

Cancer Biology & Apoptosis

How a cell is normally instructed to die, what happens when that instruction is ignored, the genes behind the breakdown, and how modern oncology fights back.

Apoptosis Pathways

Hallmarks of Cancer

Oncogenes & TSGs

PI3K/AKT/mTOR

Cancer Genomics

CSCs

Therapy

Apoptosis

Hallmarks

Classification

Common Cancers

Onco/TSG

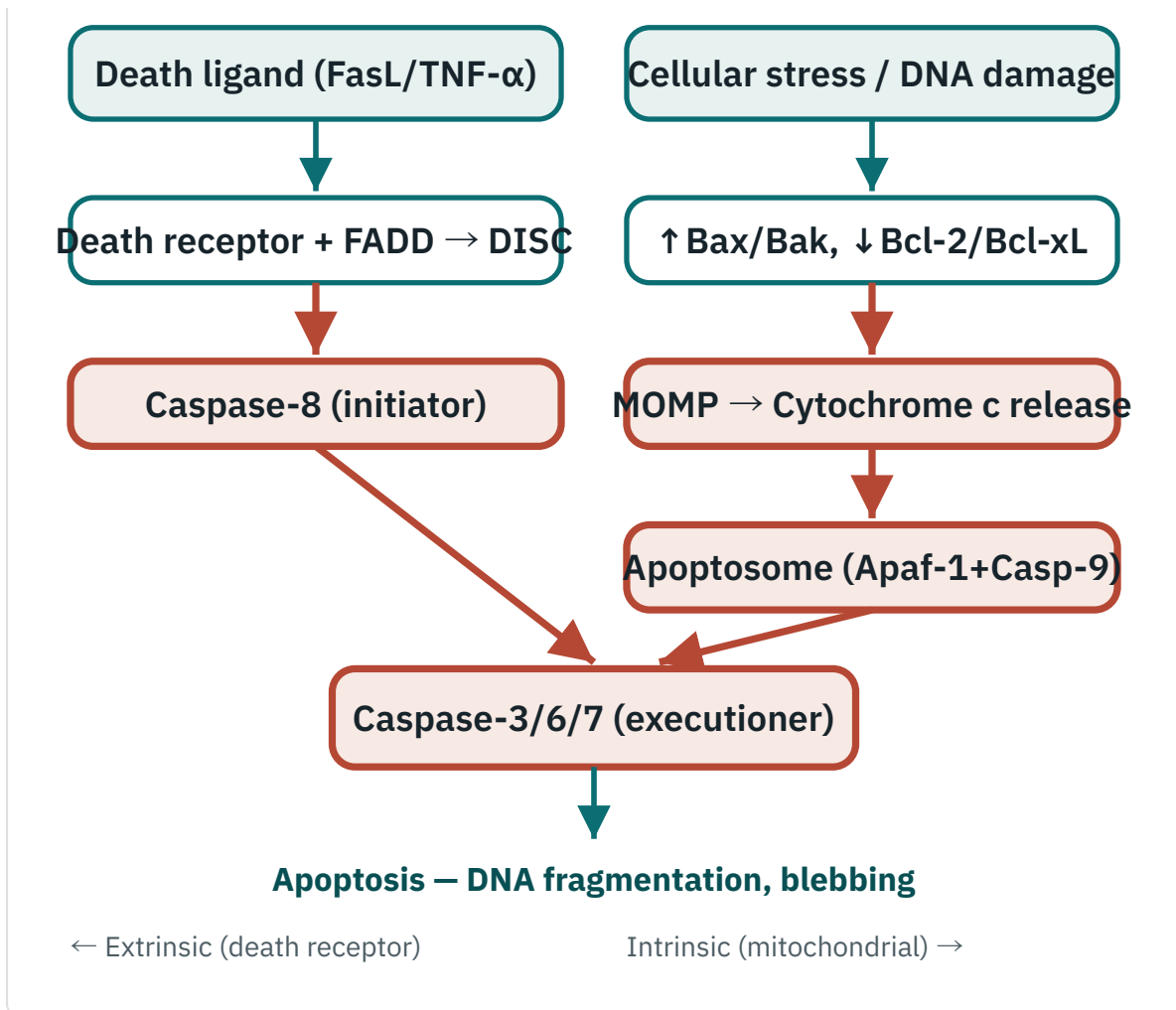
PI3K/A

1 Apoptosis

Programmed cell death — canonical and non-canonical routes

Unlike necrosis (uncontrolled, inflammatory), apoptosis is a controlled, ATP-dependent process — cell shrinkage, membrane blebbing, chromatin condensation, and tidy clearance by phagocytes without triggering inflammation.

