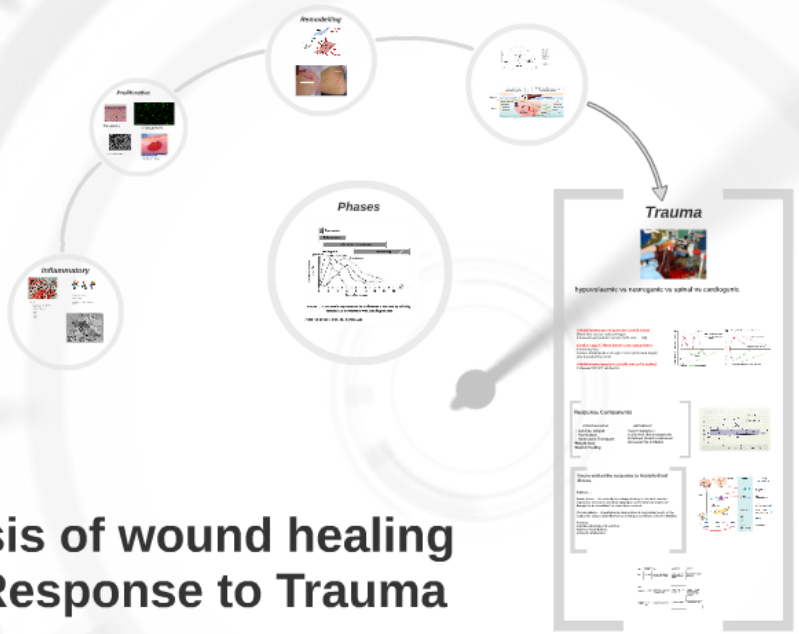
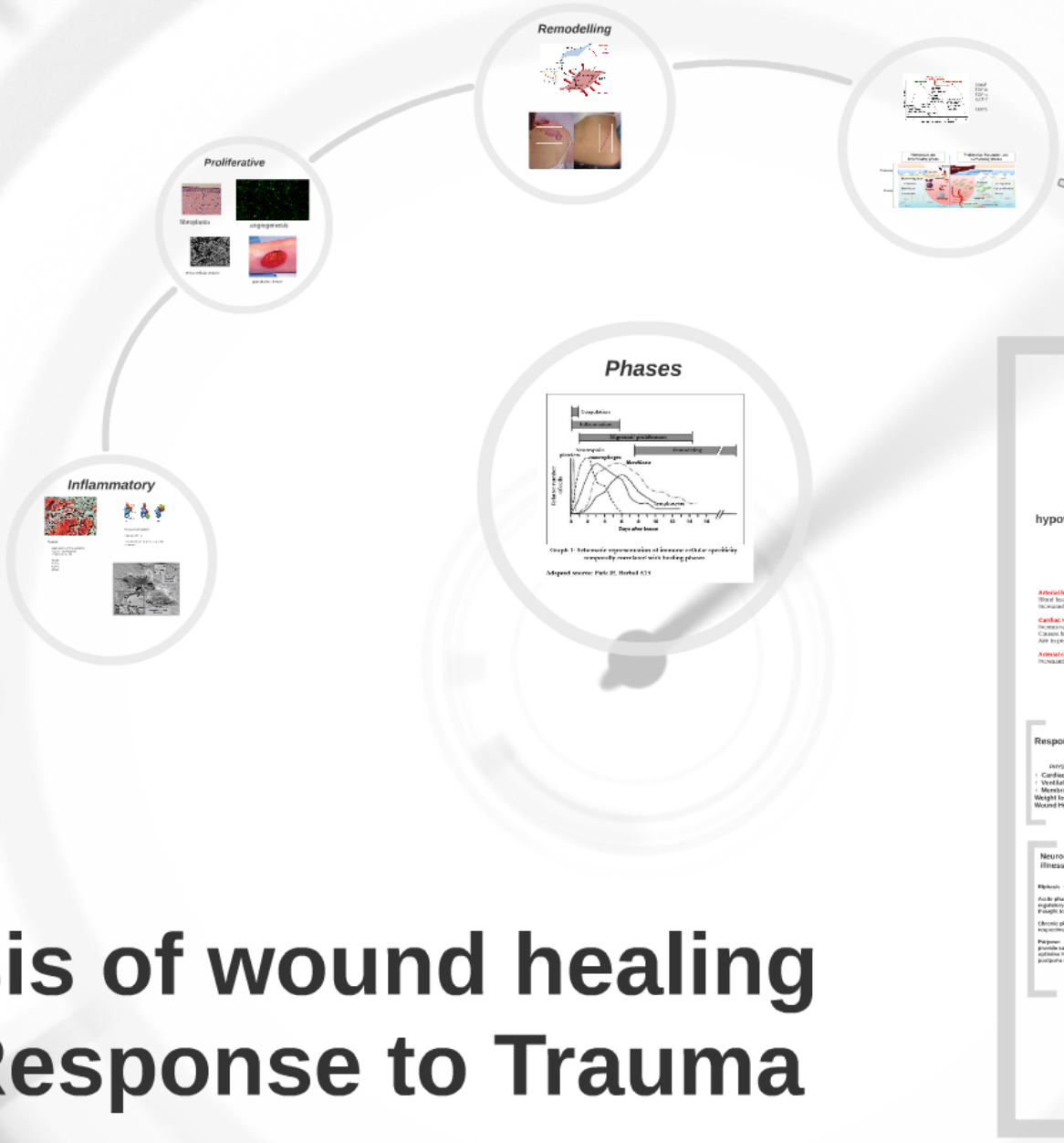


Basis of wound healing & Response to Trauma

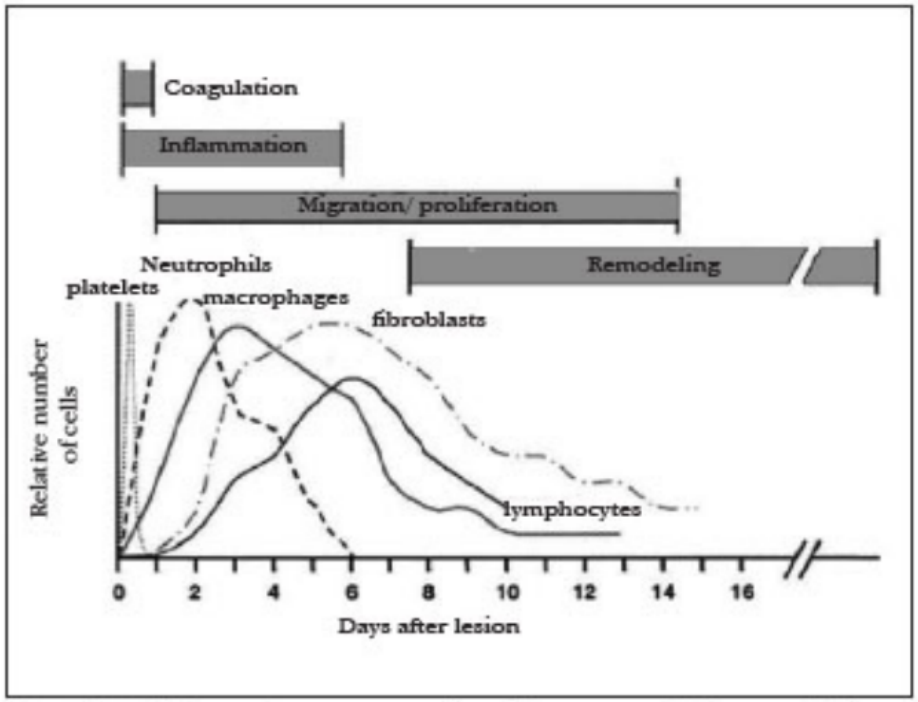
METABOLIC RESPONSE OF TISSUE TO INJURY

P[illegible]m Murali. M.S; M.B.A.



