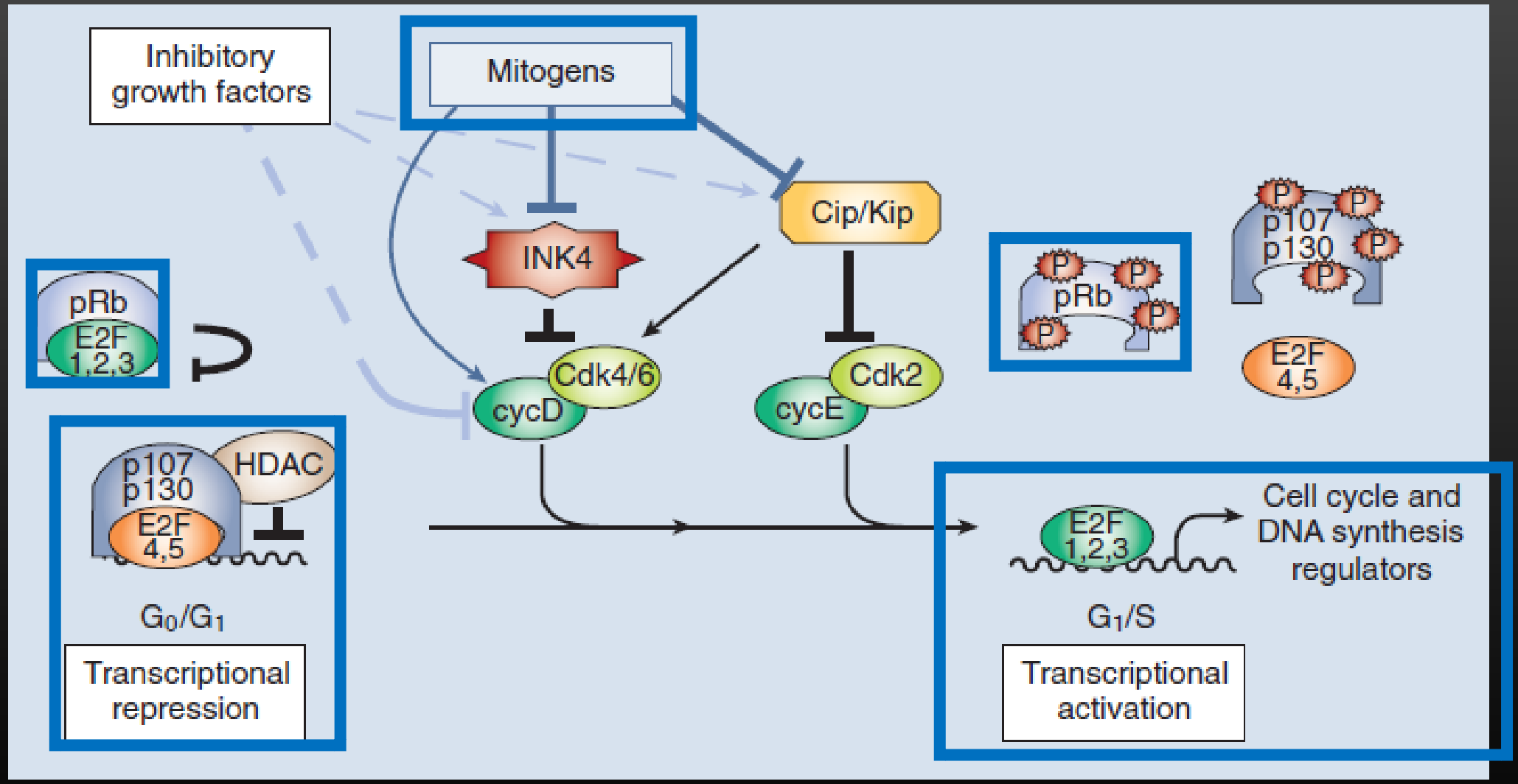
Siklus Sel

Table 4-1 Molecules Involved in Cell Cycle Regulation

TRANSCRIPTIONAL CONTROL		
Retinoblastoma family	pRb, p107, p130	Repression of the transcription of genes required for the cell cycle
E2F transcription factors	E2F1–E2F8	Transcription factors involved in G1/S transition
PHOSPHATASES		
Cdc14 phosphatases	Cdc14a, Cdc14b	Control of transcription and cell cycle progression
Cdc25 phosphatases	Cdc25a, Cdc25b, and Cdc25c	Cdk activation and cell cycle progression
PP1	Multiple complexes with different regulatory subunits	Protein dephosphorylation
PP2A	Multiple complexes with different regulatory subunits	Protein dephosphorylation; major Cdk-counteracting phosphatase
UBIQUITIN LIGASES		