Extrinsic and intrinsic pathways converge on caspase-3



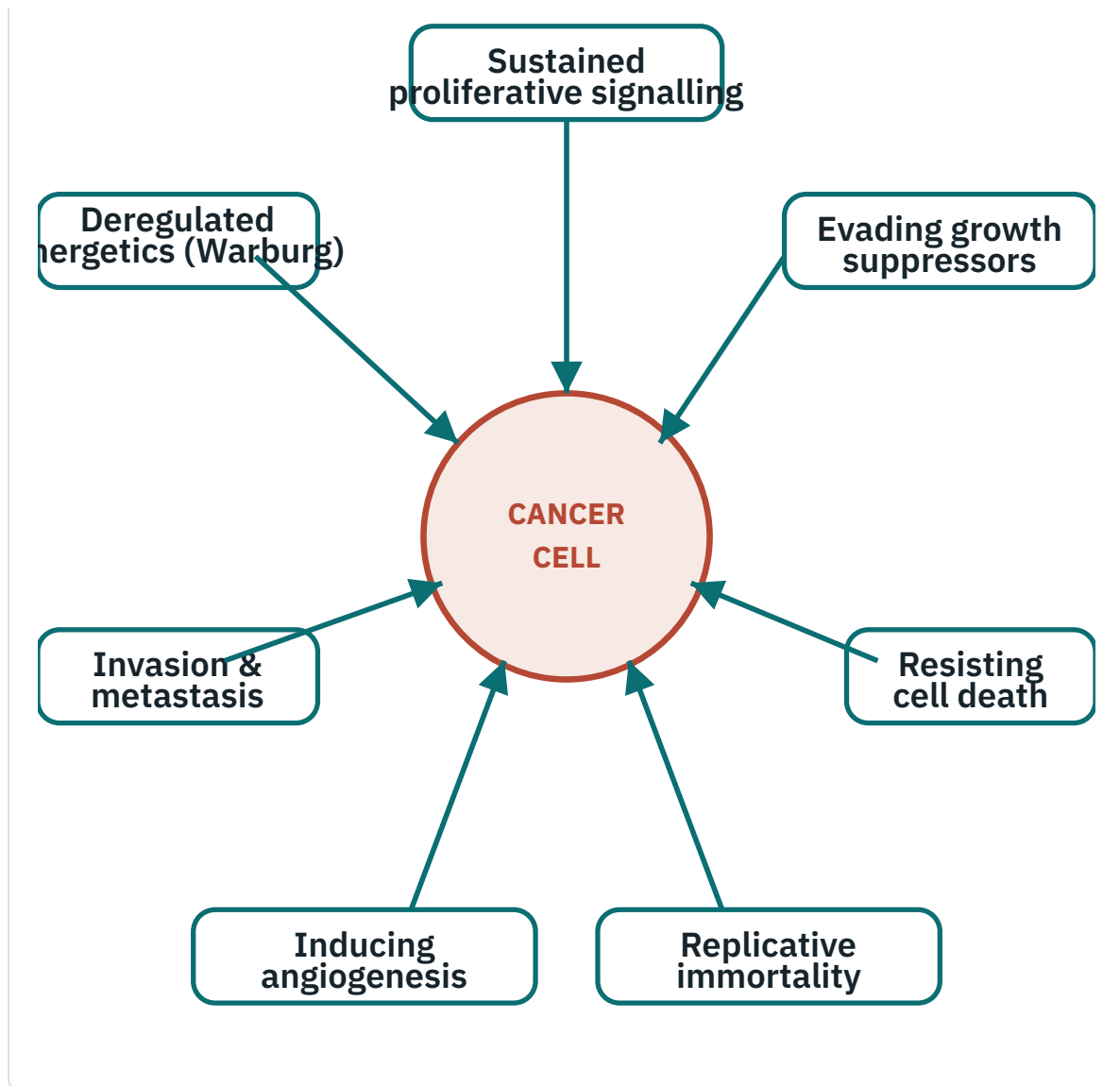
NON-CANONICAL ROUTES

Caspase-independent death can proceed via AIF (Apoptosis-Inducing Factor — released from mitochondria, causes DNA fragmentation directly in the nucleus) or granzyme B, delivered by CTLs/NK cells, which can activate caspases or cleave substrates without going through the normal initiator-caspase steps.