Basis of wound healing & Response to Trauma

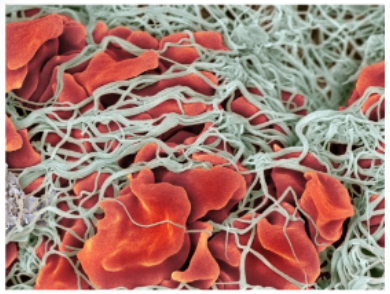
Phases



Graph 1: Schematic representation of immune cellular specificity temporally correlated with healing phases

Adapted source: Park JE, Barbul A13

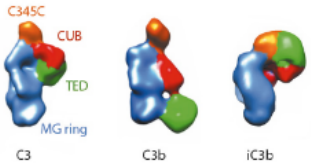
Inflammatory



Platelets

aggregates and coagulates
restore haemostasis
temporary matrix

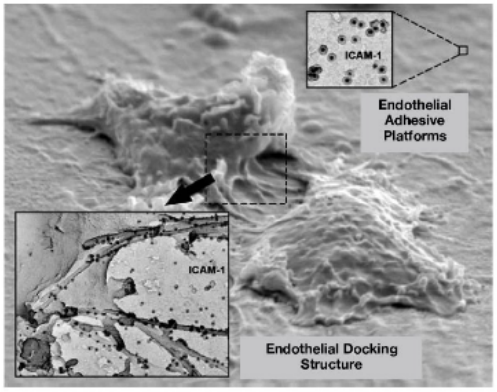
PDGF
TGF-b
TGF-a
VEGF

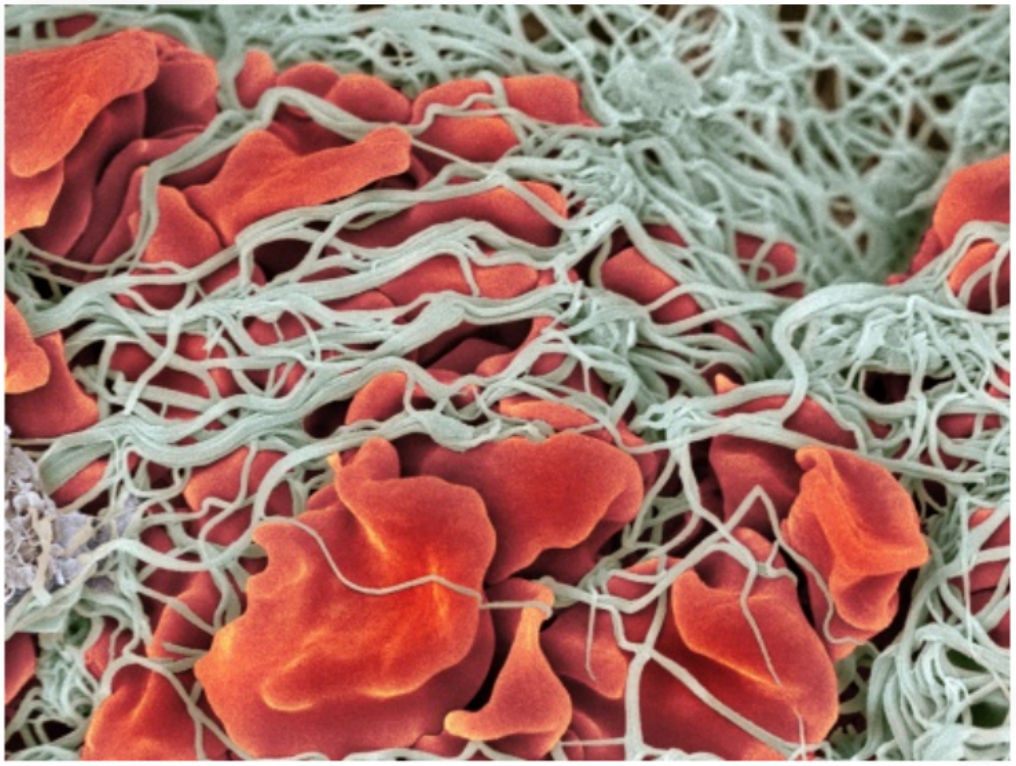


Complement system

release of GFs

recruitment of inflammatory cells
to wound





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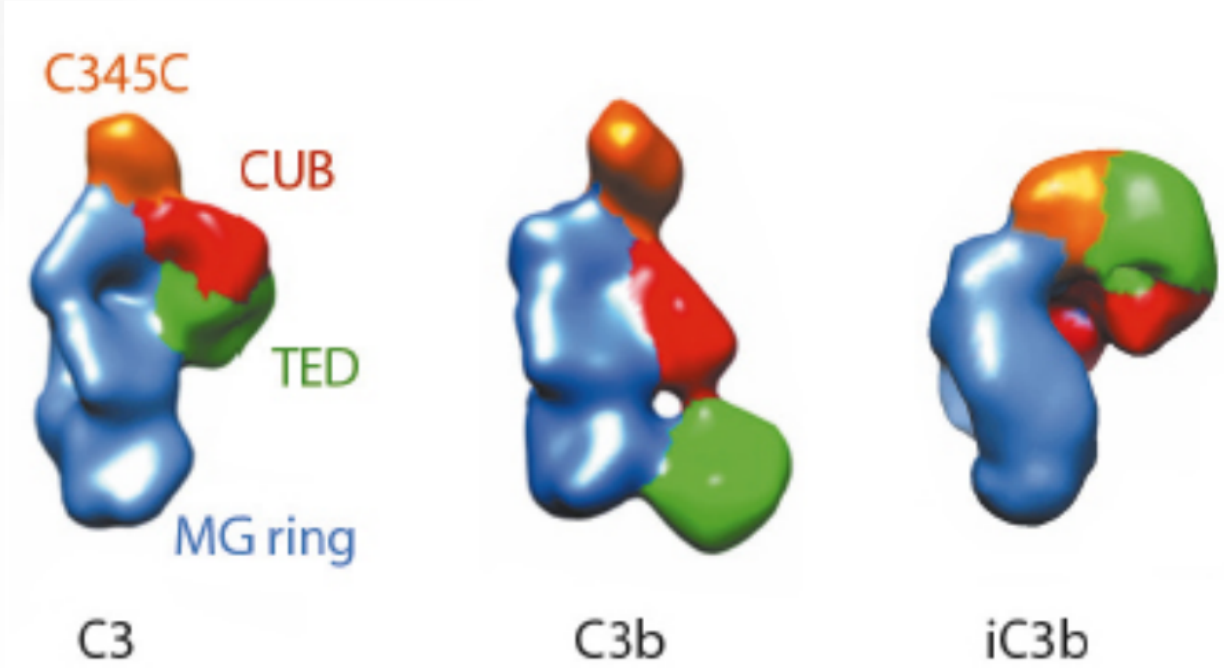
TGF-b
TGF-a
VEGF



