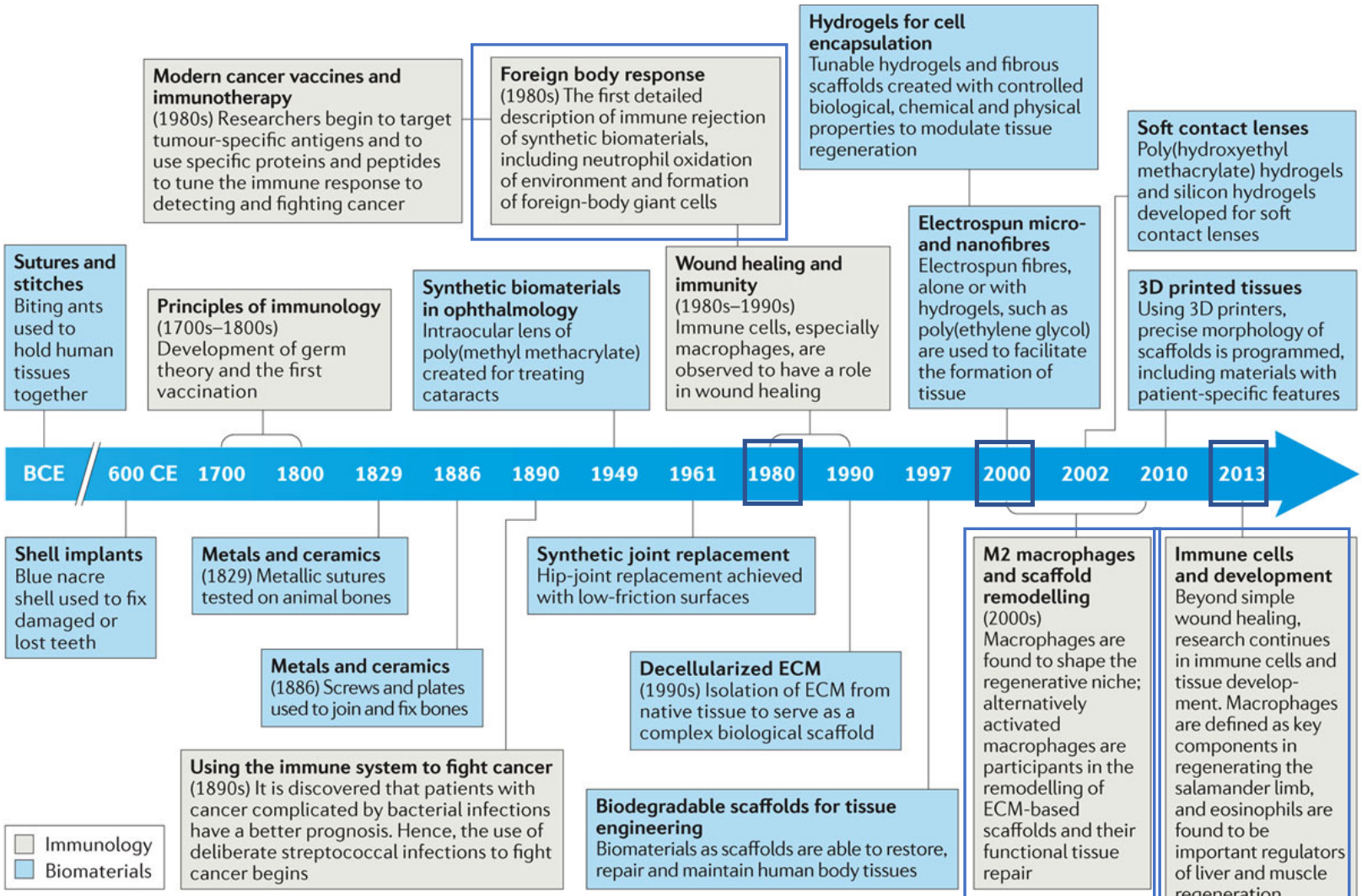
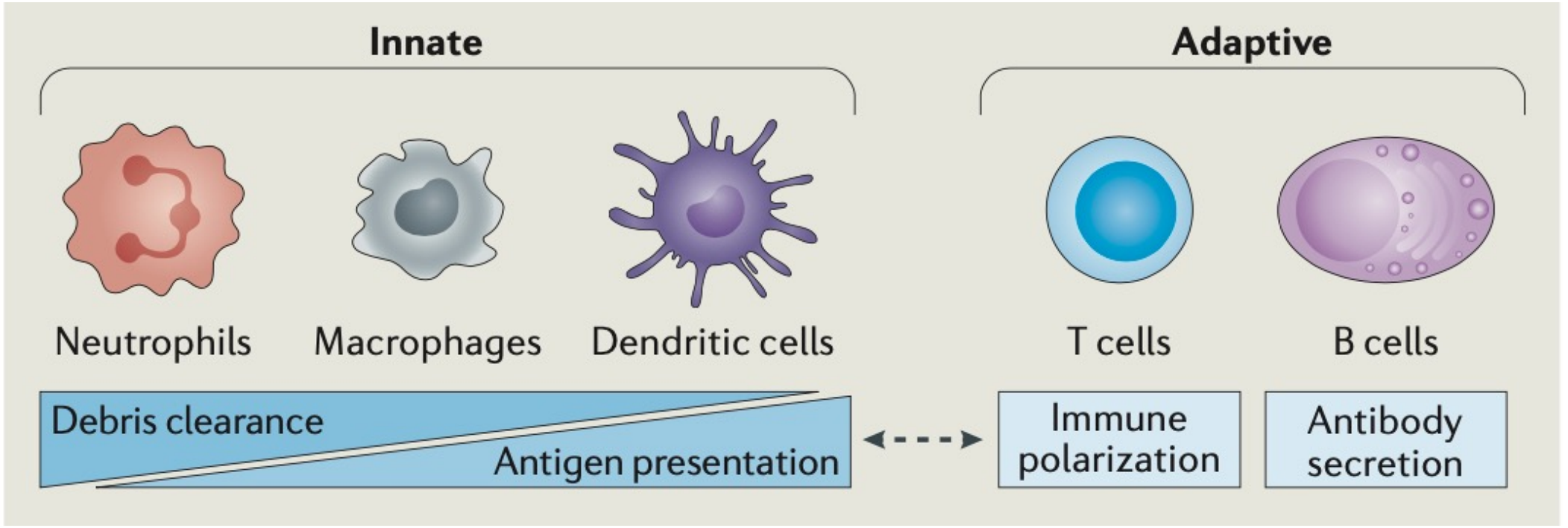
