

Components of Innate Immunity

Barriers • Cells • Soluble mediators

**Epithelial
defense**

**Cellular
effectors**

**Humoral
effectors**

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraisakhri.com

Learning outcomes

- Identify anatomic, cellular, and soluble constituents of innate immunity.
- Explain the principal functions of phagocytes, dendritic cells, NK cells, and ILCs.
- Distinguish complement, pattern recognition, and antiviral defense.
- Integrate the components in infection and tissue-injury scenarios.

Organizing question

Which component detects a threat, which eliminates it, and which connects innate defenses to adaptive immunity?

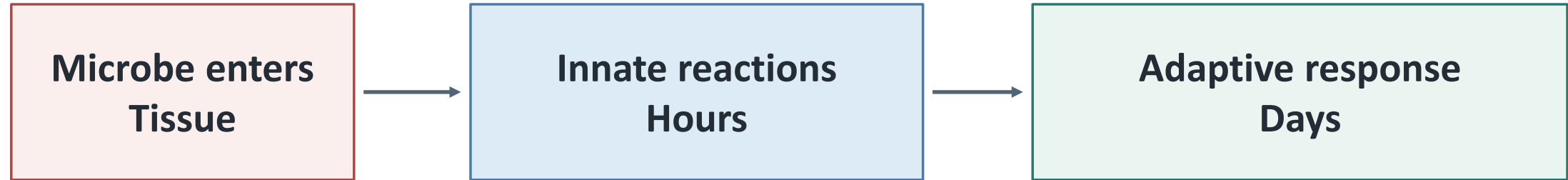
Innate immunity is present before exposure

- Intrinsic host mechanisms are poised to act immediately.
- Conserved microbial products and injury-related signals initiate responses.
- Principal purposes: Limit infection and clear damaged cells.
- It serves as the first defensive tier, not a delayed clonal response.

Contrast with adaptive immunity

Innate responses depend on germline-encoded recognition; Adaptive lymphocyte receptors undergo somatic recombination.

Response timing: Immediate versus induced



Early protection

Barrier defense, complement activation, phagocytosis, and NK-cell activity.

Later antigen-specific expansion

T- and B-lymphocyte activation, proliferation, and differentiation.

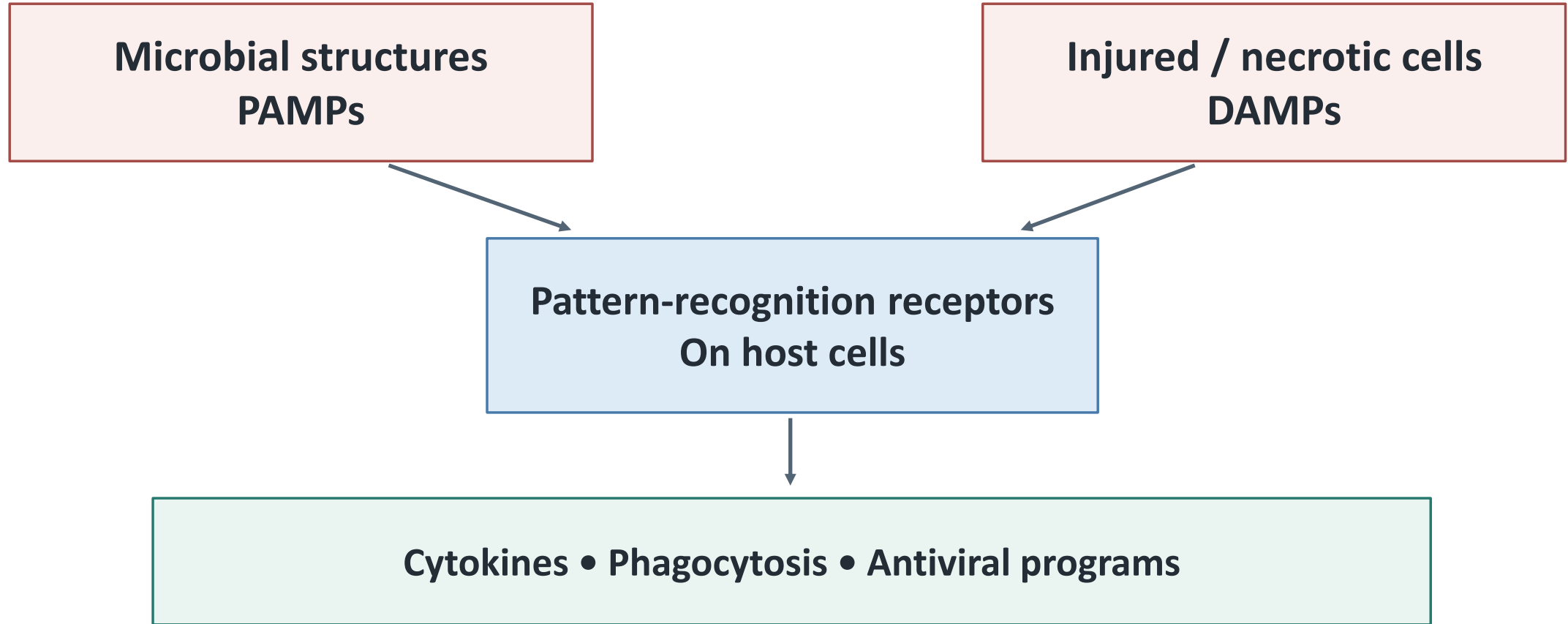
Microbial and damage signals initiate defense

**Microbial structures
PAMPs**

**Injured / necrotic cells
DAMPs**

**Pattern-recognition receptors
On host cells**

Cytokines • Phagocytosis • Antiviral programs



Defense is organized in complementary layers

Barrier exclusion

Surface epithelium restricts microbial entry before local tissue penetration.

Cellular effector defense

Resident sentinels, recruited phagocytes, NK cells and ILCs respond to danger.

Soluble effector defense

Complement and antimicrobial proteins support elimination concurrently with cellular responses.

Network principle: These components cooperate; They are not strictly sequential modules.

Cellular and humoral arms of innate immunity

Cellular arm

Neutrophils, macrophages, dendritic cells, NK cells, innate lymphoid cells, and additional tissue sentinels.

Acts through recognition, phagocytosis, cytokine production, and target-cell killing.

Humoral arm

Complement, mannose-binding lectin, C-reactive protein, and local soluble factors such as surfactant.

Acts through microbial coating, complement-mediated injury, and inflammatory amplification.

Main constituents: A functional classification

Barrier and tissue interface	Cell populations	Soluble proteins
Skin, gastrointestinal and respiratory epithelia	Neutrophils and monocyte–macrophage lineage	Complement proteins
Epithelial antimicrobial molecules	Dendritic cells and natural killer cells	Mannose-binding lectin
Epithelial resident lymphocytes	ILCs; mast cells; responsive endothelial cells	C-reactive protein; pulmonary surfactant

Epithelial surfaces block microbial entry

Skin

Continuous epithelial surface separates microbes in the external environment from deeper tissues.