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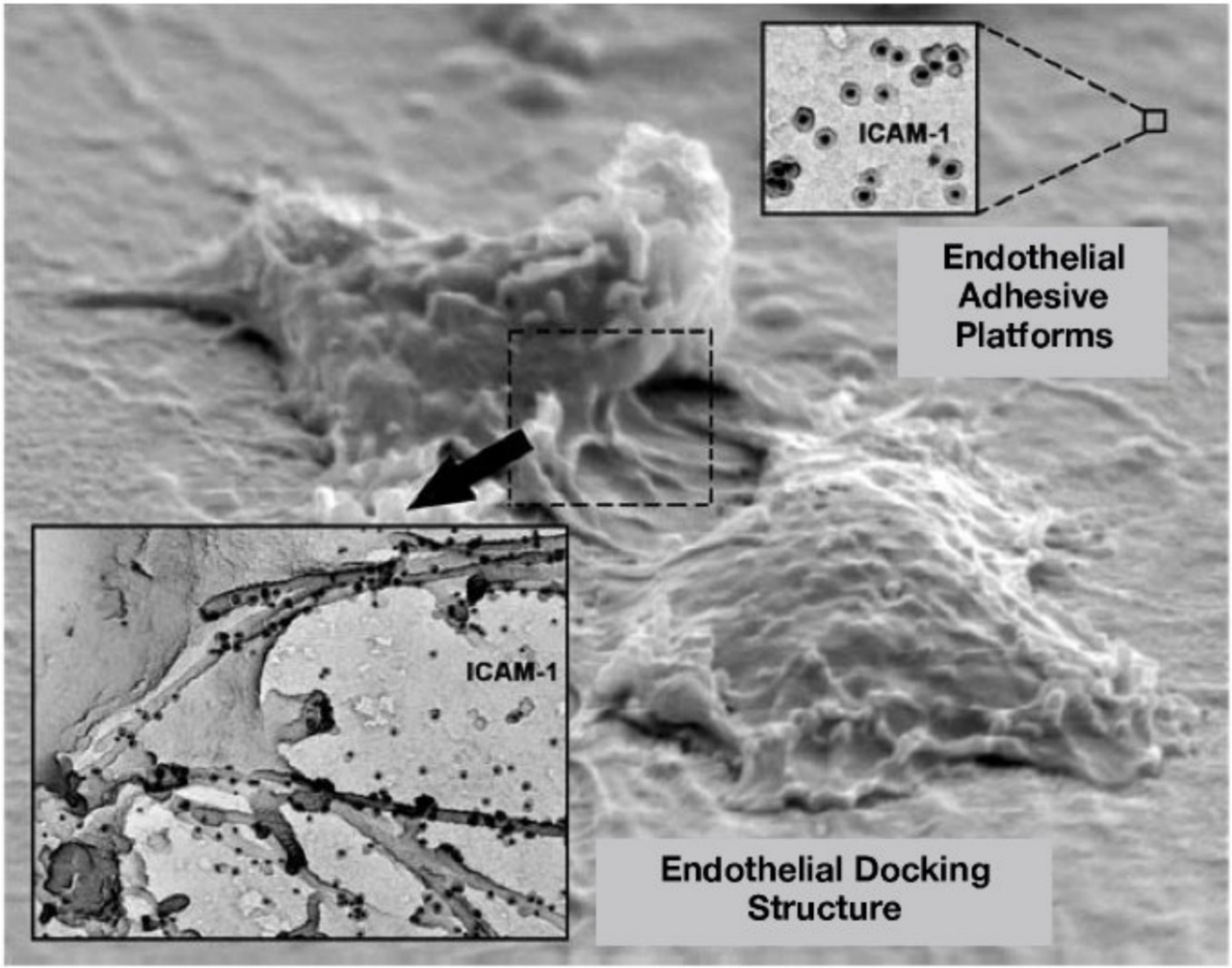
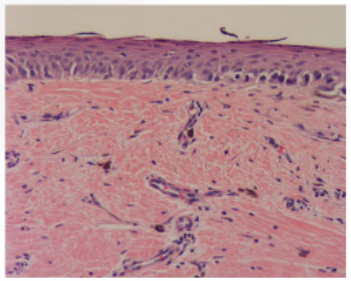
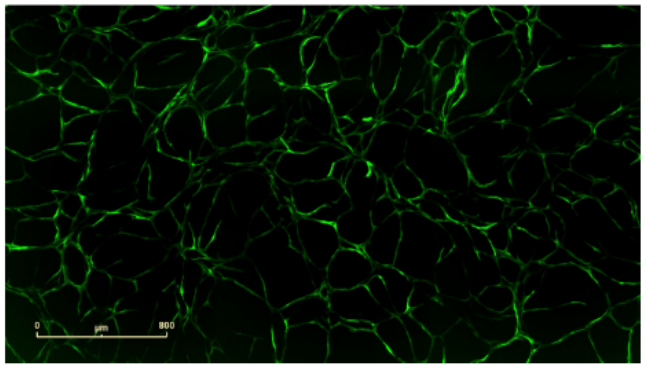

