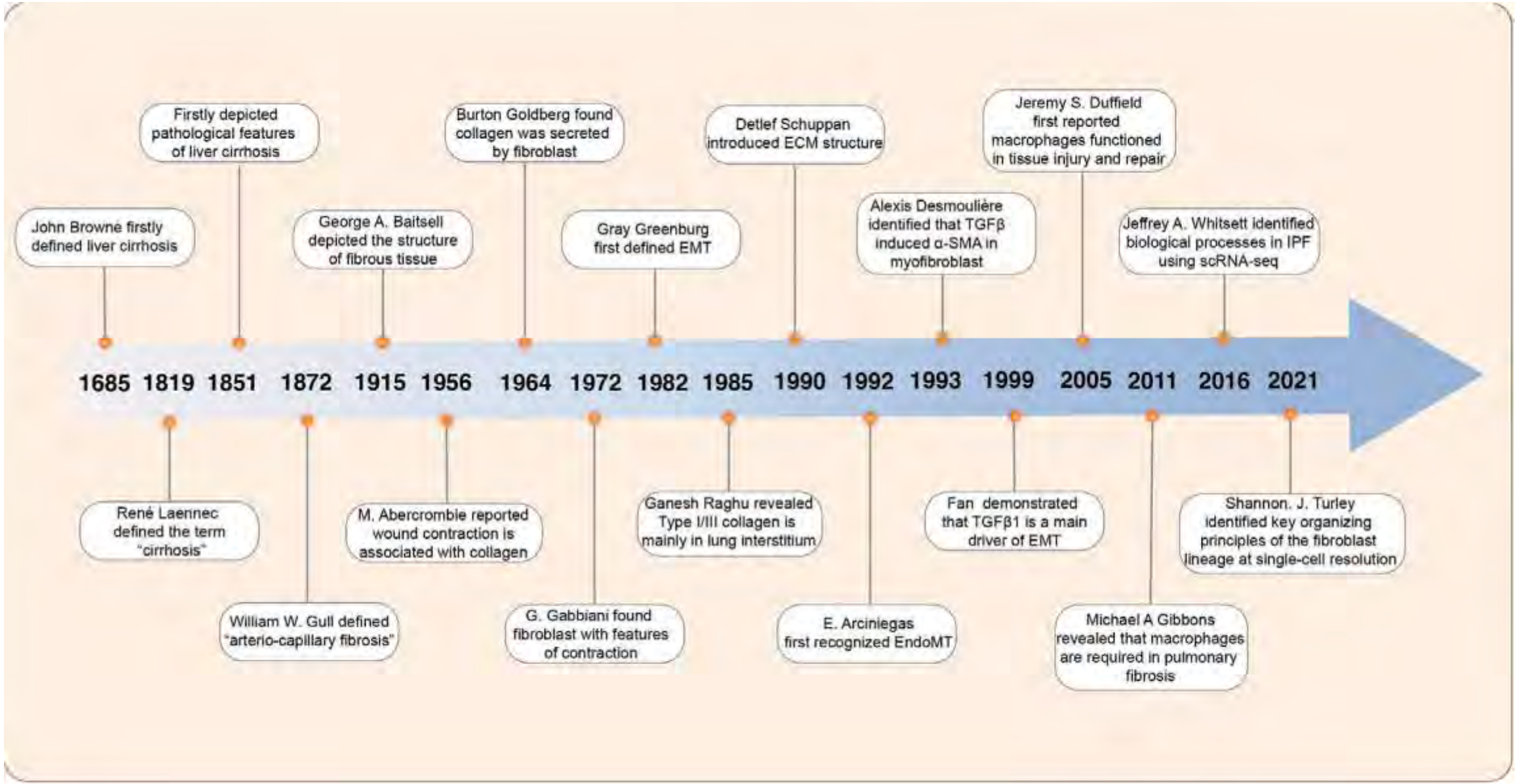
A fibrosis patofiziológiája

Szűcs Gabriella

Debreceni Egyetem

ÁOK Reumatológiai Tanszék
KK Reumatológiai és Immunológiai Klinika

IMMUNOLÓGAI ALAPFOLYAMATOK MOLEKULÁRIS MECHANIZUSAI ÉS EGYÉB ÉRDEKESSÉGEK AZ IMMUNOLÓGIA TERÜLETÉN
2026. április 29-30.
SE, Reumatológiai és Klinikai Immunológiai Klinika

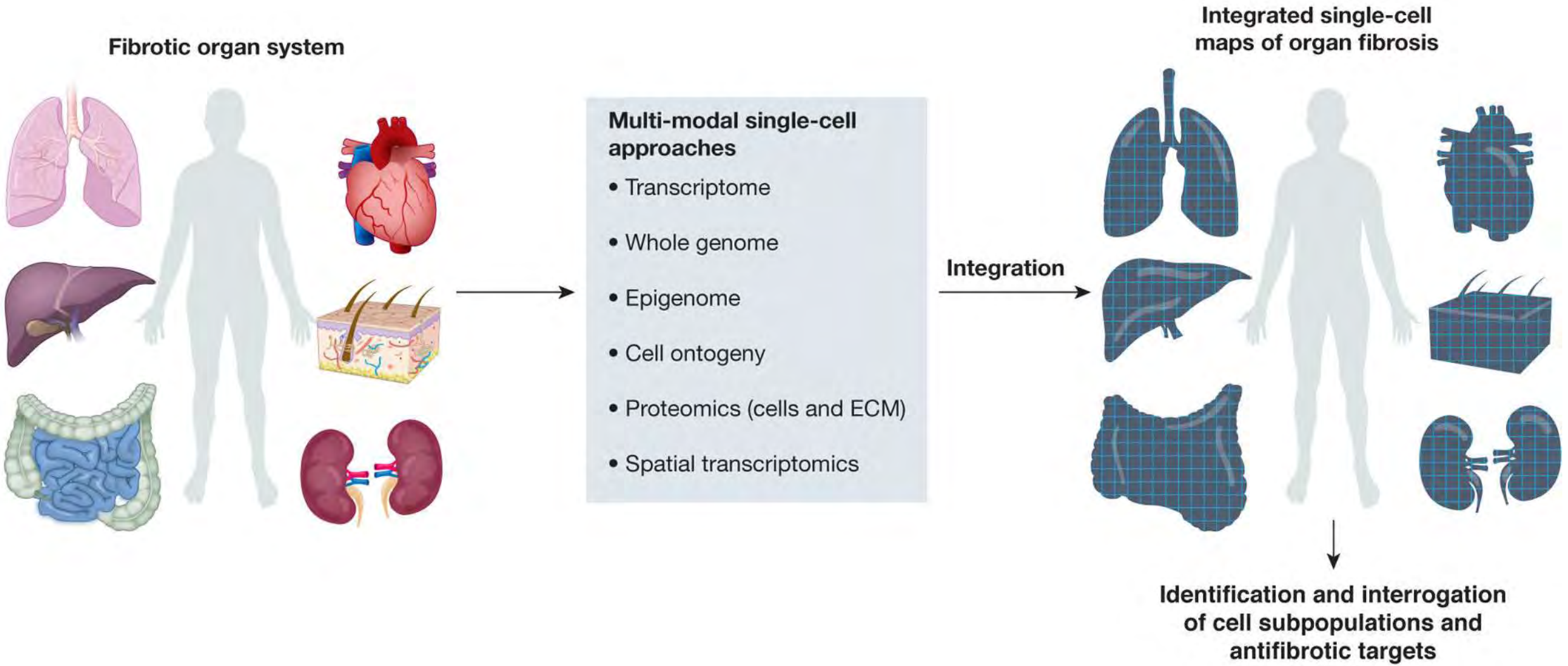


Timeline of the milestones in the investigation of fibrosis over the past 300 years

Adv. Sci. **2025**, 12, 2410416

FIBROSIS: FROM MECHANISMS TO MEDICINES

Henderson NC et al. Nature. 2020 November ; 587(7835): 555–566.



Az ipari világ halálozásának 45%-a

FIBROSIS: FROM MECHANISMS TO MEDICINES

Henderson NC et al. Nature. 2020 November ; 587(7835): 555–566.

Fibrosis, secondary to age-associated chronic low-grade inflammation (inflammaging)

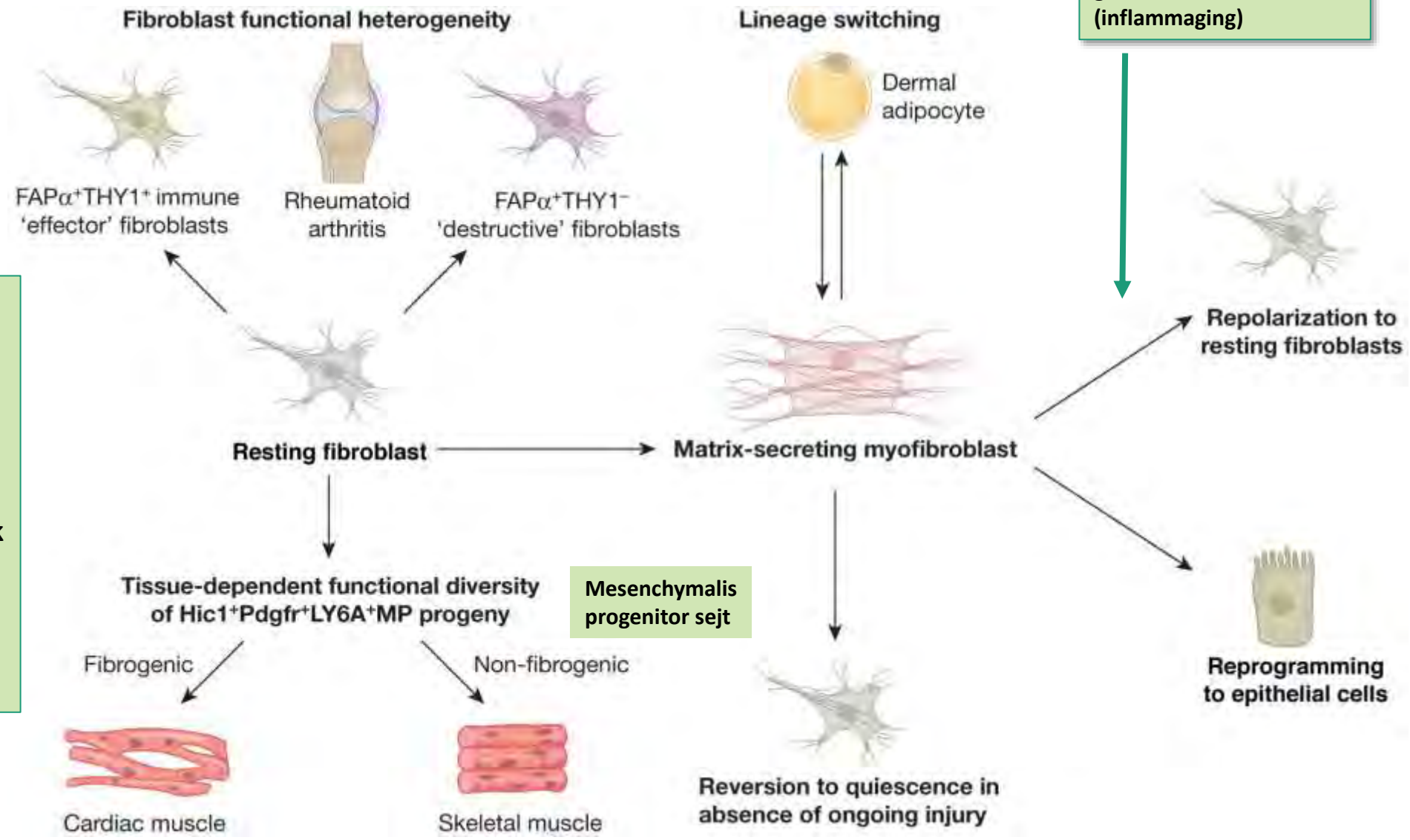
Fibrotikus szövet kialakulása – sérülés utáni normál repair

extracellular matrix (collagen, fibronectin stb) accumulatio

Pl. bőrben a fascia fibroblastok + a környező egységek (erek, macrophagok, perifériás erek)

↓

Gyógyulás



Funkcionális fibroblast heterogenitás és plaszticitás

Senescence and tissue fibrosis: opportunities for therapeutic targeting

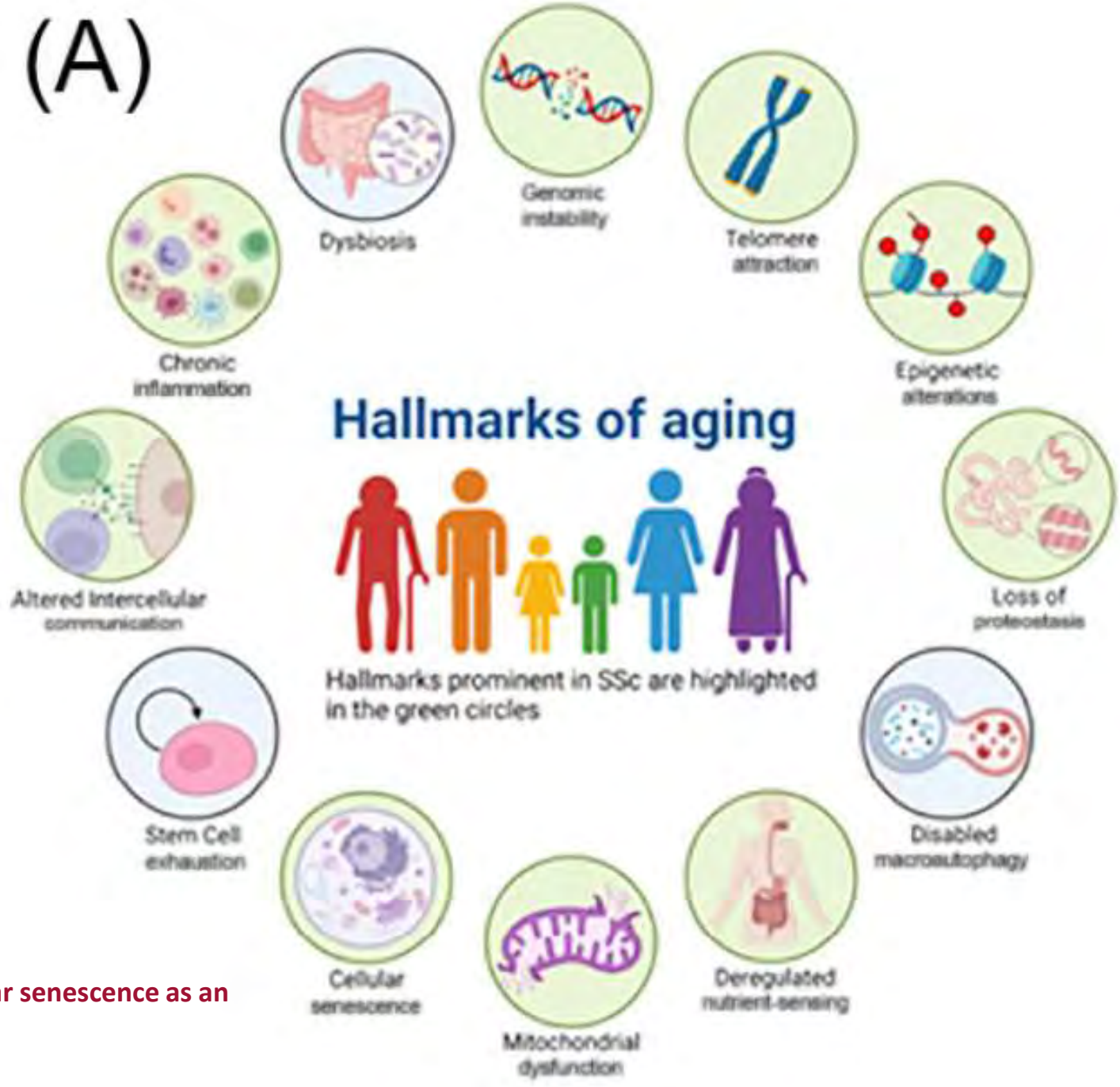


Figure 1. The 12 hallmarks of aging and targeting cellular senescence as an emerging novel therapeutic strategy for fibrosis

Trends in Molecular Medicine, December 2024, Vol. 30, No. 12

Senescence and tissue fibrosis: opportunities for therapeutic targeting

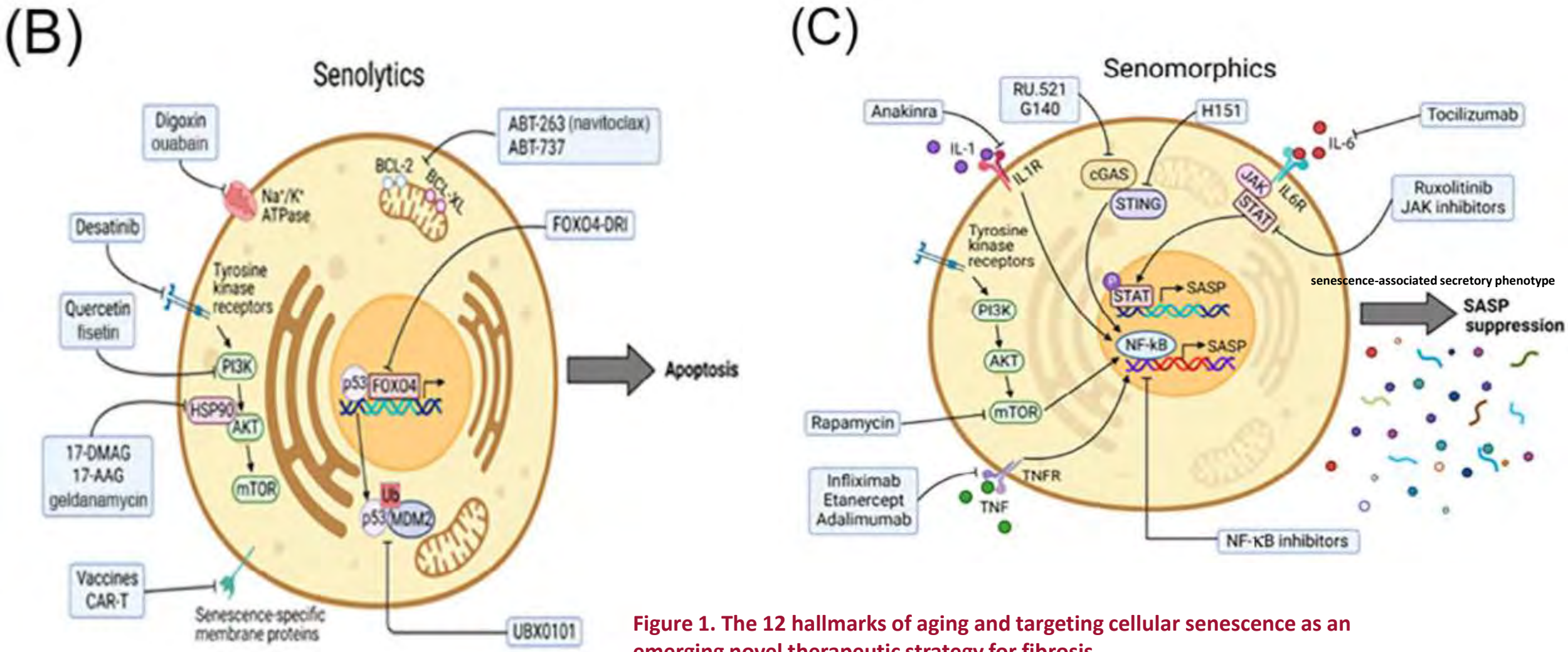
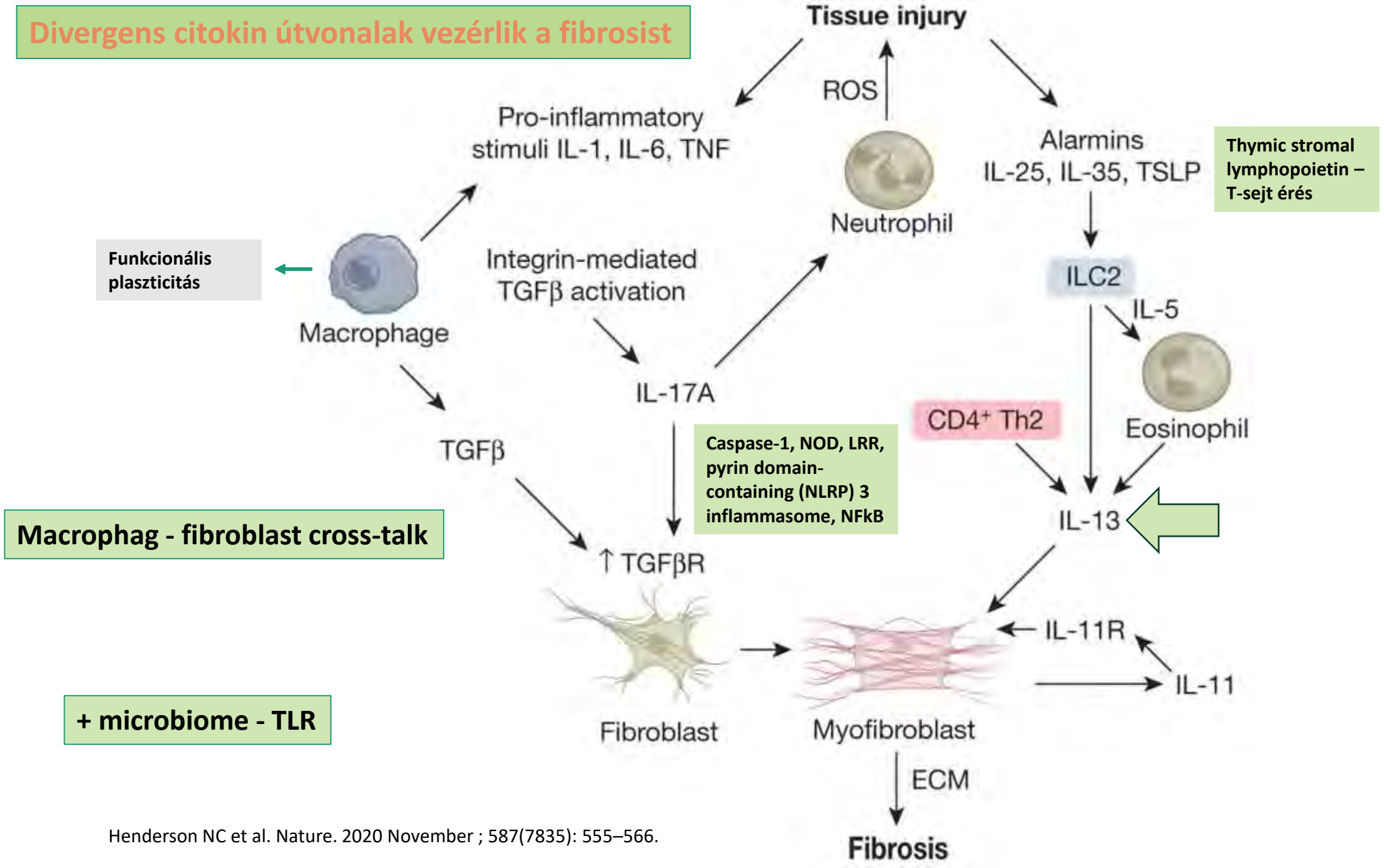


Figure 1. The 12 hallmarks of aging and targeting cellular senescence as an emerging novel therapeutic strategy for fibrosis

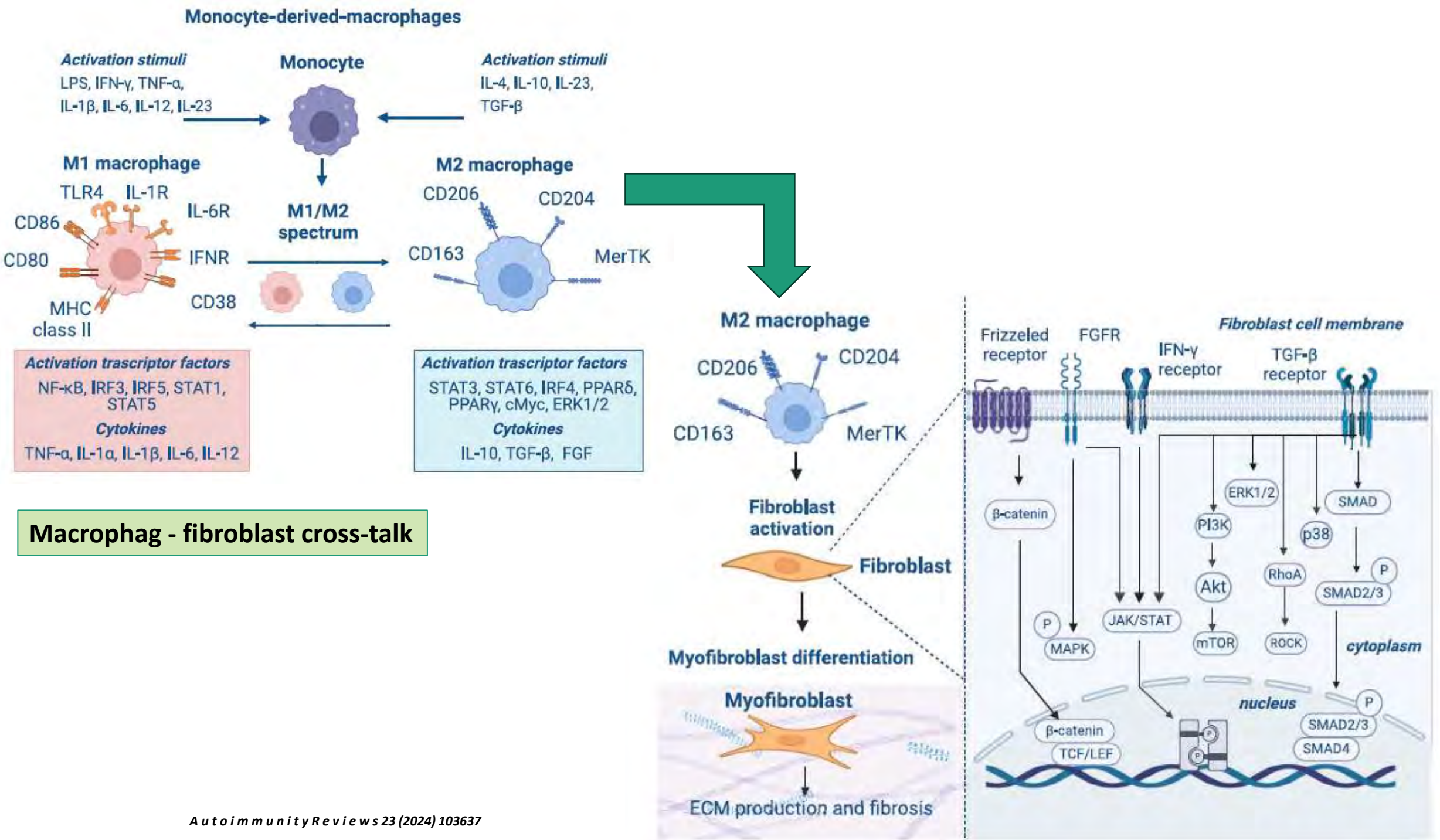
Divergens citokin útvonalak vezérlik a fibrosist