SCF	E3 ubiquitin ligase formed of Rbx1, Cul1, Skp1, and an F-box protein (e.g., Skp2 or βTrCP)	Targets multiple cell cycle regulators (e.g., $p27^{Kip1}$ or cyclin E) for ubiquitin-dependent degradation during interphase
APC/C	E3 ubiquitin ligase composed for multiple subunits including Cdc20 or Cdh1 as co-activator molecules	Targets multiple cell cycle regulators for ubiquitin-dependent degradation during mitosis (cyclin B, securin) or the mitotic/interphase transition (e.g., Aurora A, Plk1, or Tpx2)
SPINDLE REGULATORS		
Kinesins	More than 600 proteins including Eg5, CenpE, MCAK	Microtubule-based motor proteins that hydrolyze ATP to generate energy for movement along microtubule fibers

Sumber:
1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.

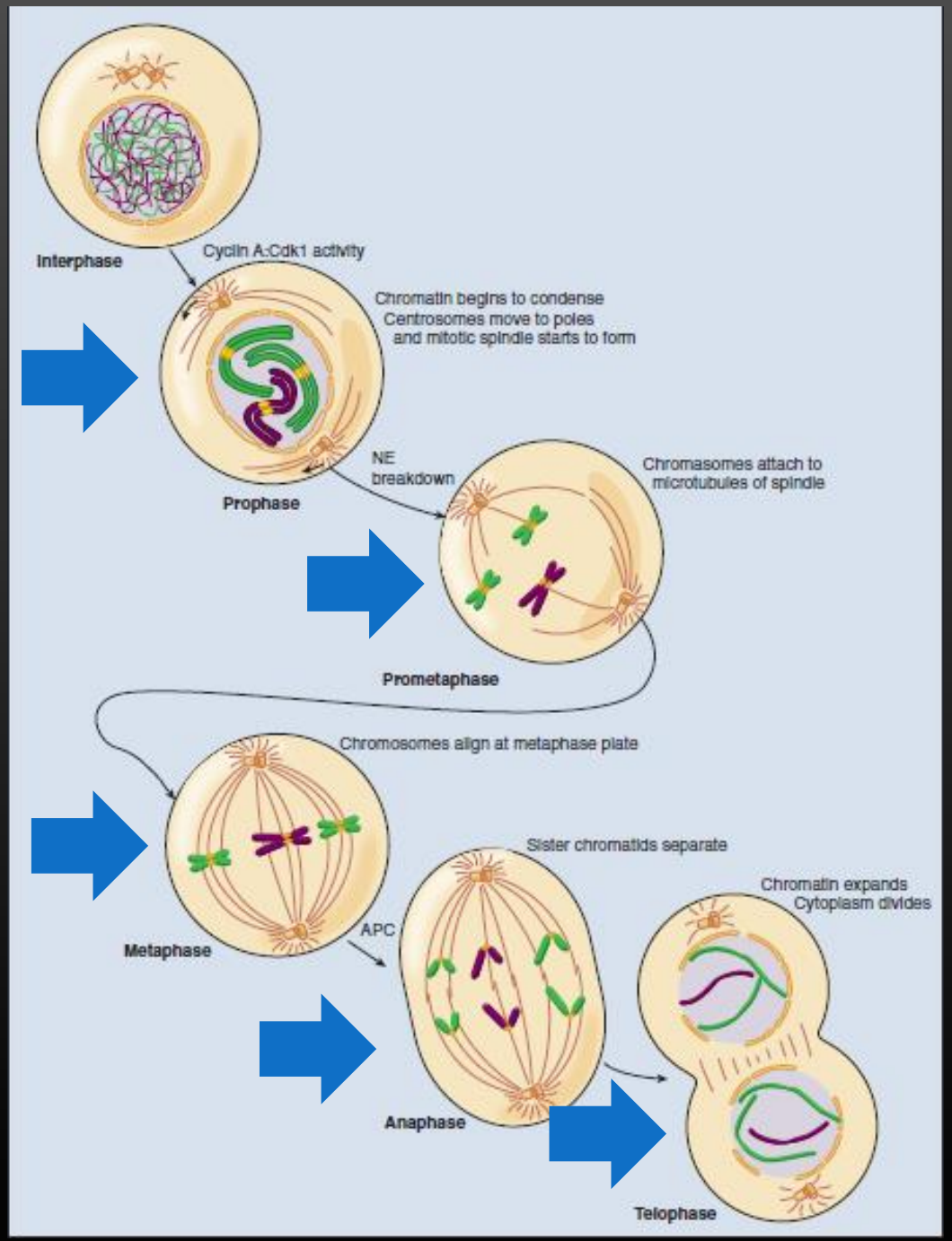
Siklus Sel – Inisiasi Siklus Sel



Sumber:

1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.