ICAM-1
Endothelial
Adhesive
Platforms
ICAM-1
Endothelial Docking
Structure

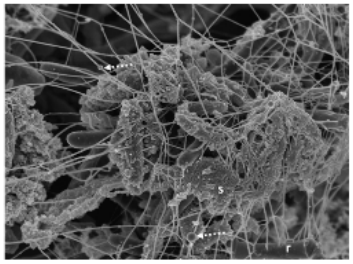
Proliferative



fibroplasia

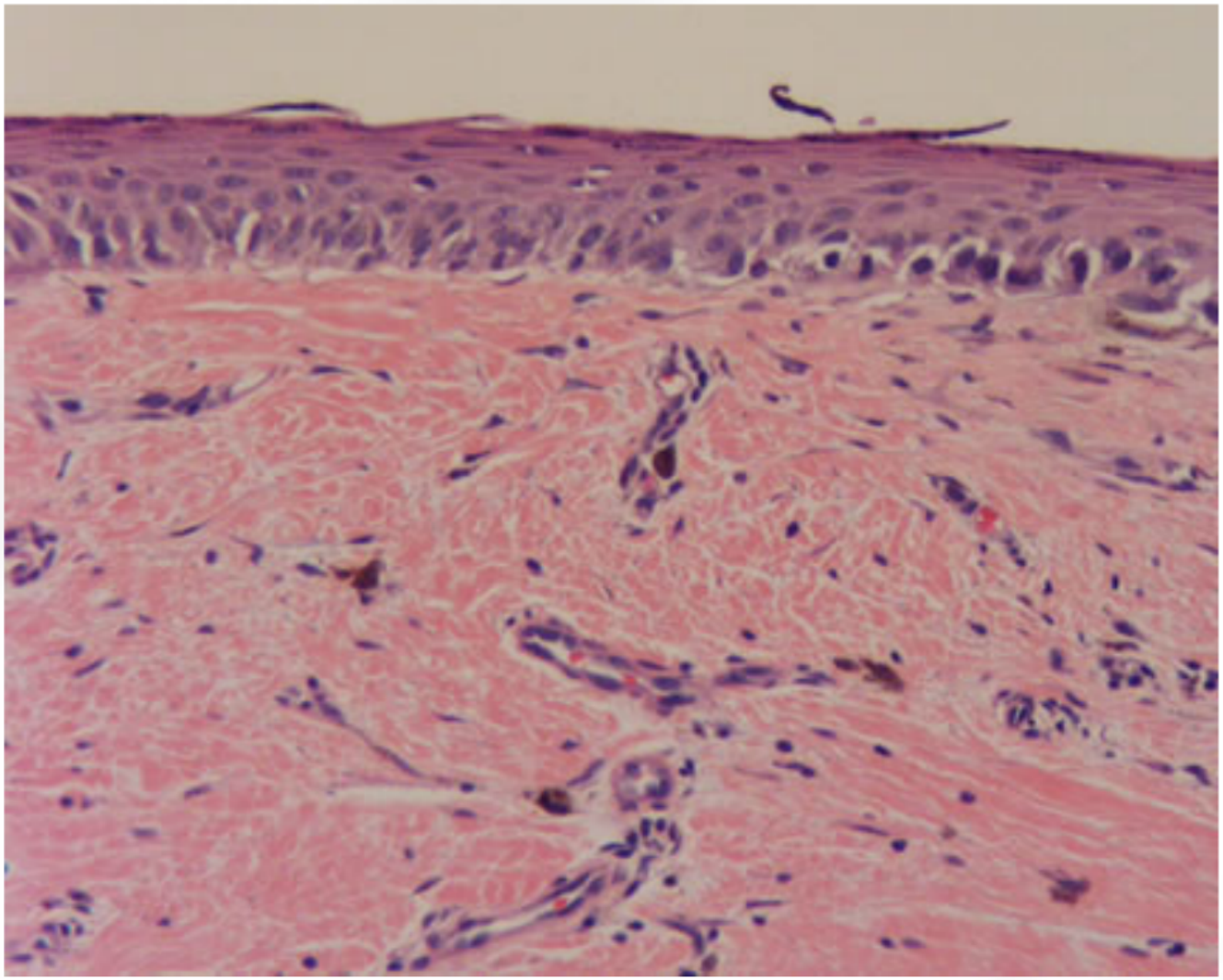


angiogenesis

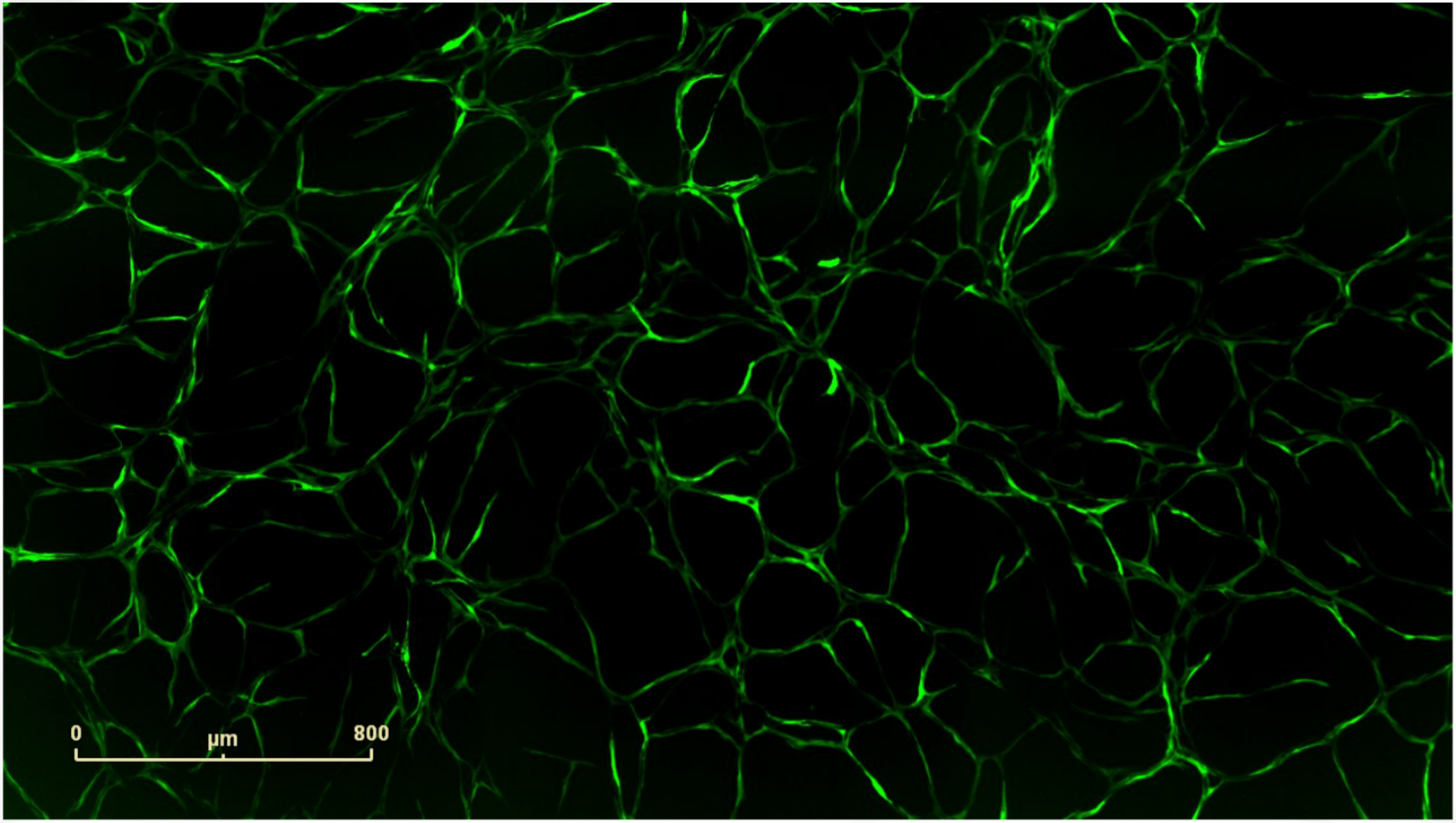


extra-cellular matrix

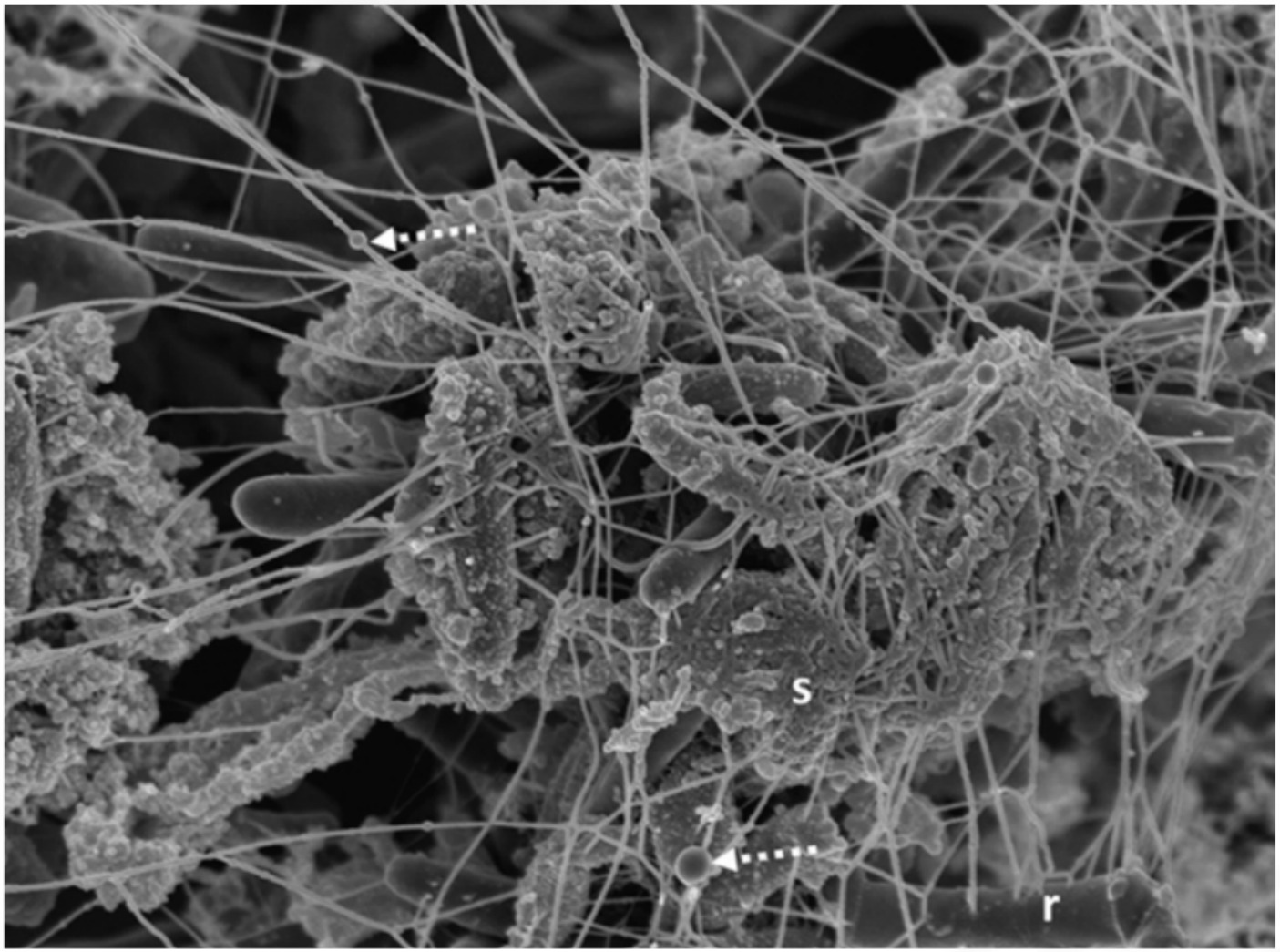
granulation tissue



fibroplasia



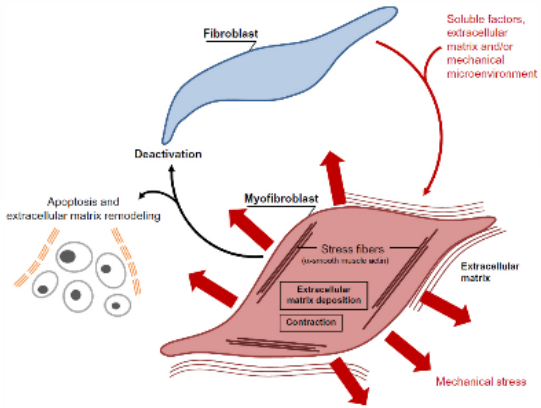
angiogenesis

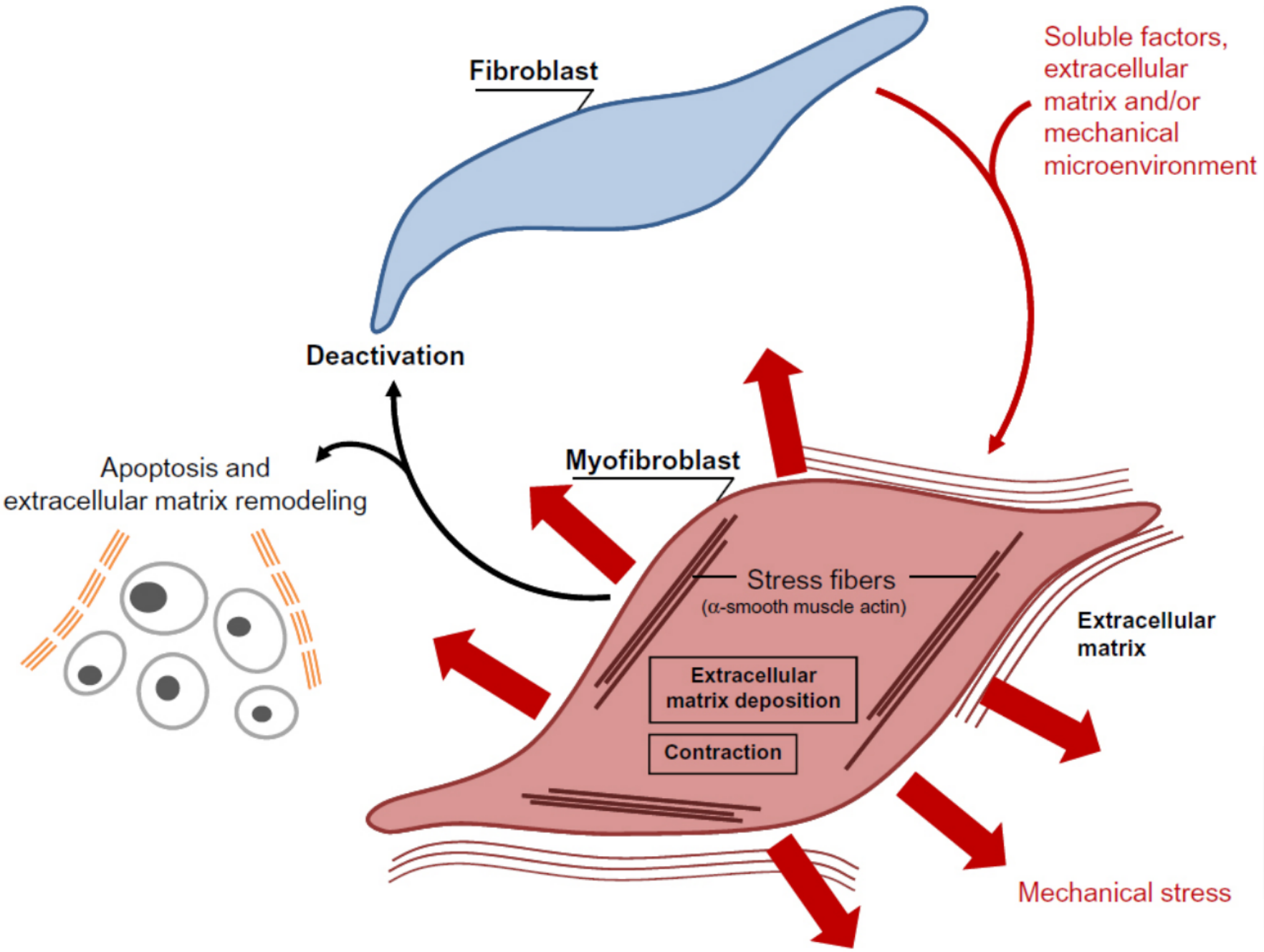