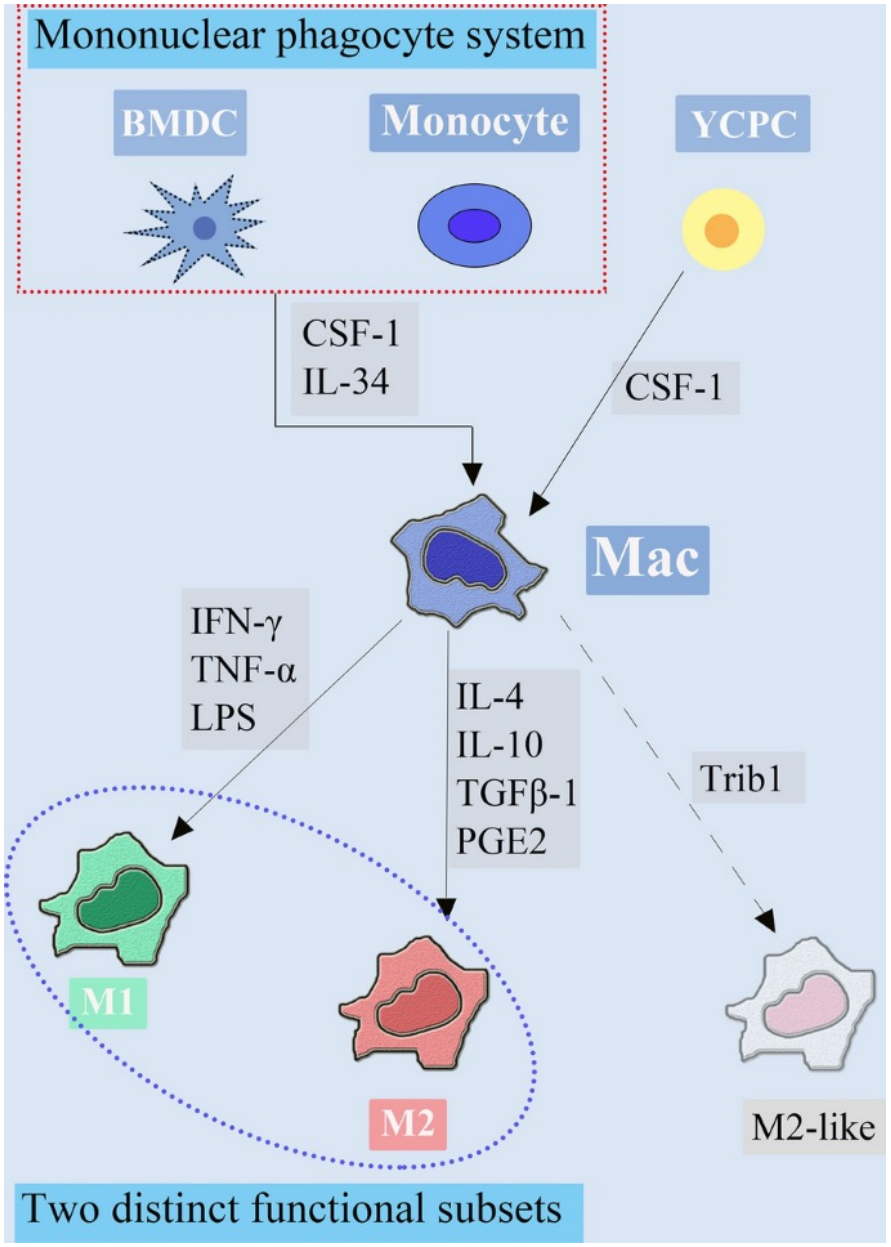
IMMUNOENGINEERING