Gastrointestinal tract

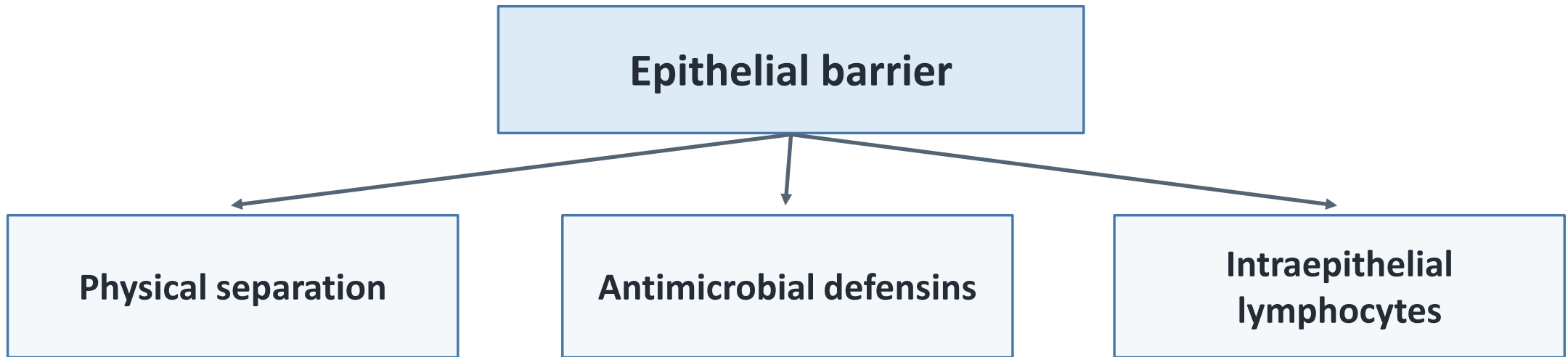
Epithelial lining restricts microbial penetration at a heavily exposed interface.

Respiratory tract

Epithelial surface blocks entry of inhaled microbes; Local soluble factors add protection.

Functional principle: Mechanical exclusion is protective before any leukocyte recruitment occurs.

Barrier protection is not only mechanical



Result: Parallel mechanical, molecular, and cellular protection at exposed surfaces.

Defensins: An epithelial antimicrobial product

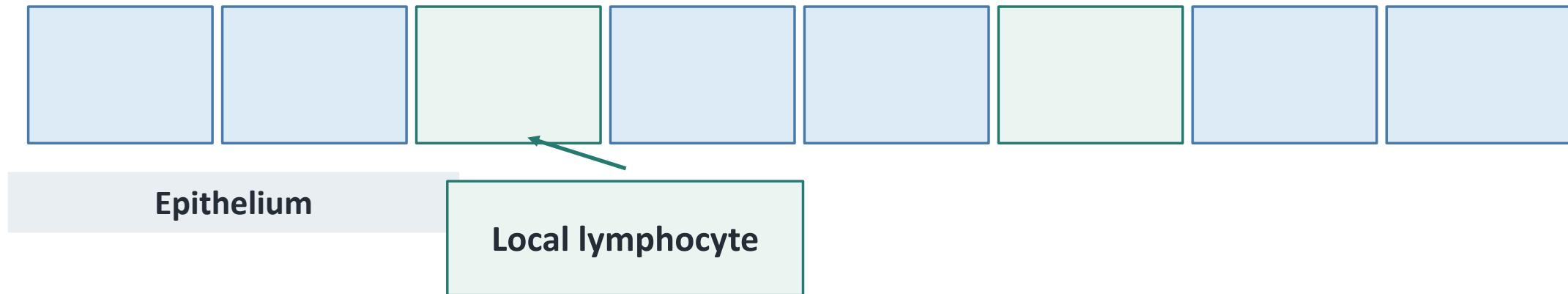
- Epithelial cells synthesize defensins as part of local innate defense.
- Defensins act at the exposed tissue interface.
- Antimicrobial production complements the epithelial physical barrier.
- Barrier-derived defense operates even before recruited phagocytes arrive.

Teaching distinction

A protective barrier is an active host tissue, not simply an impermeable covering.

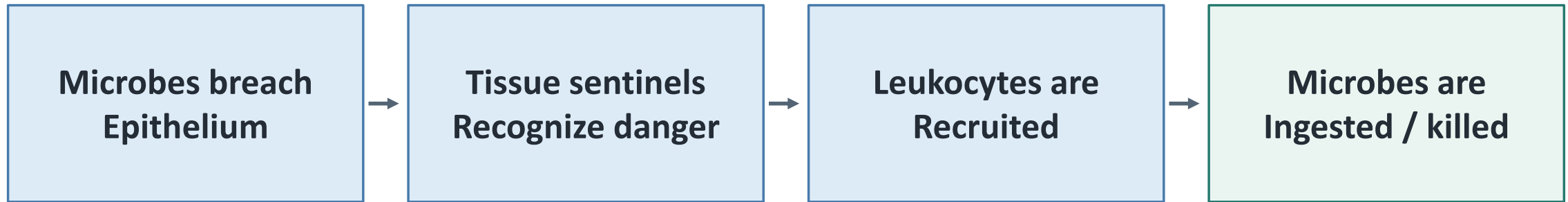
Intraepithelial lymphocytes defend surface tissues

External microbial challenge



Lymphocytes positioned in epithelia combat microbes where they first encounter the host.

When epithelia are breached, deeper defenses engage



Mechanism: Barrier failure changes the response from exclusion to recognition and clearance.

Principal phagocytes circulate and enter tissues

Neutrophils

Circulating granulocytes that can be rapidly recruited into sites of infection.

Provide strong short-lived antimicrobial responses.

Monocytes → macrophages

Blood monocytes enter tissues and mature into macrophages.

Macrophages phagocytose organisms and coordinate longer inflammatory responses.

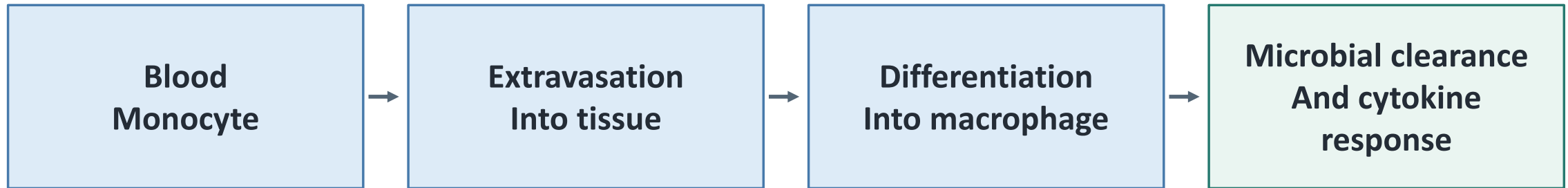
Neutrophils: Rapid recruited phagocytes

- Present in blood before tissue infection develops.
- Rapid recruitment brings microbicidal activity into infected tissue.
- Phagocytosis, granule products, and reactive oxygen species eliminate microbes.
- Predominate in the early inflammatory leukocyte infiltrate.

Relation to inflammation

Neutrophils are a hallmark effector of acute inflammation; Their destructive molecules may also injure host tissue.

Monocytes differentiate into tissue macrophages



Macrophages remain important after early neutrophil-dominant inflammation and contribute to chronic inflammatory responses.

Tissue-resident macrophages occupy sentinel niches

Tissue	Resident macrophage population	Functional relevance
Liver	Kupffer cells	Local tissue surveillance and clearance
Central nervous system	Microglia	Resident immune sentinel population
Lung	Alveolar macrophages	Defense within the respiratory compartment

Macrophage origins include embryonic precursors

Developmental resident pool

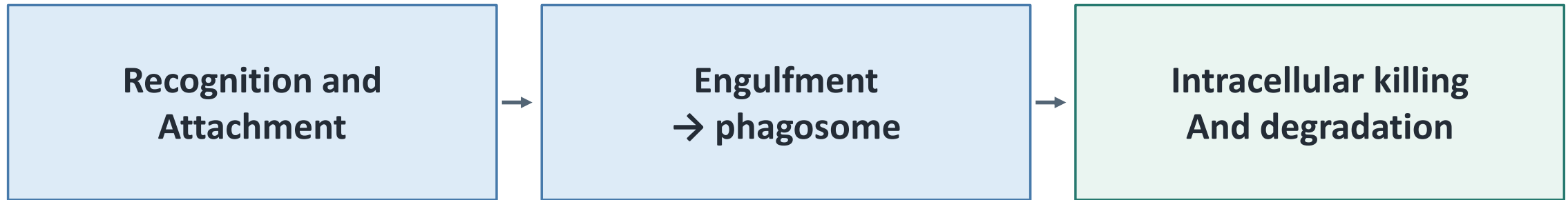
Some long-lived tissue-resident macrophages originate from progenitors in the yolk sac or fetal liver early in development.