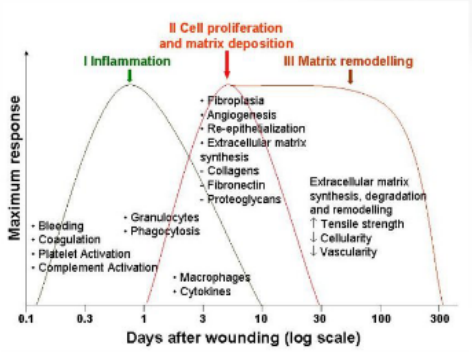
extra-cellular matrix

granulation tissue

Remodelling

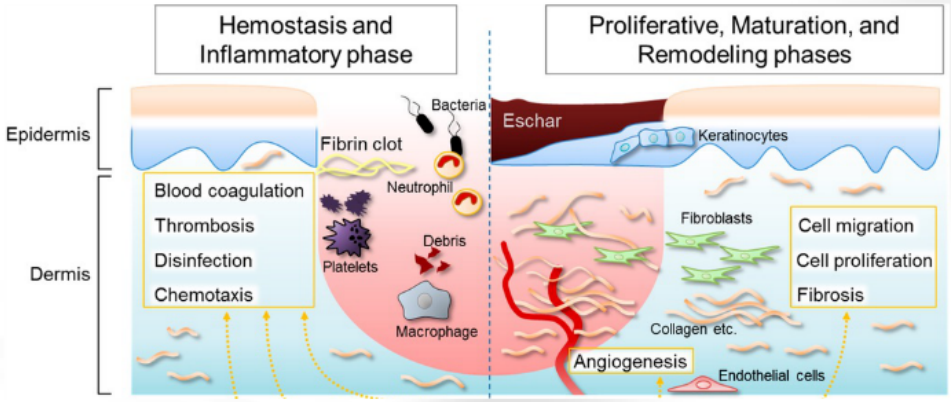


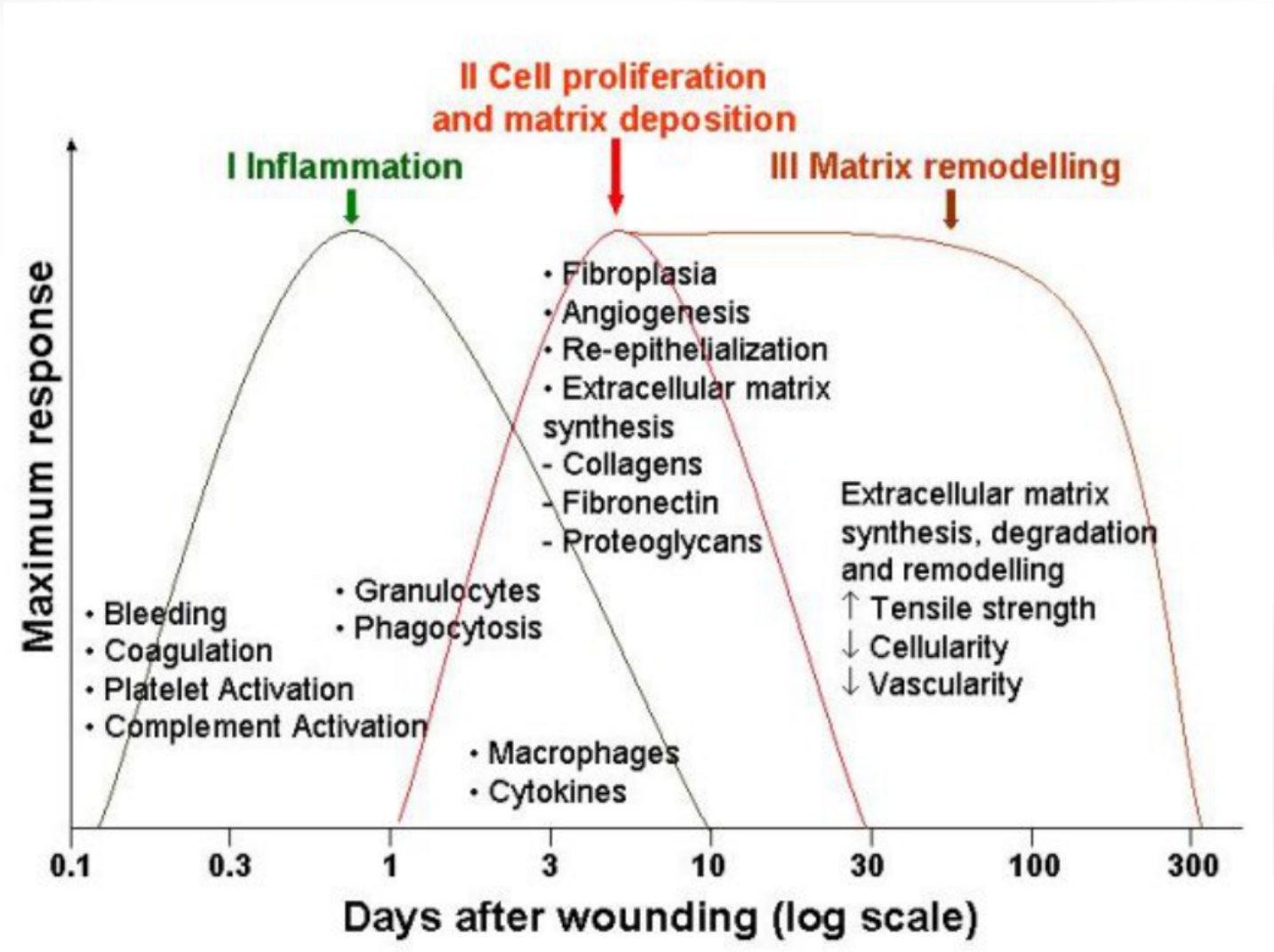

Fibroblast
Soluble factors, extracellular matrix and/or mechanical microenvironment
Deactivation
Apoptosis and extracellular matrix remodeling
Myofibroblast
Stress fibers
(α-smooth muscle actin)
Extracellular matrix
Extracellular matrix deposition
Contraction
Mechanical stress