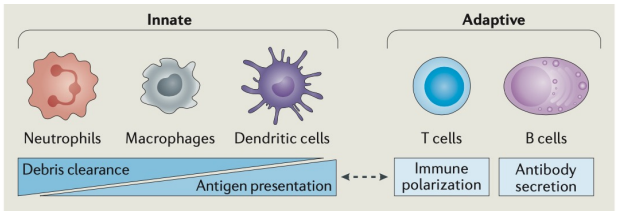
Shift in function of biomaterial scaffolds from passive physical structures to bio-interactive structures

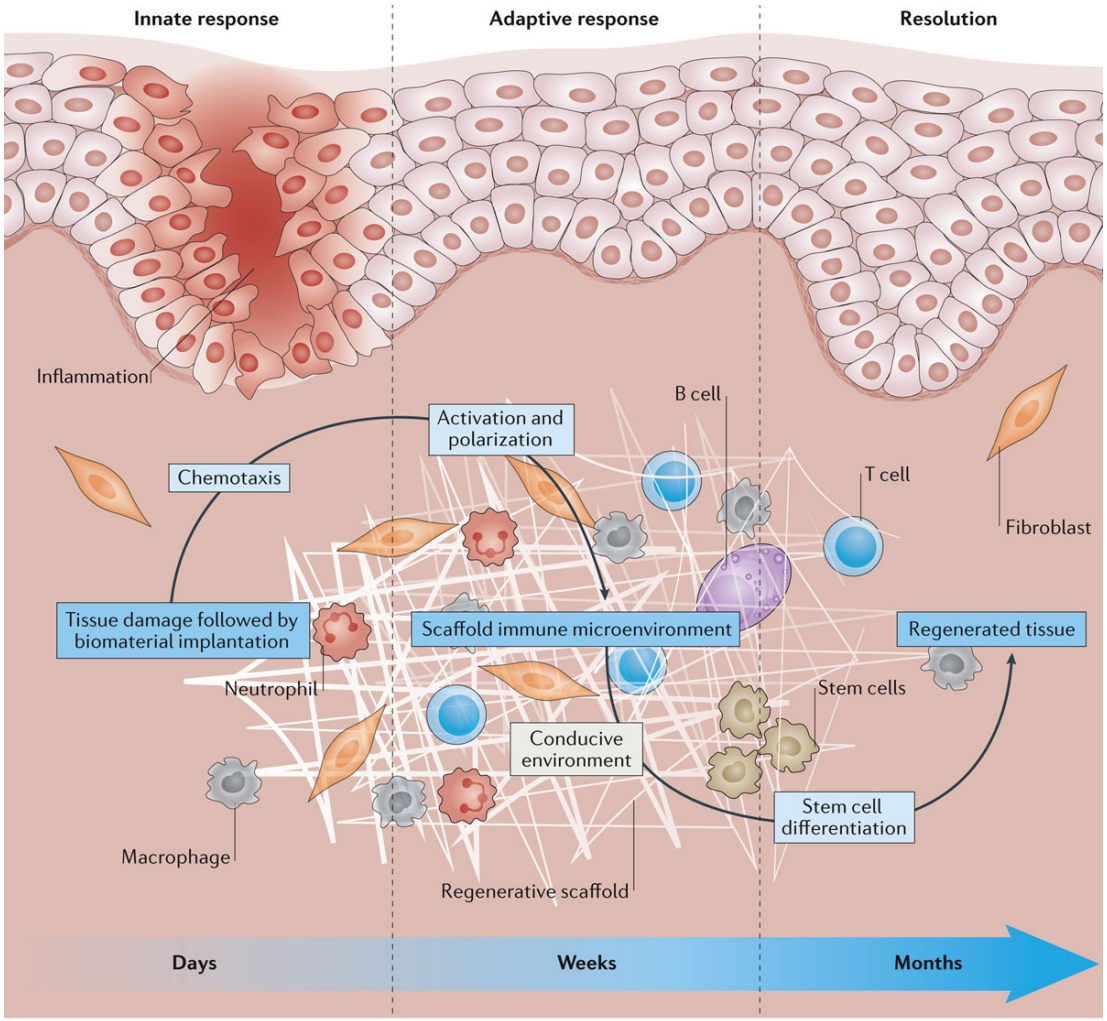



Innate
Adaptive
Neutrophils
Macrophages
Dendritic cells
T cells
B cells
Debris clearance
Antigen presentation
Immune polarization
Antibody secretion