Macrophag - fibroblast cross-talk

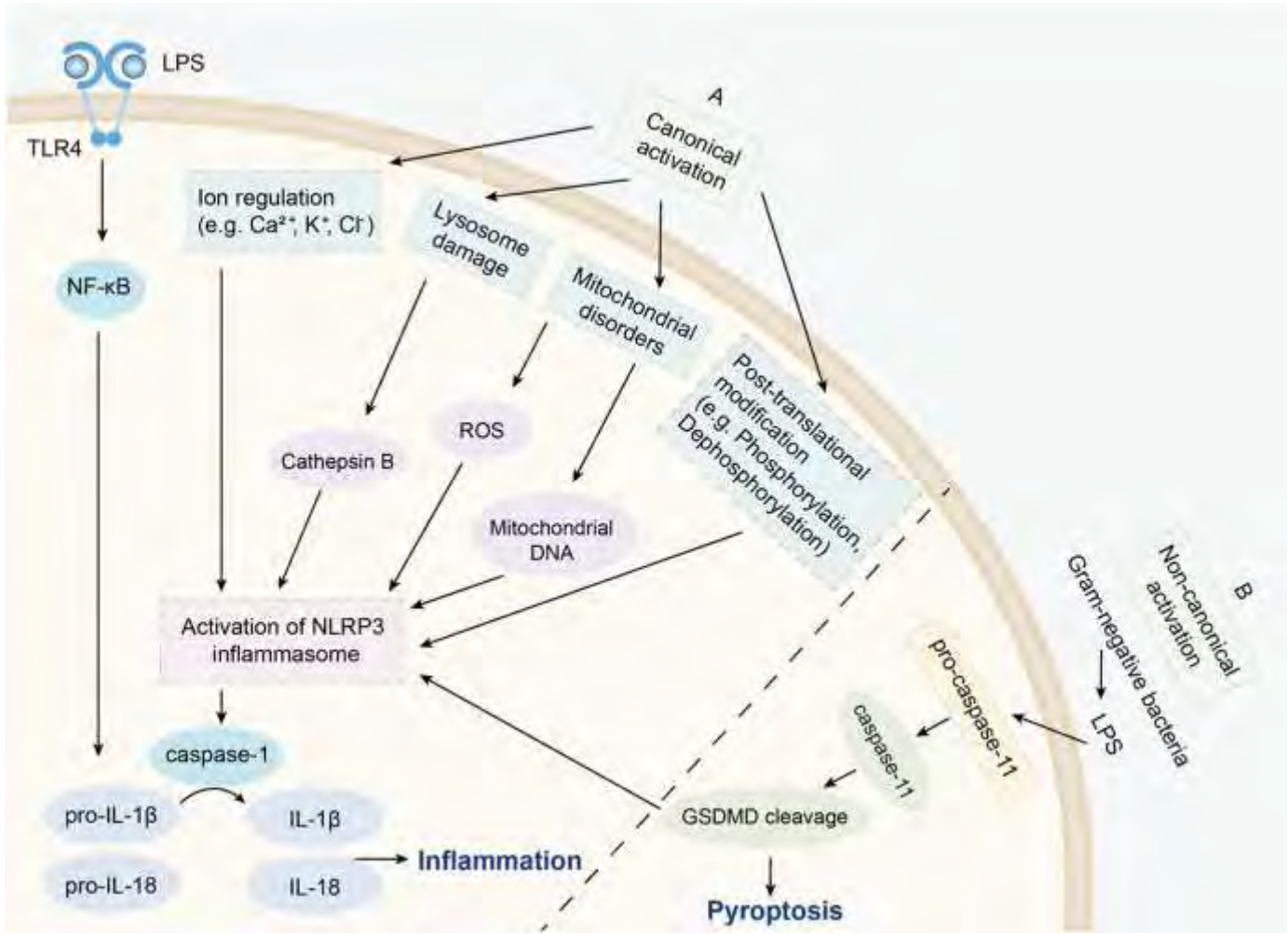
+ microbiome - TLR

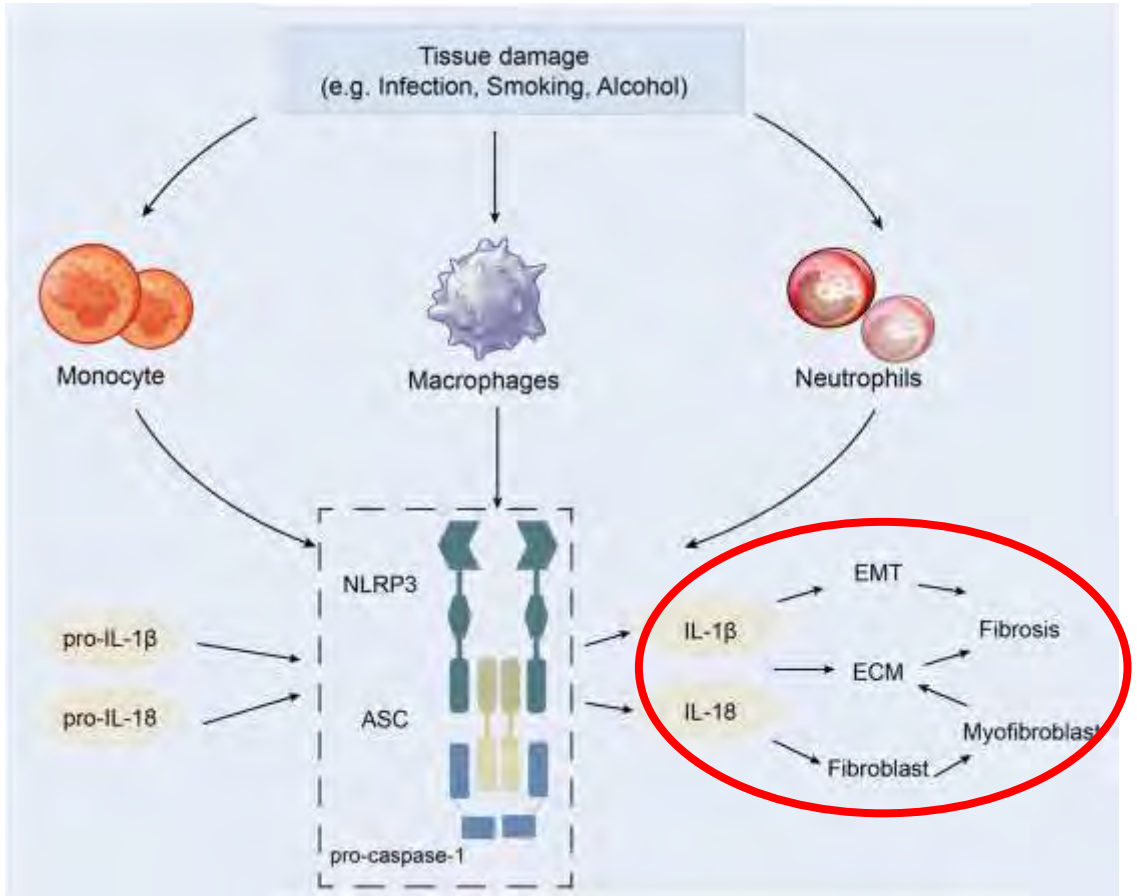
Henderson NC et al. Nature. 2020 November ; 587(7835): 555–566.



Macrophag - fibroblast cross-talk

The NLRP3 inflammasome in fibrosis and aging: The known unknowns





ASC: apoptosis-associated speck-like protein

Fig. 1. Regulatory mechanism of the NLRP3 inflammasome.

FIBROSIS: FROM MECHANISMS TO MEDICINES

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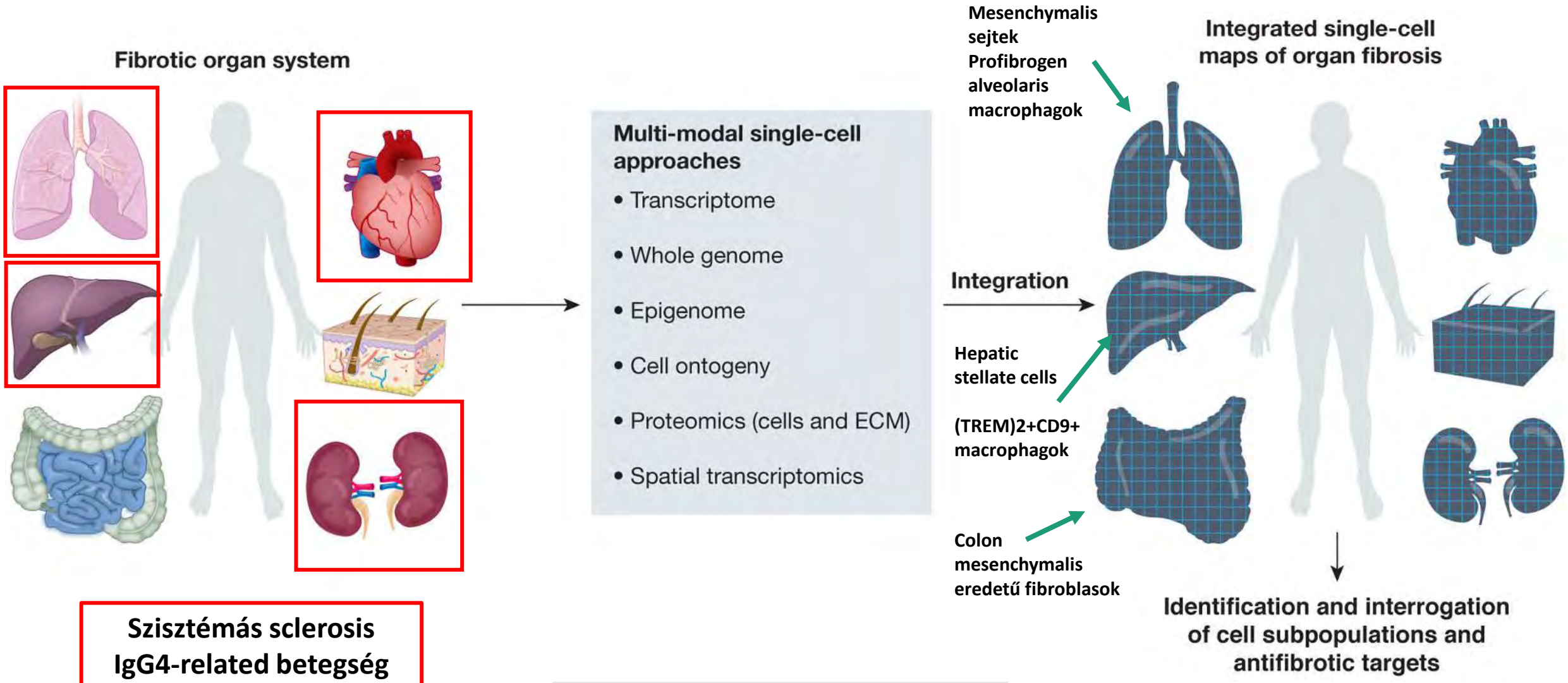


Szisztémás sclerosis
IgG4-related betegség

Az ipari világ halálozásának 45%-a

Inflammation and immunity in IPF pathogenesis and treatment

Heukels P et al. Respiratory Medicine 147 (2019) 79–91.

Incidencia: 3-9/100 000
>65 év: 94/100 000,
prevalencia 494/100 000

Repetitív alveolaris epithelialis sérülés

+

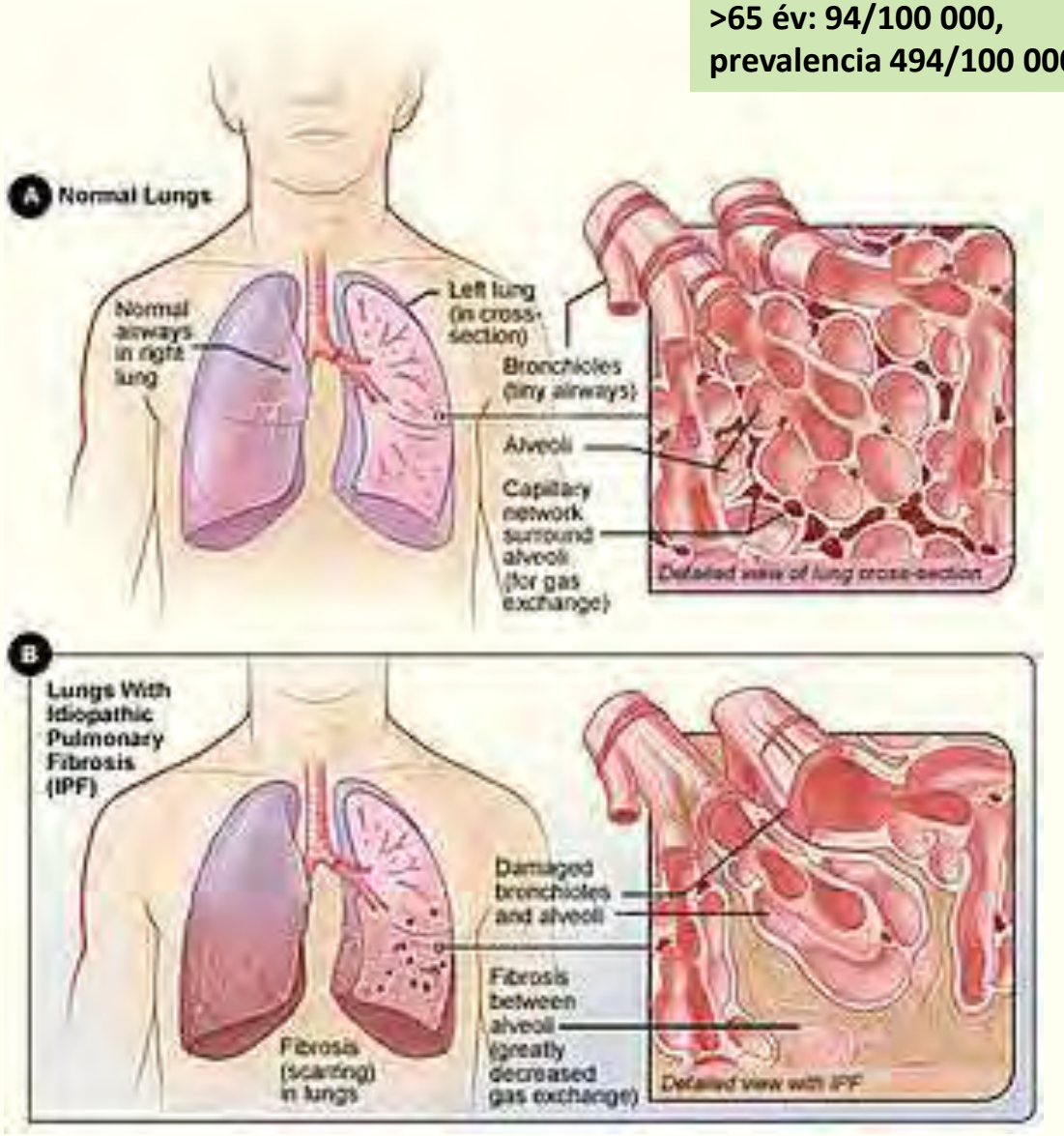
Repair mechanizmusok diszregulációja

+

fibroblast diszfunkció

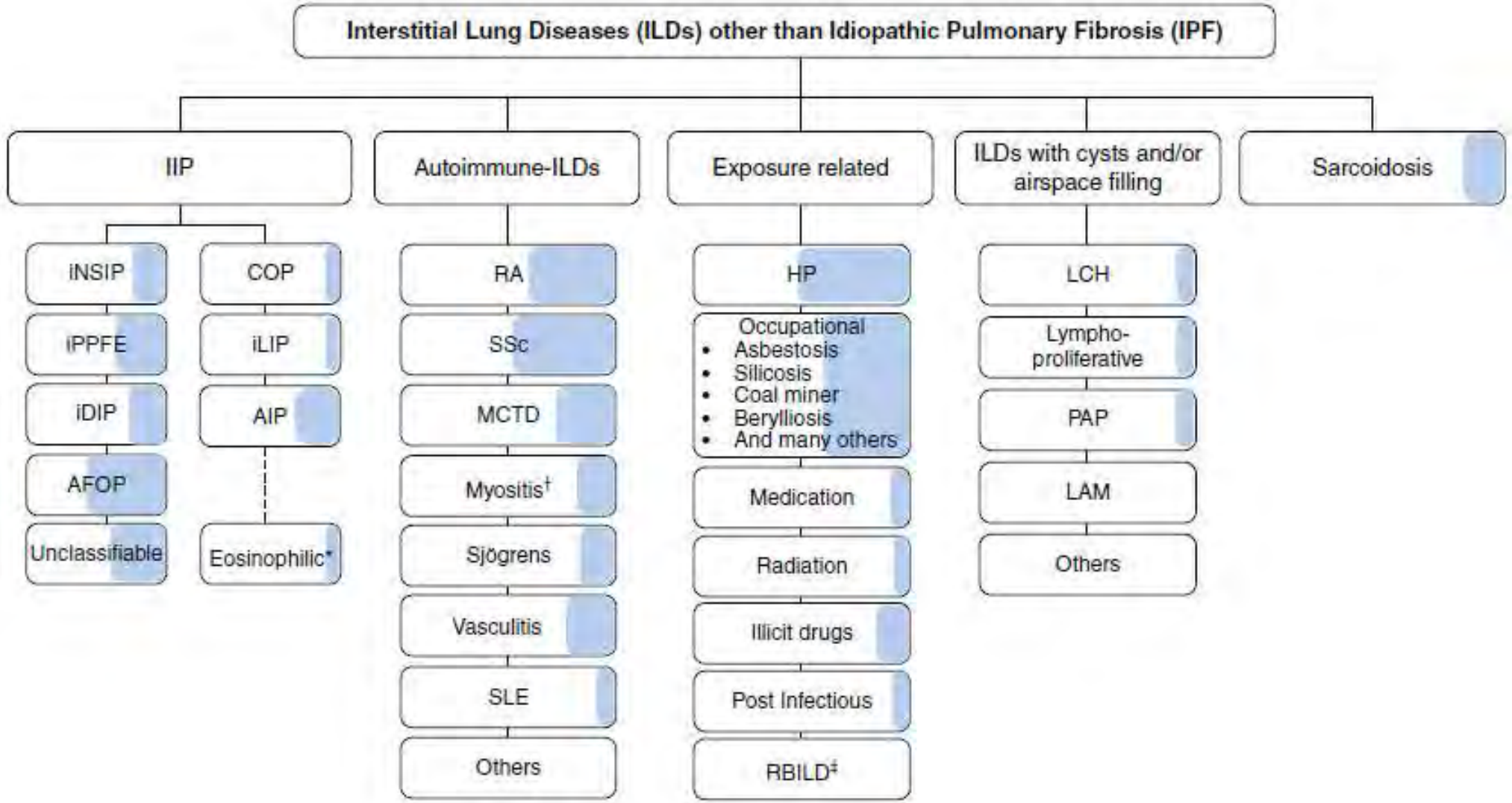
↓

fibrosis

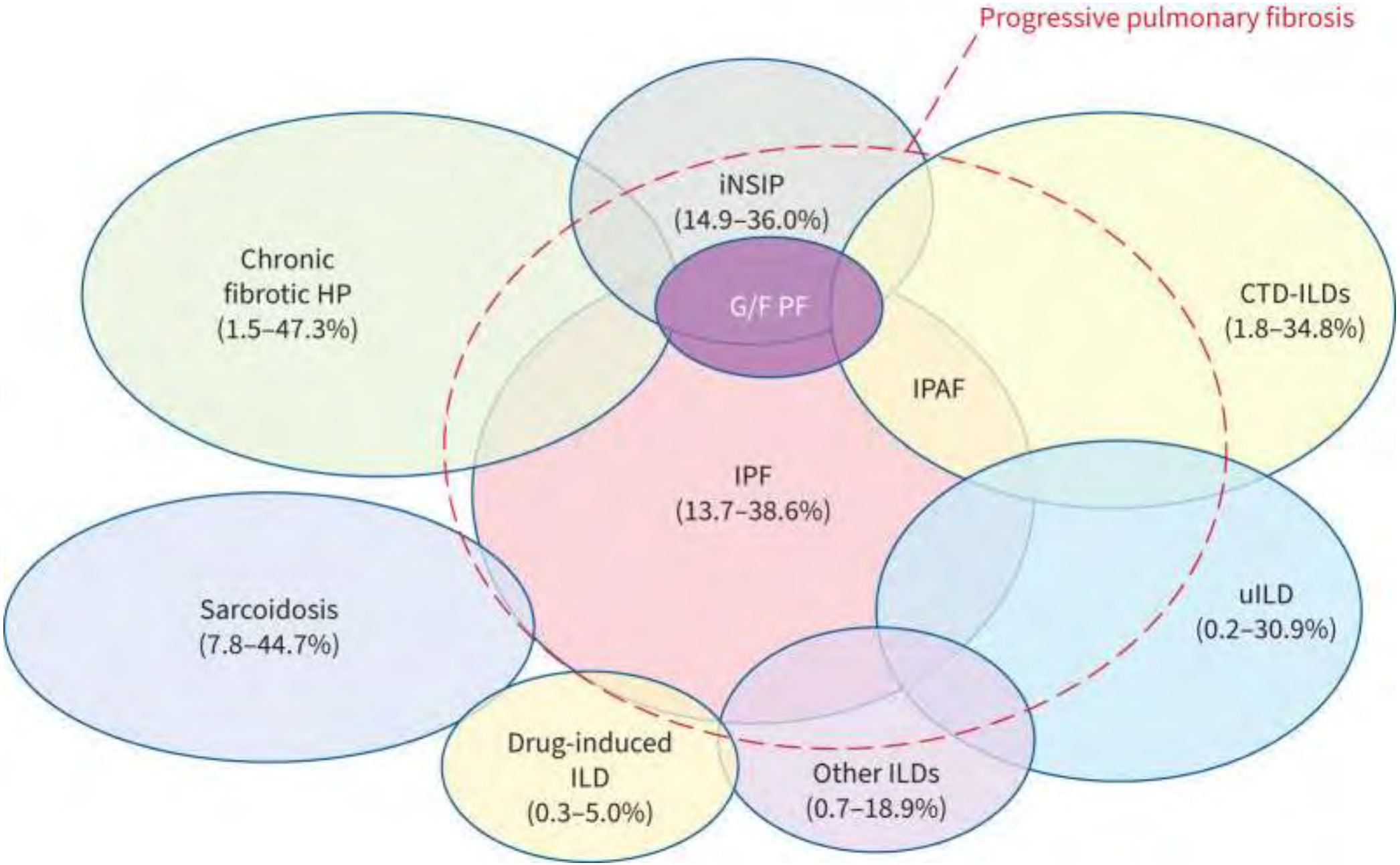


Genetikai vizsgálatok vizsgálatok:
***FAM13A* (4q22), *DSP* (6p24), *OBFC1* (10q24)**
WNT, TGF, NOTCH, sonic hedgehog (SHH)
***TOLLIP (*Toll-interacting protein), the inhibitory protein of the Toll-like receptor (TLR)**
DRB1*15:01* and *DQB1*06:02
MUC5B gén

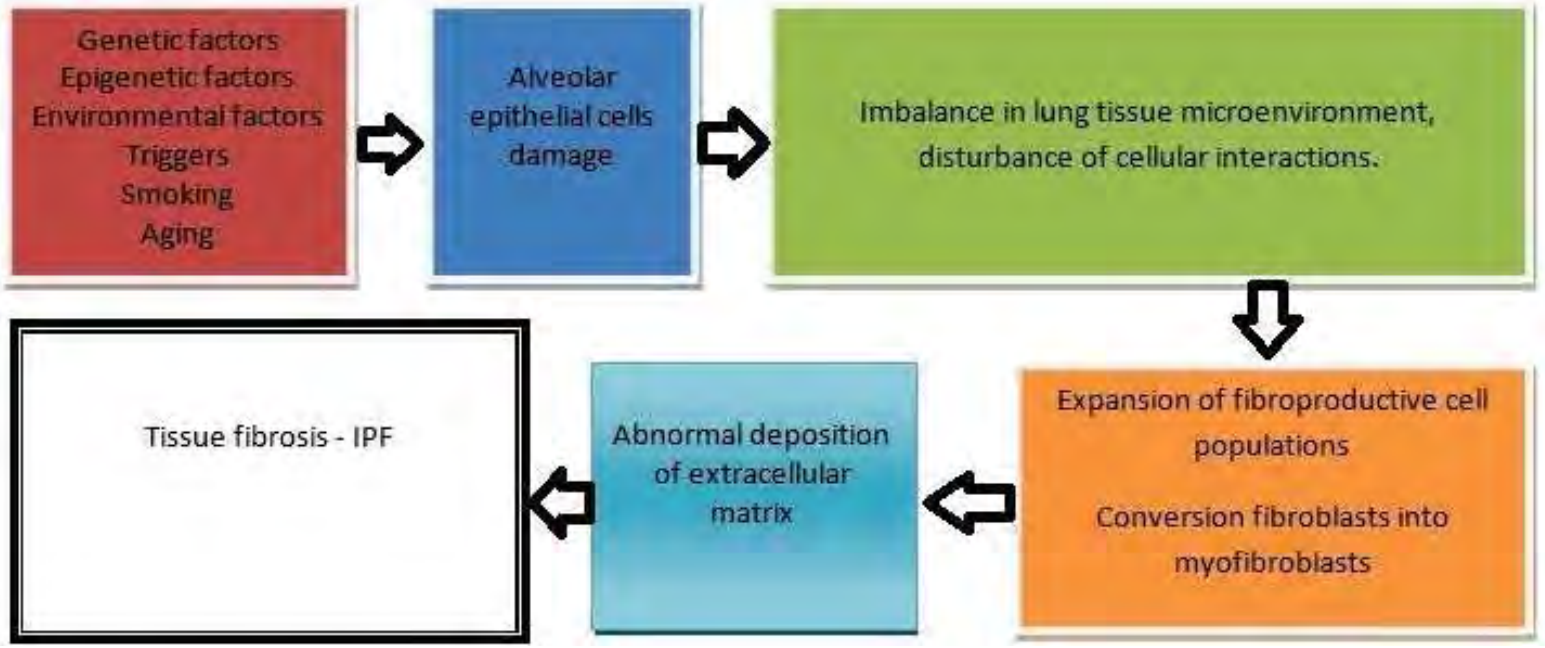
Az ILD klasszifikációja

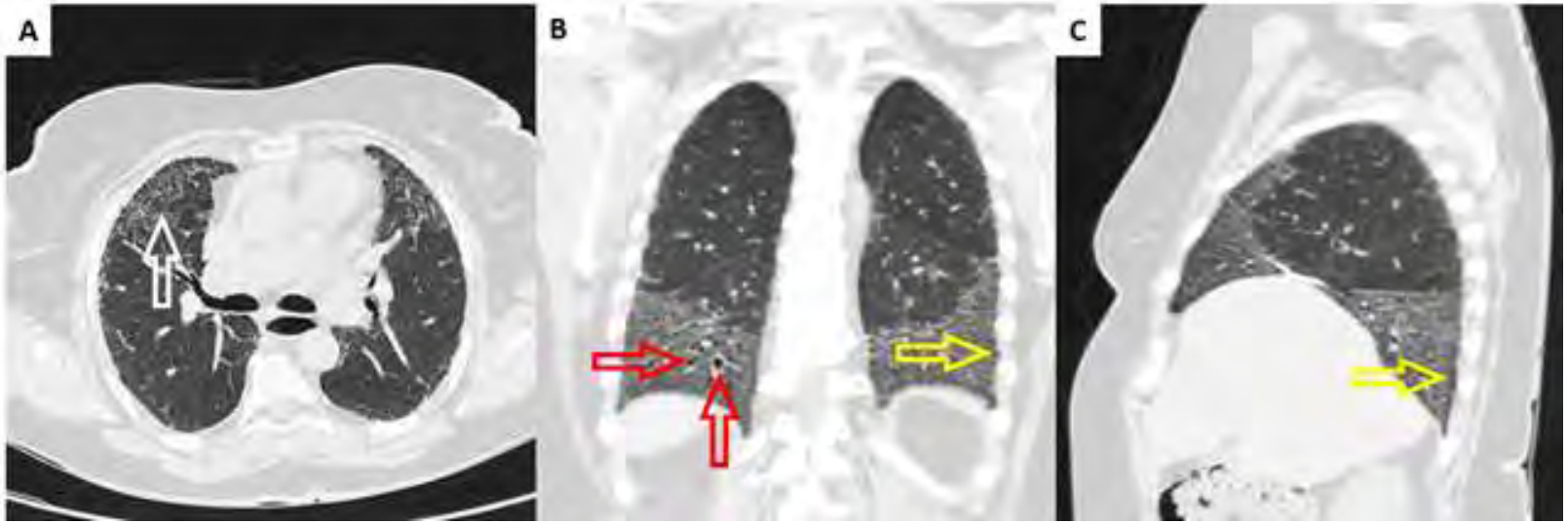


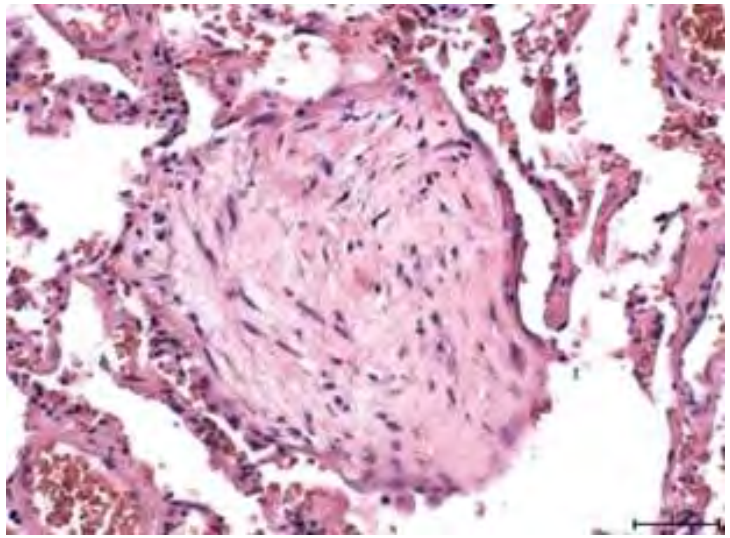
Am J Respir Crit Care Med Vol 205, Iss 9, pp e18–e47, May 1, 2022