Recruited inflammatory pool

Circulating monocytes from hematopoietic production enter tissues and generate macrophages during inflammatory reactions.

Implication: Macrophages in tissue are not all recently recruited from blood.

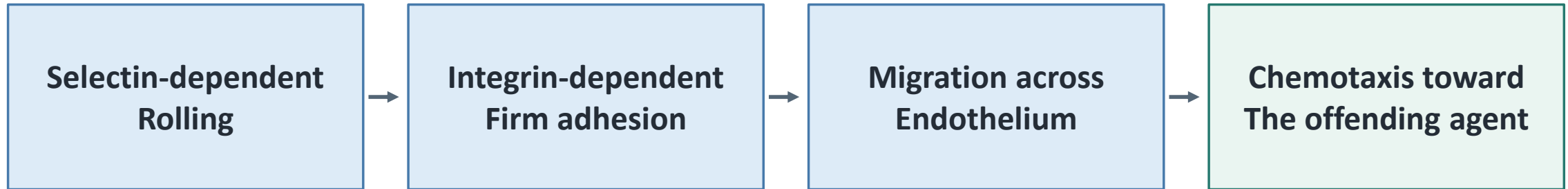
Phagocytes carry out a three-stage program



Biological purpose

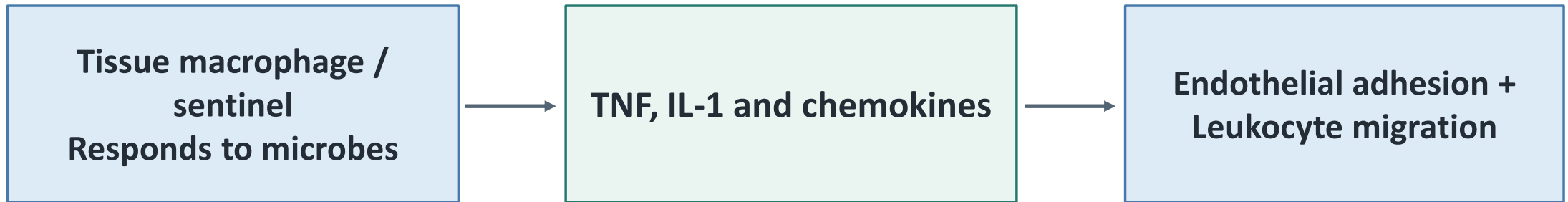
Capture a threat, isolate it in an intracellular compartment, then destroy and digest the material.

Leukocyte recruitment is a multistep process



Coordination: Cytokines and chemokines generated in tissue regulate each recruitment step.

Inflammatory cytokines activate the vascular gateway

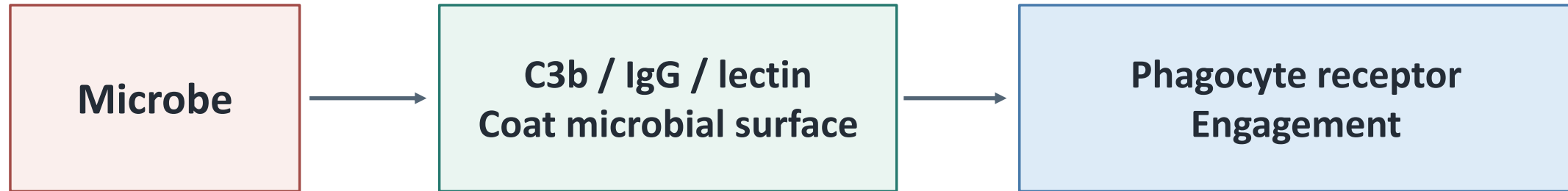


Selectins support rolling; Activated integrins support firm adhesion; Chemoattractants direct migration.

Phagocytic receptors recognize microbial surfaces

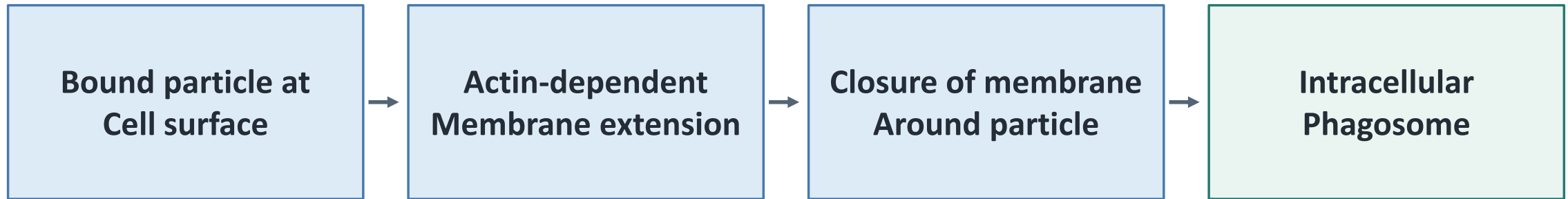
Receptor group	Recognized feature	Result
Mannose receptors	Terminal mannose/fucose on microbial structures	Preferential microbial recognition
Scavenger receptors	Diverse microbial ligands	Binding and uptake
Opsonin receptors	Microbes coated with IgG or complement fragments	Efficient phagocytic attachment

Opsonization increases phagocytic efficiency



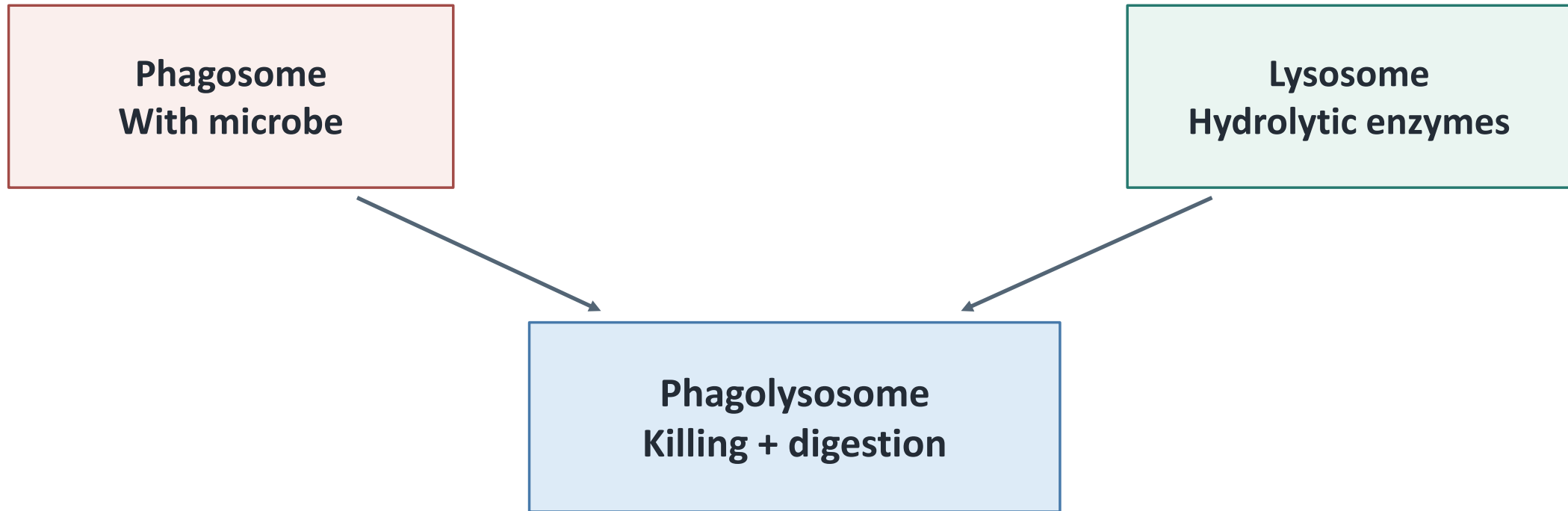
An opsonin provides a recognizable ligand for the phagocyte, converting weaker attachment into effective engulfment.