Siklus Sel: Mitosis



Sumber:
1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.

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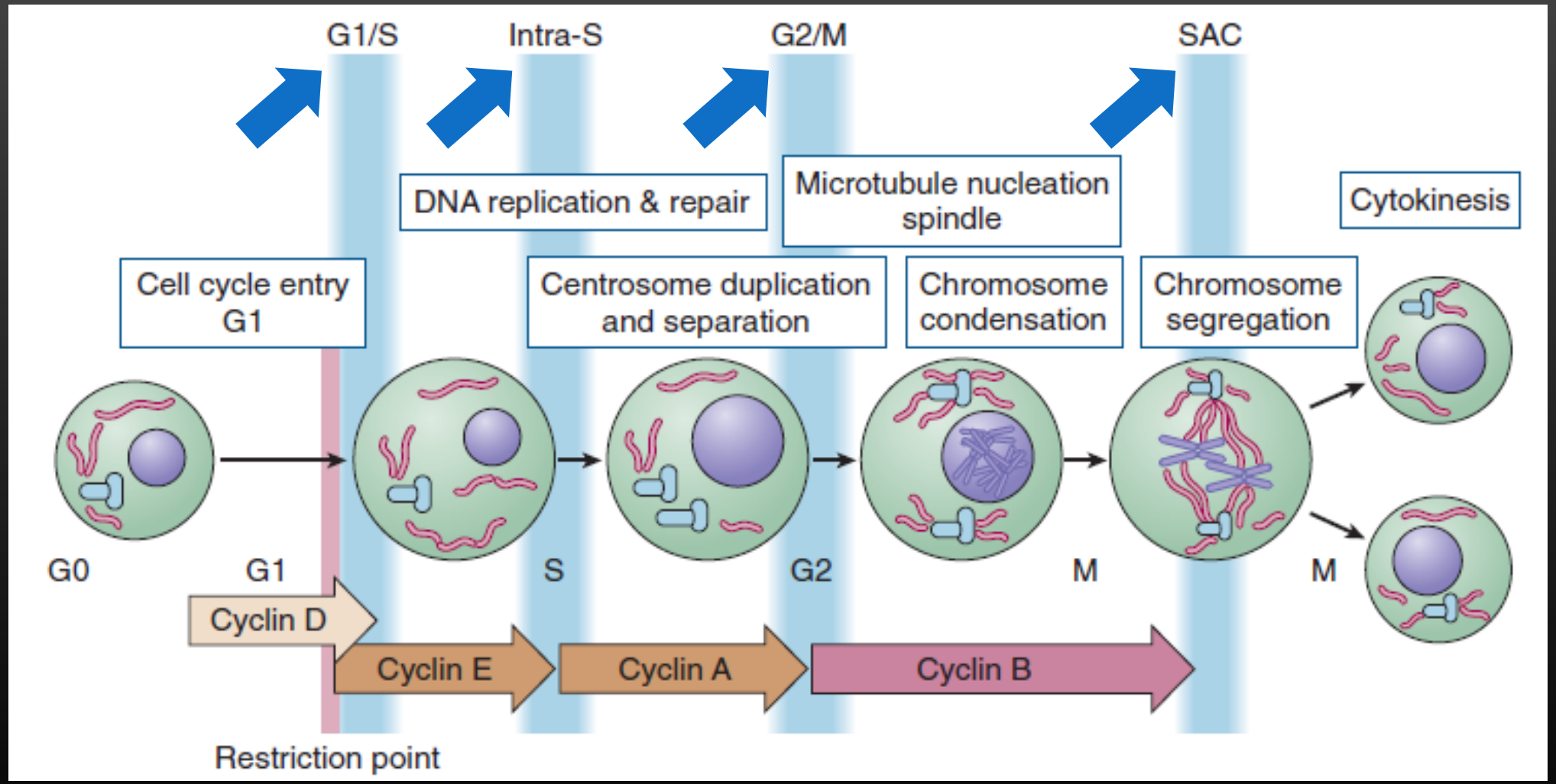


Sumber:

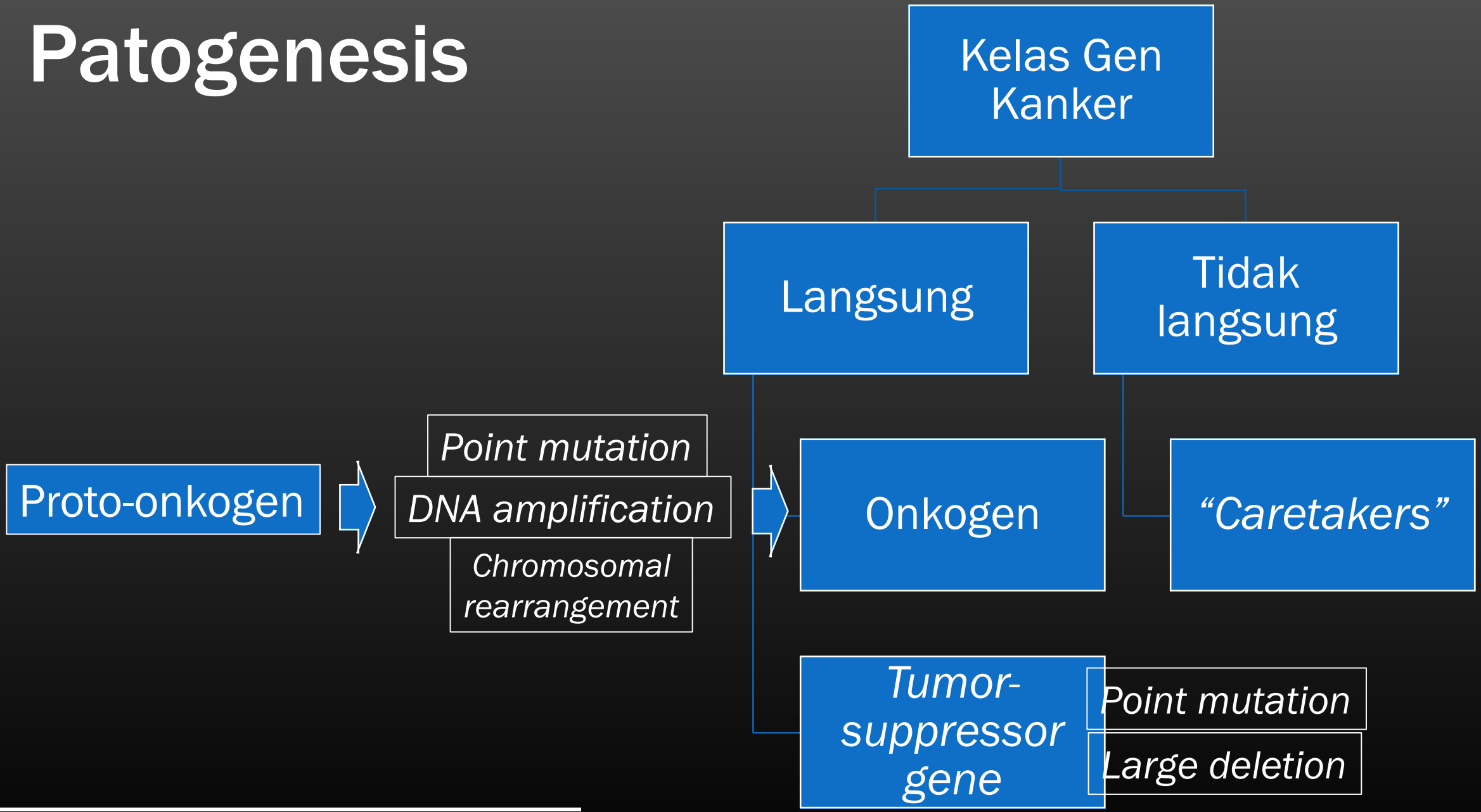
1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.

Siklus Sel pada Kanker

Entry	*Checkpoint*	Jumlah Kromosom
• ⬇ tumor suppressor • Ekpresi berlebih	• ⬇ tumor suppressor p53	• Jumlah kromosom abnormal

Sumber:
1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.

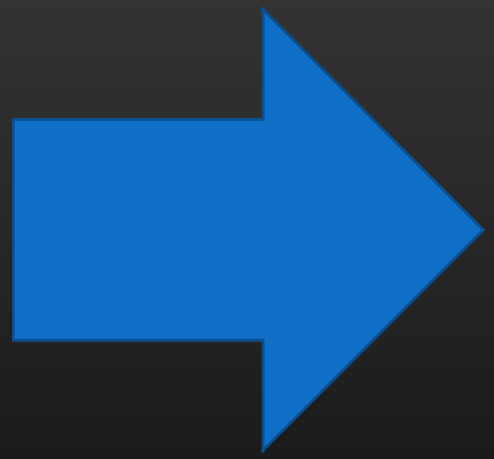
Patogenesis



Sumber:
2. Morin PJ, Trent JM, Collins FS, Vogelstein B. Cancer genetics. In: Longo DL, editor. Harrison's Hematology and Oncology. McGraw-Hill Companies, Inc; 2010.
3. Mendelsohn J, Gray JW, Howley PM, Israel MA, Thompson CB. The molecular basis of cancer. 4th ed. Saunders; 2015.