Eur Respir J 2023; 61: 2103187


Genetic factors
Epigenetic factors
Environmental factors
Triggers
Smoking
Aging
Alveolar epithelial cells damage
Imbalance in lung tissue microenvironment, disturbance of cellular interactions.
Expansion of fibroproductive cell populations
Conversion fibroblasts into myofibroblasts
Abnormal deposition of extracellular matrix
Tissue fibrosis - IPF


A
B
C



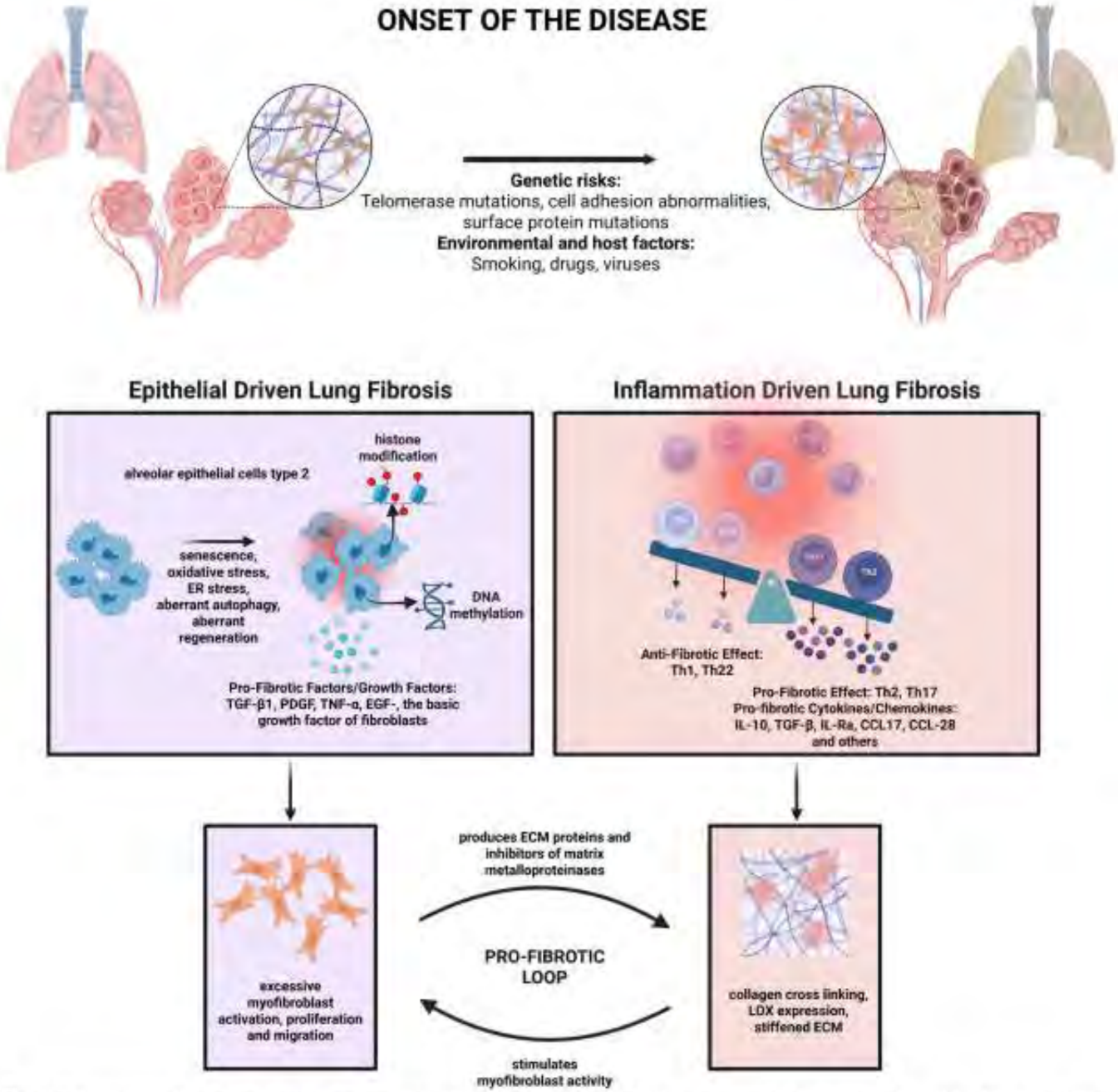
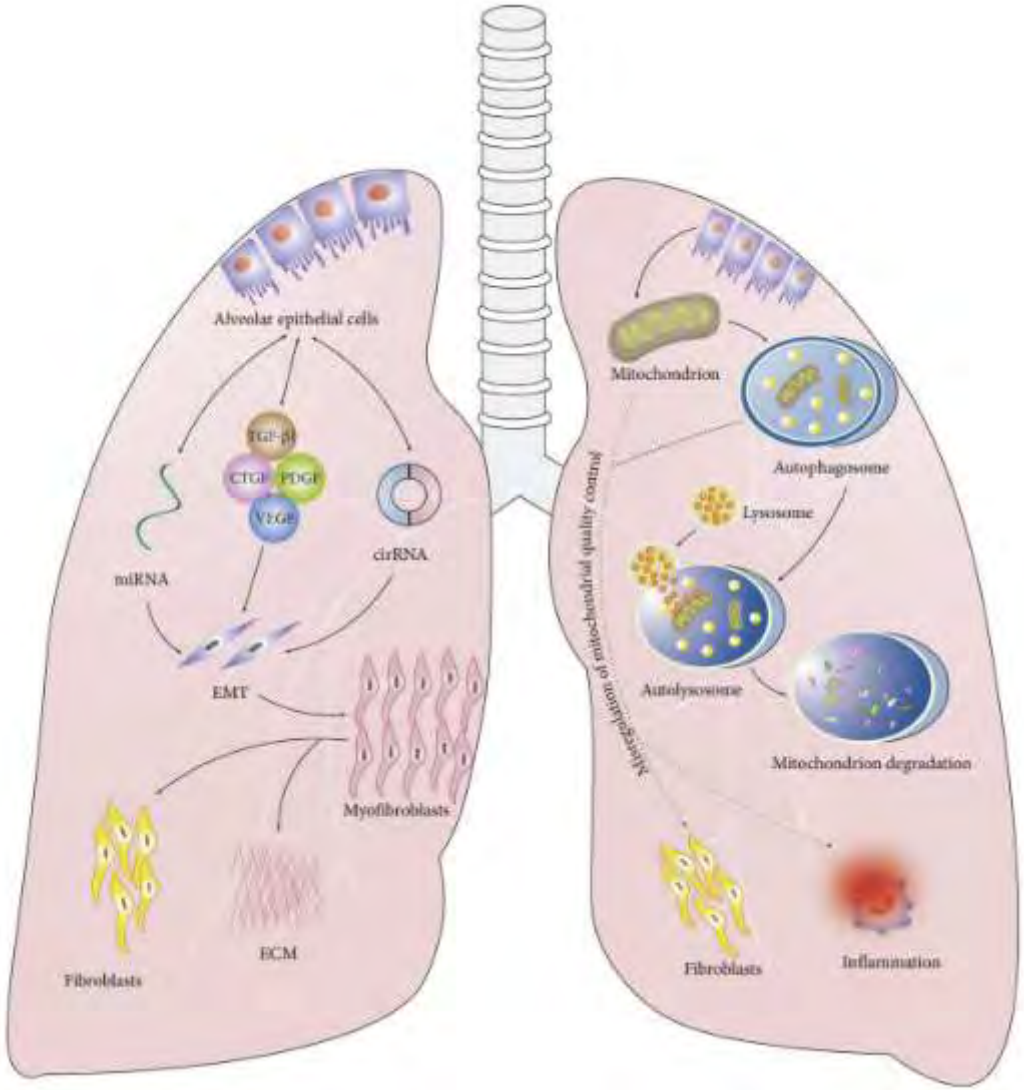


Fig. 1 Pathogenesis of lung fibrosis [27]. The scheme shows epithelia-driven lung fibrosis pathway and inflammation-driven lung fibrosis pathway



Fibrocyta – myofibroblast átalakulás

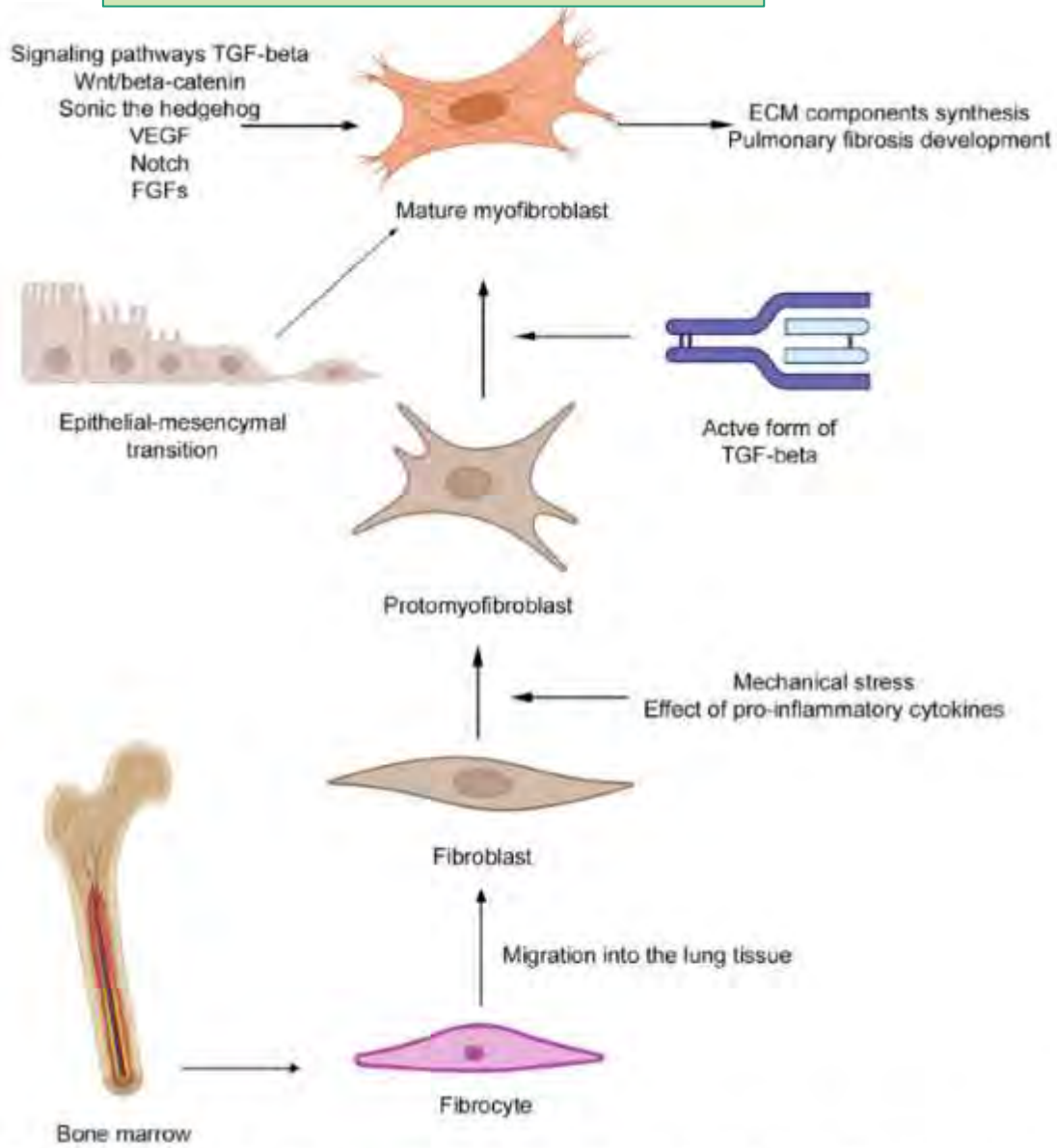


Figure 2. Evolution of fibrocyte to myofibroblast—main effector cell in pulmonary fibrosis development.

Szignál-transzdukció folyamata

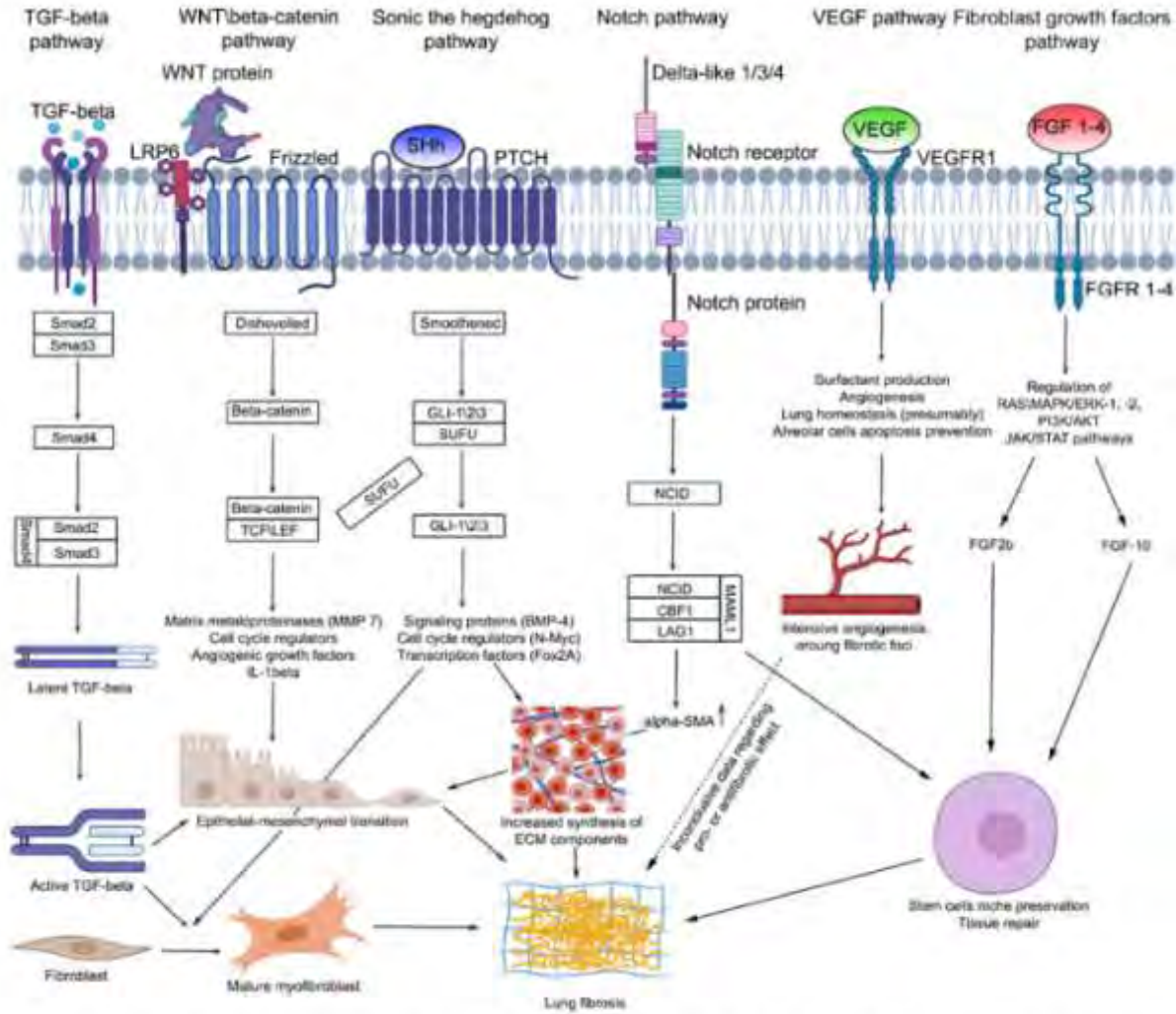


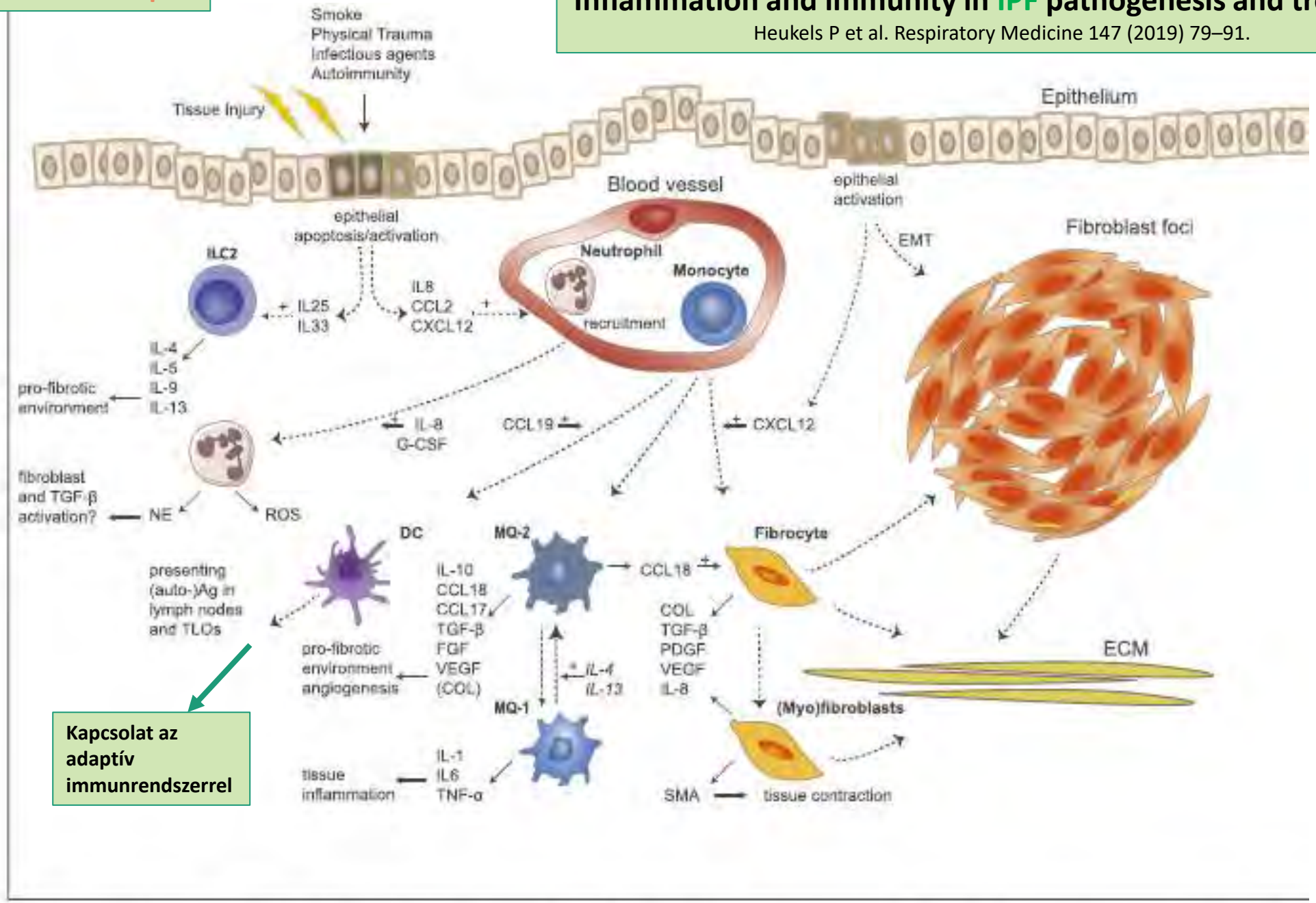
Figure 3. Overview of particular signaling pathways regulating pulmonary fibrosis development.

Int. J. Mol. Sci. 2022, 23, 14959. https://doi.org/10.3390/ijms232314959

Innate immunrendszer szerepe

Inflammation and immunity in IPF pathogenesis and treatment

Heukels P et al. Respiratory Medicine 147 (2019) 79–91.



Kapcsolat az adaptív immunrendszerrel

Fig. 1. Schematic overview of the role of the innate immune system in IPF pathogenesis. Abbreviations: EMT = epithelial–mesenchymal transition, IL

Adaptív immunrendszer szerepe

Inflammation and immunity in IPF pathogenesis and treatment

Heukels P et al. Respiratory Medicine 147 (2019) 79–91.