2 Characteristics of Cancer Cells

The Hanahan & Weinberg hallmarks

Hallmarks radiating from the cancer cell



EMERGING HALLMARKS

Genome instability/mutation, tumour-promoting inflammation, and avoiding immune destruction are increasingly recognised alongside the original six – the last of these is the entire rationale behind checkpoint-inhibitor immunotherapy.

3 Classification of Cancer

Named by tissue of origin

Category	Tissue of origin	Example
Carcinoma	Epithelium (~85–90% of all cancers)	Adenocarcinoma (glandular – breast, colon); squamous cell carcinoma (skin, cervix)

Sarcoma	Mesenchyme/connective tissue	Osteosarcoma (bone), liposarcoma (fat), rhabdomyosarcoma (muscle)
Leukaemia	Bone marrow blood-forming cells	Circulates in blood rather than forming a solid mass — ALL, AML, CLL, CML
Lymphoma	Lymphocytes	Solid tumours in lymph nodes — Hodgkin (Reed-Sternberg cells) vs. Non-Hodgkin

4 Overview of Common Cancers

Breast, lung, prostate, colon, and blood cancer at a glance

Cancer	Key point
Breast	Commonest cancer in women; BRCA1/2, family history, hormonal exposure; subtyped by ER/PR/HER2 status, incl. triple-negative
Lung	Leading cause of cancer death; strongly smoking-linked; NSCLC (~85%) vs. aggressive neuroendocrine SCLC (~15%)
Prostate	Commonest cancer in men (excl. skin); age-related; usually slow-growing adenocarcinoma; PSA screening
Colon	Adenoma-carcinoma sequence — APC mutation early, then KRAS, TP53; colonoscopy screening
Blood	Leukaemia/lymphoma/myeloma — not solid tumours; diagnosed via blood counts, marrow biopsy, flow cytometry

5 Oncogenes & Tumour Suppressor Genes

Two opposite ways to lose control of the cell cycle

	Proto-oncogene → Oncogene	Tumour suppressor gene
Normal role	Promotes growth/division	Restrains growth, repairs DNA, triggers apoptosis