Transmisi Sinyal pada Kanker

Proliferasi dan Kematian



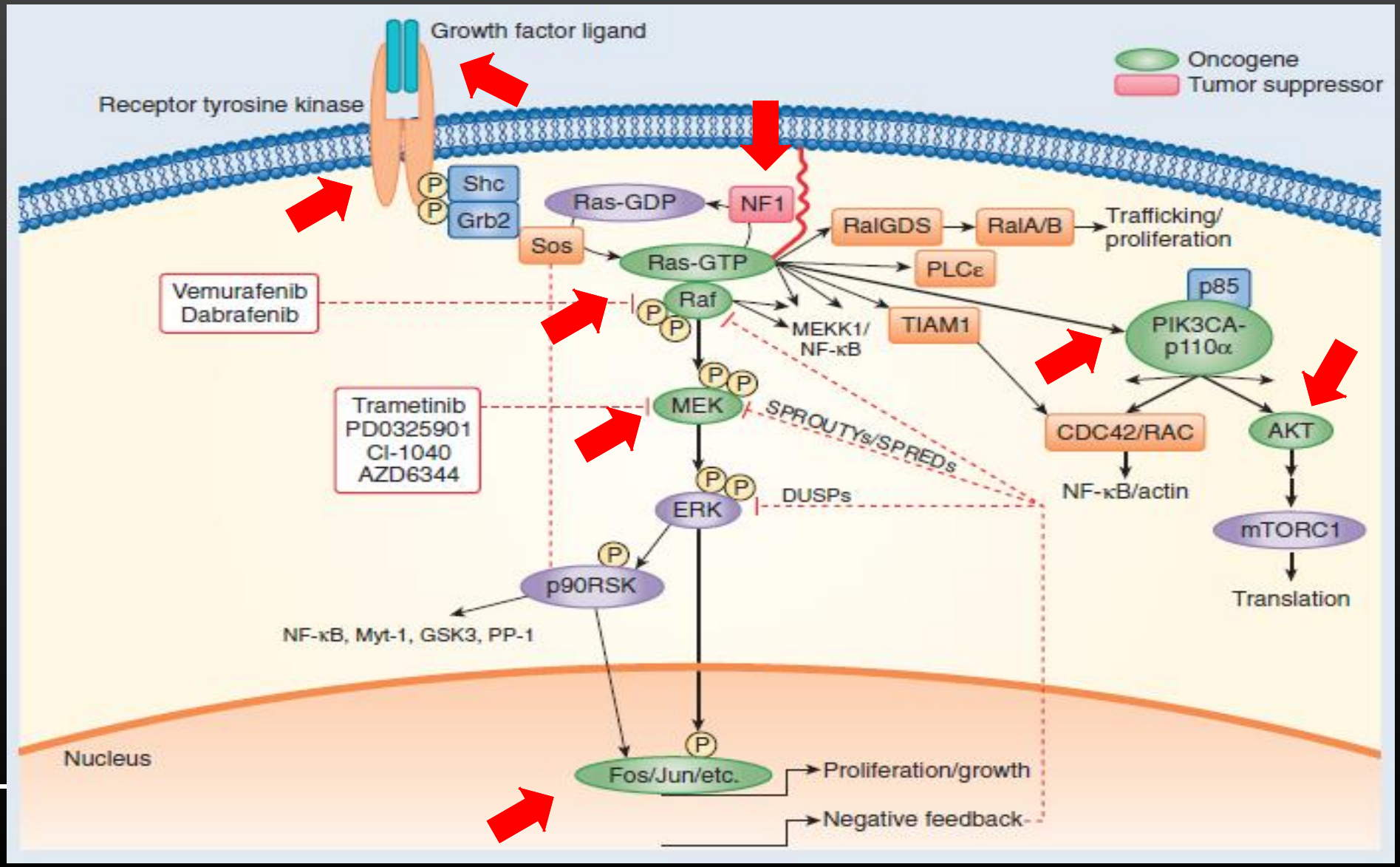
Transmisi Sinyal Intraseluler

Sumber:
1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.