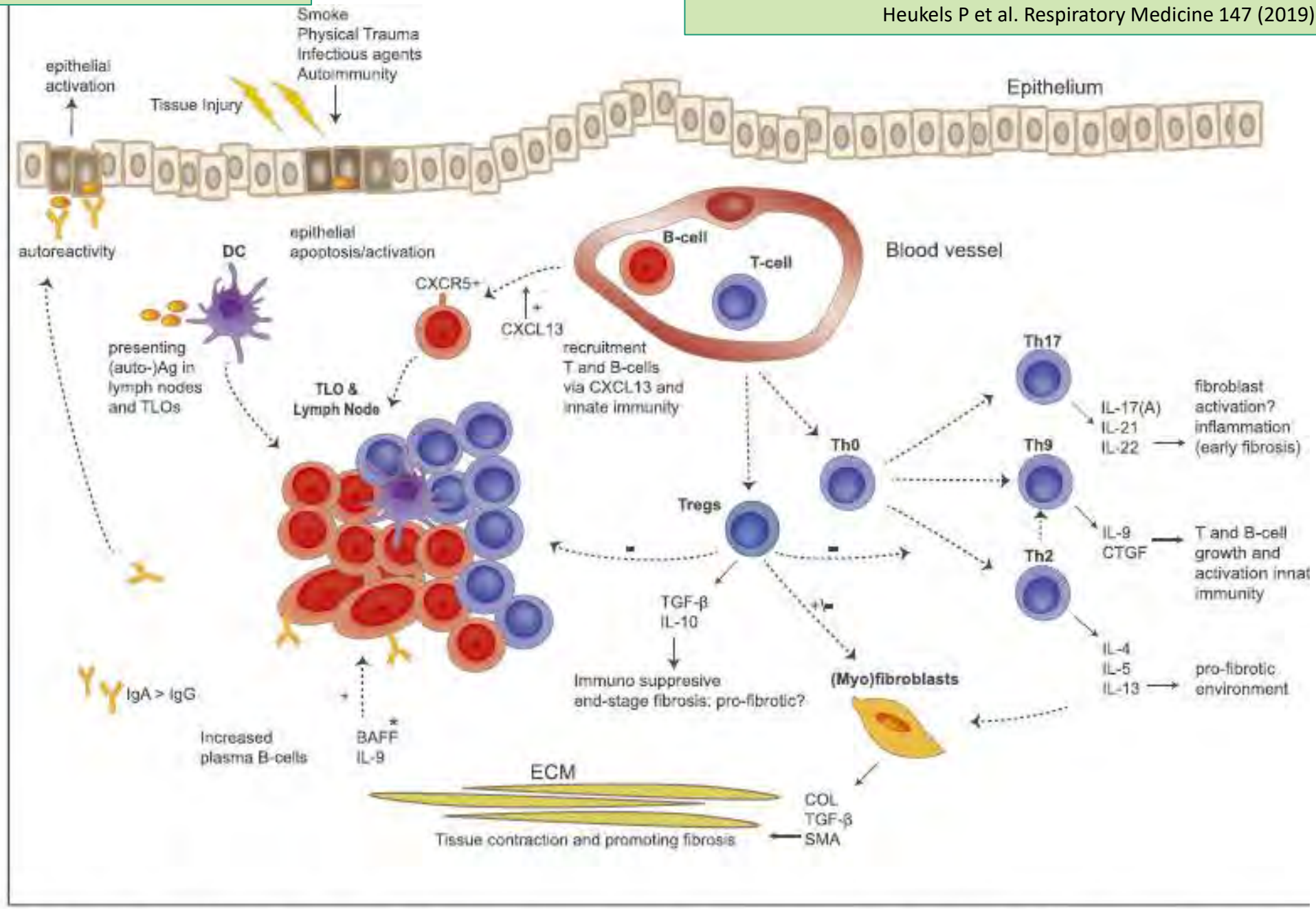
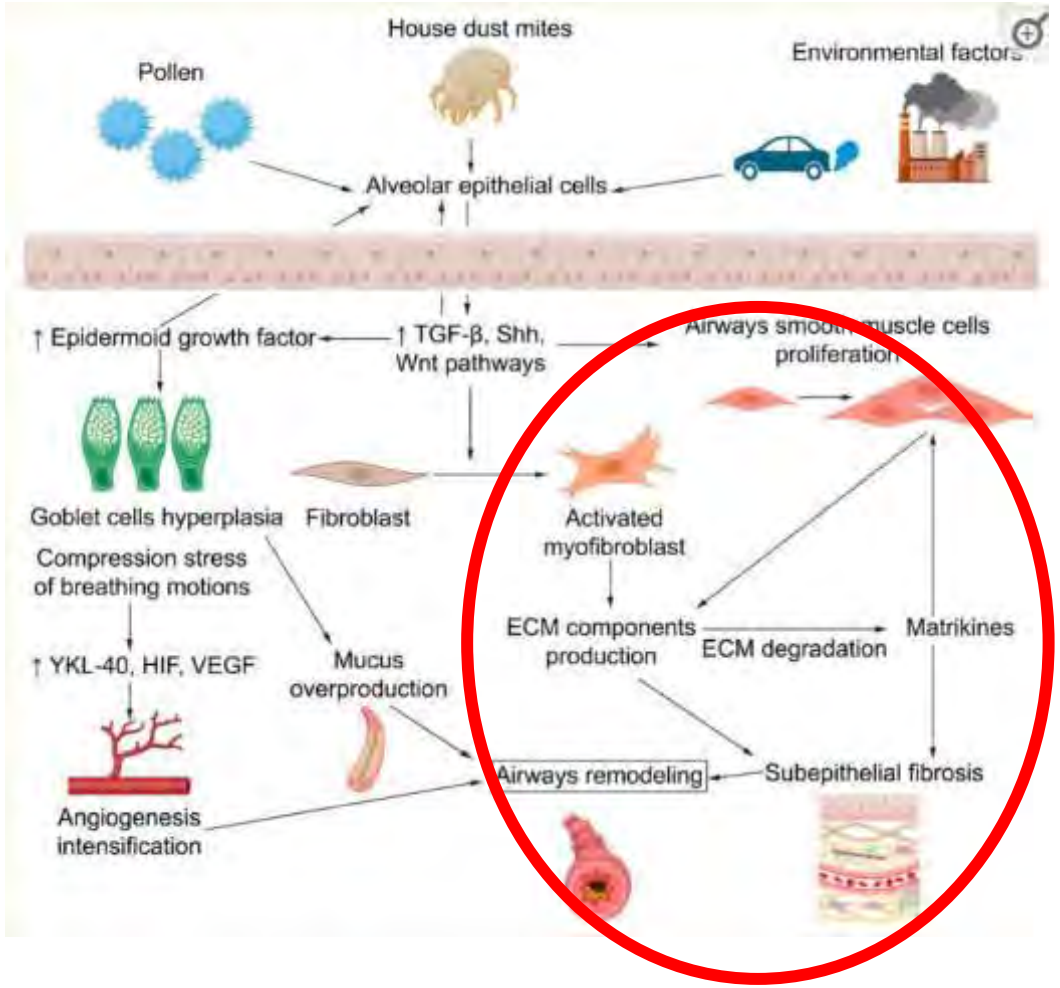


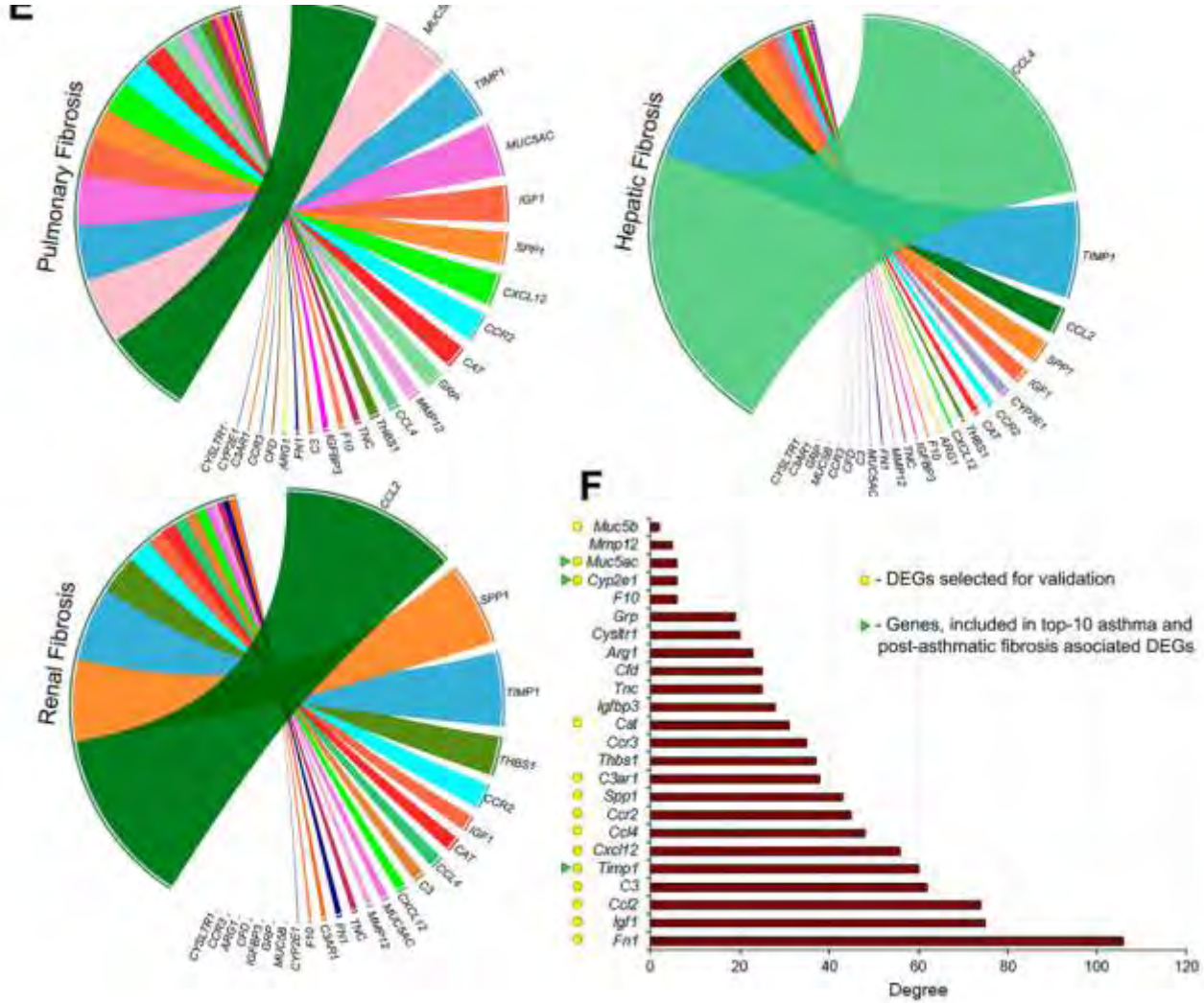
Fig. 2. Schematic overview of the role of the adaptive immune system in IPF pathogenesis. * also known as B lymphocyte stimulator (BL

Asthma és fibrosis



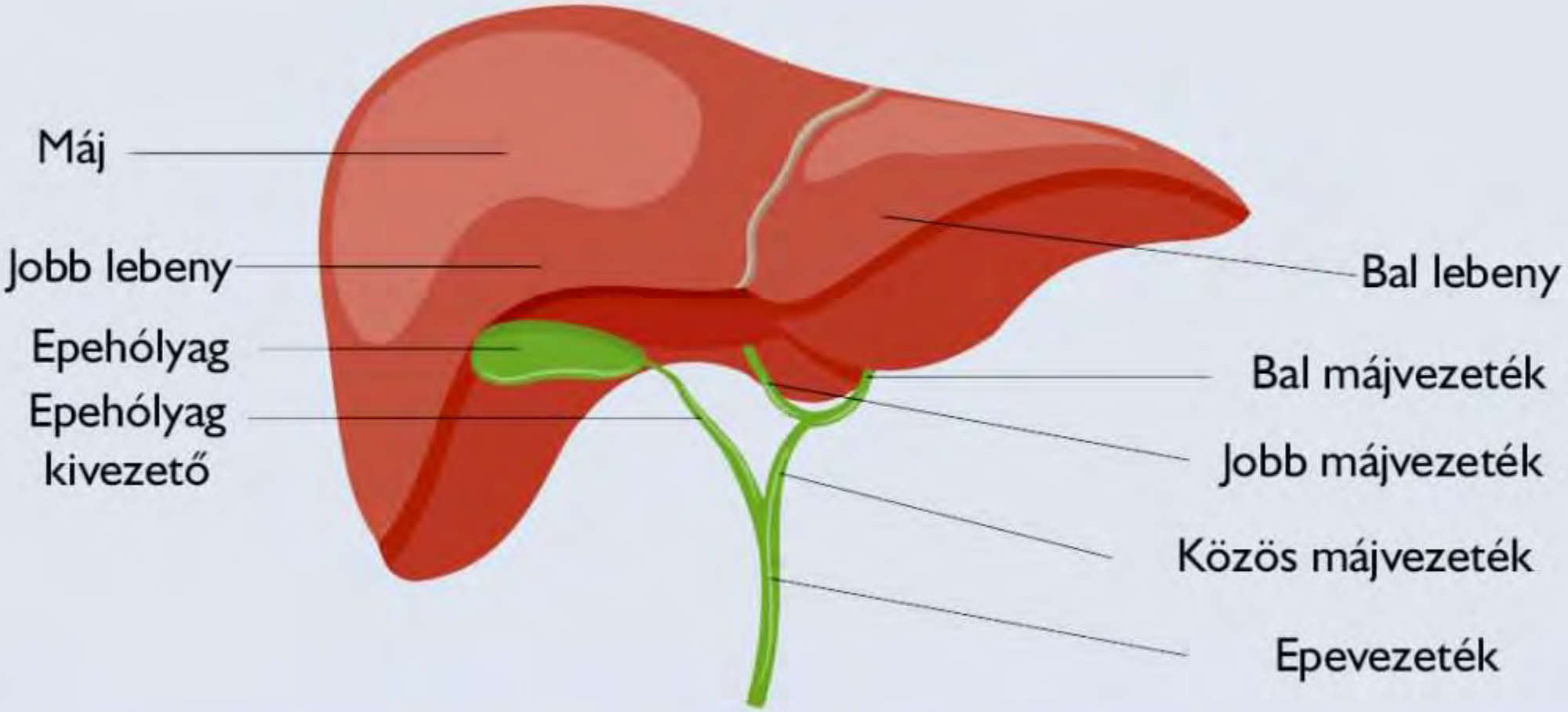
Principal pathophysiological components of airway remodeling emergence in allergic asthma.

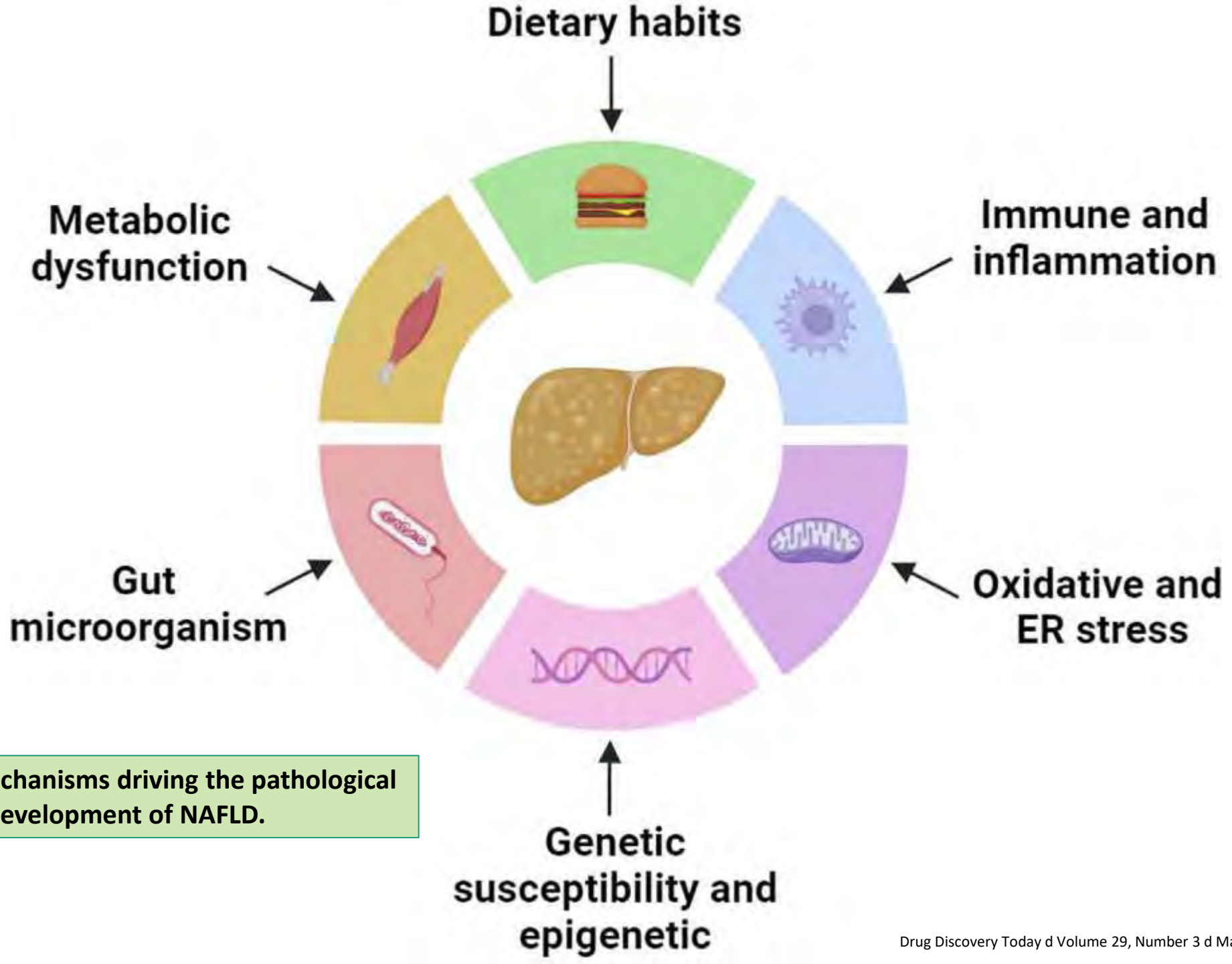
• . 2023 Nov 7;24(22):16042. doi: 10.3390/ijms242216042.



Asthma and Post-Asthmatic Fibrosis

Biomedicines **2022**, 10, 17.


Máj
Jobb lebeny
Epehólyag
Epehólyag kivezető
Bal lebeny
Bal májvezeték
Jobb májvezeték
Közös májvezeték
Epevezeték



Complex mechanisms driving the pathological development of NAFLD.

Immune mechanisms linking metabolic injury to inflammation and fibrosis in fatty liver disease – novel insights into cellular communication circuits

Peiseler M et al. Journal of Hepatology 2022 vol. 77 j 1136–1160.

Előfordulás: 6-35%/populáció

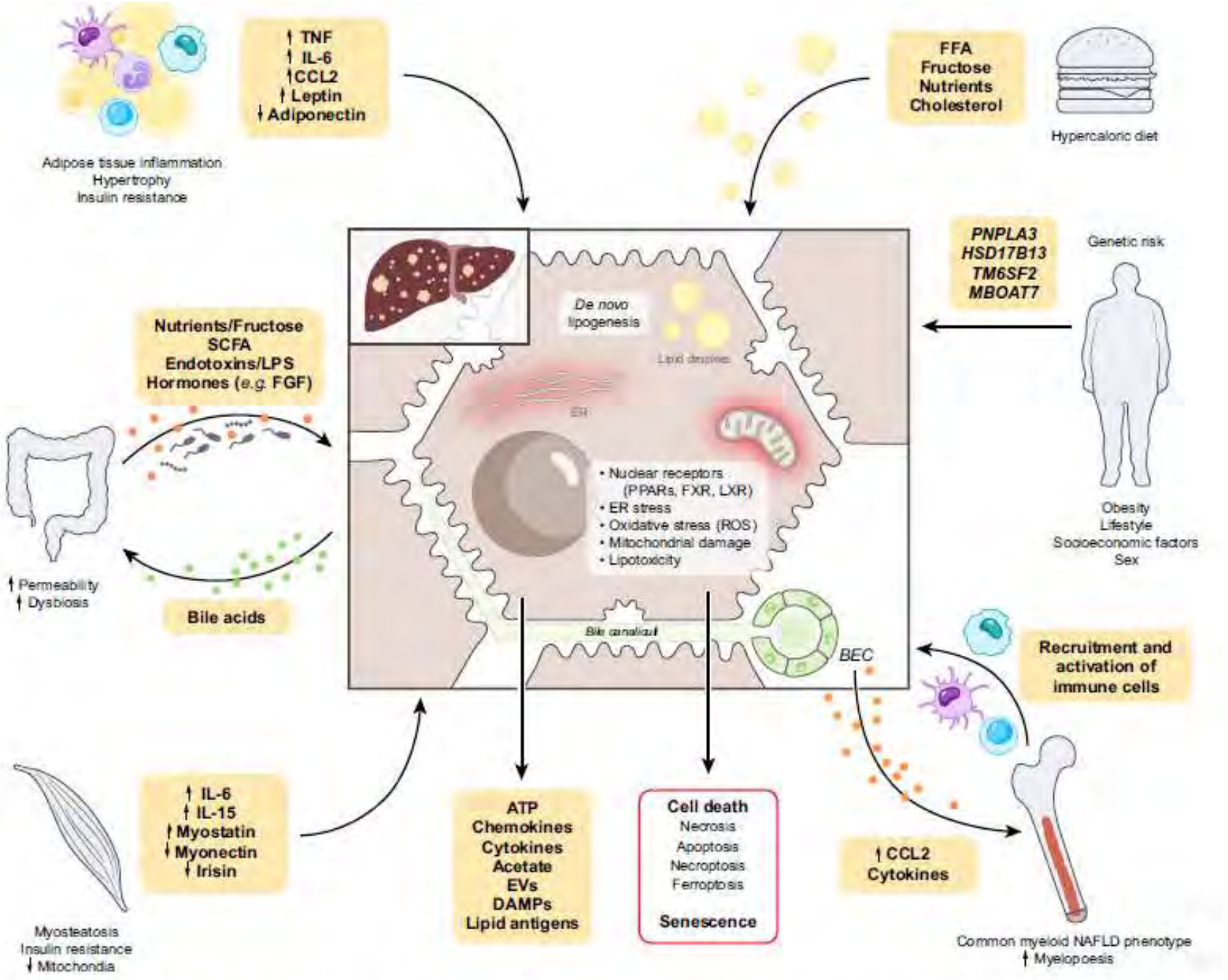


Fig. 1. Triggers of inflammation in NAFLD. Intra- and extrahepatic factors trigger inflammation in NAFLD. Hypercaloric diet, obesity, lifestyle, and genetic risk

Metabolic reprogramming in liver fibrosis

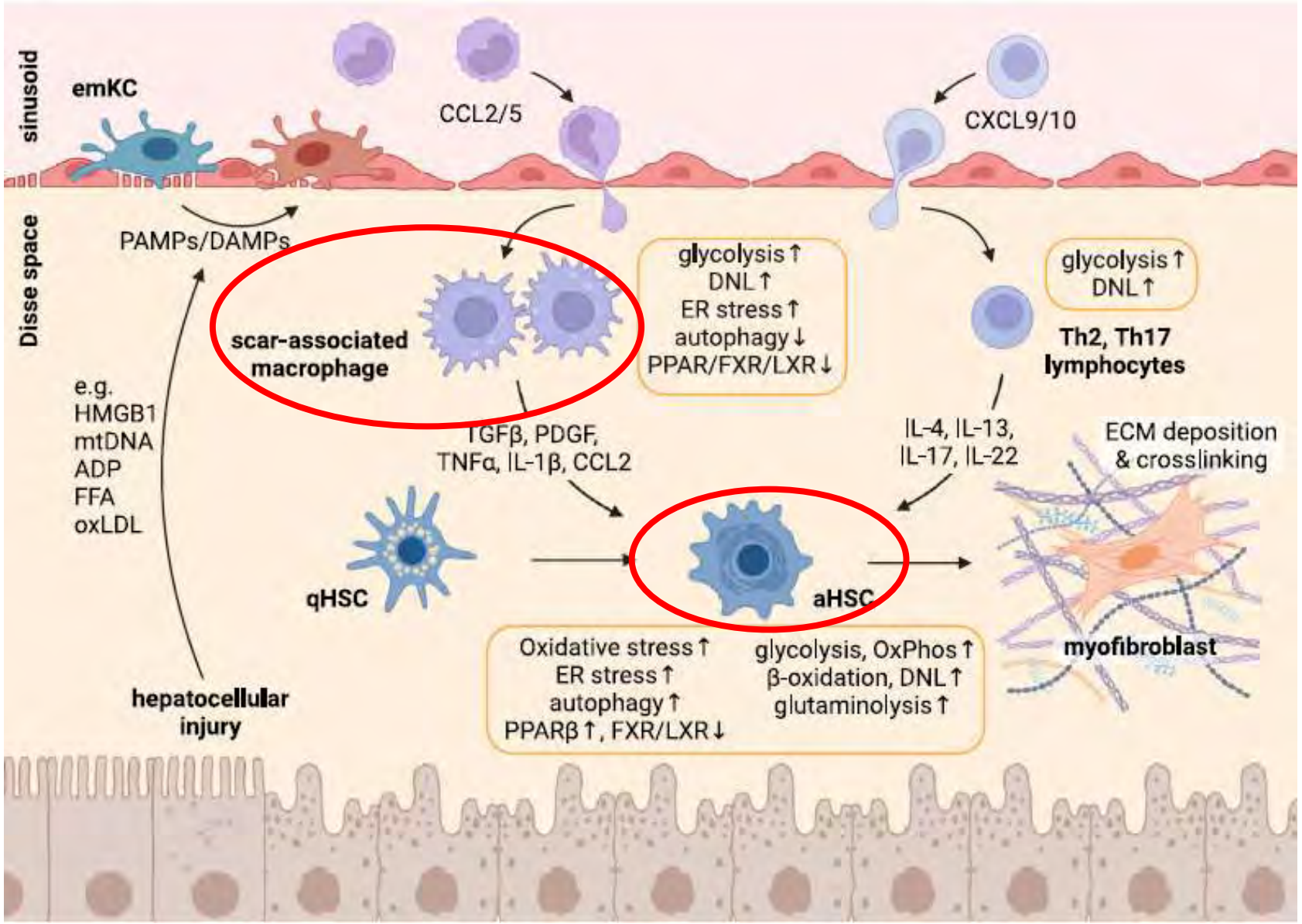
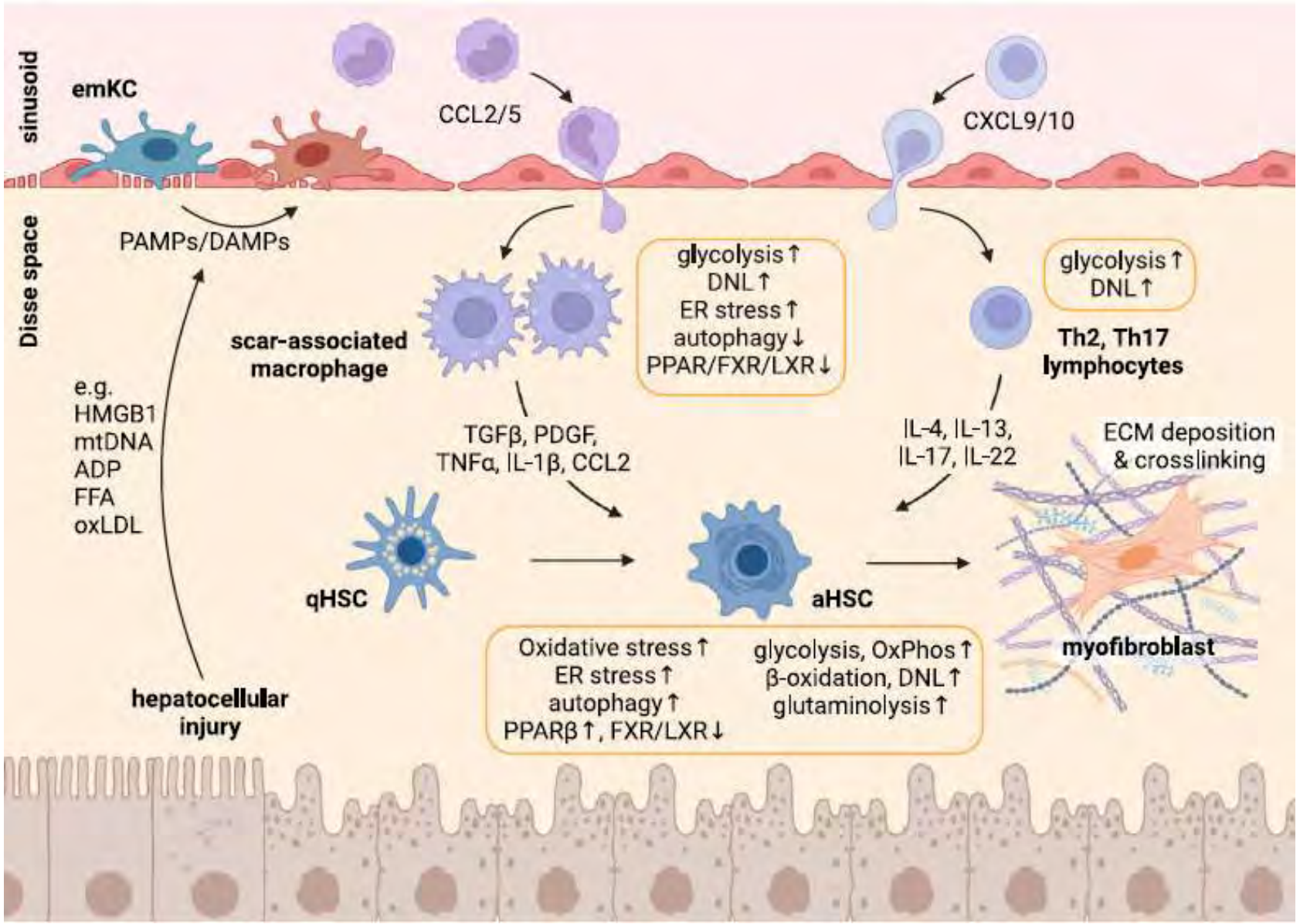