PDGF
TGF-b
TGF-a
KGF-7

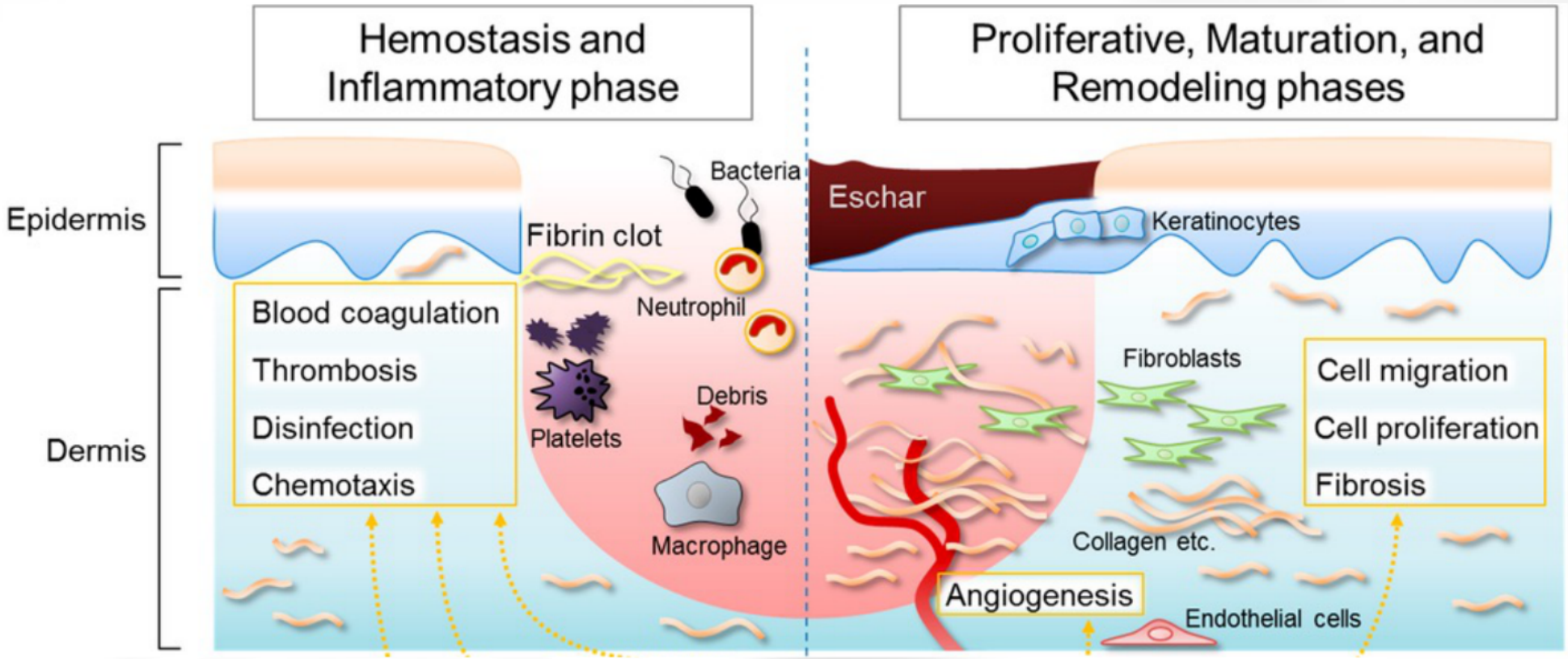
MMPs



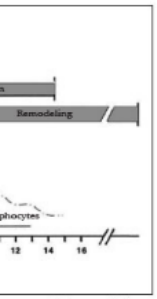


PDGF
TGF-b
TGF-a
KGF-7

MMPs


Hemostasis and Inflammatory phase
Proliferative, Maturation, and Remodeling phases
Epidermis
Dermis
Bacteria
Eschar
Keratinocytes
Fibrin clot
Neutrophil
Blood coagulation
Thrombosis
Disinfection
Chemotaxis
Platelets
Debris
Macrophage
Fibroblasts
Cell migration
Cell proliferation
Fibrosis
Collagen etc.
Angiogenesis
Endothelial cells

es



mmune cellular specificity
ealing phases

ling
uma

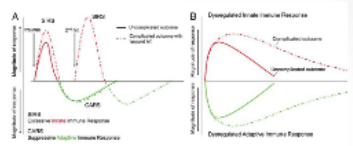
Trauma

hypovolaemic vs neurogenic vs spinal vs cardiogenic

Arterial baroreceptors (arch and carotid sinus)
Blood loss causes reduced vagus
Increased sympathetic activity (SVR and +/- HR)

Cardiac vagal C-fibres (ventricular myocardium)
Increasing loss
Causes bradycardia and hypotension (increased vagal)
Aim to protect the heart

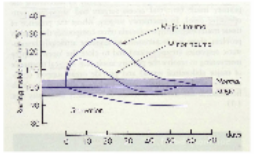
Arterial chemoreceptors (carotid and aortic bodies)
Increased RR with acidaemia



Response Components

PHYSIOLOGICAL
↑ Cardiac Output
↑ Ventilation
↑ Membrane Transport
Weight loss
Wound Healing

METABOLIC
Hypermetabolism
Acclerated Gluconeogenesis
Enhanced Protein breakdown
Increased Fat oxidation



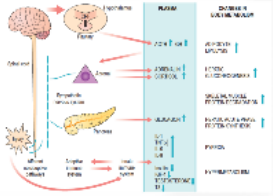
Neuro-endocrine response to injury/critical illness

Biphasic :

Acute phase - An actively secreting pituitary & elevated counter regulatory hormones (cortisol, glucagon, adrenaline).Changes are thought to be beneficial for short-term survival.

Chronic phase - Hypothalamic suppression & low serum levels of the respective target organ hormones. Changes contribute chronic wasting.

Purpose:
provide substrates for survival
optimise host defence
postpone anabolism



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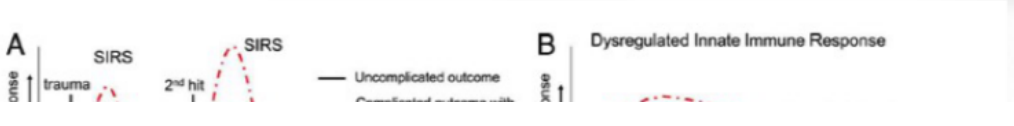