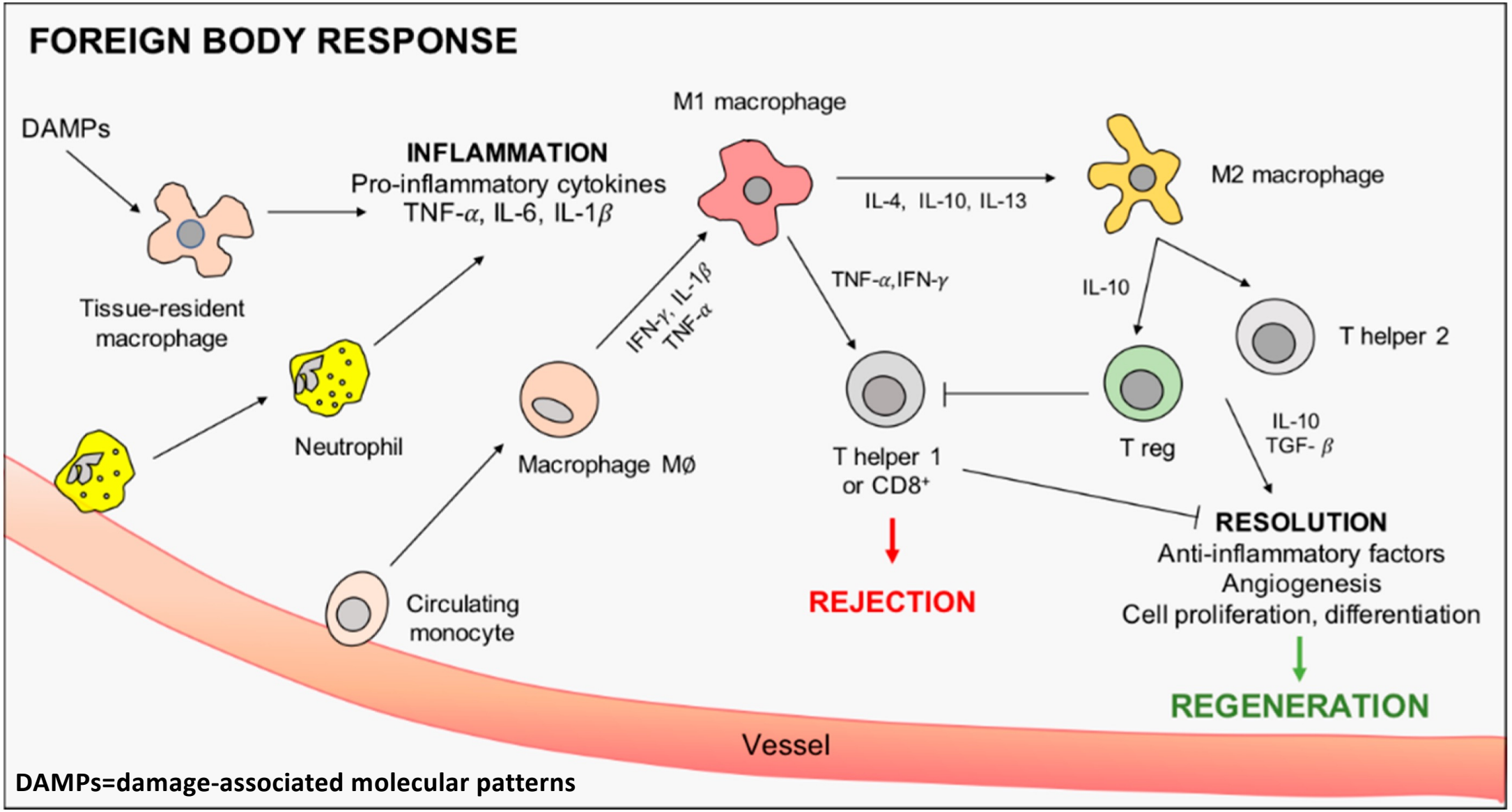

Mononuclear phagocyte system
BMDC
Monocyte
YCPC
CSF-1
IL-34
CSF-1
Mac
IFN-γ
TNF-α
LPS
IL-4
IL-10
TGFβ-1
PGE2
Trib1
M1
M2
M2-like
Two distinct functional subsets