Engulfment produces an intracellular phagosome



Mechanism: Receptor-initiated signals reorganize membrane and cytoskeleton during particle uptake.

Phagosome–lysosome fusion enables degradation



Controlled compartmentalization limits damage to the phagocyte

Phagocytes use multiple microbicidal effectors

Reactive oxygen species

Phagocyte oxidase generates oxidative intermediates for antimicrobial action.

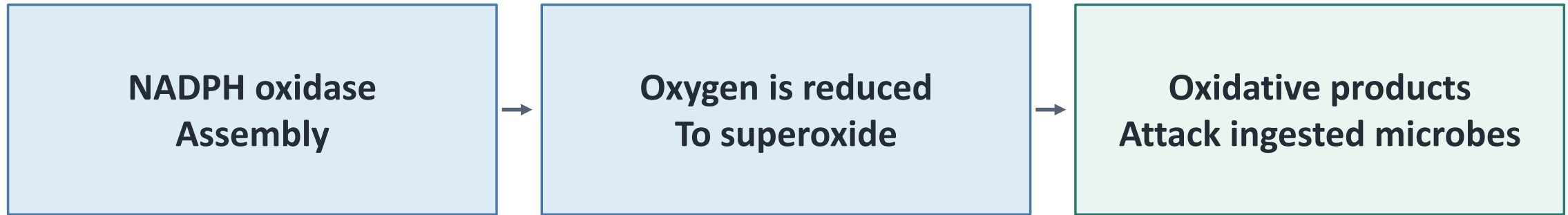
Reactive nitrogen species

Nitric oxide-derived chemistry contributes to killing of ingested microbes.

Lysosomal enzymes

Degradation proceeds inside phagolysosomes through enzyme-rich compartments.

Respiratory burst links oxygen use to microbicidal ROS



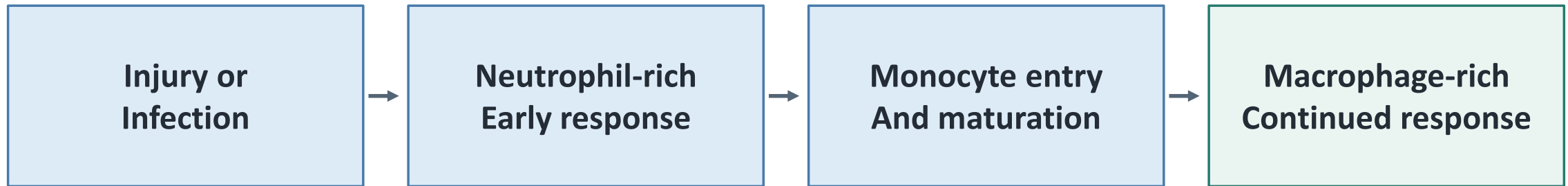
Why compartmentalization matters

Phagocytes generate potent toxic mediators; Concentrating them in microbicidal compartments helps preserve host-cell integrity.

Neutrophils and macrophages are not interchangeable

Characteristic	Neutrophils	Macrophages
Response profile	Rapid; short-lived	Sustained; gene-expression dependent
Granule release	Prominent	Less prominent
Cytokine production	Limited compared with macrophages	Major functional activity
Reactive intermediates	Rapid oxidase assembly / ROS	iNOS-derived nitric oxide; ROS

Acute cellular defense evolves over time



Clinical link: Neutrophils dominate many early acute lesions; Macrophages are important in persistent inflammation.

Dendritic cells are distributed tissue sentinels

Epithelial sites

Dendritic cells position microbial sensing near the host–environment interface.

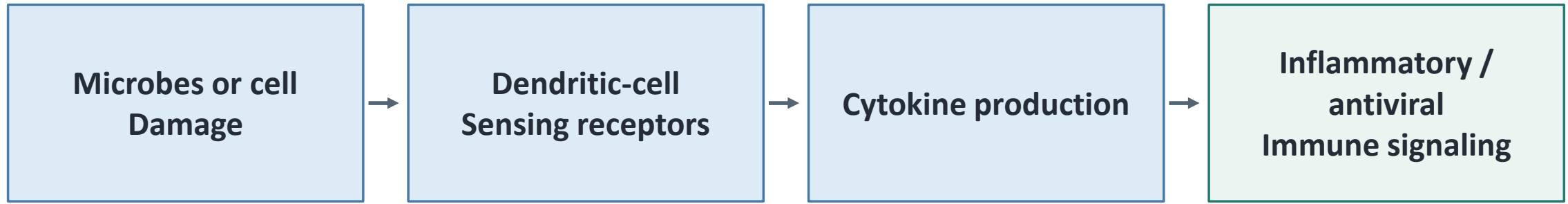
Peripheral tissues

They sample antigens and danger signals in most tissues.

Lymphoid organs

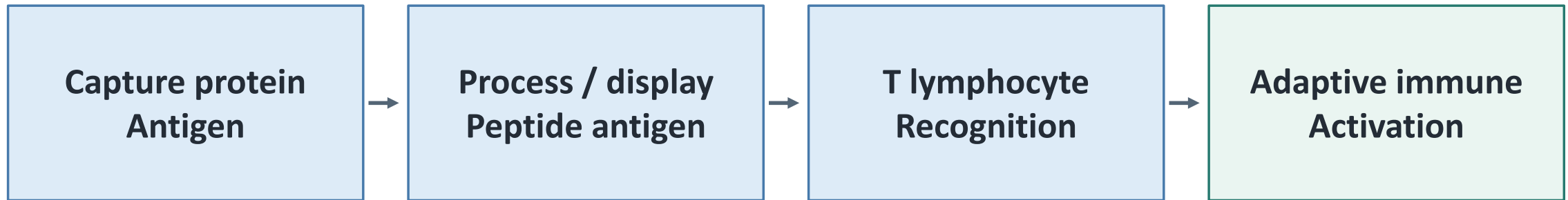
They display captured peptide antigens to T lymphocytes.

Dendritic cells detect danger and signal it



Key contrast: Dendritic cells are chiefly sentinels and coordinators, not the main cells that digest and destroy microbes.

Dendritic cells connect innate and adaptive immunity



Two roles in one cell

Innate detection of danger and presentation of antigen to adaptive lymphocytes are coordinated in dendritic cells.

Macrophages and dendritic cells: Division of labor

Macrophage emphasis

Engulfment and destruction of offending agents; Secretion of inflammatory cytokines; Clearance of damaged tissue.

Dendritic-cell emphasis

Environmental sensing, cytokine signaling, antigen capture, and display of peptides to T lymphocytes.