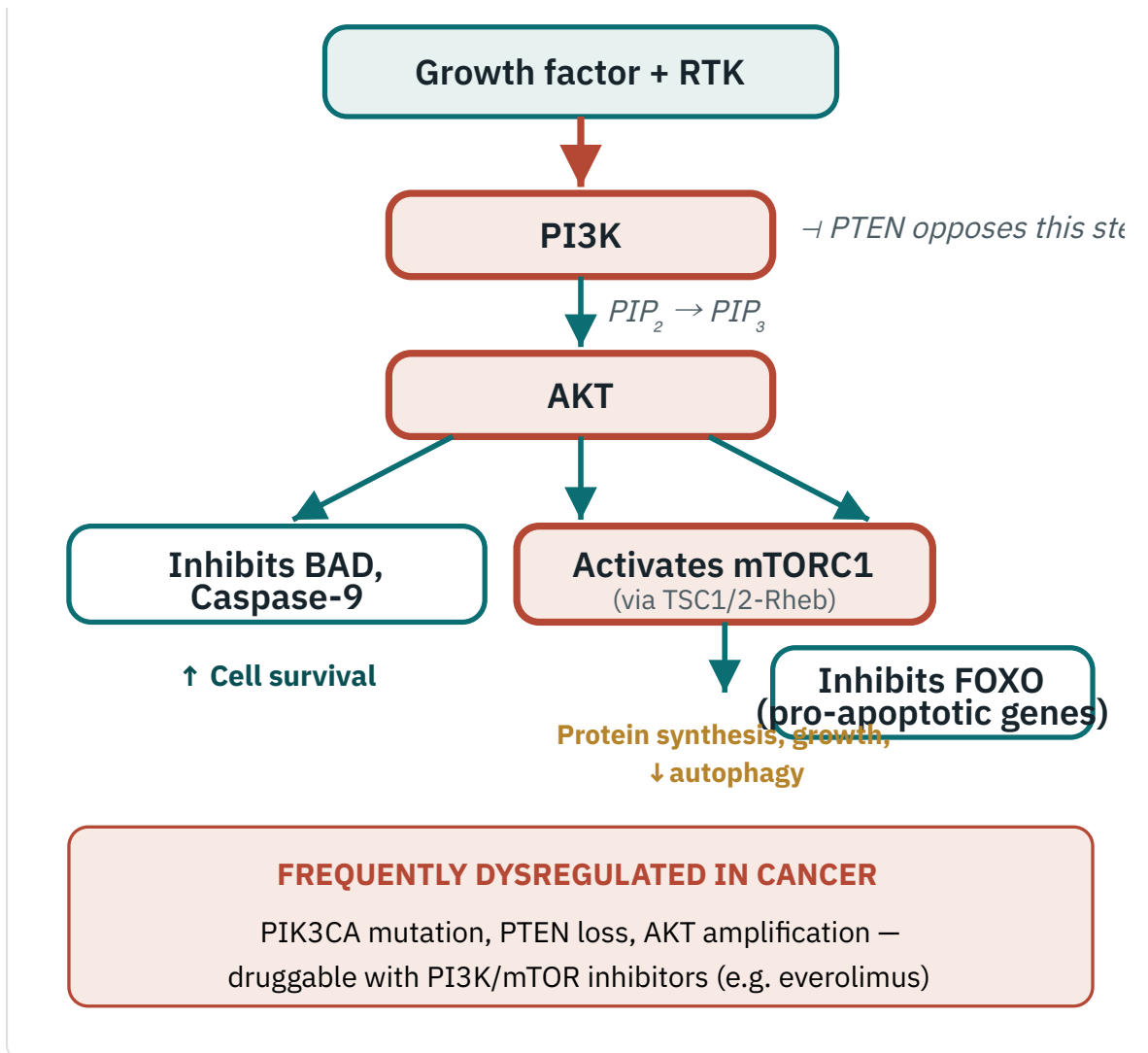
Cancer-causing change	Gain-of-function	Loss-of-function
Genetics	Dominant — one mutant allele suffices	Recessive at the cell level — Knudson's "two-hit" hypothesis
Analogy	Accelerator stuck down	Brakes cut

Gene	Type	Role
RAS	Proto-oncogene	GTPase relaying growth-factor signal to MAPK/ERK; mutations lock it GTP-bound (constitutively active) — mutated in ~20–30% of all cancers
MYC	Proto-oncogene	Transcription factor driving cell-cycle/growth genes; overexpression (e.g. t(8;14) in Burkitt lymphoma) drives excess proliferation
TP53	Tumour suppressor	"Guardian of the genome" — triggers cell-cycle arrest, DNA repair, or apoptosis after damage; most commonly mutated gene in cancer; germline loss → Li-Fraumeni syndrome
BRCA1/2	Tumour suppressor	DNA double-strand break repair (homologous recombination); germline loss → hereditary breast/ovarian cancer; basis for PARP-inhibitor synthetic lethality

6 PI3K/AKT/mTOR Pathway

One of the most frequently hijacked survival pathways in cancer

From growth-factor receptor to cell growth and survival



7 Cancer Genomics

Sequencing as both a research and a clinical tool

Next-generation sequencing (NGS) of tumour DNA/RNA identifies **point mutations** (distinguishing driver from passenger mutations), **chromosomal alterations** (translocations, amplifications, deletions — e.g. BCR-ABL in CML, HER2 amplification in breast cancer), and **gene expression patterns** (RNA-seq-based molecular subtyping, e.g. breast cancer's Luminal A/B, HER2-enriched, and basal-like/triple-negative groups).

CLINICAL PAYOFF

Precision oncology matches therapy to a tumour's specific mutations (EGFR inhibitors for EGFR-mutant lung cancer, BRAF inhibitors for BRAF-mutant

melanoma); **liquid biopsy** tracks circulating tumour DNA non-invasively; **tumour mutational burden** helps predict immunotherapy response.