Transmisi Sinyal pada Kanker

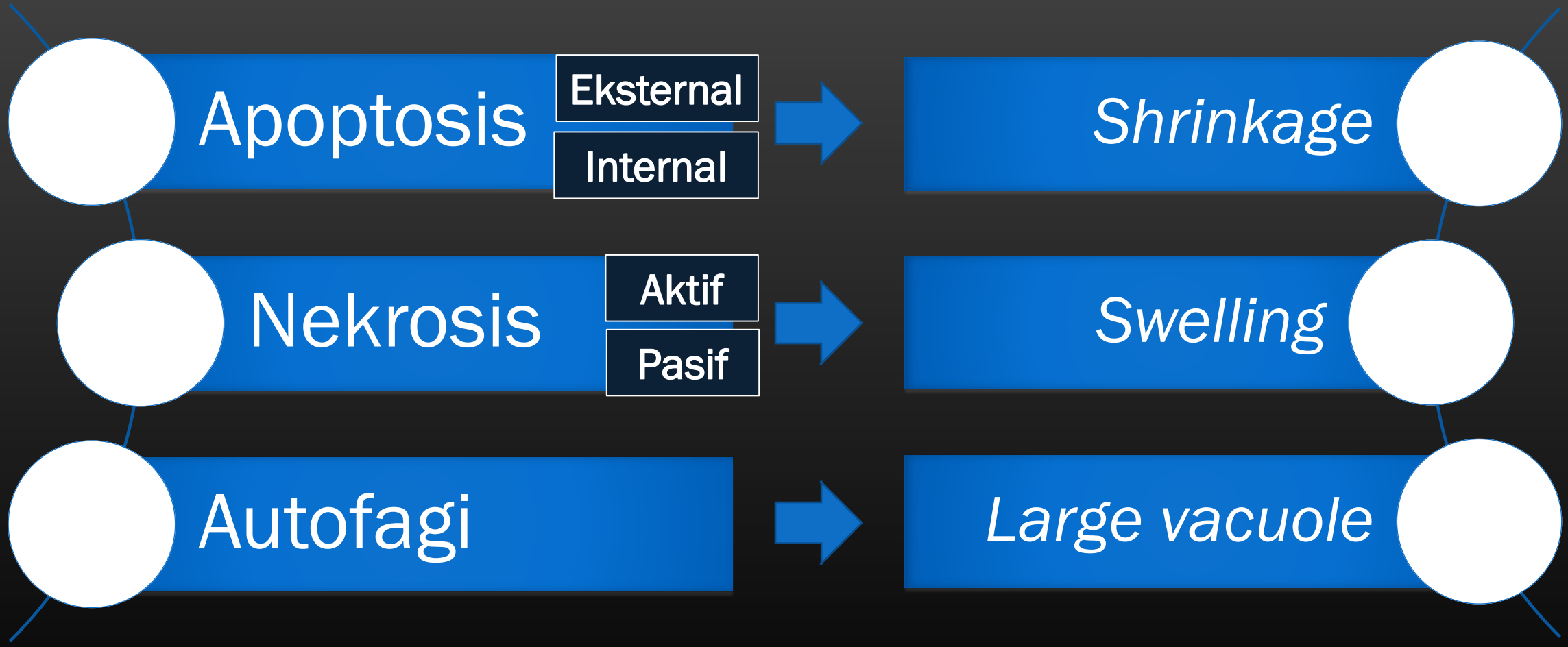
Sumber:
1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.

Transmisi Sinyal pada Kanker



Sumber:
1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.

Kematian Sel



Sumber:
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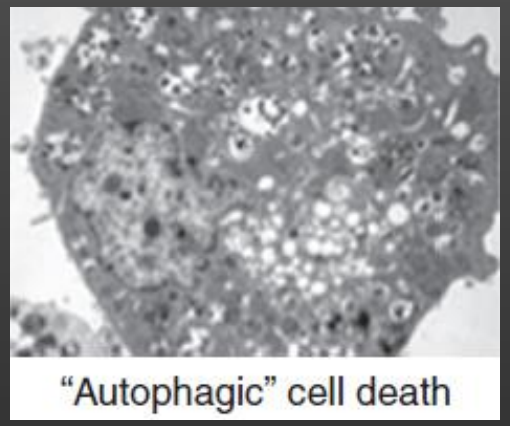
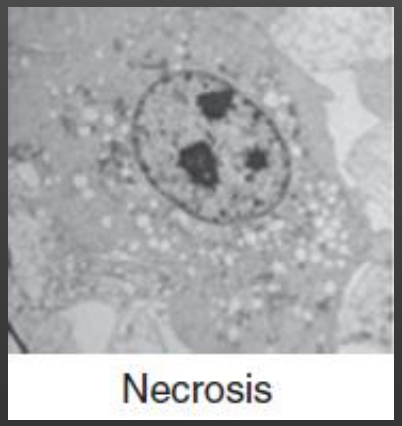
3. Mendelsohn J, Gray JW, Howley PM, Israel MA, Thompson CB. The molecular basis of cancer. 4th ed. Saunders; 2015.