Biomaterials-directed regenerative immunology



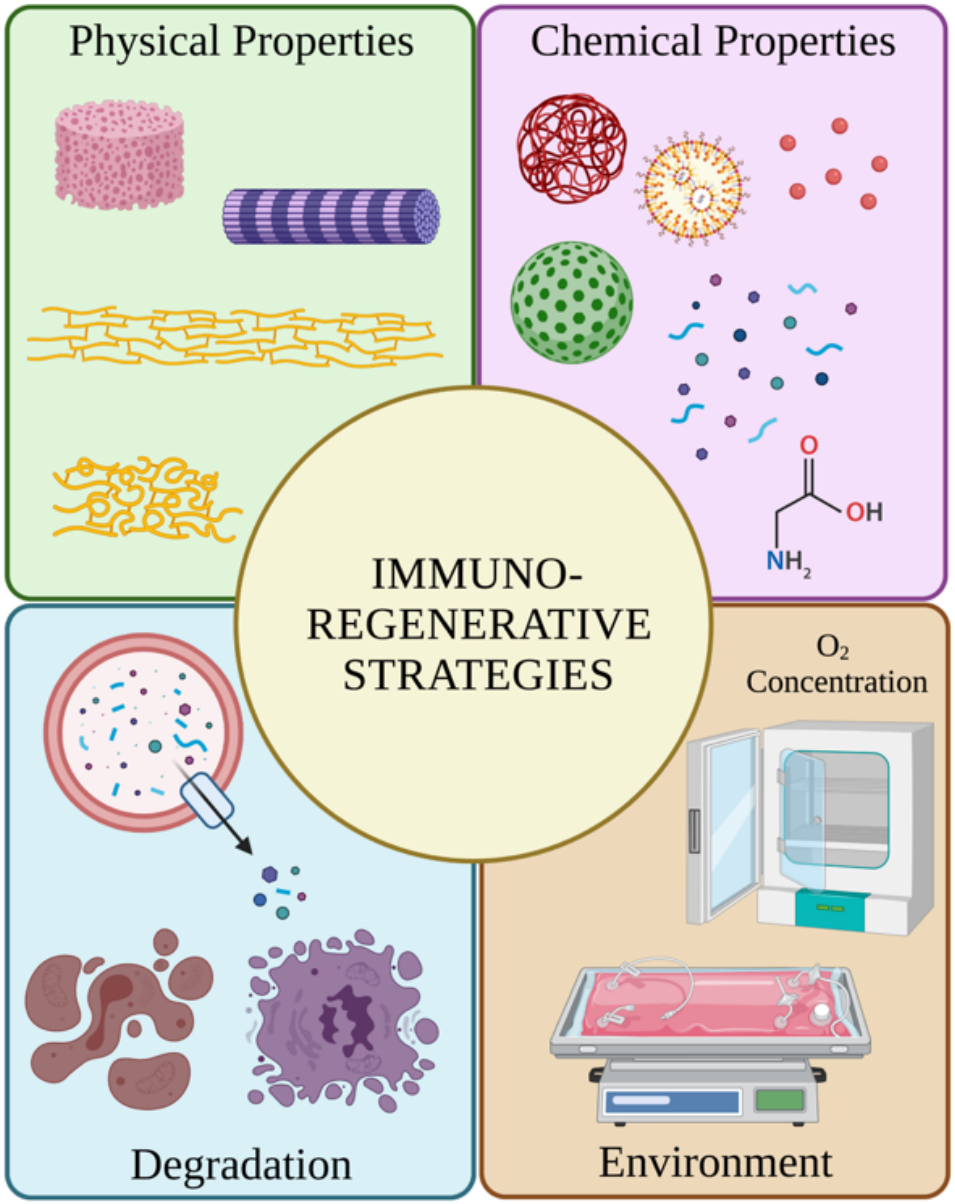


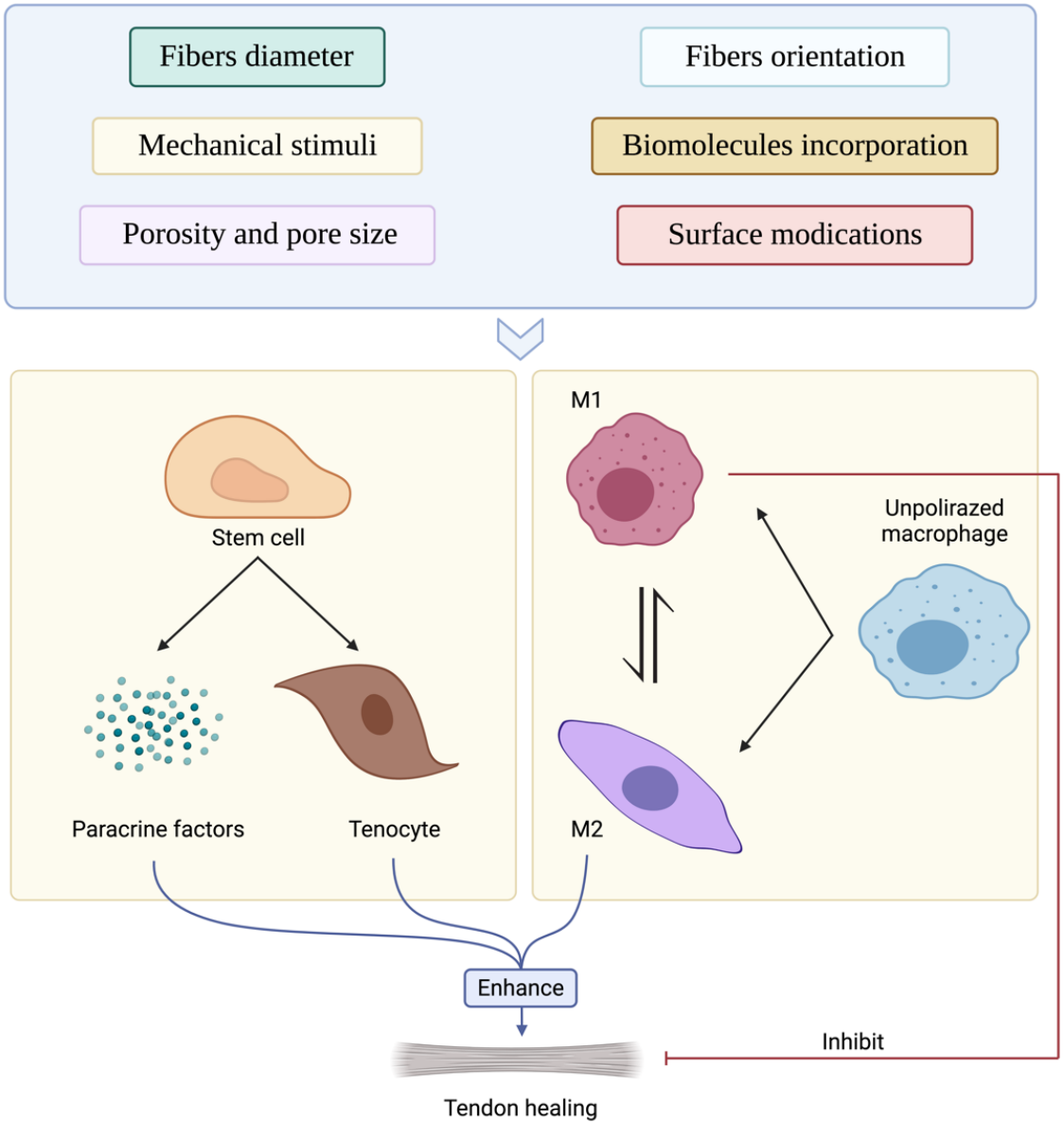
Nature Reviews | Materials



DAMPs=damage-associated molecular patterns


Pore size-mediated
Macrophage