Innate lymphoid cells respond without antigen receptors

- ILCs are tissue-resident lymphocytes lacking T-cell antigen receptors.
- They respond to cytokines and local mediators associated with tissue injury.
- They provide early sources of cytokines during immune reactions.
- They are distinct from antigen-specific T lymphocytes.

ILC groups parallel helper-T-cell functional profiles

Innate lymphoid group	Corresponding helper-T subset	Shared organizing principle
Group 1 ILCs	Th1	Related dominant cytokine patterns
Group 2 ILCs	Th2	Related dominant cytokine patterns
Group 3 ILCs	Th17	Related dominant cytokine patterns

Boundary: Functional parallels do not mean ILCs carry T-cell antigen receptors.

NK cells detect abnormal host cells

Virus-infected cells

Early surveillance detects altered self surfaces during viral infection.

Other stressed cells

Activating ligands can appear following injury or DNA damage.

Neoplastic cells

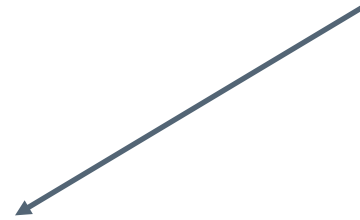
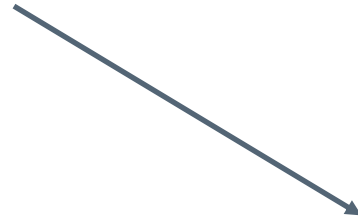
Tumor transformation may reduce self MHC class I and raise activating ligands.

NK activity balances two receptor inputs

**Activating receptor
Stress ligand**

**Inhibitory receptor
Self MHC class I**

**Net signal determines
NK-cell killing**



Normal MHC class I restrains NK-cell cytotoxicity



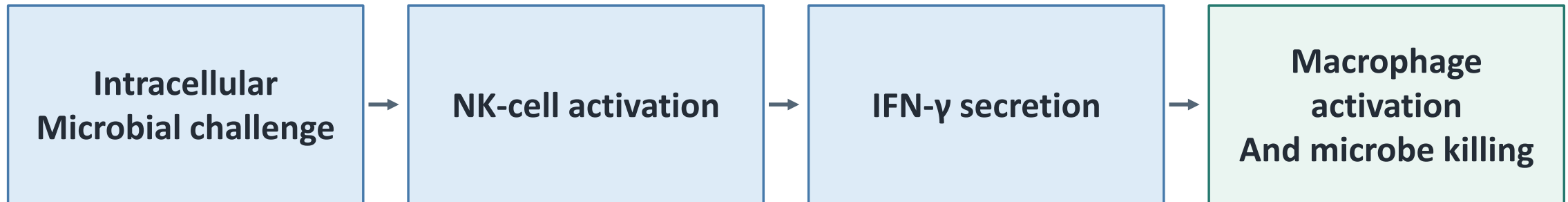
Logic: Inhibitory recognition prevents the immune system from destroying ordinary healthy cells.

Stressed cells can escape NK inhibition



Distinction: NK cells kill abnormal host cells rather than engulfing free extracellular microbes.

NK-cell IFN- γ helps macrophage control infection



Innate cytotoxic lymphocytes also influence the antimicrobial programs of phagocytes.

NK cells can mediate antibody-dependent cytotoxicity



Important connection: This is antibody-dependent cellular cytotoxicity (ADCC): An innate effector cell uses an adaptive antibody.

Mast cells serve as innate inflammatory sensors



Complement cooperation

C3a and C5a can trigger mast-cell mediator release, linking plasma proteins to vascular changes.

Epithelial and endothelial cells also react to microbes

Epithelial cells

Serve as a physical barrier and produce antimicrobial molecules; Can also sense microbial danger at the surface.

Endothelial cells

Respond to inflammatory mediators by expressing leukocyte adhesion machinery that permits recruitment into tissue.

Soluble innate defense operates in tissue fluids

Complement cascade

Plasma proteins amplify recognition and mediate opsonization, inflammatory effects, and selected microbial lysis.

Opsonizing proteins

Mannose-binding lectin and C-reactive protein coat microbes for phagocytic recognition.

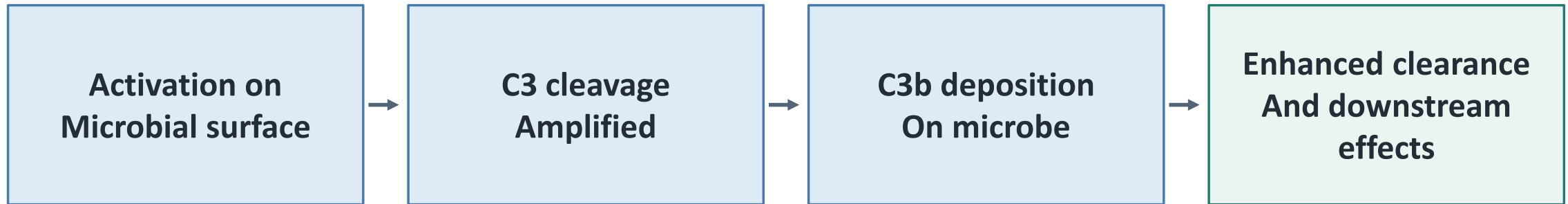
Pulmonary surfactant

A local component of respiratory innate defense against inhaled microbes.

Complement connects innate and adaptive immunity

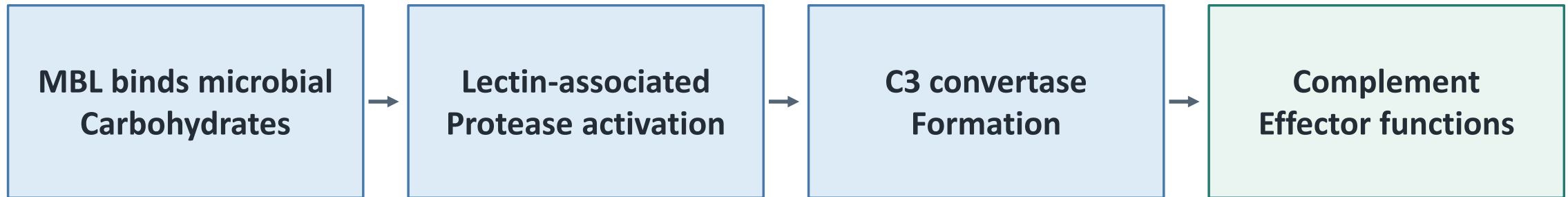
Activation route	Initiating recognition	Immune context
Alternative	Microbial surfaces without antibody requirement	Innate
Lectin	Mannose-binding lectin bound to microbial carbohydrates	Innate
Classical	Antigen–antibody complexes activating C1	Adaptive-linked

Alternative complement activation is antibody-independent



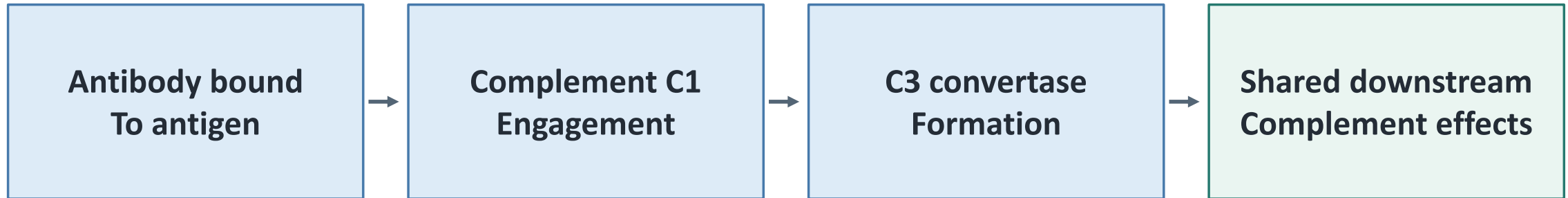
Principle: Antibody is not necessary for this pathway to participate in early host defense.