Figure 1. General mechanisms of liver fibrosis and main metabolic adaptations in macrophages, lymphocytes, and activated hepatic stellate cells

Metabolic reprogramming in liver fibrosis



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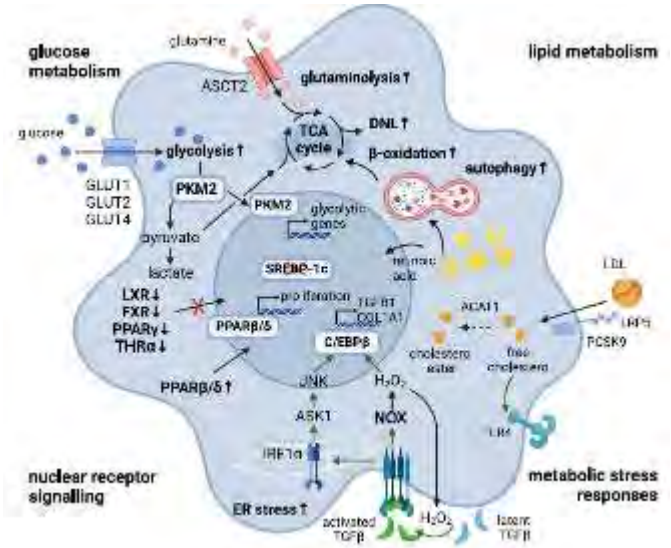


Figure 3. Metabolic reprogramming in fibrogenic hepatic stellate cell activation

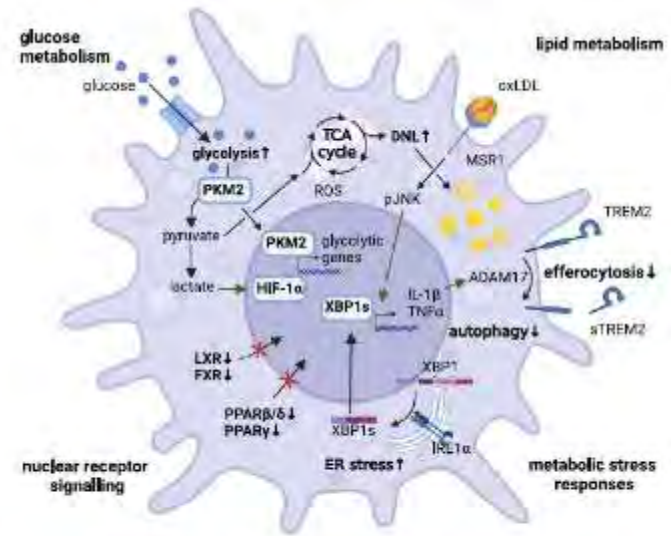


Figure 2. Metabolic reprogramming in hepatic macrophage activation during liver fibrogenesis

Autoimmun májbetegségek és fibrosis

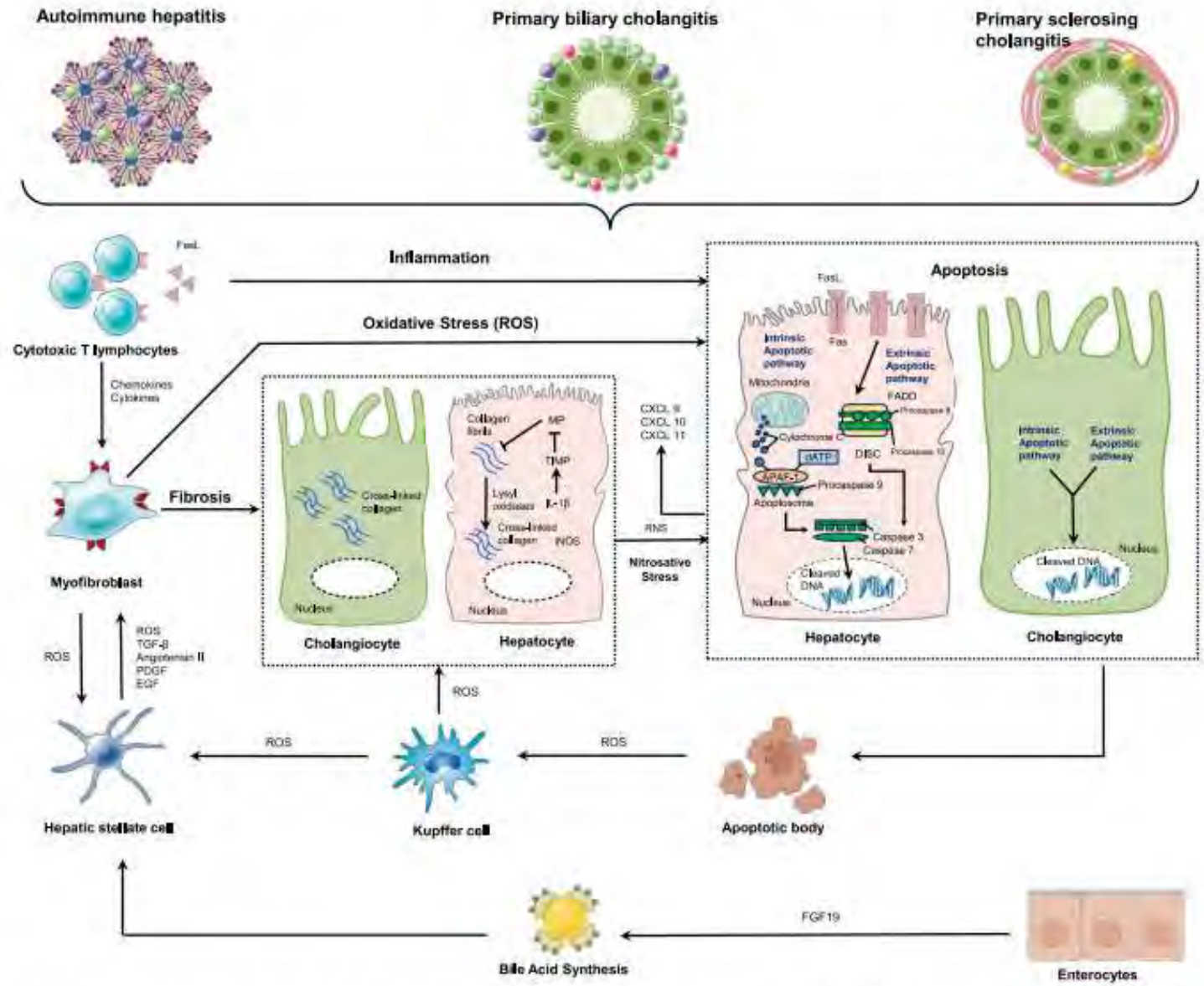


FIGURE 1 | Mechanisms of hepatic fibrosis associated with liver inflammation, oxidative stress, nitrosative stress and apoptosis in AILD.

Liver International, 2025; 45:e70190

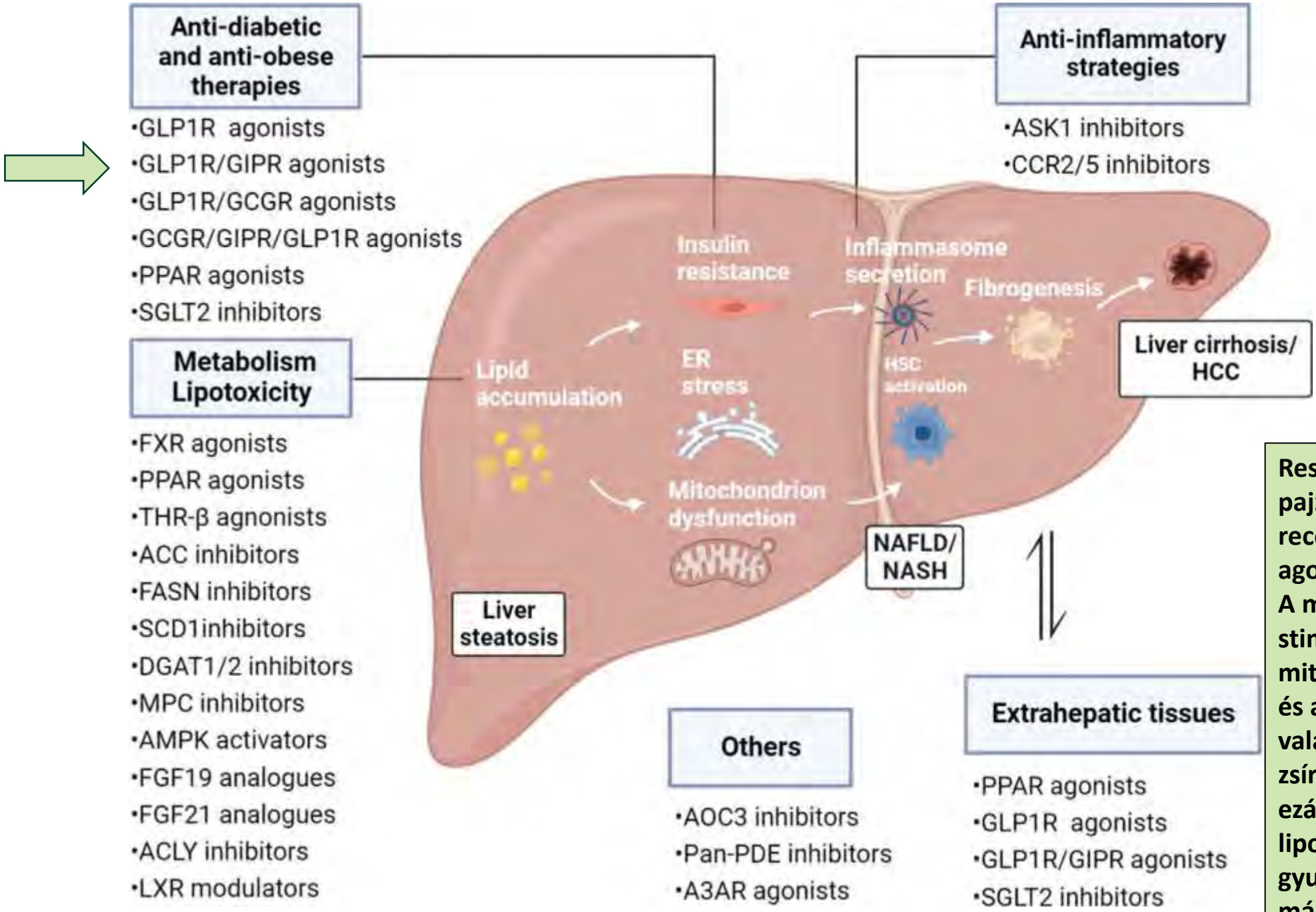
Autoimmun májbetegségek és fibrosis

TABLE 1 | Non-invasive biomarker-based scores for liver fibrosis and parameters required for their calculation.

Score	Age	Sex	ALT	AST	GGT	Platelet count	RDW	INR	PT	Albumin	Total bilirubin	Urea	HA	Hyaluronate	PIIINP	TIMP-1	α-2-macroglobulin
APRI				X		X											
FIB-4 score	X		X	X		X											
AAR			X	X													
GPR					X	X											
ELF score													X		X	X	
ALBI grade										X	X						
FibroQ	X		X	X		X		X									
Fibrometer	X			X		X			X			X		X			X
Hepascore	X	X			X						X		X				X
RPR						X	X										

Abbreviations: AAR, AST/ALT ratio; ALBI grade, Albumin-Bilirubin grade; ALT, alanine transaminase; APRI, AST/platelet ratio index; AST, aspartate transaminase; ELF score, Enhanced Liver Fibrosis score; FIB-4 score, Fibrosis-4; GGT, gamma-glutamyl transferase; GPR, GGT to platelet ratio; HA, hyaluronic acid; INR, international normalised ratio; PIIINP, propeptide of type III procollagen; PT, prothrombin time; RDW, red cell distribution width; RPR, RDW to platelet count ratio; TIMP-1, tissue inhibitor of metalloproteinase type 1; α-2-macroglobulin, alpha-2-macroglobulin.

Liver International, 2025; 45:e70190



Resmetirom: pajzsmirigyhormon-receptor-β (THR-β) agonista
A májban a THR-β stimulációja javítja a mitokondriális funkciót és a lipidanyagcserét, valamint növeli a zsírsav-β-oxidációt, ezáltal csökkentve a lipotoxikus májzsírt, a gyulladást és a májfibrózist

Drug Discovery Today d Volume 29, Number 3 d March 2024

Diffuse myocardial fibrosis: mechanisms, diagnosis and therapeutic approaches

Begoña López[1,2,4], Susana Ravassa[1,2,4], María U. Moreno[1,2,4], Gorka San José[1,2], Javier Beaumont[1,2], Arantxa González[1,2]✉ and Javier Díez[1,2,3]✉

Box 1 | **Conditions associated with diffuse myocardial fibrosis**

Ischaemic heart disease
- Coronary artery disease[a]
- Alterations of the coronary microcirculation caused by hypertension[a] or diabetes mellitus[a]

Cardiac pressure overload
- Systemic arterial hypertension[a]
- Aortic stenosis[a,10]
- Coarctation of the aorta[a,12]
- Pulmonary arterial hypertension[a,b,12]

Cardiac volume overload
- Obesity[a,b,13]
- Aortic regurgitation[a,14]
- Mitral regurgitation[a,b,15]

Cardiac inflammation
- Myocarditis[16]
- Sarcoidosis[a,17]

Genetic cardiac diseases
- Hypertrophic cardiomyopathy[a,18]

Cardiac metabolic alterations
- Obesity[a,b,13]
- Diabetes mellitus[a,19]
- Chronic kidney disease[a,b,20]

Infiltrative cardiac alterations
- Amyloidosis[21]

Cardiac storage diseases
- Anderson–Fabry disease[a,b,22]

Congenital heart diseases
- Tetralogy of Fallot[23]
- Ebstein anomaly[a,b,24]
- Transposition of the great arteries[a,b,25]

Other conditions
- Ageing[26]
- Non-ischaemic dilated cardiomyopathy[27]
- Atrial fibrillation-mediated cardiomyopathy[28]
- Exposure to pharmacological cardiotoxic agents[29]

[a]Conditions in which diffuse myocardial fibrosis was identified by cardiovascular MRI instead of endomyocardial biopsy, which was performed in the other conditions.

Nature Reviews Cardiology **volume 18**, pages479–498 (2021)

Diffuse myocardial fibrosis: mechanisms, diagnosis and therapeutic approaches

Begoña López[1,2,4], Susana Ravassa[1,2,4], María U. Moreno[1,2,4], Gorka San José[1,2], Javier Beaumont[1,2], Arantxa González[1,2]✉ and Javier Díez[1,2,3]✉

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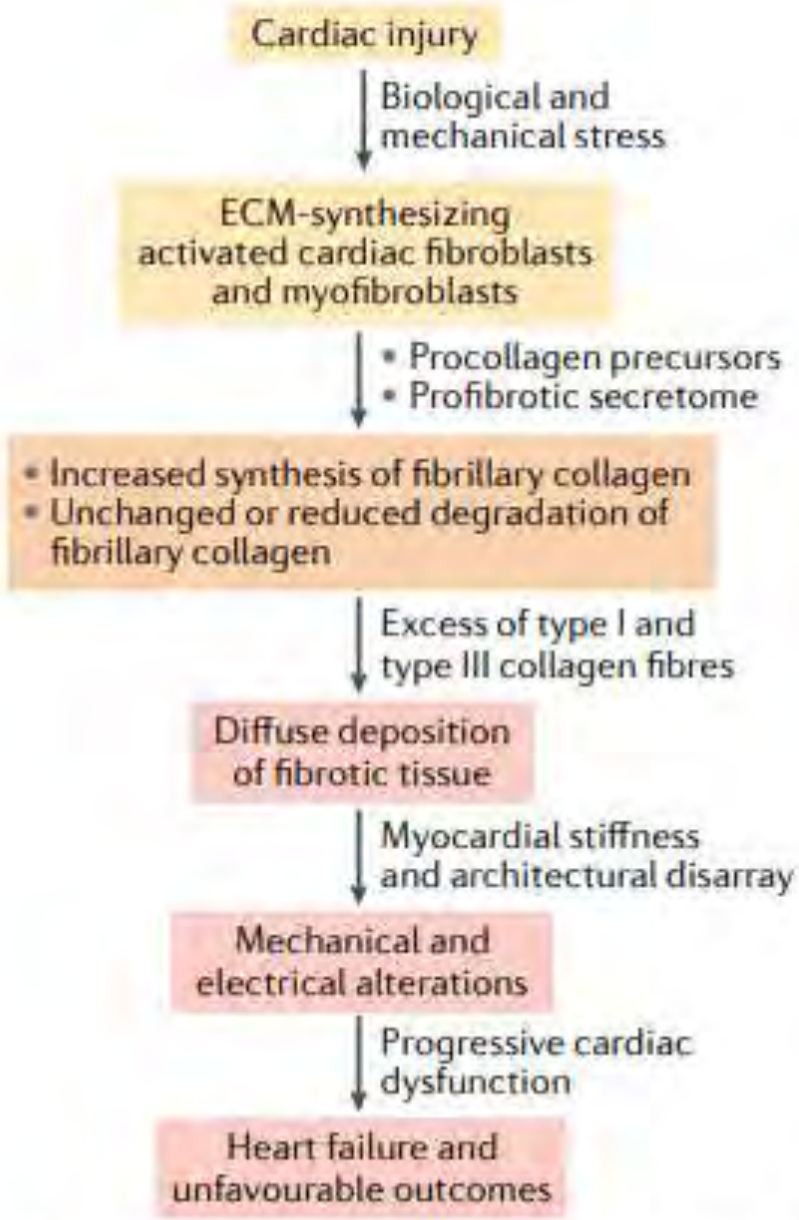


Fig. 1 | **Pathogenesis and consequences of diffuse myocardial fibrosis.** In response to cardiac injury,

Nature Reviews Cardiology **volume 18**, pages479–498 (2021)

Diffuse myocardial fibrosis: mechanisms, diagnosis and therapeutic approaches

Begoña López[1,2,4], Susana Ravassa[1,2,4], María U. Moreno[1,2,4], Gorka San José[1,2], Javier Beaumont[1,2], Arantxa González[1,2]✉ and Javier Díez[1,2,3]✉

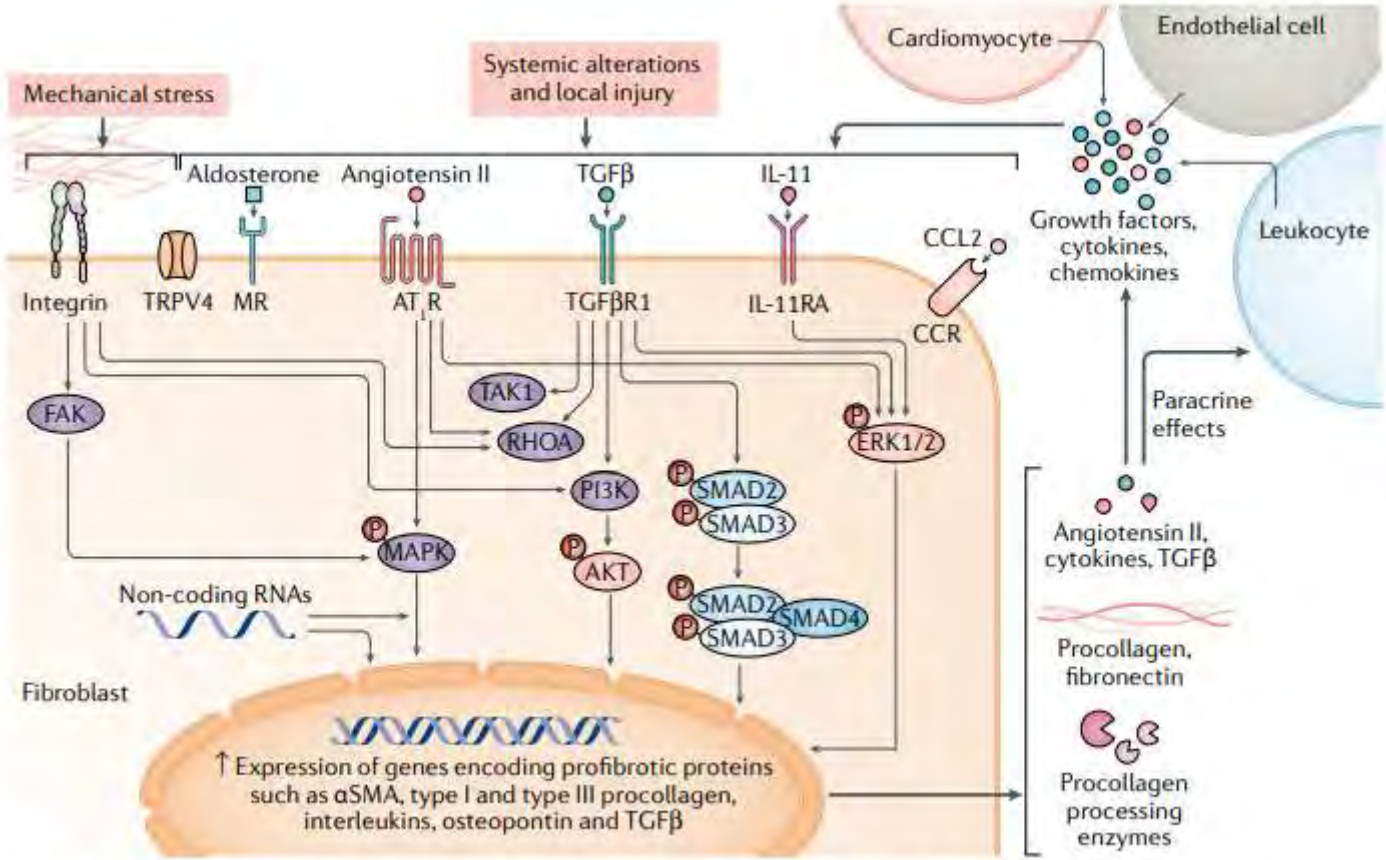
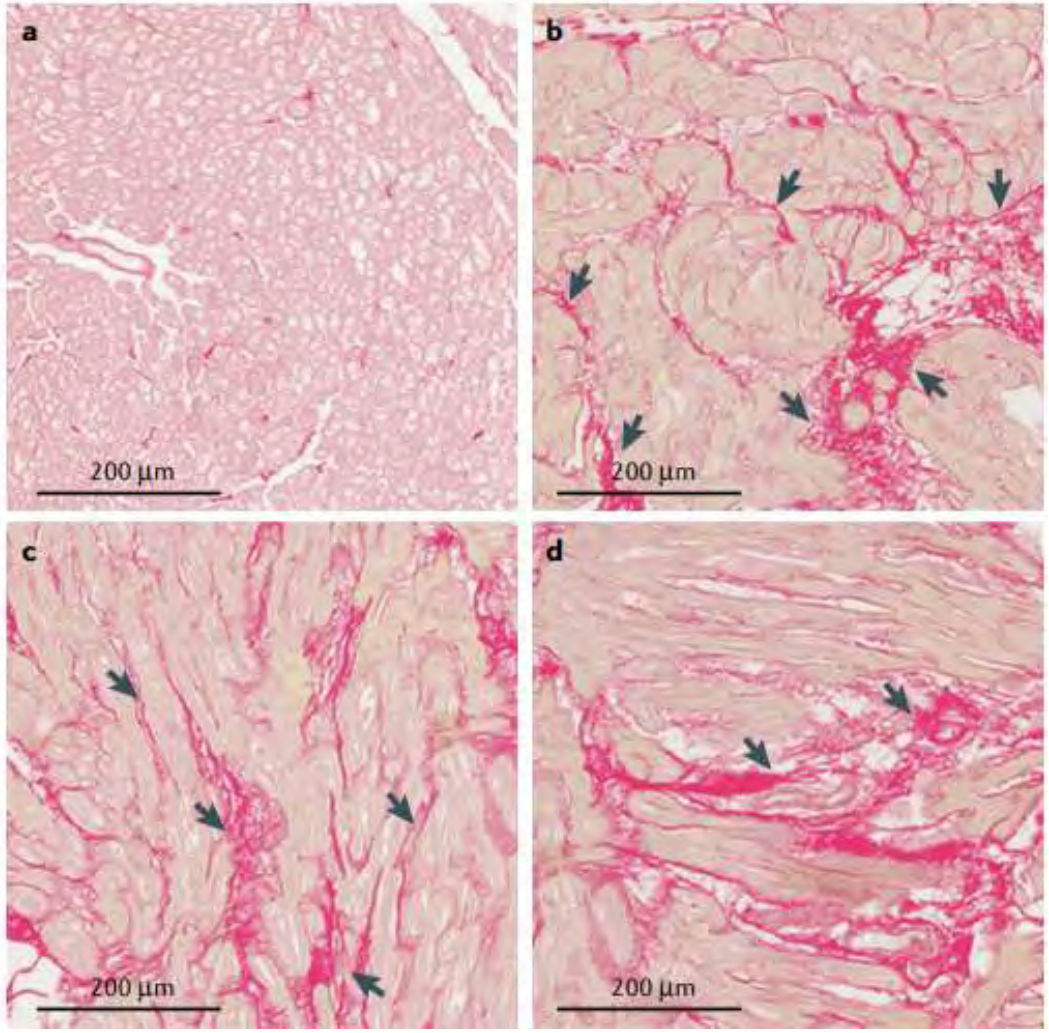


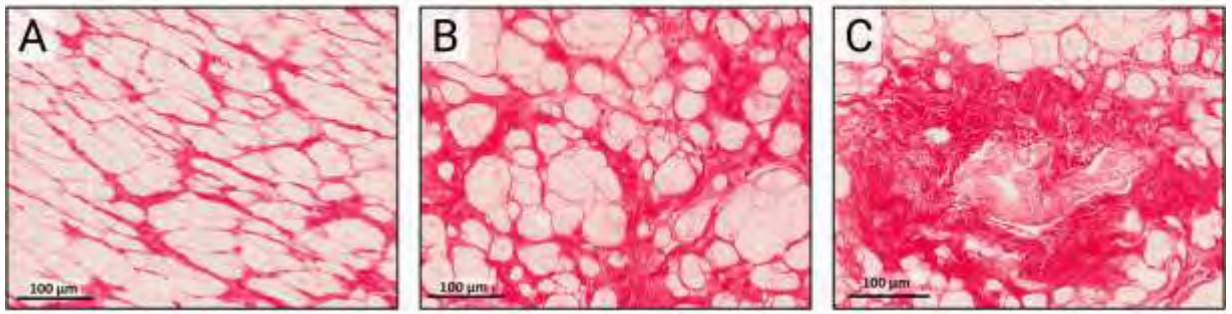
Fig. 3 | **Major signalling pathways involved in the activation of cardiac fibroblasts** In response to increased



Nature Reviews Cardiology **volume 18**, pages479–498 (2021)