M1-to-M2 transition
Promotion
Porous scaffold
Angiogenesis and vascularization


Physical Properties
Chemical Properties
IMMUNO-
REGENERATIVE
STRATEGIES
O
OH
NH2
O2
Concentration
Degradation
Environment

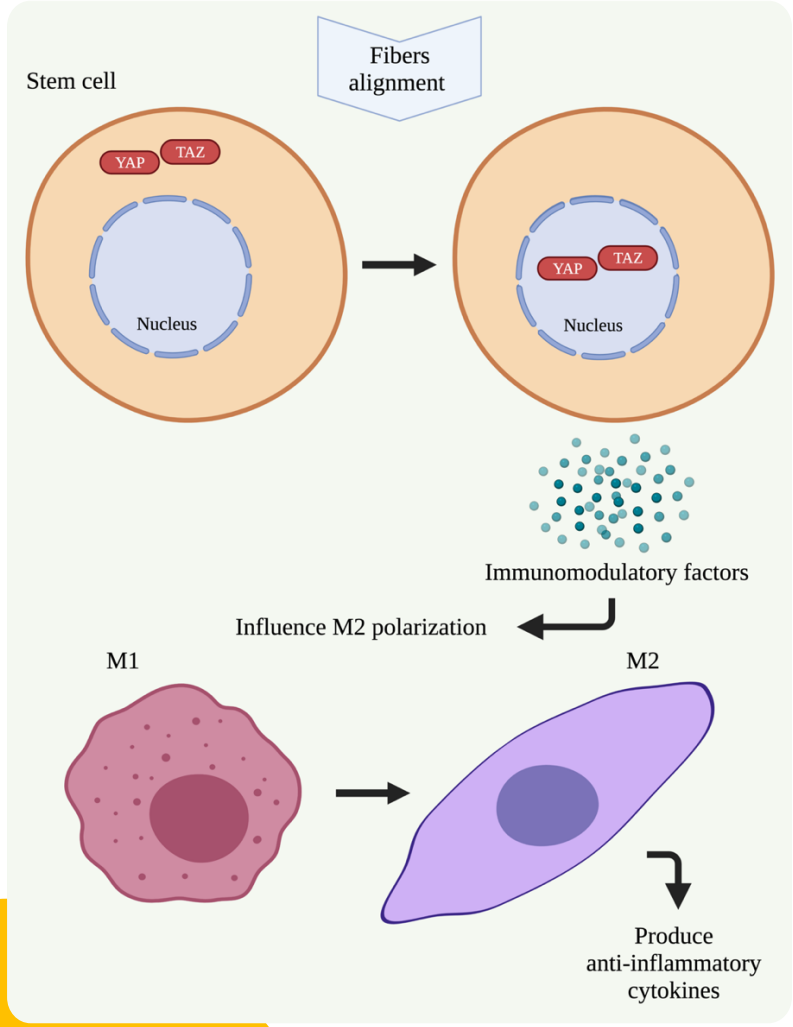

Fibers diameter
Fibers orientation
Mechanical stimuli
Biomolecules incorporation
Porosity and pore size
Surface modications
Stem cell
Paracrine factors
Tenocyte
M1
Unpolirazed
macrophage
M2
Enhance
Inhibit
Tendon healing