Lectin pathway couples microbial sugar recognition to C3



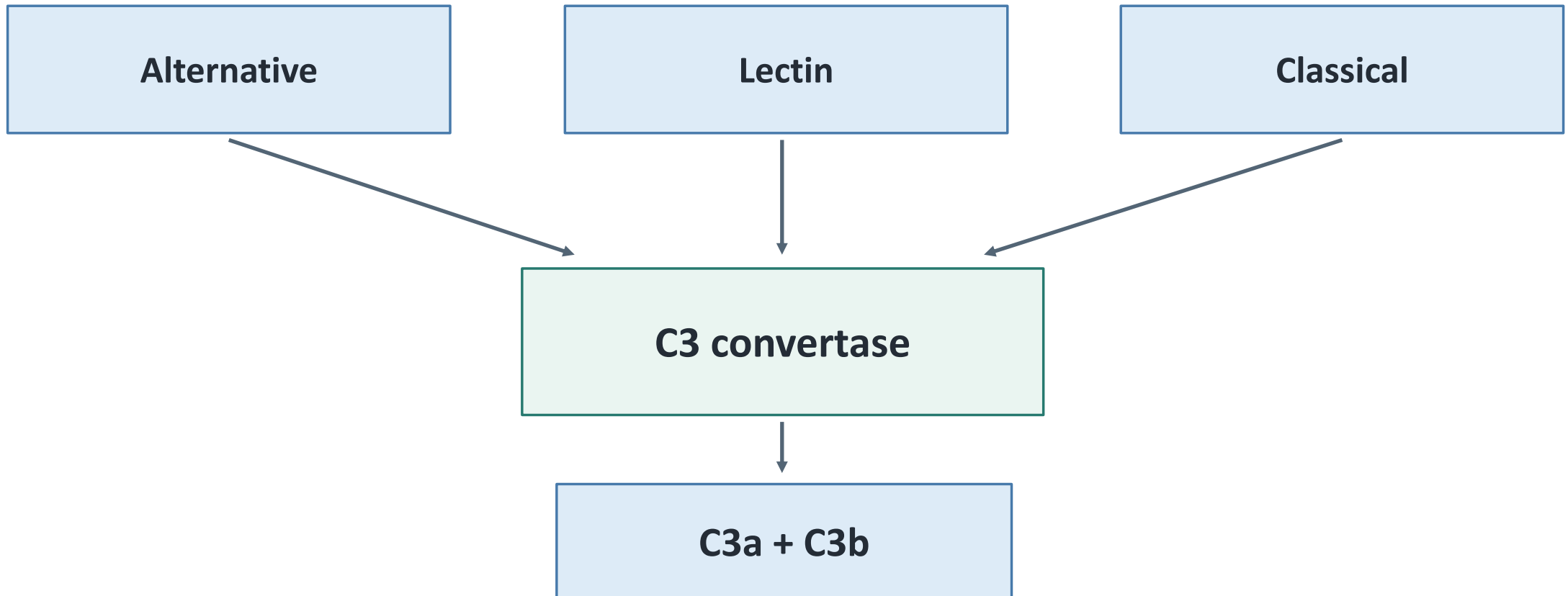
Specificity: Recognition is directed at characteristic microbial carbohydrate patterns.

Classical complement activation depends on antibodies



Boundary: The classical pathway illustrates cooperation with adaptive immunity rather than purely innate triggering.

All complement pathways converge at C3



Complement mediates three distinct host effects

Inflammation

C3a and C5a promote vascular changes; C5a also recruits leukocytes.

Opsonization

C3b and iC3b on microbes support phagocyte receptor binding.

Cell lysis

Terminal C5b–C9 membrane attack complexes can disrupt selected microbes.

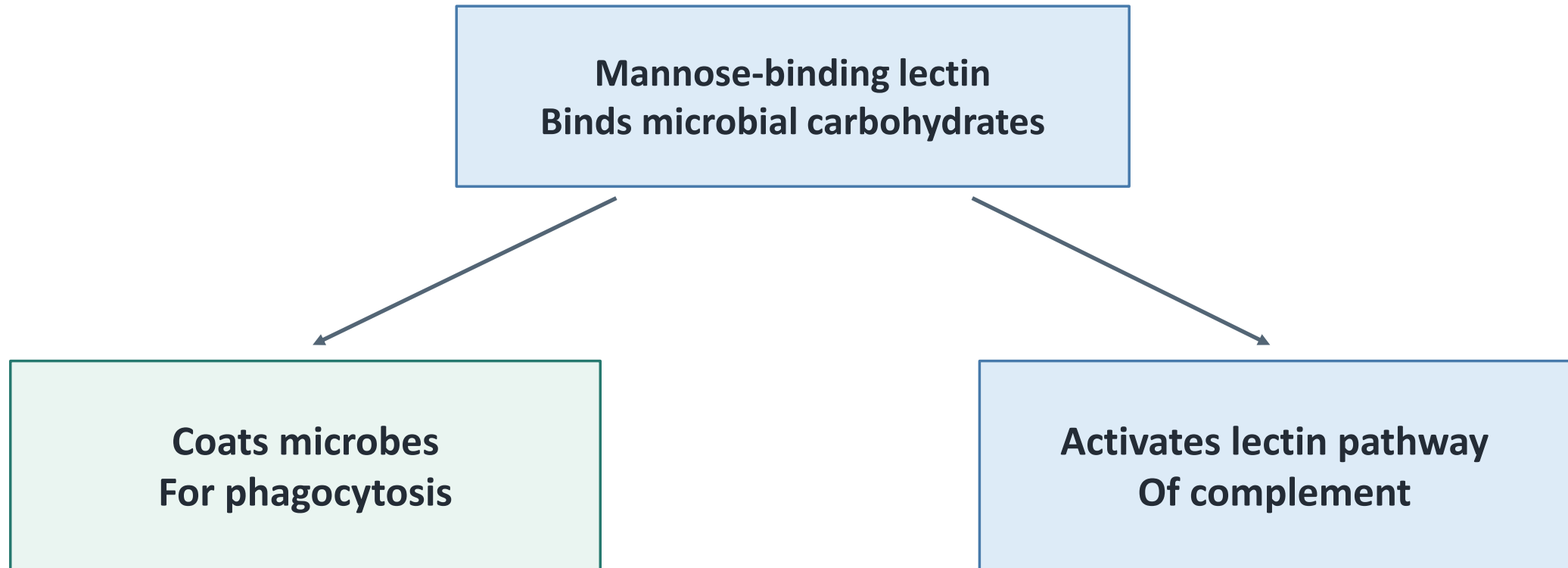
Complement regulators prevent self-injury



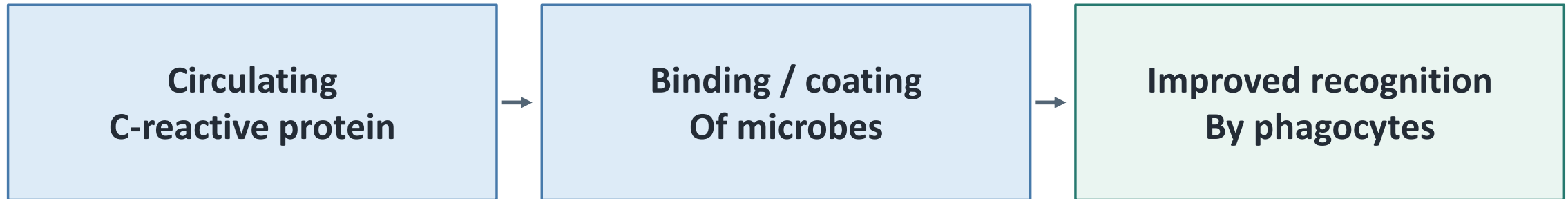
When regulation fails

Excess complement activation can contribute to tissue damage even though complement normally protects against microbes.