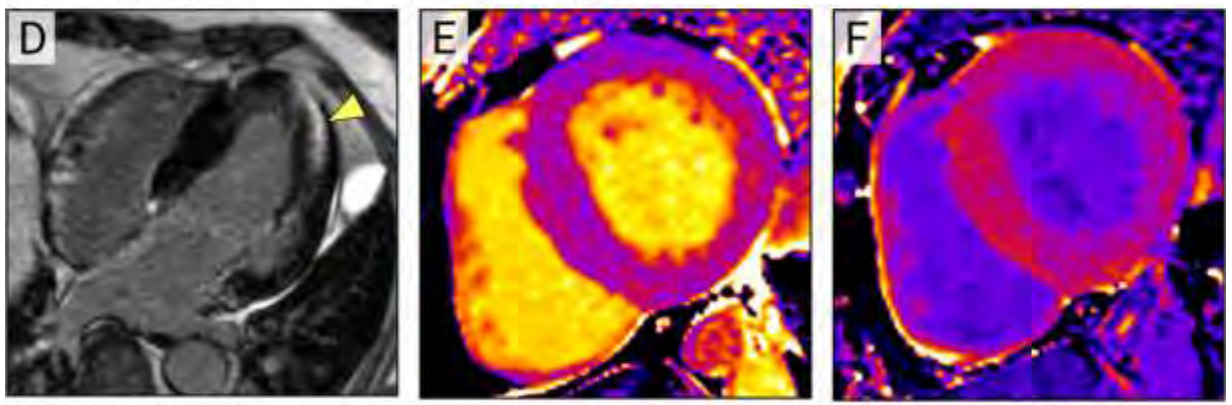
Myocardial fibrosis from the perspective of the extracellular matrix: Mechanisms to clinical impact

Endomyocardial biopsy (EMB)



Reactive interstitial fibrosis | Focal replacement fibrosis | Perivascular fibrosis

Cardiac magnetic resonance (CMR) imaging



Late gadolinium enhancement (LGE) | Native T1 mapping | Post-contrast T1 mapping

Biomarkers of cardiac fibrosis

Endomyocardial biopsy (EMB)

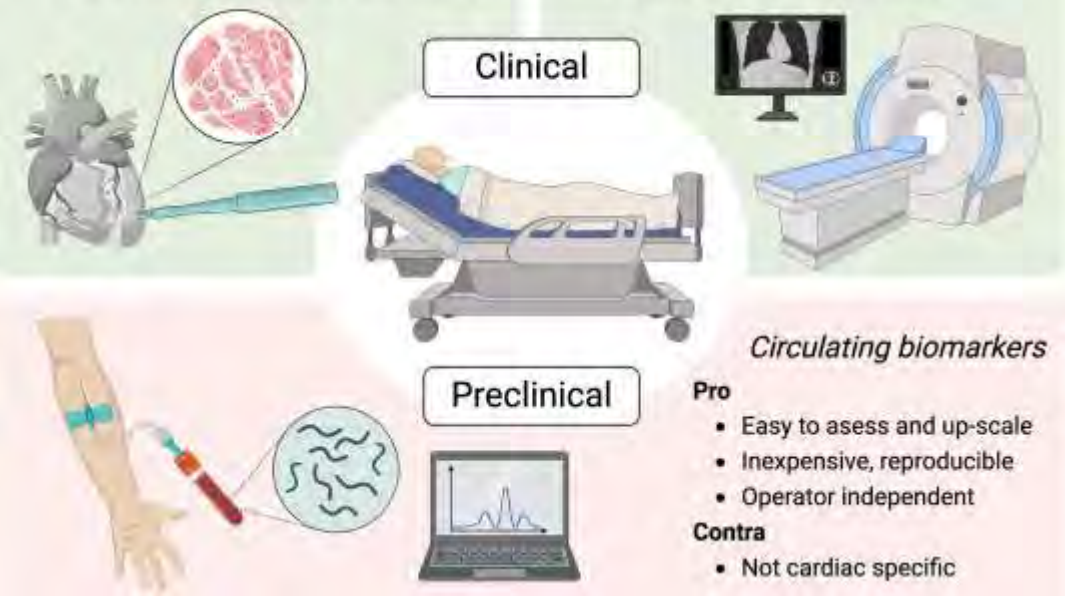
Pro
- Direct and specific assessment of myocardial collagen

Contra
- Invasive procedure
- Vulnerable to sampling bias
- Screening is logistically challenching

Cardiac MRI or CT

Pro
- Repeatable, non-invasive procedure
- Whole-heart visualisation

Contra
- Low resolution (0.5 - 2.0 mm)
- Limited ability to discriminate tissues
- Mostly detects focal fibrosis



Circulating biomarkers

Pro
- Easy to asess and up-scale
- Inexpensive, reproducible
- Operator independent

Contra
- Not cardiac specific

Myocardial fibrosis from the perspective of the extracellular matrix: Mechanisms to clinical impact

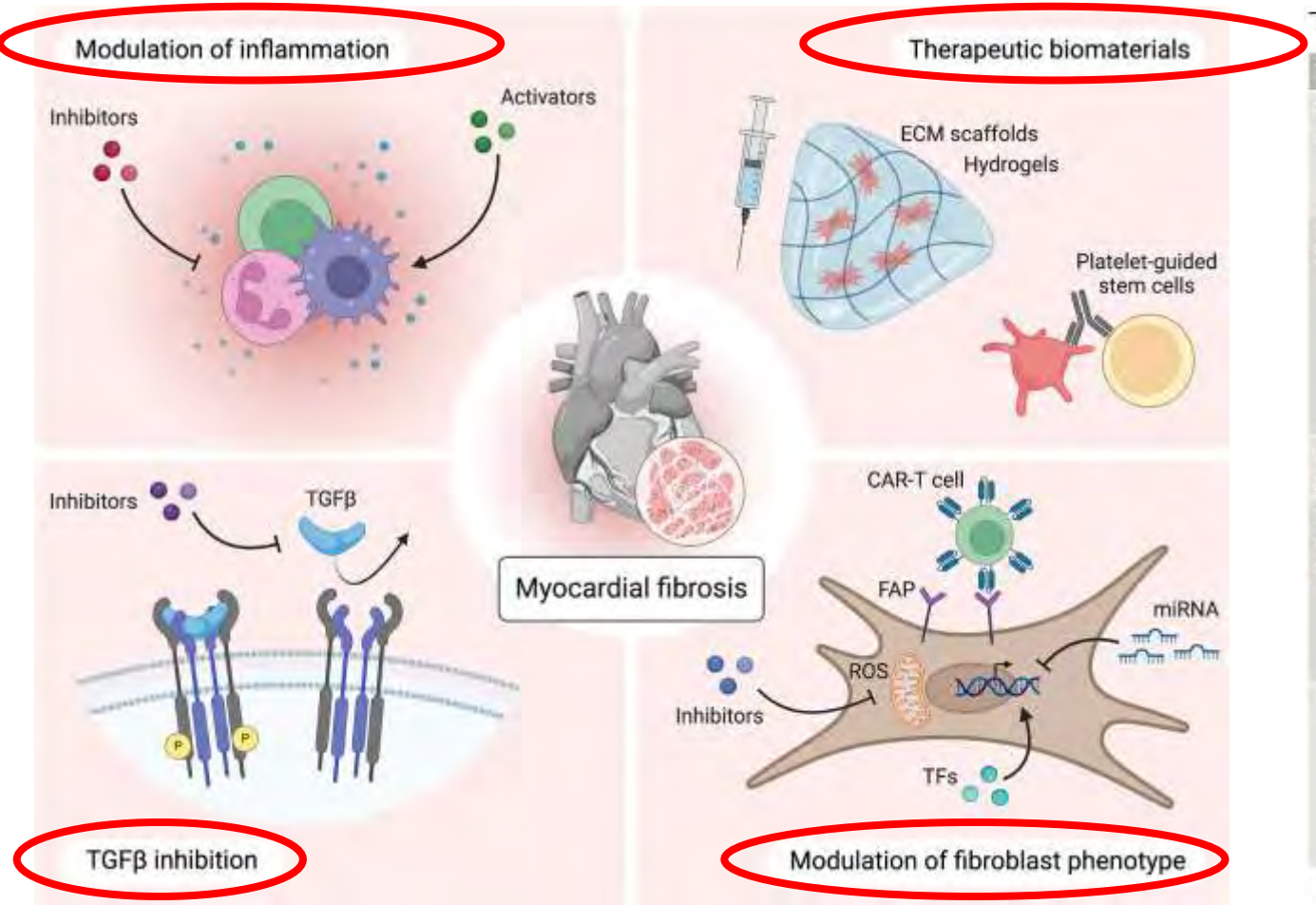


Table 3 | **Novel therapies potentially applicable to reverse diffuse myocardial fibrosis**

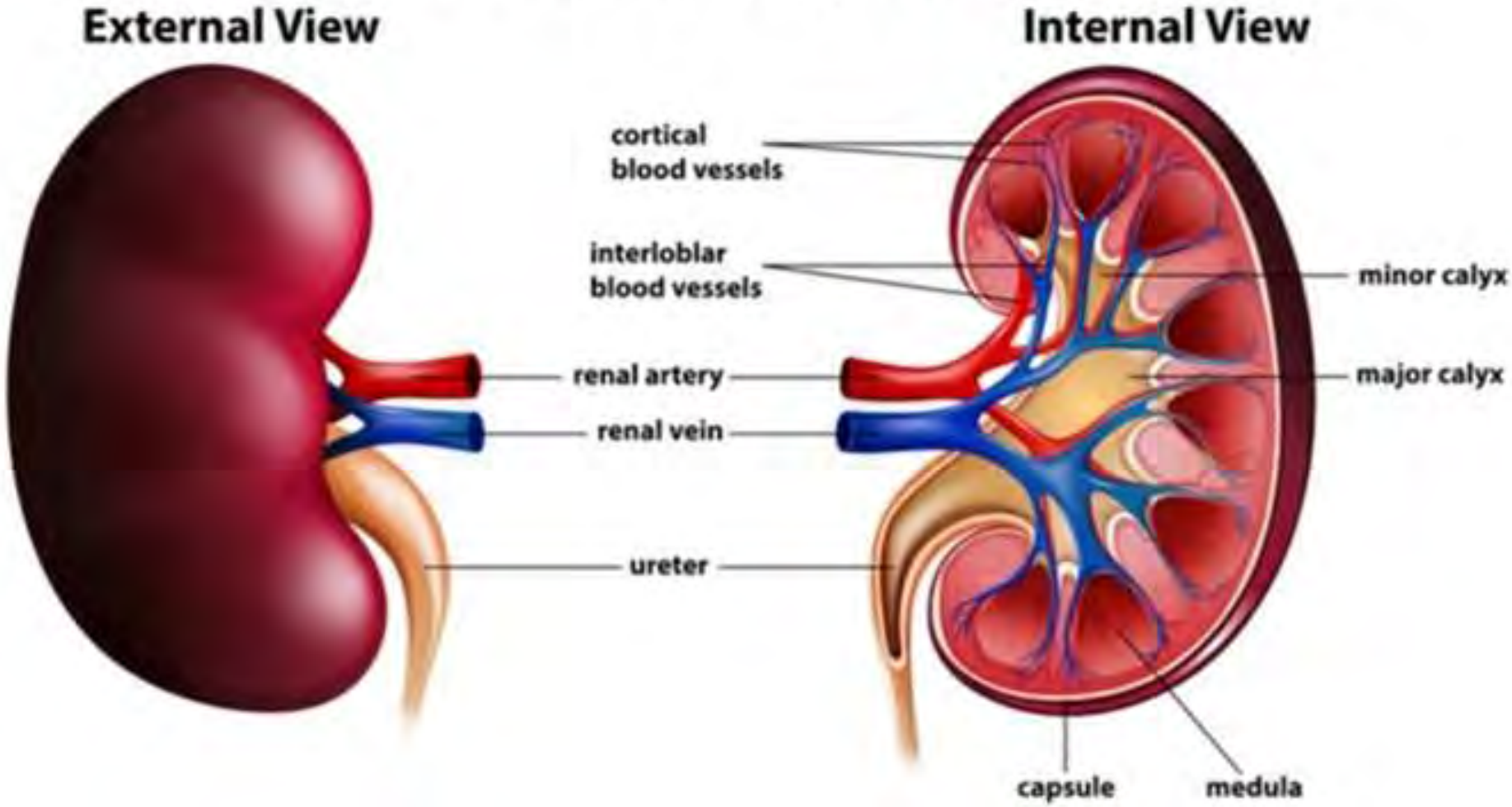
Target	Therapeutic strategy	Study stage	Status	Ref.
TGFβ1 signalling	Inhibiting connective tissue growth factor activity with the monoclonal antibody pamrevlumab	Phase II trial in patients with idiopathic pulmonary fibrosis	Completed	
		Phase III trial in patients with idiopathic pulmonary fibrosis	Ongoing	
Non-coding RNAs	Inhibiting miR-21 with RG-012	Phase I trials in patients with Alport syndrome	Completed	
		Phase II trials in patients with Alport syndrome	Ongoing	
	Mimicking miR-29a with remlarsen	Phase I trial in healthy volunteers	Completed	
		Phase II trial in patients with cutaneous fibrosis	Ongoing	
Metabolic pathways	Omega-3 fatty acid supplementation	Phase III clinical trial in patients with myocardial infarction	Completed	
Extracellular collagen processing	LOXL2 inhibition with simtuzumab	Phase II clinical trial in patients with idiopathic pulmonary fibrosis	Completed	
	Matrix metalloproteinase inhibition with low-dose doxycycline	Phase II clinical trials in patients with acute myocardial infarction and heart failure	Completed	
		Phase II trial in patients with myocardial infarction	Ongoing	
Inflammation	Therapy with modified citrus pectin (a galectin 3 inhibitor)	Phase I trial in patients with chronic kidney disease	Ongoing	
	Therapy with BLD-2660 (a calpain inhibitor)	Phase IIa trial in patients with idiopathic pulmonary fibrosis	Ongoing	
	Therapy with sodium thiosulfate (a hydrogen sulfide-releasing agent)	Phase II trial in patients with myocardial infarction	Ongoing	

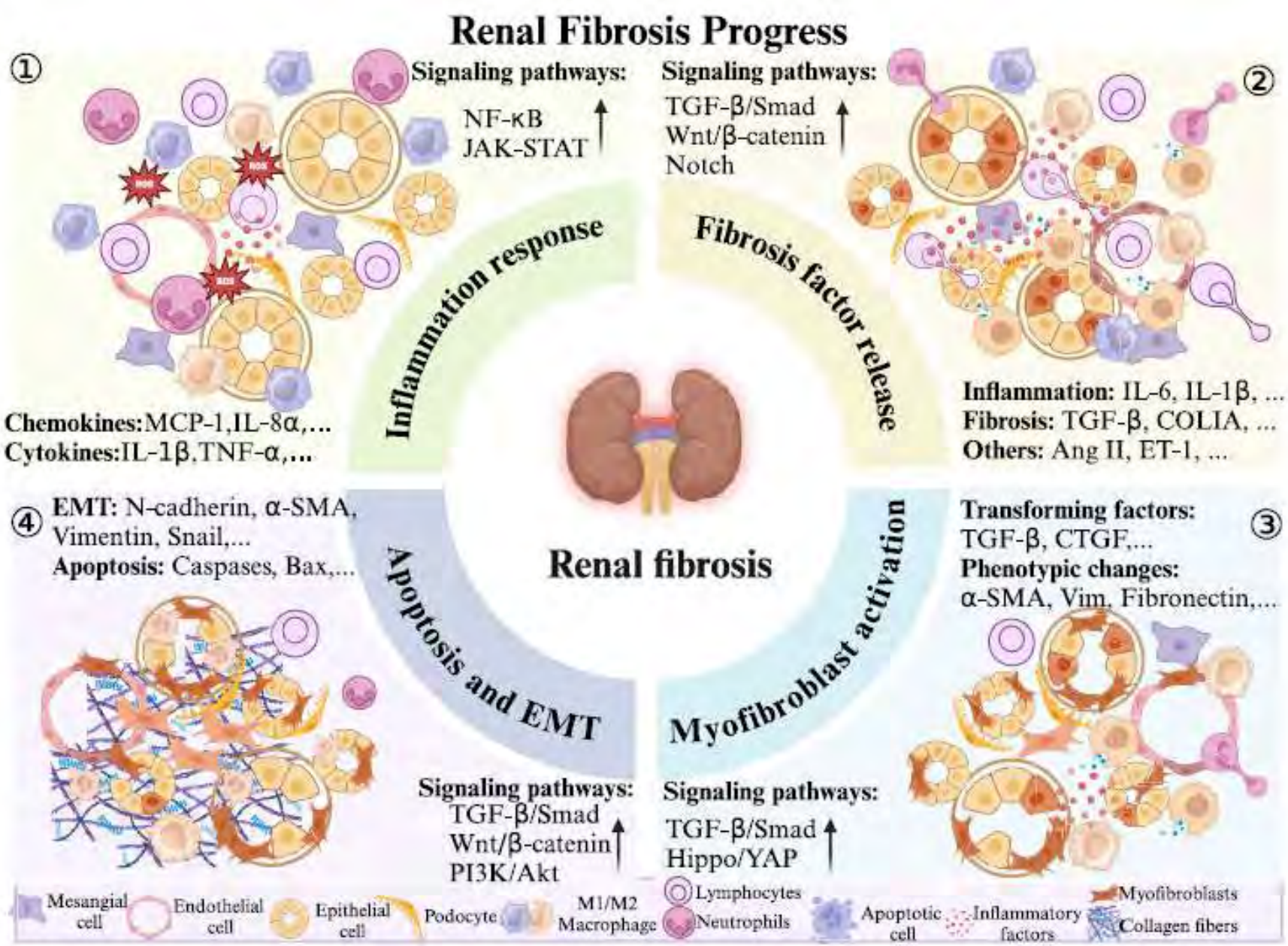
LOXL2, lysyl oxidase homologue 2; TGFβ1, transforming growth factor-β1.

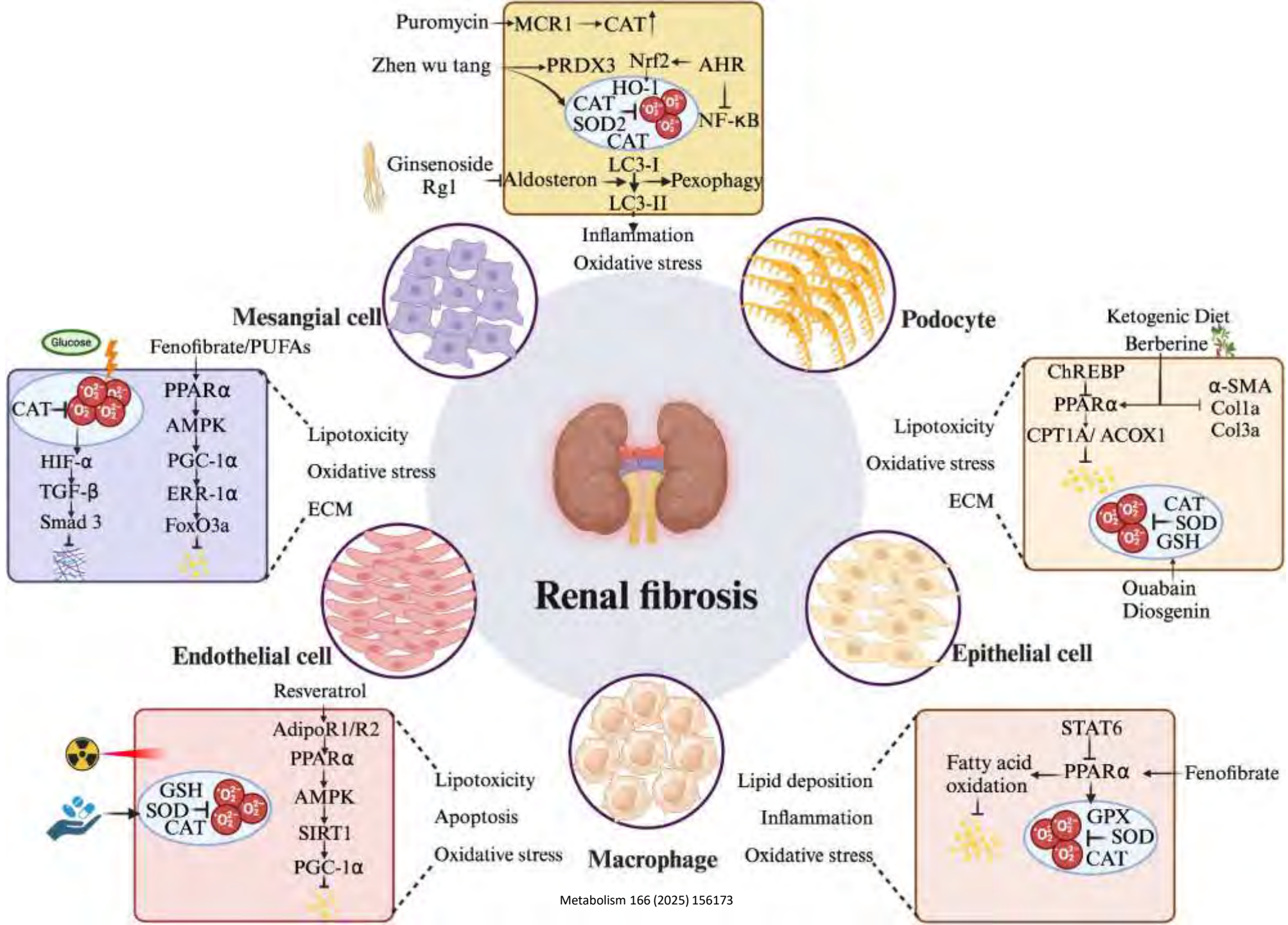
Matrix Biology 134 (2024) 1–22

Nature Reviews Cardiology **volume 18**, pages479–498 (2021)

Human Kidney Anatomy




Renal Fibrosis Progress
①
Signaling pathways:
NF-κB
JAK-STAT
Chemokines:MCP-1,IL-8α,...
Cytokines:IL-1β,TNF-α,...
Inflammation response
Signaling pathways:
TGF-β/Smad
Wnt/β-catenin
Notch
Fibrosis factor release
②
Inflammation: IL-6, IL-1β, ...
Fibrosis: TGF-β, COLIA, ...
Others: Ang II, ET-1, ...
Renal fibrosis
④
EMT: N-cadherin, α-SMA, Vimentin, Snail,...
Apoptosis: Caspases, Bax,...
Apoptosis and EMT
Signaling pathways:
TGF-β/Smad
Wnt/β-catenin
PI3K/Akt
Myofibroblast activation
Signaling pathways:
TGF-β/Smad
Hippo/YAP
③
Transforming factors:
TGF-β, CTGF,...
Phenotypic changes:
α-SMA, Vim, Fibronectin,...
Mesangial cell
Endothelial cell
Epithelial cell
Podocyte
M1/M2 Macrophage
Lymphocytes
Neutrophils
Apoptotic cell
Inflammatory factors
Myofibroblasts
Collagen fibers


Puromycin
MCR1
CAT
Zhen wu tang
PRDX3
Nrf2
AHR
HO-1
CAT
SOD2
CAT
NF-κB
Ginsenoside Rg1
Aldosteron
LC3-I
LC3-II
Pexophagy
Inflammation
Oxidative stress
Mesangial cell
Podocyte
Glucose
Fenofibrate/PUFAs
CAT
PPARα
AMPK
PGC-1α
ERR-1α
FoxO3a
HIF-α
TGF-β
Smad 3
Lipotoxicity
Oxidative stress
ECM
Ketogenic Diet
Berberine
ChREBP
PPARα
CPT1A/ ACOX1
α-SMA
Col1a
Col3a
Lipotoxicity
Oxidative stress
ECM
CAT
SOD
GSH
Ouabain
Diosgenin
Renal fibrosis
Endothelial cell
Epithelial cell
Resveratrol
AdipoR1/R2
PPARα
AMPK
SIRT1
PGC-1α
GSH
SOD
CAT
Lipotoxicity
Apoptosis
Oxidative stress
Macrophage
STAT6
Fatty acid oxidation
PPARα
Fenofibrate
GPX
SOD
CAT
Lipid deposition
Inflammation
Oxidative stress