Overview of the influence of different electrospun scaffolds proprieties on immune cells

Material	Scaffold proprieties	Immune response
PCL	7 and 12% cyclic uniaxial strains (0.8 Hz)	7% mechanical strain → ↑ MCP-1, IL-6, IL-10, and MMP-9 (M2 markers) 12% strain → M1 proinflammatory phenotype
CE-UPy-PCL	Cyclic strains: 0%, 8% and 14% strain at 0.8 Hz	High strains addressed a pro-inflammatory condition
PCL	Random and aligned fiber orientation	Aligned fibers → least amount of monocyte adhesion with a thinner fibrous capsule and more fibroblasts infiltration compared to randomly oriented fibers
PCL	25-hydroxyvitamin D_3 elution	↓ TNF-a, IL-6 and ↑ IL-4, IL-10
PDO	Different fibers diameter size (0.35, 2.20, and 2.80 µm)	Increasing fiber diameter → ↑ M2 macrophages expression
PDO	Different pore size (0.96, 10.57, and 14.73 µm)	14.73 µm pore size → M2 macrophage polarization, ↑Arginase I and ↓iNOS
PLA	Ibuprofen-loading	↓TNF-α expression and collagen III deposition,
PCL	Anti-inflammatory cytokine IL-4 binding	↑M2 macrophage markers (Arginase I, CD206…)
PLLA	Five different types scaffolds: aligned microfibers, aligned nanofibers, random microfibers, random nanofibers, and on film	Nanofibrous PLLA scaffolds ↓ inflammatory response than films and microfibrous scaffolds PLLA film ↑ number of foreign body giant cells than the micro- and nanofibrous scaffolds
PCL	Random and aligned fiber orientation	Random fibers ↑ pro-inflammatory response compared to aligned fibers
PCL	Static culture (1% constant strain) and dynamic loading (7% cyclic strain at 1Hz)	Dynamic loading → ↑ CCR7 (M1 marker)
PCL	Different Fiber diameters (0.69 and 5.59 µm)	Increased fiber diameter size (5.59 µm) → ↑ M2 macrophages expression
PELA	NSAIDs-loading (e.g., Ibuprofen and Celecoxib)	↓ inflammatory response and ↓TA

Overview of the influence of different electrospun scaffolds properties on the immunomodulatory properties of stem cells

Material	Stem Cell Type	Propriety	Outcomes
PCL	Rat ADMSCs	Randomly oriented, aligned and mesh like electrospun fibers	↑ gene expression of PGE_2, iNOS, and VEGF within ADMSCs engineered within aligned fibers
PLLA	Human ADMSCs	Randomly oriented and highly aligned electrospun fibers	↑ gene expression of COX-2, TGF-β, TSG-6, and M-CSF in ADMSCs cultured within aligned fibers. ↑ protein expression of COX-2 and TSG-6 and ↑ secreted levels of PGE_2 in ADMSCs on aligned fibers
PLGA	Ovine AECs	Electrospun PLGA scaffolds with two different diameter size (1.27 and 2.50 µm)	↑ gene expression of IL-4 and IL-10 and ↓ gene expression of IL-12 and IL-6 within small fiber diameter size (1.27 µm)
PCL/SF	Human BMMSCs	Functionalization of electrospun aligned fibers with MSCs-derived ECM	In vitro: ↑ M2 macrophage polarization & ↓ IL -1β, IL-6, CXCL11, IL-10, IL-1R2 and TGF-β1 In vivo: ↓ FBR, thinner fibrotic capsule formation and ↑ M2 macrophage polarization
PCL	Human ADMSCs	Electrospun PCL-DT-NPs yarns cultivated under static and magnetic stimulation conditions	↑ gene expression of MMP-1, MMP-2, MMP-3, TIMPs, IL-10, and IL-4 with ↓ gene expression of IL-6 and COX-2 under magnetic stimulation condition



Mechanotransduction cues effects on YAP/TAZ cellular distribution and their influence on stem and immune cell immunomodulation