Mannose-binding lectin supports two defenses



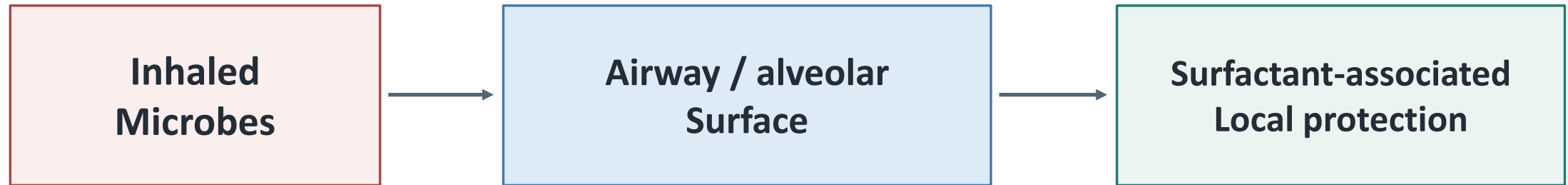
C-reactive protein is an innate opsonin



Functional distinction

CRP is included here because of its host-defense role as a microbial coating protein, not solely because clinicians measure it during inflammation.

Pulmonary surfactant has an immune-defense role



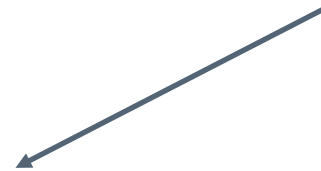
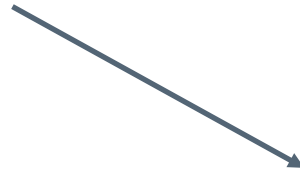
Scope: Surfactant is explicitly included among innate immune components protecting against inhaled microbes.

Pattern recognition links constituents to danger

**PAMPs: Shared microbial
Molecular structures**

**DAMPs: Signals from
Damaged / necrotic cells**

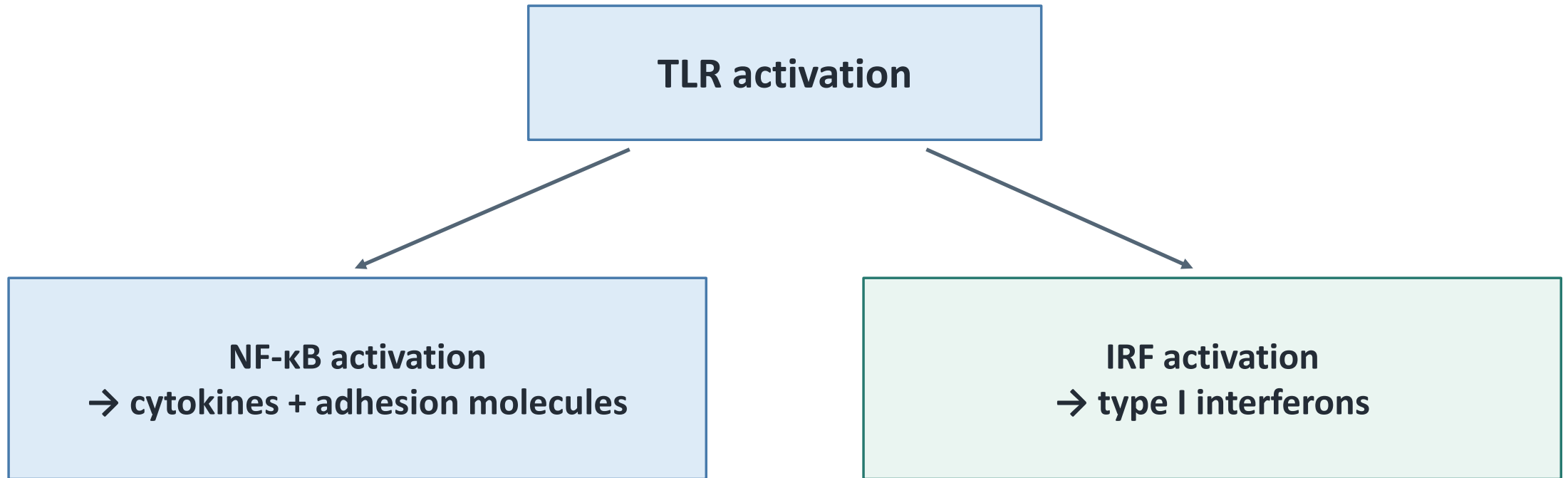
**Germline-encoded
Pattern-recognition receptors**



Recognition systems survey different compartments

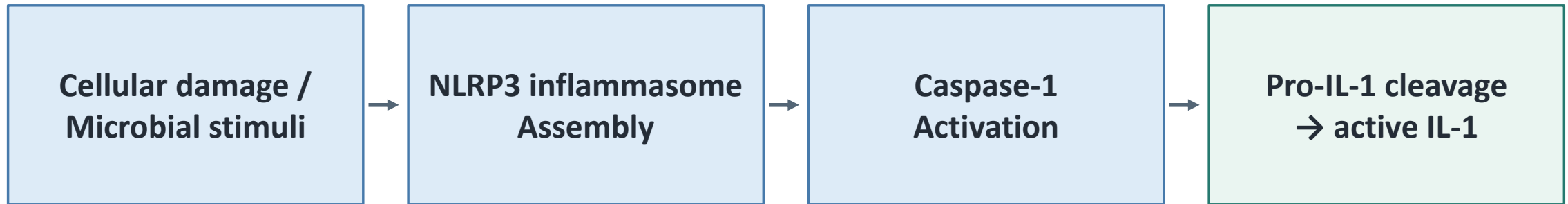
Receptor location	What can be sensed	Biologic rationale
Cell surface	Extracellular microbial ligands	Signals before cellular entry
Endosomal vesicles	Products of internalized microbes	Detects ingested microbial contents
Cytosol	Microbes or intracellular danger signals	Detects danger within the cell

Toll-like receptor signaling has two major outputs



Outcome: Coordinated leukocyte recruitment and antiviral protection.

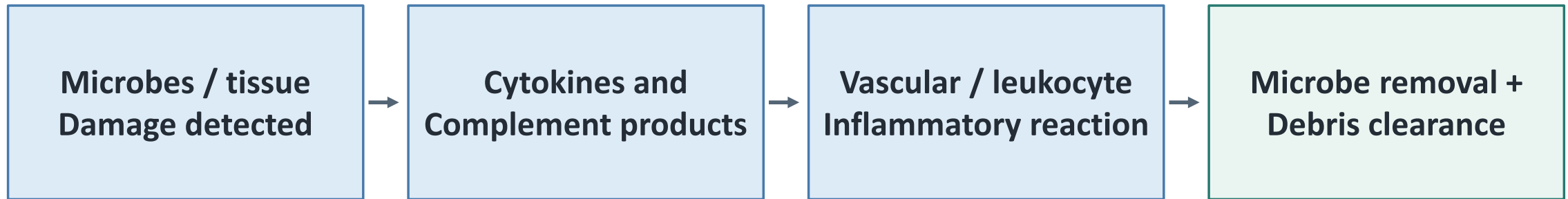
Inflammasomes convert danger sensing into IL-1



Inflammatory result

Active IL-1 contributes to recruitment of leukocytes and fever.