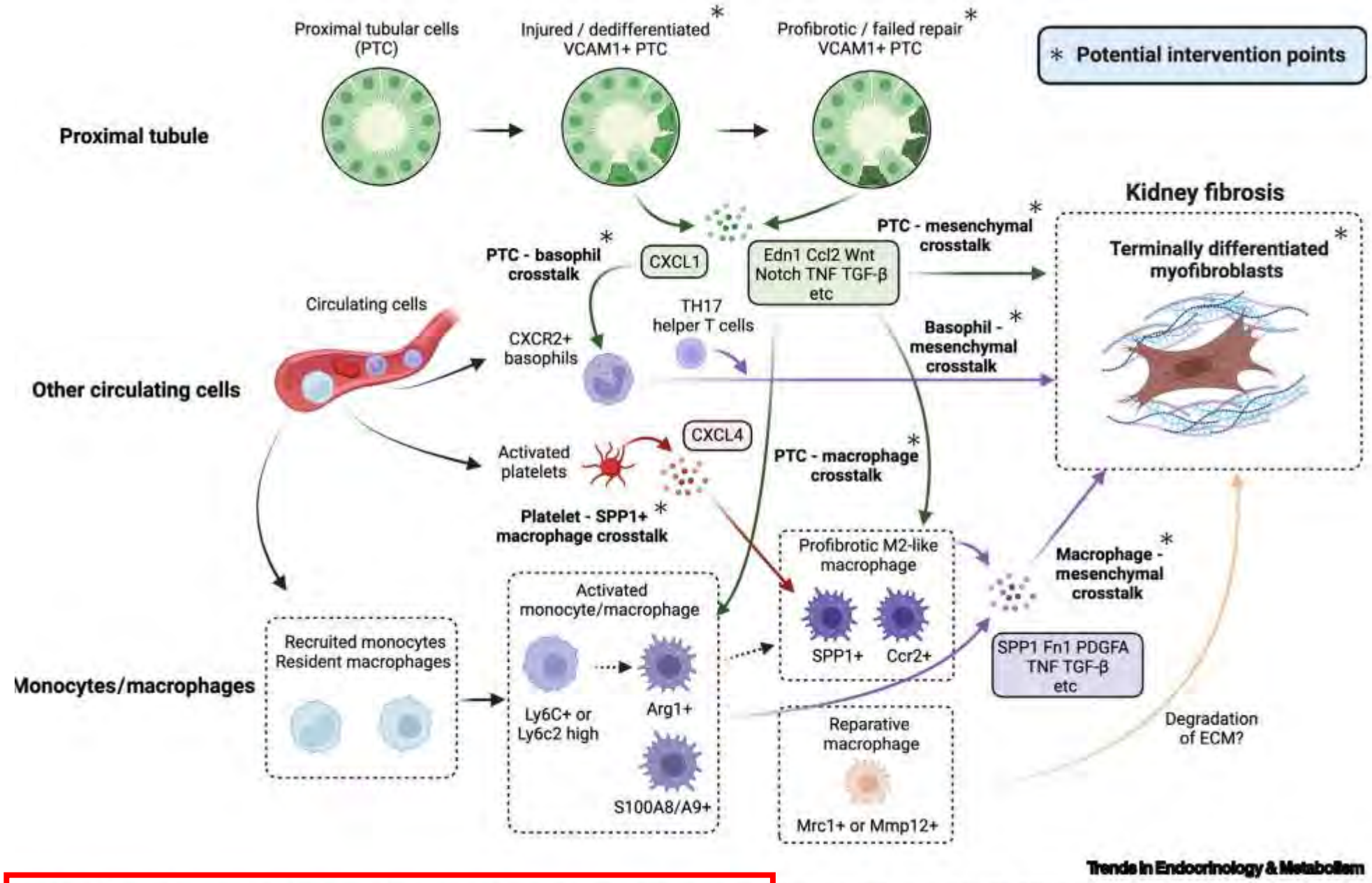
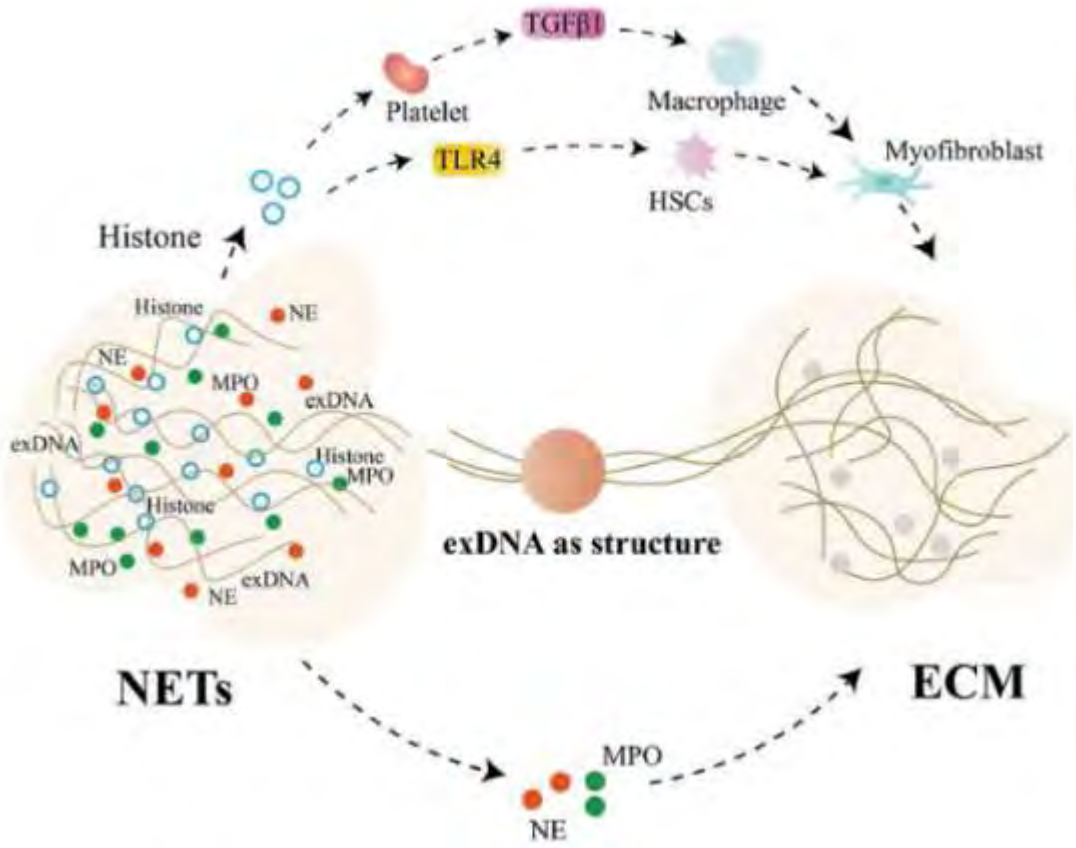
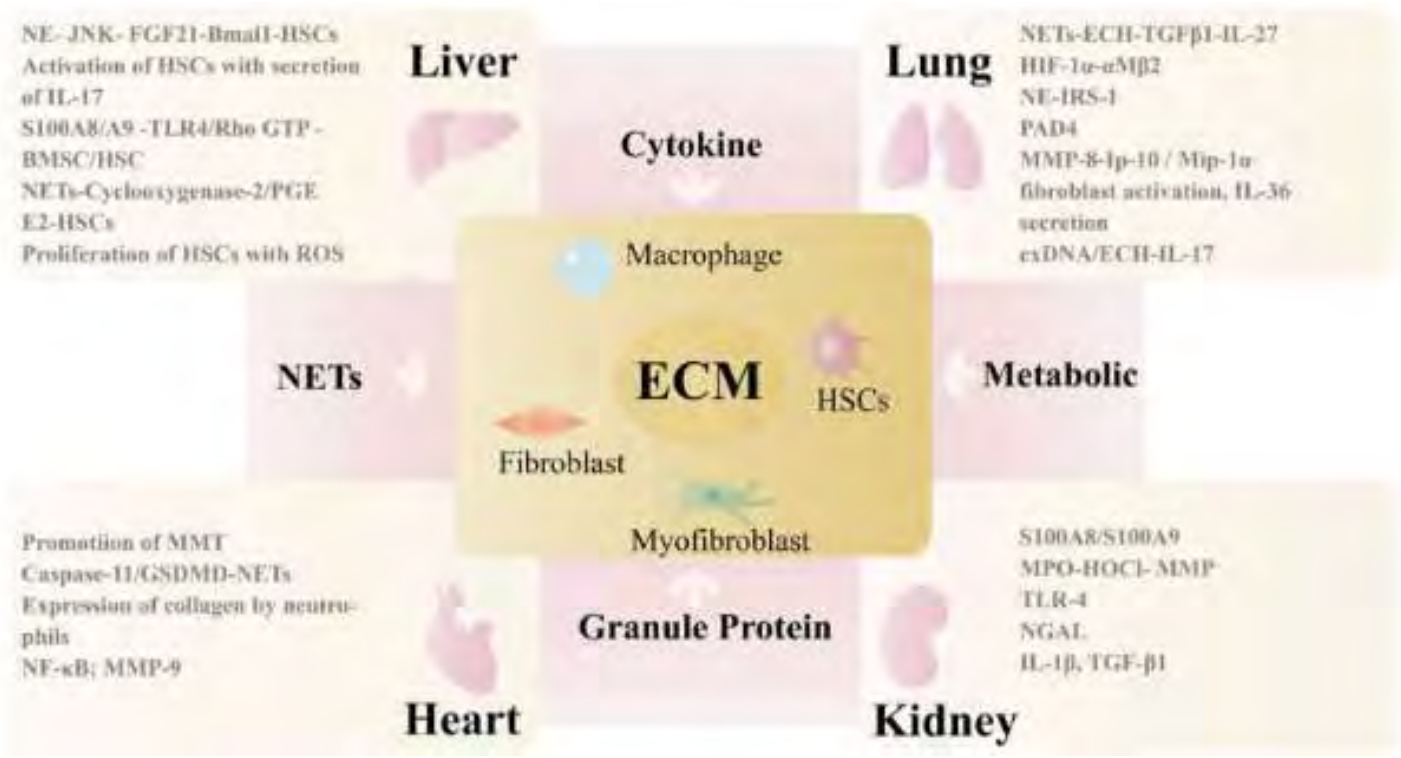


Figure 2. Cellular crosstalk driving kidney fibrosis, and potential intervention points. Proximal tubular epithelial cells (PTCs) are the major cellular component of the

- **SGLT2 Inhibítorok (Dapagliflozin, empagliflozin)**
- **Mineralocorticoid Antagonisták: Finerenone**
- **Új target: TRPC6** inhibitor és **TGF-β** blokkoló

Neutrofil sejtek és fibrosis



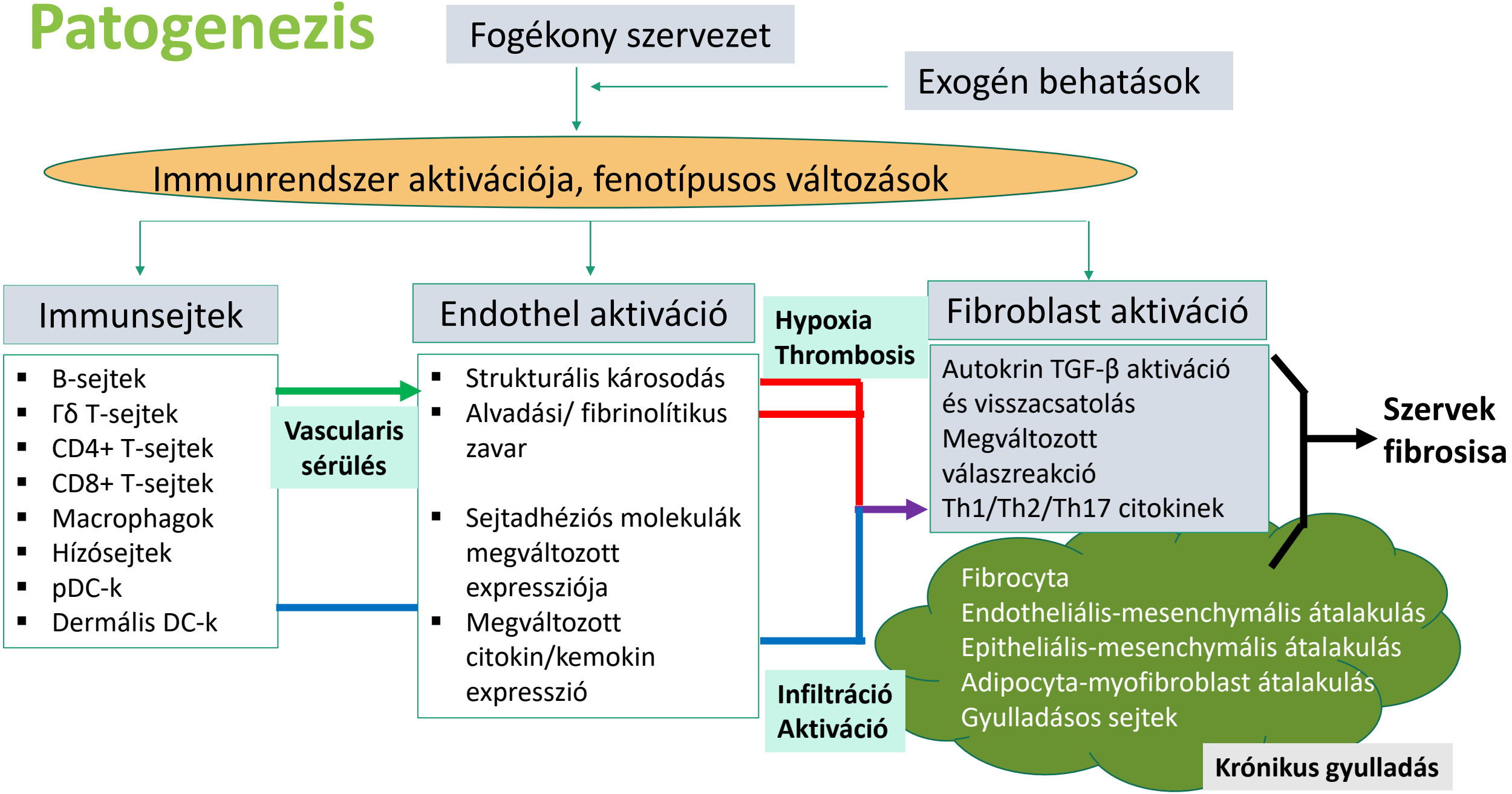


The FASEB Journal, 2025; 39:e70992

Szisztémás sclerosis

„scleroderma”: „sclero” (kemény) + „derma” (bőr)

Patogenezis



Raynaud tünet

Vazokonstrikció ↑

A simaizomsejtek α-2 adrenoreceptorok reaktivitása ↑

A digitalis artériák hideghatásra, vagy emocionális stresszre bekövetkező kóros válaszreakciója, fokozott vasokonstrikciója

Endothel sérülés

Sejtek közötti adhézió, tight junction fellazulása

Idegrostok (szimpatikus és szenzoros)

Simaizomsejtek

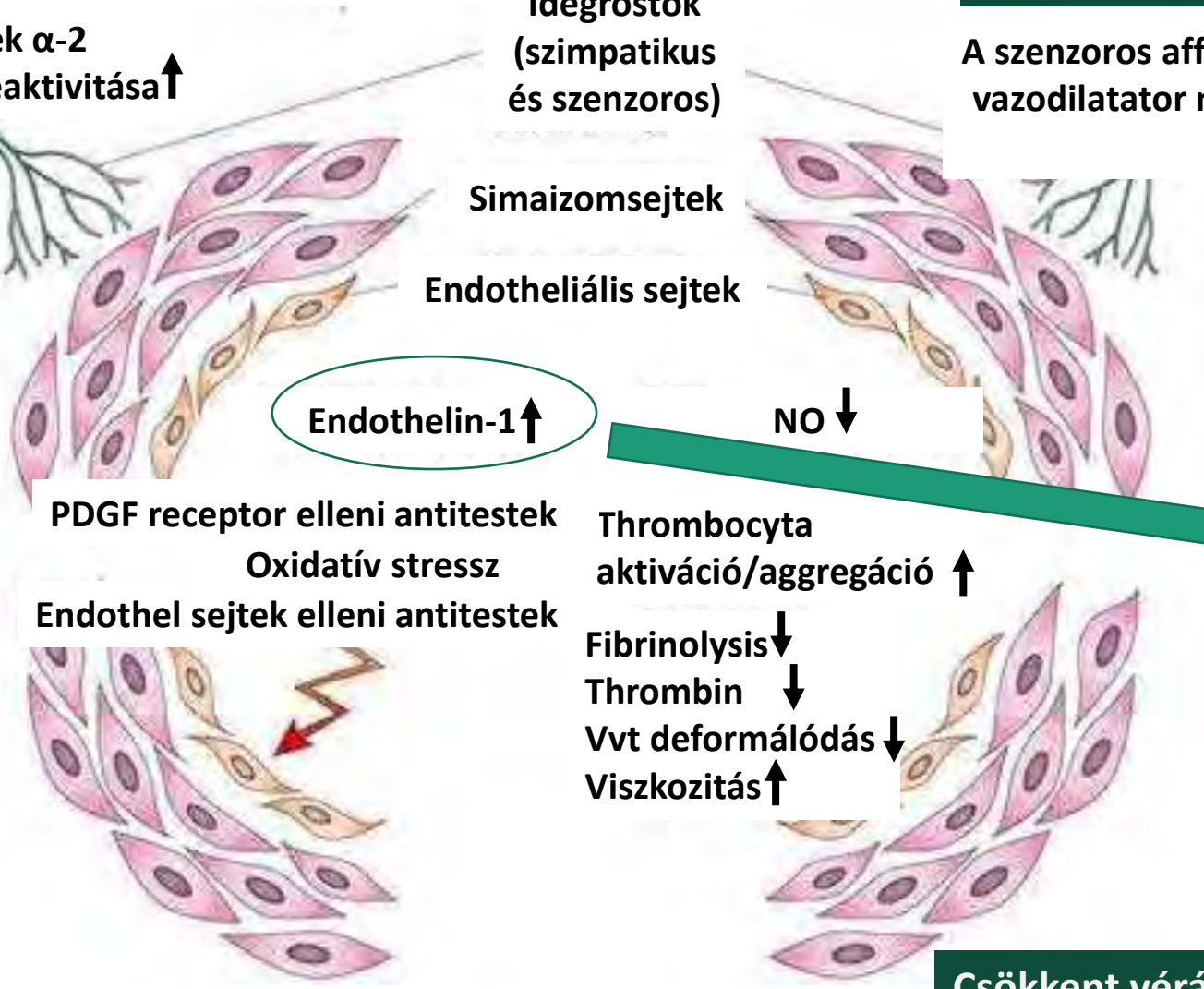
Endotheliális sejtek

Endothelin-1 ↑

PDGF receptor elleni antitestek

Oxidatív stressz

Endothel sejtek elleni antitestek



Vazodilatáció ↓

A szenzoros afferens rostokból származó vazodilatator neuropeptidek (pl. CGRP) szintje ↓

NO ↓

Thrombocyta aktiváció/aggregáció ↑

Fibrinolysis ↓

Thrombin ↓

Vvt deformálódás ↓

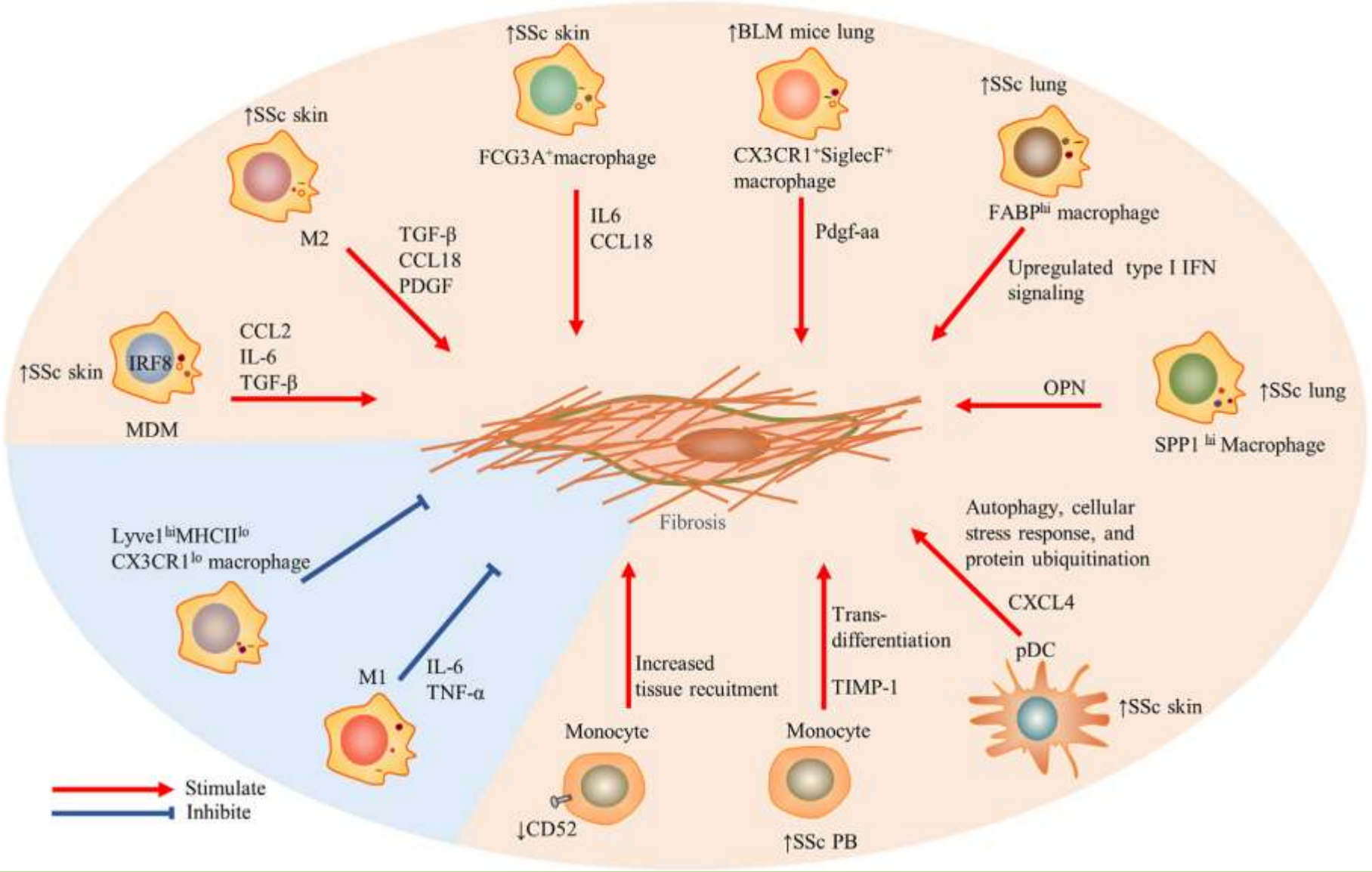
Viszkozitás ↑

Fibrosis

Csökkent véráramlás/ prokoaguláns állapot

Contributions of Immune Cells and Stromal Cells to the Pathogenesis of Systemic Sclerosis: Recent Insights

Bingying Dai et al. 2022. Front. Pharmacol. 13:826839.



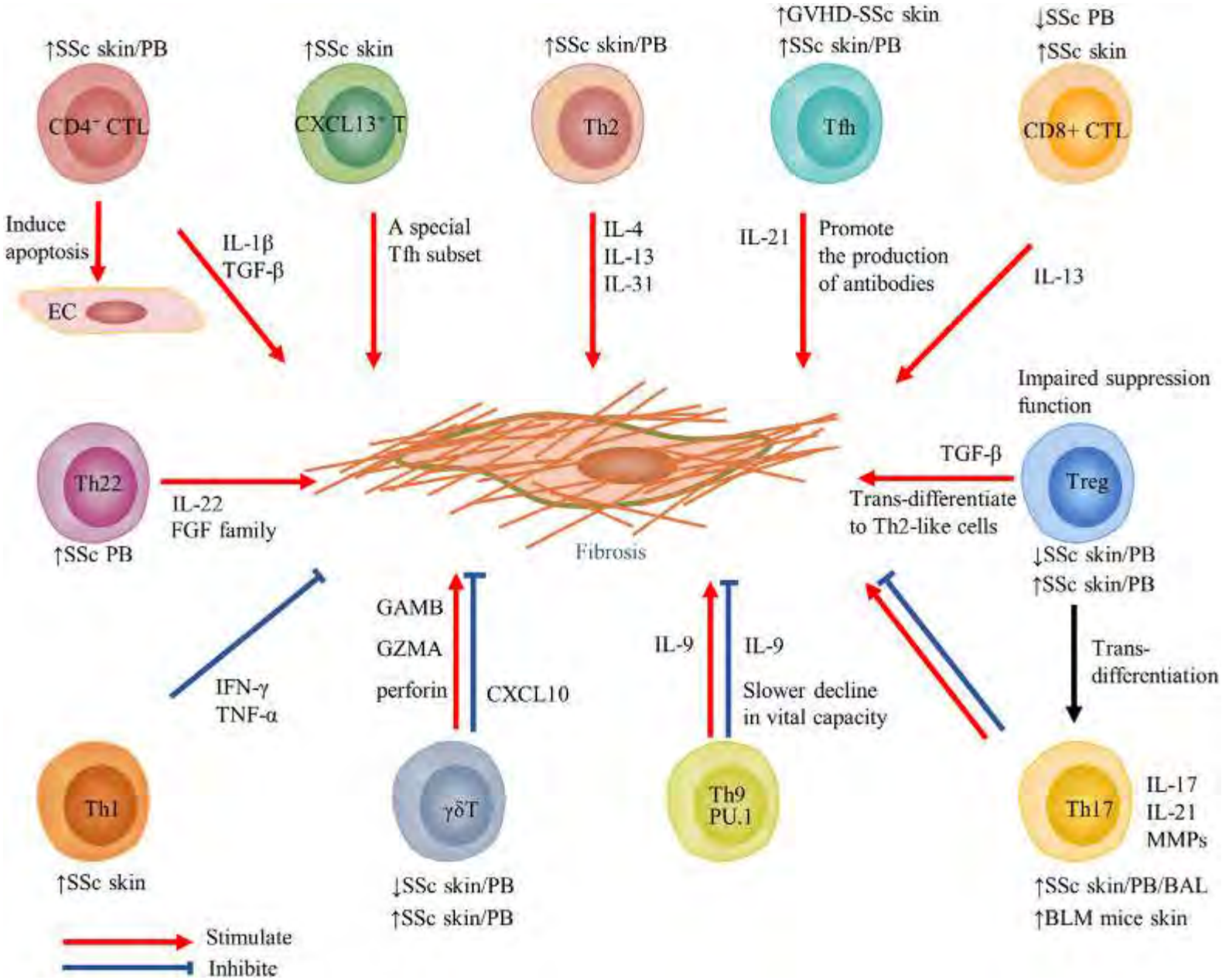
The role of innate immune cells including monocytes, macrophages, and dendritic cells in the fibrosis in SSc.

Contributions of Immune Cells and Stromal Cells to the Pathogenesis of Systemic Sclerosis: Recent Insights

Bingying Dai et al. 2022. Front. Pharmacol. 13:826839.