Apoptosis


"Autophagic" cell death


Necrosis

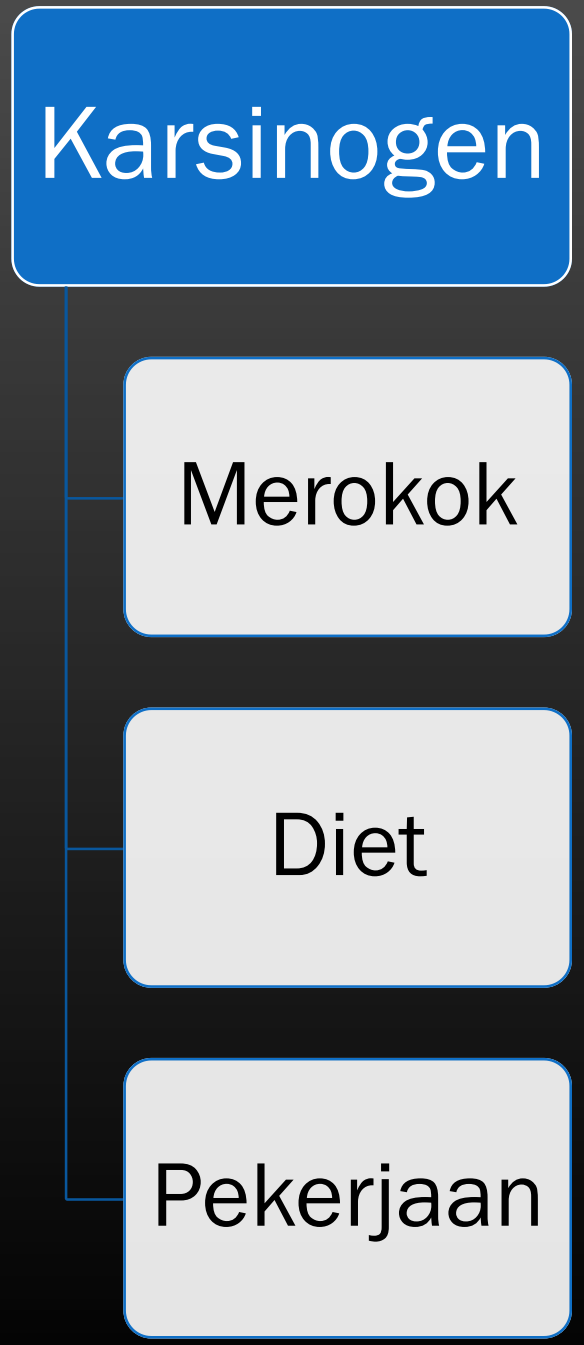
Kematian Sel

- Mode
  - Aktif
    - Apoptosis
    - Nekroptosis
    - Autofagi
  - Pasif
    - Nekrosis

Sumber:
1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.
3. Mendelsohn J, Gray JW, Howley PM, Israel MA, Thompson CB. The molecular basis of cancer. 4th ed. Saunders; 2015.

FAKTOR RISIKO KANKER

Faktor Risiko Kanker



Sumber:
3. Mendelsohn J, Gray JW, Howley PM, Israel MA, Thompson CB. The molecular basis of cancer. 4th ed. Saunders; 2015.

Karsinogen

Cancer Site	Carcinogenic Agents with Sufficient Evidence in Humans	Agents with Limited Evidence in Humans
Oral cavity	Alcohol, betel quid, HPV, tobacco smoking, smokeless tobacco	Solar radiation
Stomach	*Helicobacter pylori*, rubber production industry, tobacco smoking, x-rays, gamma radiation	Asbestos, Epstein-Barr virus, lead, nitrate, nitrite, pickled vegetables, salted fish
Colon and rectum	Alcohol, tobacco smoking, radiation	Asbestos, *Schistosoma japonicum*
Liver and bile duct	Aflatoxins, alcohol, *Clonorchis sinensis*, estrogen-progestin contraceptives, HBV, HCV, *Opisthorchis viverrini*, plutonium, thorium-232, vinyl chloride	Androgenic steroids, arsenic, betel quid, HIV, poly-chlorinated biphenyls, *Schistosoma japonicum*, trichloroethylene, x-rays, gamma radiation
Pancreas	Tobacco smoking, smokeless tobacco	Alcohol, thorium-232, x-rays, gamma radiation, radioiodines
Lung	Tobacco smoking, aluminum production, arsenic, asbestos, beryllium, bis (chloromethyl) ether, chloromethyl methyl ether, cadmium, chromium, coal combustion and coal tar pitch, coke production, hematite mining, iron and steel founding, MOPP, nickel, painting, plutonium, radon, rubber production, silica dust, soot, sulfur mustard, x-rays, gamma radiation	Acid mists, manufacture of glass, indoor emissions from household combustion, carbon electrode manufacture, chlorinated toluenes and benzoyl chloride, cobalt metal with tungsten carbide, creosotes, engine exhaust, insecticides, dioxin, printing processes, welding fumes
Skin—melanoma	Solar radiation, UV-emitting tanning devices	
Other skin cancers	Arsenic, azathiopurine, coal tar pitch, coal tar distillation, cyclosporine, methoxsalen plus UVA, mineral oils, shale oils, solar radiation, soot, x-rays, gamma radiation	Creosotes, HIV, HPV, nitrogen mustard, petroleum refining, UV-emitting tanning devices

Sumber:
3. Mendelsohn J, Gray JW, Howley PM, Israel MA, Thompson CB. The molecular basis of cancer. 4th ed. Saunders; 2015.