Inflammation is a principal innate reaction



After control: Inflammation also supports the subsequent repair of damaged tissues.

Type I interferons establish an antiviral state



Complementary response: NK cells recognize and eliminate virus-infected host cells.

Innate immunity provides activation cues to adaptive cells



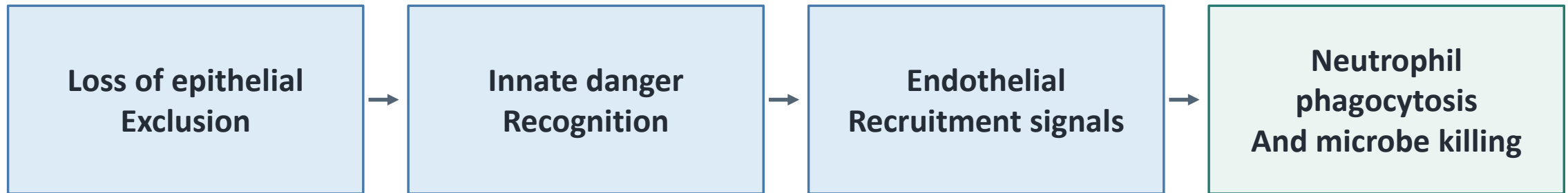
Two systems cooperate

Innate effector functions buy time and deliver inflammatory and antigen-presentation signals that support adaptive immunity.

Case application: Contaminated skin wound

Clinical situation

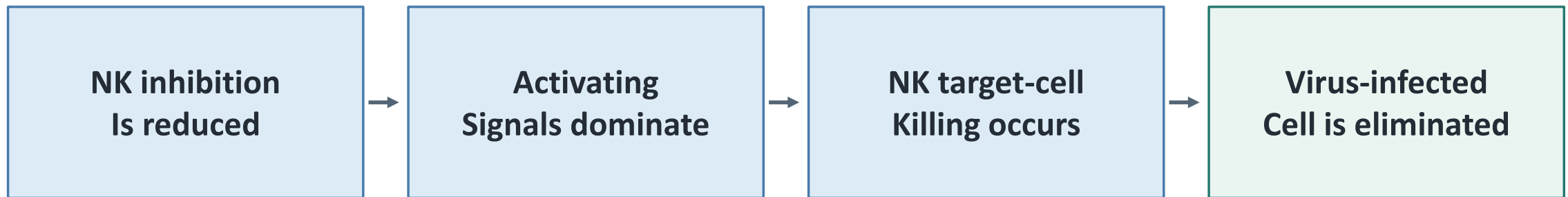
A break in the skin is followed by microbial entry into deeper tissues and a neutrophil-rich early inflammatory response.



Case application: Virus-infected cell with low MHC I

Clinical situation

An infected cell reduces surface MHC class I while displaying stress-induced activating ligands.

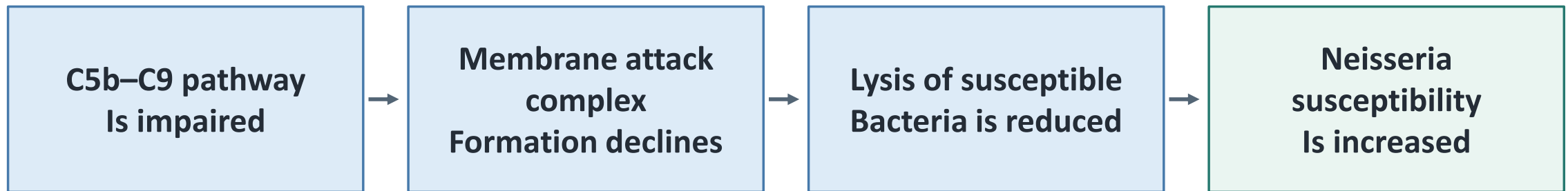


Parallel defense: Type I interferons also inhibit viral replication in nearby cells.

Case application: Susceptibility to Neisseria infection

Mechanistic vignette

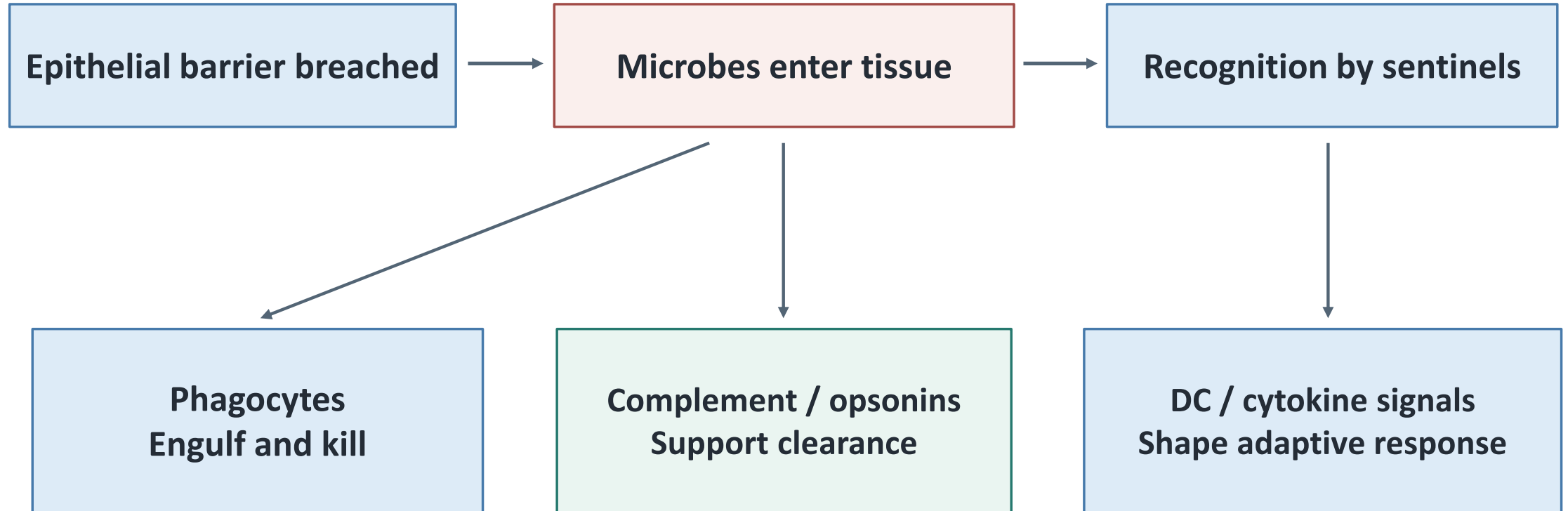
A patient with deficient terminal complement components cannot assemble an effective membrane attack complex.



Synthesis: Match each component to its job

Constituent	Principal task	Primary outcome
Epithelium / defensins	Block access; local antimicrobial action	Exclusion
Neutrophils / macrophages	Engulf and kill microbes	Clearance
Dendritic cells / ILCs	Sense danger; produce signals; present antigen (DCs)	Coordination
NK cells	Recognize abnormal cells; cytotoxicity / IFN- γ	Infected-cell control
Complement / MBL / CRP	Opsonization, inflammation; sometimes cell lysis	Soluble protection

Integrating the host-defense network



References and source scope

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026).

Normal Immune Response; Components of Innate Immunity.

Cellular Receptors; Natural Killer Cells; Reactions of Innate Immunity.

Leukocyte activation and phagocytosis.

Complement System.

Conceptual diagrams in this lecture are original editable teaching schematics.