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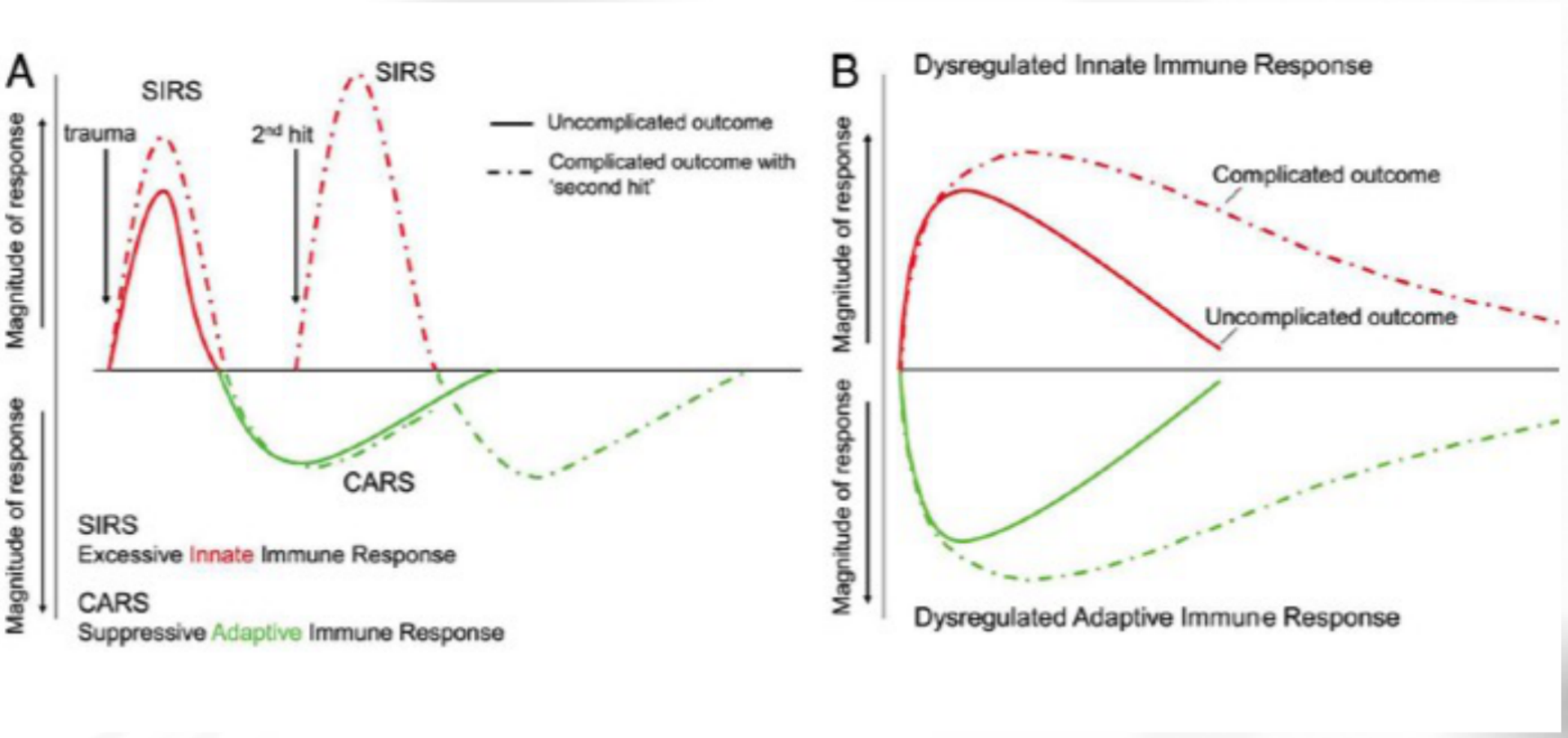
A
SIRS
SIRS
trauma
2nd hit
Uncomplicated outcome
Complicated outcome with 'second hit'
Magnitude of response
Magnitude of response
CARS
SIRS
Excessive Innate Immune Response
CARS
Suppressive Adaptive Immune Response
B
Dysregulated Innate Immune Response
Magnitude of response
Complicated outcome
Uncomplicated outcome
Magnitude of response
Dysregulated Adaptive Immune Response

Response Components

PHYSIOLOGICAL

↑ Cardiac Output
↑ Ventilation
↑ Membrane Transport
Weight loss
Wound Healing

METABOLIC

Hypermetabolism
Acclerated Gluconeogenesis
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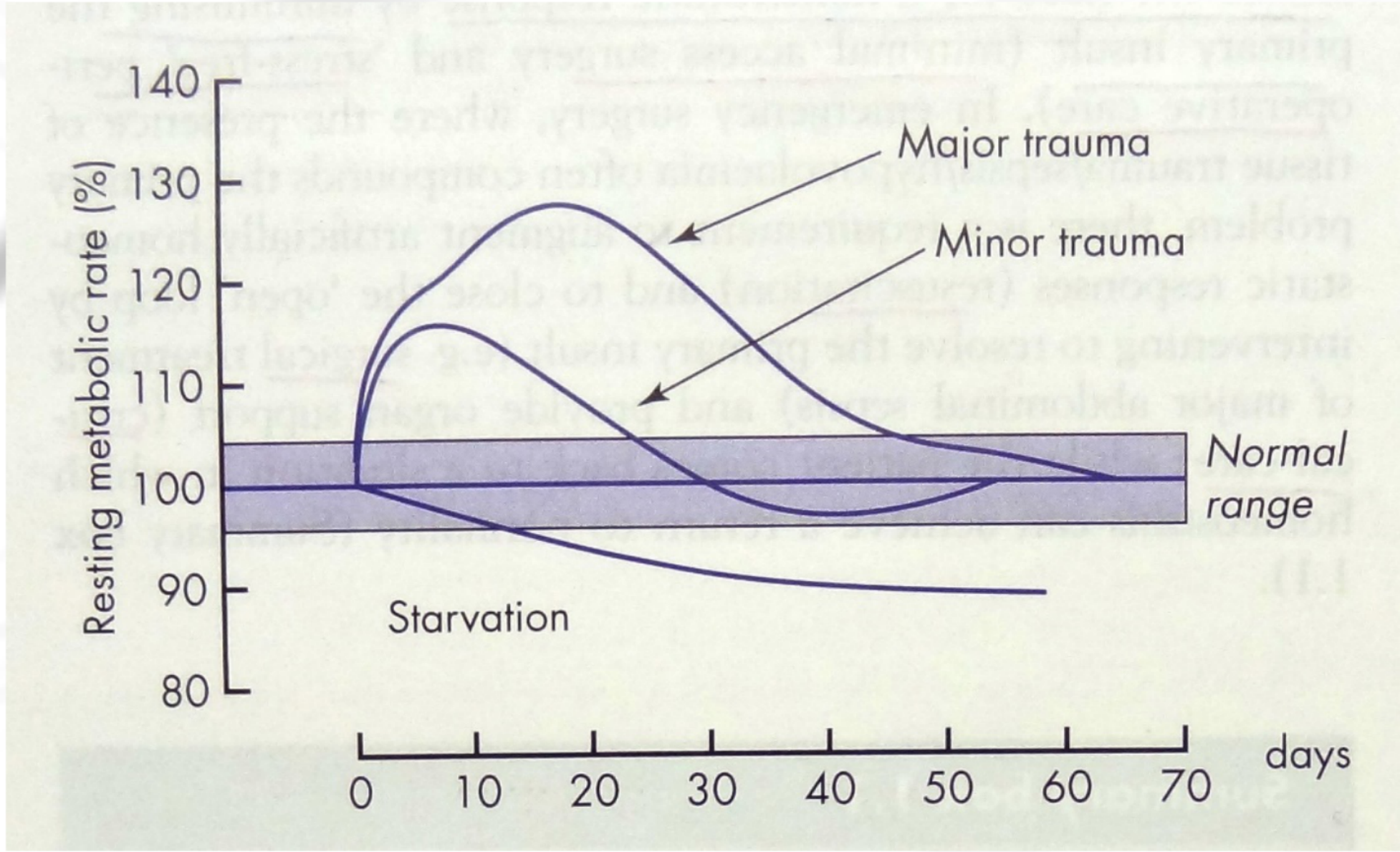
Neuro-endocrine response to injury/critical


Resting metabolic rate (%)
140
130
120
110
100
90
80
Major trauma
Minor trauma
Normal range
Starvation
0
10
20
30
40
50
60
70
days