8 Cancer Stem Cells (CSCs)

The small subpopulation that survives treatment

- **Self-renewal** and **multipotency** — can regenerate a heterogeneous tumour cell population
- **Tumour-initiating capacity** — reliably form new tumours on transplantation, unlike bulk tumour cells
- **Relative quiescence** — slow-cycling, which lets them evade chemotherapy aimed at rapidly dividing cells
- **Therapy resistance** — enhanced DNA repair, drug-efflux (ABC transporter) pumps, strong anti-apoptotic signalling
- Marked by surface markers that vary by cancer (e.g. CD44⁺/CD24⁻ in breast cancer, CD133⁺ in several tumour types)

WHY CSCS MATTER CLINICALLY

Because they survive treatments that kill the rapidly dividing tumour bulk, CSCs are widely thought to be the source of relapse and metastasis even after apparently successful therapy — a major rationale for developing CSC-targeted drugs.

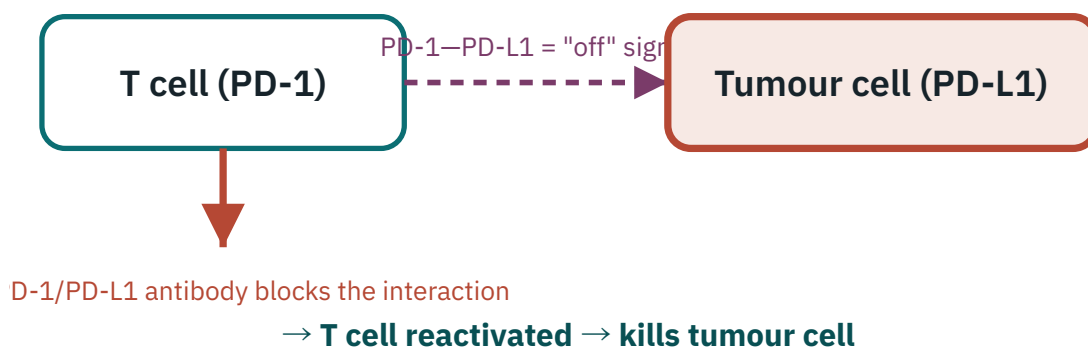
9 Chemotherapy, Radiotherapy & Immunotherapy

Three very different ways to attack a tumour

Modality	Mechanism	Example agents
Chemotherapy	Cytotoxic drugs targeting rapidly dividing cells — also harms normal fast-dividing tissue (marrow, gut, hair)	Alkylating agents, antimetabolites (methotrexate, 5-FU), anthracyclines, taxanes

Radiotherapy	Ionizing radiation damages DNA directly/via free radicals — most effective on actively dividing cells	External beam, brachytherapy
Immunotherapy	Harnesses the patient's immune system against the tumour	Checkpoint inhibitors, CAR-T cells, monoclonal antibodies

Checkpoint inhibition — releasing the brakes on T cells



10 Minimum Residual Disease (MRD)

The gap between "no visible disease" and "no disease"

MRD refers to the small number of cancer cells left in the body during or after treatment, at a level too low for conventional imaging or clinical exam to detect — the patient looks to be in remission, but disease persists below the radar.

DETECTING IT

Flow cytometry (aberrant immunophenotypes), PCR for specific genetic markers (e.g. BCR-ABL transcript monitoring in CML), and NGS-based assays (sensitive enough to find one cancer cell among a million+ normal cells) are the main tools — most established in leukaemias, increasingly used in solid tumours via ctDNA liquid biopsy.

WHY IT MATTERS

MRD positivity after treatment is one of the strongest predictors of relapse, and is increasingly used to guide how intensively — or for how long — treatment should continue.

11 Exam Corner

Practice question set — end-semester format

B.Sc. Biochemistry — End-Semester Examination

Paper: Cancer Biology & Apoptosis

Full Marks: 30

Time: 1.5 Hrs

GROUP A — LONG ANSWER (ANSWER ANY TWO)

1. Describe the extrinsic and intrinsic pathways of apoptosis with a labelled diagram, indicating where they converge. **10**
2. Discuss the roles of RAS, MYC, TP53, and BRCA1/2 in cancer development, contrasting oncogene and tumour suppressor gene behaviour. **10**
3. Describe the PI3K/AKT/mTOR signalling pathway and explain why it is frequently dysregulated in cancer. **10**

GROUP B — SHORT NOTES (ANSWER ANY TWO)

- a. Hallmarks of cancer cells **5**
- b. Cancer stem cells and therapy resistance **5**
- c. Minimum residual disease **5**