Karsinogen

Cancer Site	Carcinogenic Agents with Sufficient Evidence in Humans	Agents with Limited Evidence in Humans
Mesothelioma	Asbestos, erionite, painting	
Breast	Alcohol, diethylstilbestrol, estrogen-progesterone contraceptive and menopausal therapy, x-rays, gamma radiation	Estrogen menopausal therapy, ethylene oxide, shift work resulting in circadian disruption, tobacco smoking
Uterine cervix	Diethylstilbestrol (exposure in utero), estrogen-progestogen contraception, HIV, HPV, tobacco smoking	Tetrachloroethylene
Ovary	Asbestos, estrogen menopausal therapy, tobacco smoking	Talc-based body powder, x-rays, gamma radiation
Prostate		Androgenic steroids, arsenic, cadmium, rubber production industry, thorium-232, x-rays, gamma radiation, diethylstilbestrol (exposure in utero)
Kidney	Tobacco smoking, x-rays, gamma radiation	Arsenic, cadmium, printing processes
Urinary Bladder	Aluminum production, 4-aminobiphenyl, arsenic, auramine production, benzidine, chlornaphazine, cyclophosphamide, magenta production, 2-naphthylamine, painting, rubber production, *Schistosoma haematobium*, tobacco smoking, toluidine, x-rays, gamma radiation	Coal tar pitch, coffee, dry cleaning, engine exhaust, printing processes, occupational exposures in hair dressing and barbering, soot, textile manufacturing
Brain	X radiation, gamma radiation	
Leukemia and/or lymphoma	Azathiopurine, benzene, busulfan, 1,3-butadiene, chlorambucil, cyclophosphamide, cyclosporine, Epstein-Barr virus, etoposide with cisplatin and bleomycin, fission products, formaldehyde, *Helicobacter pylori*, HCV, HIV, human T-cell lymphotropic virus type 1, Kaposi's sarcoma herpesvirus, melphalan, MOPP, phosphorus-32, rubber production, semustine, thiotepa, thorium-232, tobacco smoking, treosulfan, X radiation, gamma radiation	Bischloroethyl nitrosourea, chloramphenicol, ethylene oxide, etoposide, HBV, magnetic fields, mitoxantrone, nitrogen mustard, painting, petroleum refining, polychlorophenols, radioiodines, radon-222, styrene, teniposide, tetrachloroethylene, trichloroethylene, dioxin, tobacco smoking (childhood leukemia in smokers' children)

Sumber:
3. Mendelsohn J, Gray JW, Howley PM, Israel MA, Thompson CB. The molecular basis of cancer. 4th ed. Saunders; 2015.

TUMOR MARKER

Tumor Marker

- CEA
  - *Carcinoembryonic Antigen*
- NSE
  - *Neuron-Specific Enolase*
- CYFRA21-1
  - Cytokeratin 19
- AFP
  - Alfa-fetoprotein
- CA-125, CA-19.9
  - Carbohydrate antigen 125, Carbohydrate antigen 19.9
- PSA
  - *Prostate-Specific Antigen*

Sumber:
4. Li X, Lu J, Ren H, Chen T, Gao L, Di L, et al. Combining multiple serum biomarkers in tumor diagnosis: A clinical assessment. Mol Clin Oncol. 2012;1(1):153–60.
2. Longo DL, editor. Harrison's Hematology and Oncology. 17th ed. McGraw-Hill Companies, Inc; 2010.

Kesimpulan

Onkologi dasar mencakup pembahasan mengenai kanker, terutama faktor risiko, patogenesis serta patofisiologi yang kompleks. Ketiga hal tersebut sangat penting untuk diketahui karena berhubungan dengan diagnosis dan terapi kasus-kasus kanker

Daftar Pustaka

1. Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, editors. Abeloff's clinical oncology. 5th ed. Philadelphia: Saunders; 2014. Saunders.
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4. Li X, Lu J, Ren H, Chen T, Gao L, Di L, et al. Combining multiple serum biomarkers in tumor diagnosis: A clinical assessment. Mol Clin Oncol. 2012;1(1):153–60.

TERIMA KASIH

Jangan lupa untuk mengerjakan soal latihan ya!