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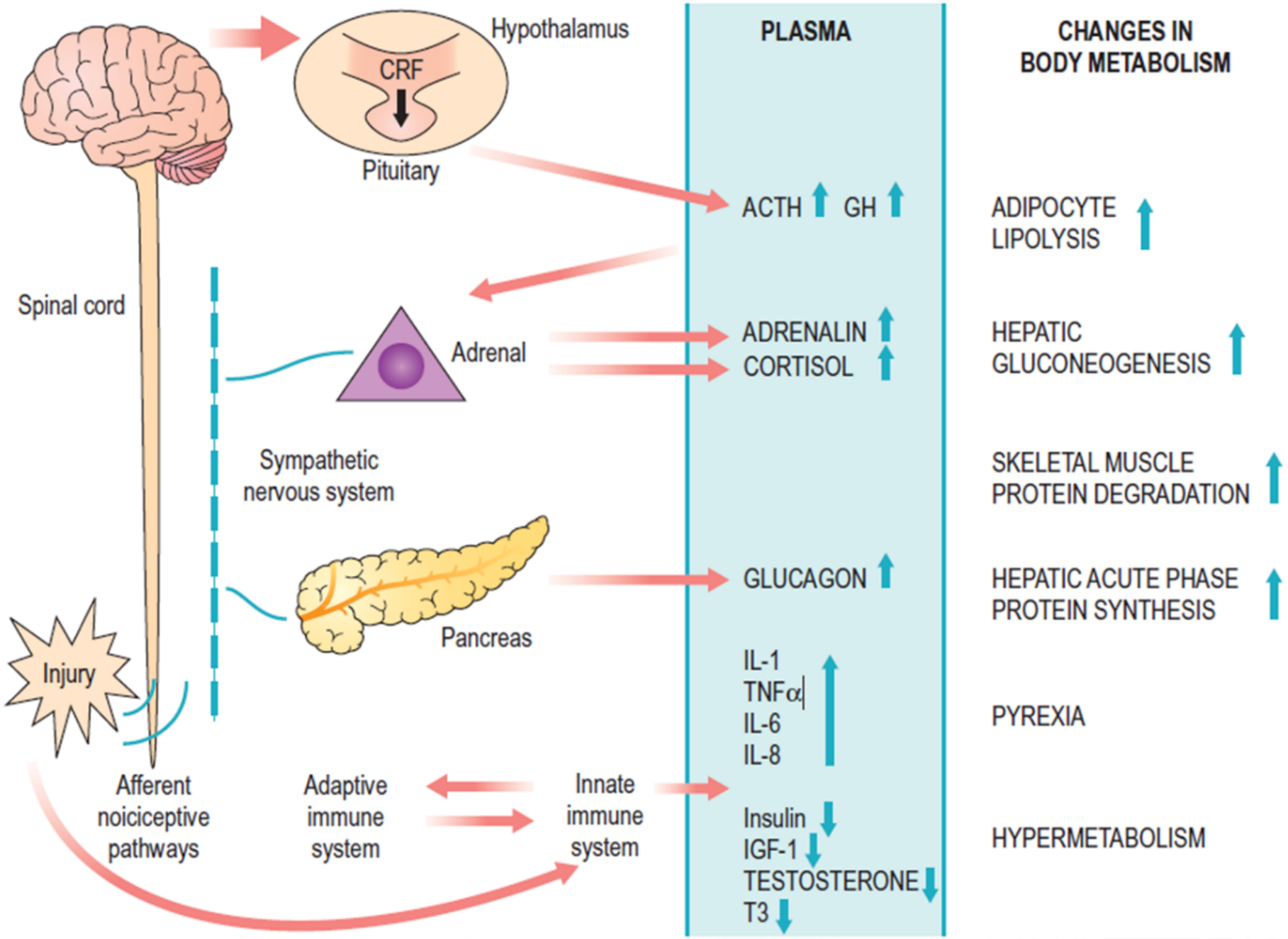
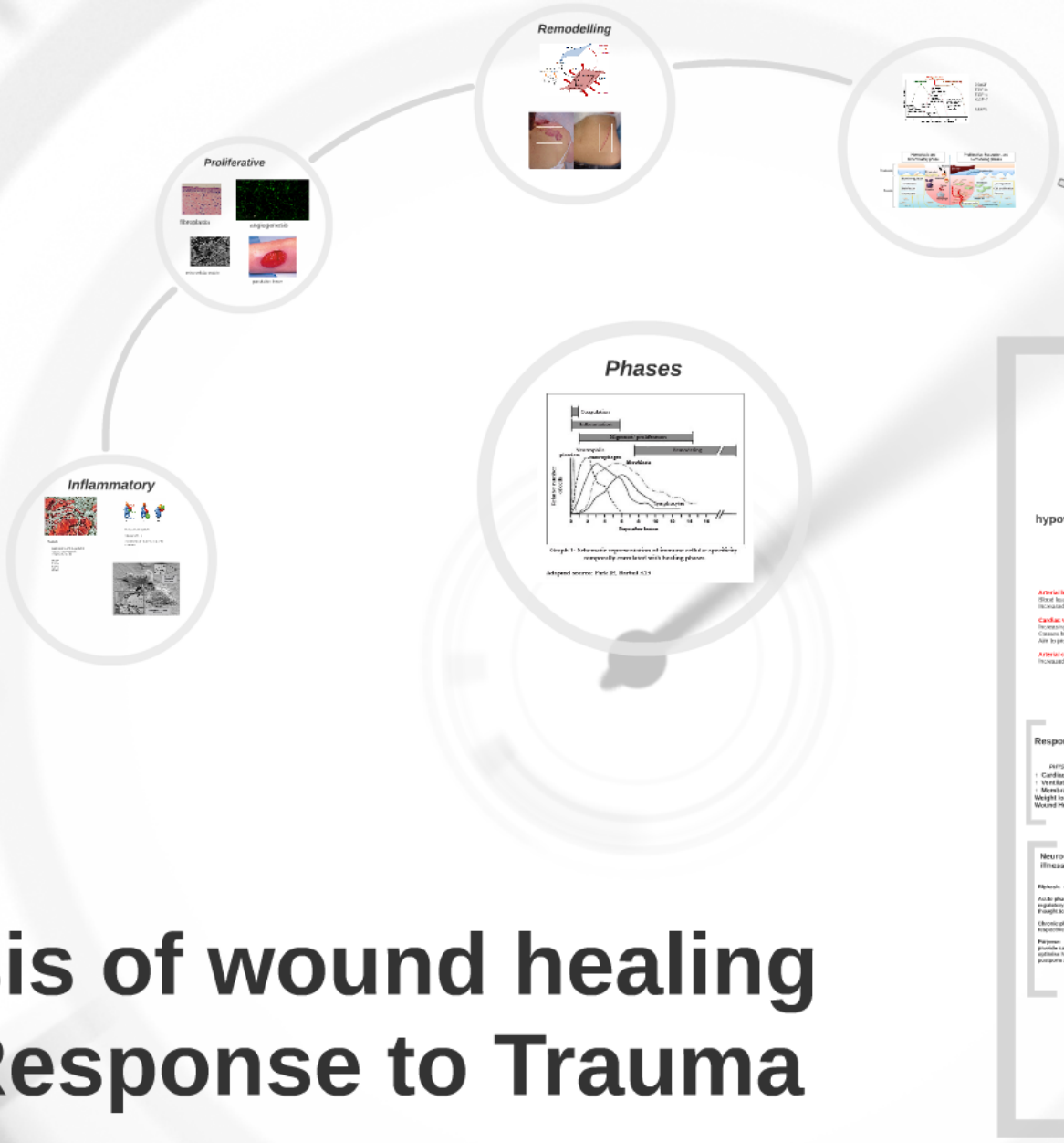

Hypothalamus
CRF
Pituitary
PLASMA
CHANGES IN BODY METABOLISM
ACTH
GH
ADIPOCYTE LIPOLYSIS
Spinal cord
Adrenal
ADRENALIN
CORTISOL
HEPATIC GLUCONEOGENESIS
Sympathetic nervous system
SKELETAL MUSCLE PROTEIN DEGRADATION
GLUCAGON
HEPATIC ACUTE PHASE PROTEIN SYNTHESIS
Pancreas
Injury
IL-1
TNFα
IL-6
IL-8
PYREXIA
Afferent noiciceptive pathways
Adaptive immune system
Innate immune system
Insulin
IGF-1
TESTOSTERONE
T3
HYPERMETABOLISM

Phase	Duration	Role	Physiological	Hormones
Ebb	24 - 48 hrs	Conserve - blood volume & energy reserves - Repair	↓ BMR, ↓ temp, ↓ CO, hypovolaemia, lactic acidosis	Catecholamines, Cortisol, aldosterone
Flow				
Catabolic	3 – 10 days	Mobilisation of energy stores – Recovery & Repair	↑ BMR, ↑ Temp, ↑ O2 consump, ↑ CO	Cytokines + ↑ Insulin, Glucagon, Cortisol, Catechol but insulin resistance
Anabolic	10 – 60 days	Replacement of lost tissue	+ve Nitrogen balance	Growth hormone, IGF



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