Adaptív immunitás

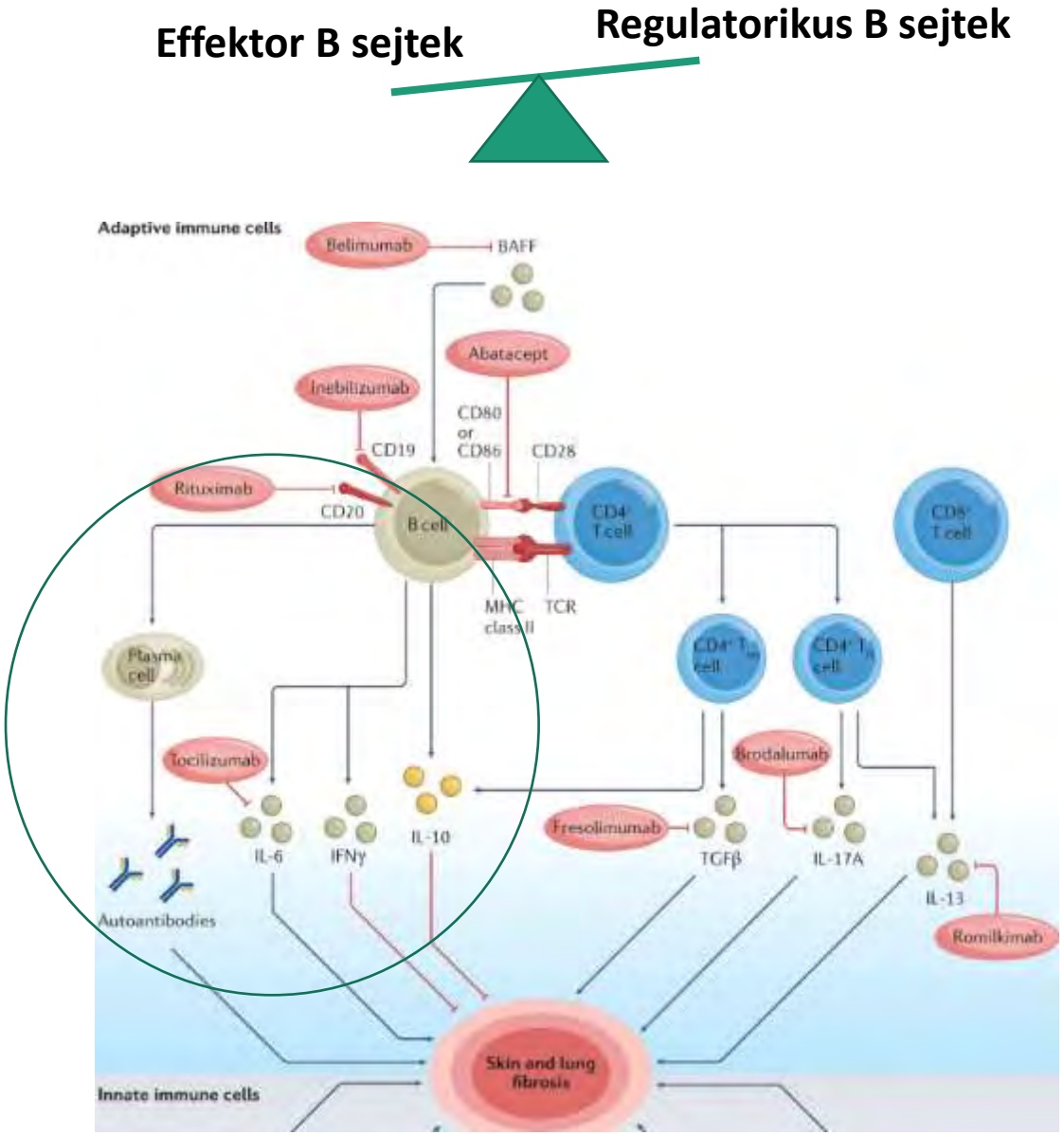
Contribution of T-cell subsets and their cytokines to fibrosis in SSc



Adaptív immunitás

B-sejtek:

- Antitest termelés, citokin szekréció
- IL-6, IFNγ, GM-CSF
- Breg sejtek száma és funkciója is csökken: IL-10
- BAFF: B-sejtek profibrotikus aktivitása nő, fokozódik a citokin szekréció
- Macrophagok M2 polarizációjában, T-sejtek, dendritikus sejtek aktivációjában is részt vesznek: innate-adaptív immunitás összeköttetés



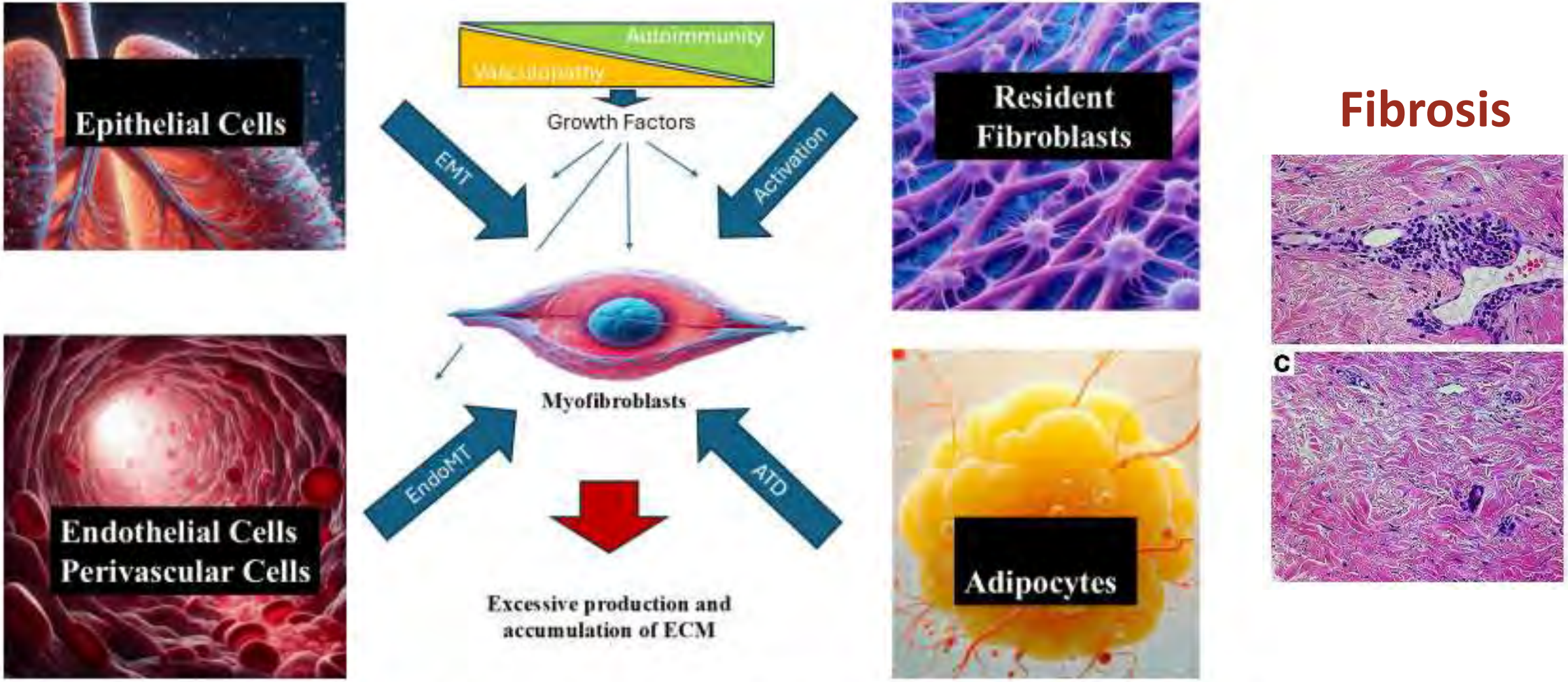
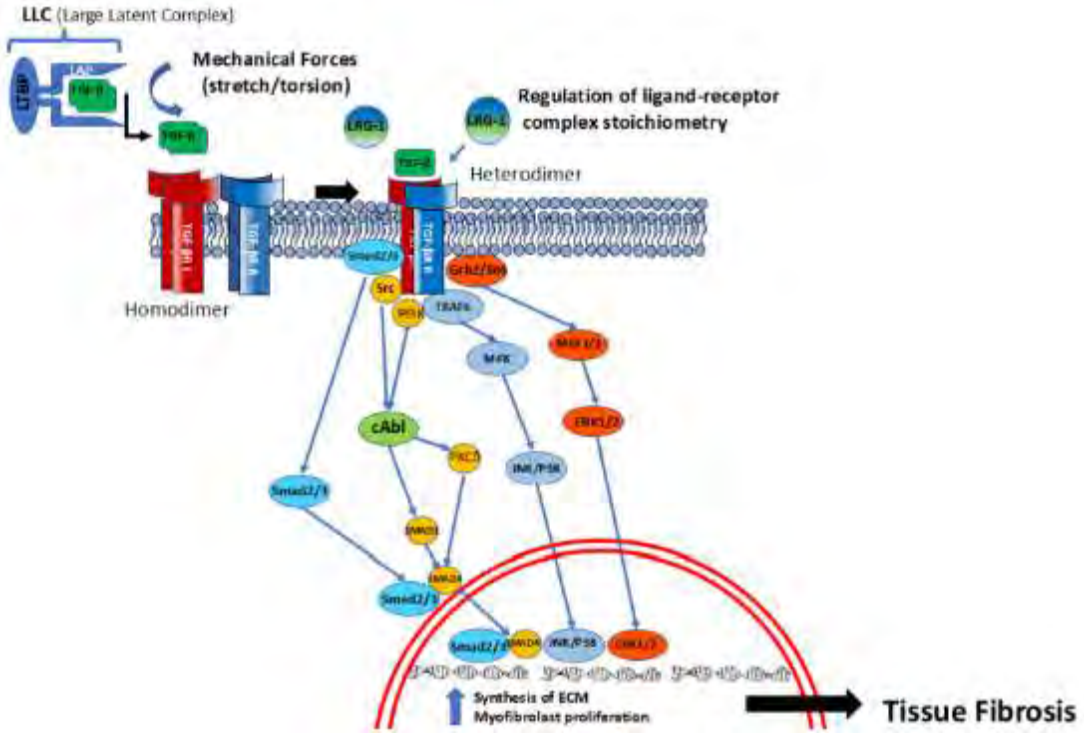


Figure 1. Pathophysiology of SSc. Early events, including endothelial cell dysfunction, vasculopathy,

Növekedési faktorok és fibrosis

TGF-β



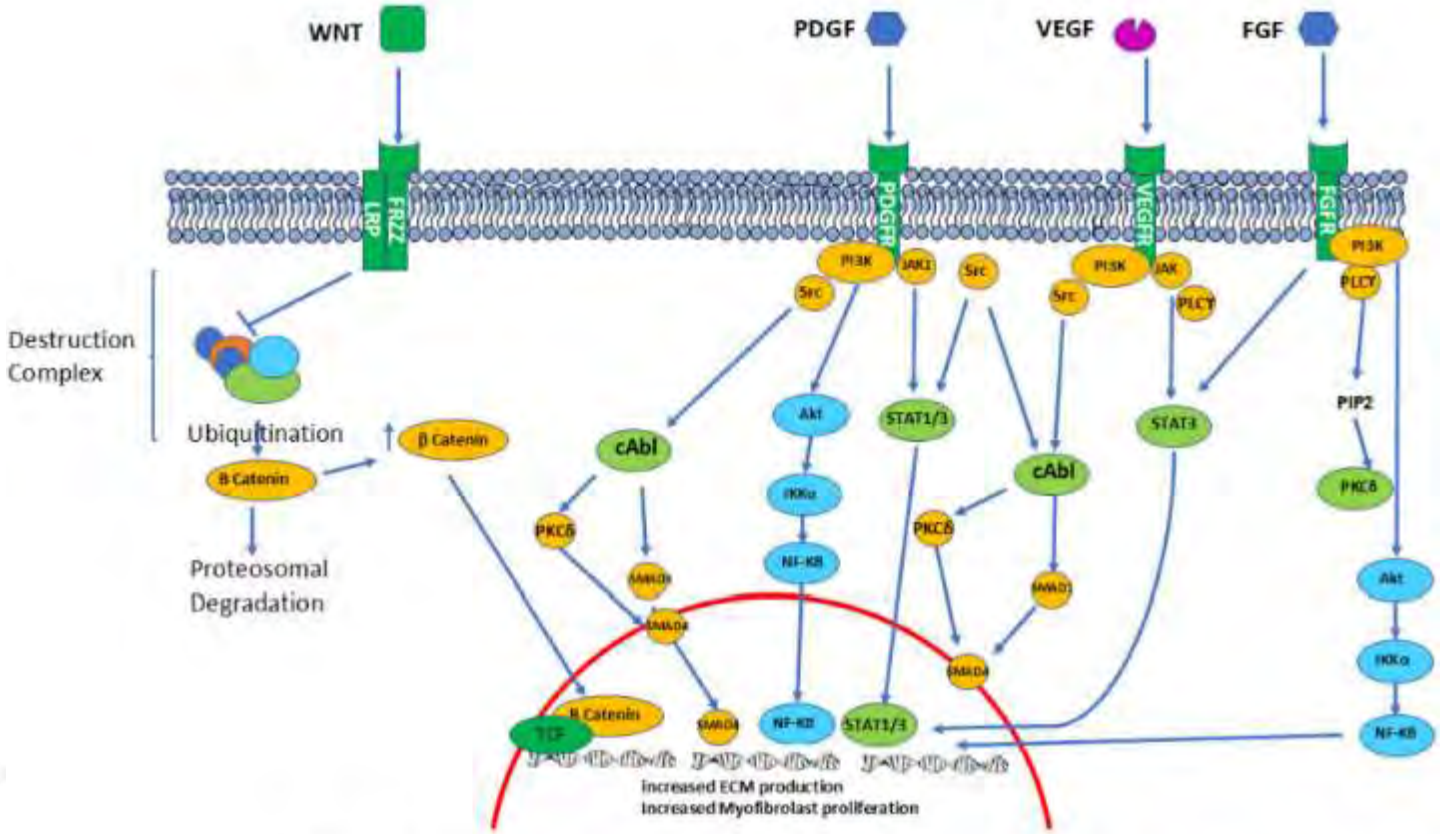
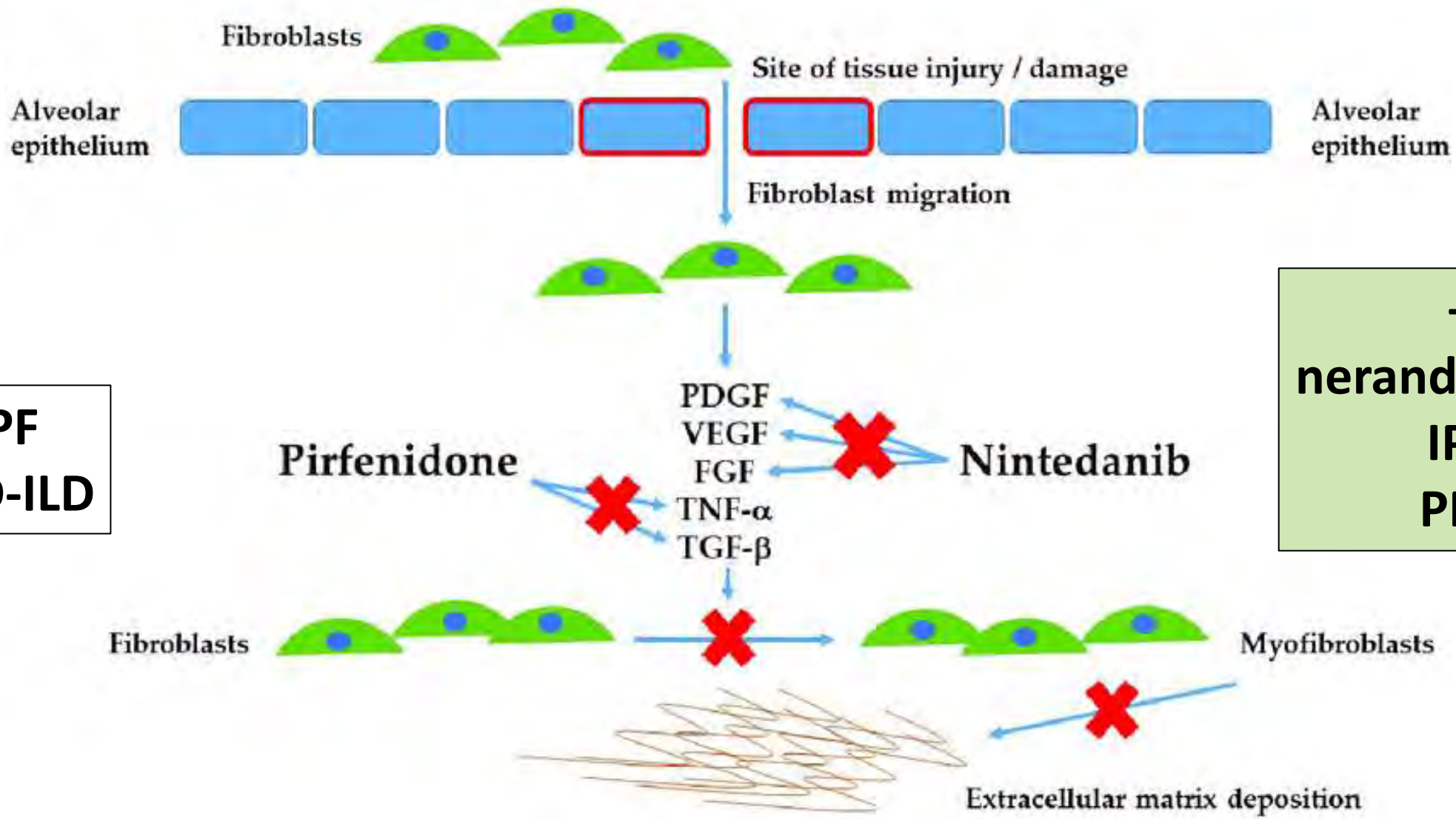


Figure 3. Intracellular pathways of selected pro-fibrotic molecules. Schematic intracellula

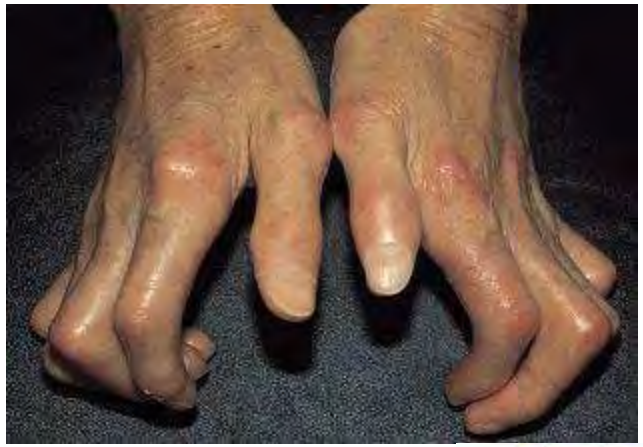


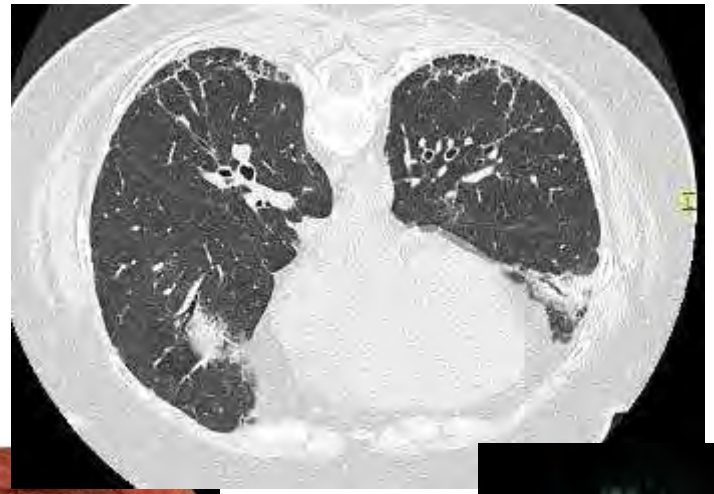
IPF
CTD-ILD

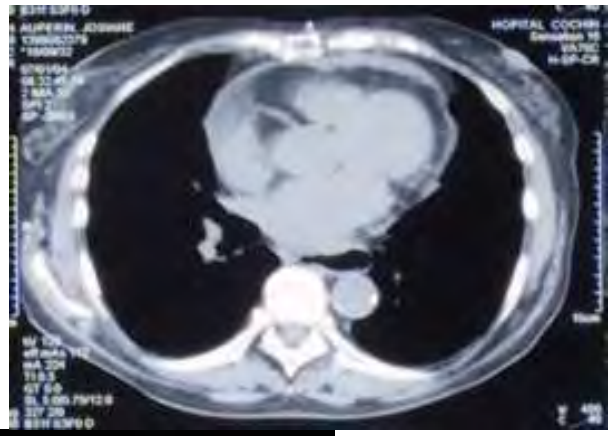
+
nerandomilast
IPF
PPF

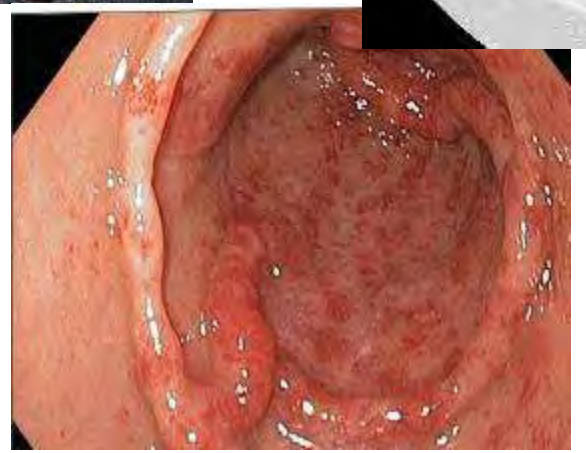
Int. J. Mol. Sci. 2025, 26, 9596

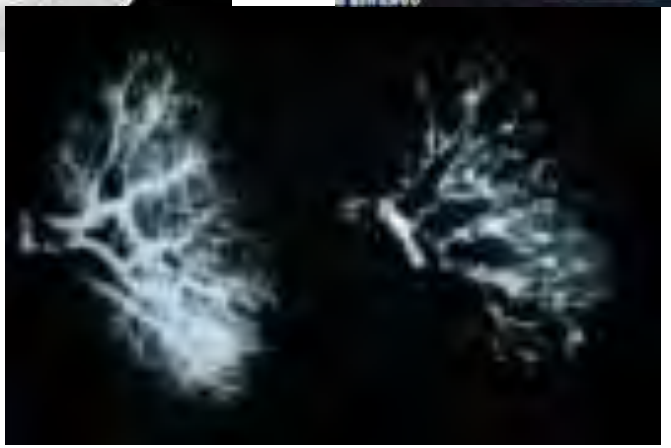
Szervi érintettségek pathogenezise





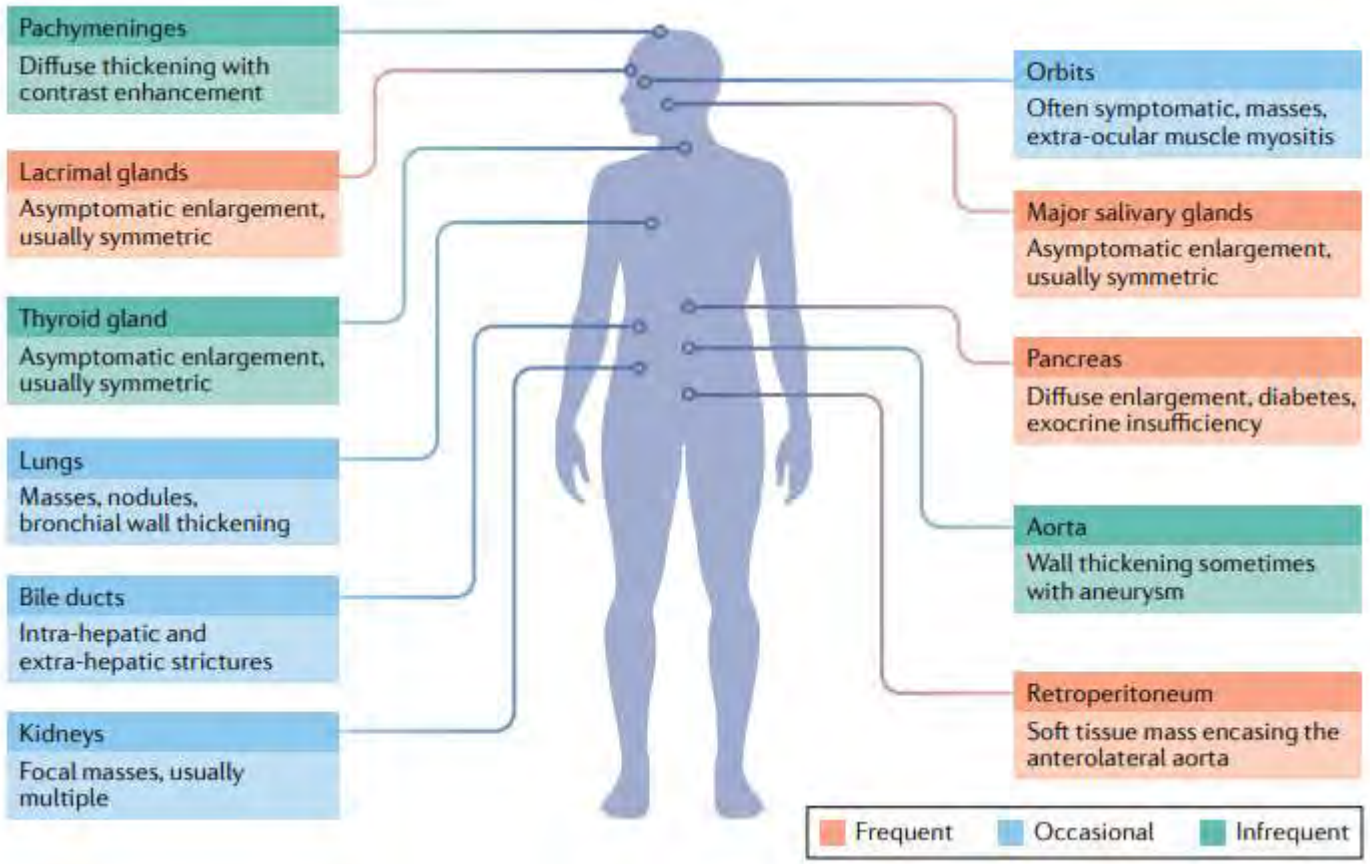


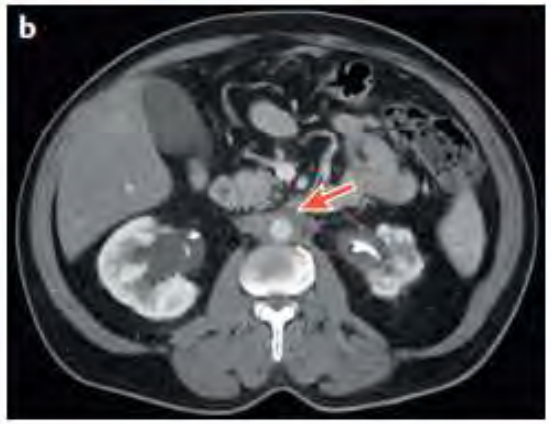


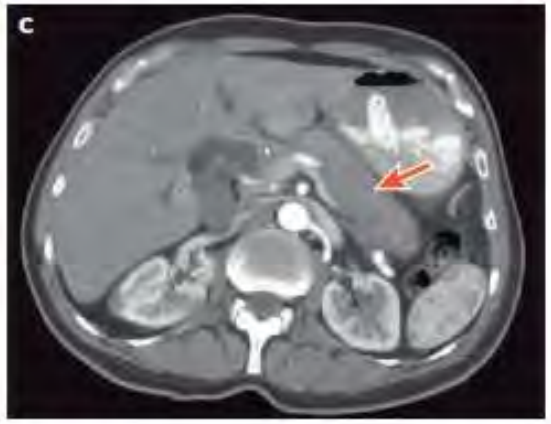


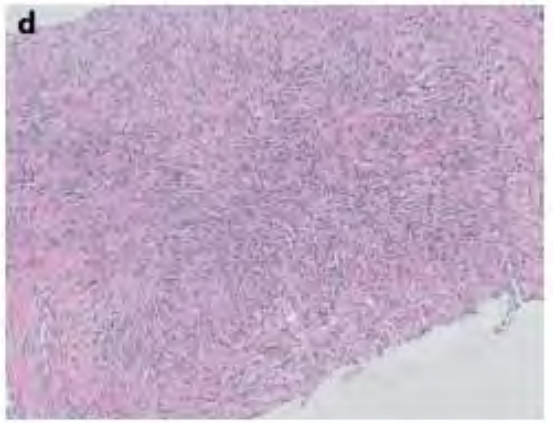
IgG4-related disease: an update on pathophysiology and implications for clinical care

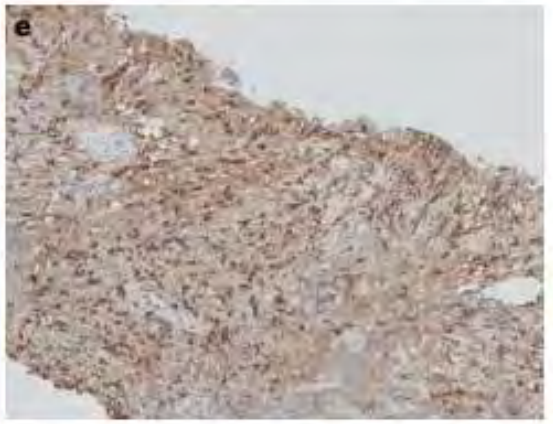
Cory A. Perugino[1,2] and John H. Stone[1] ✉







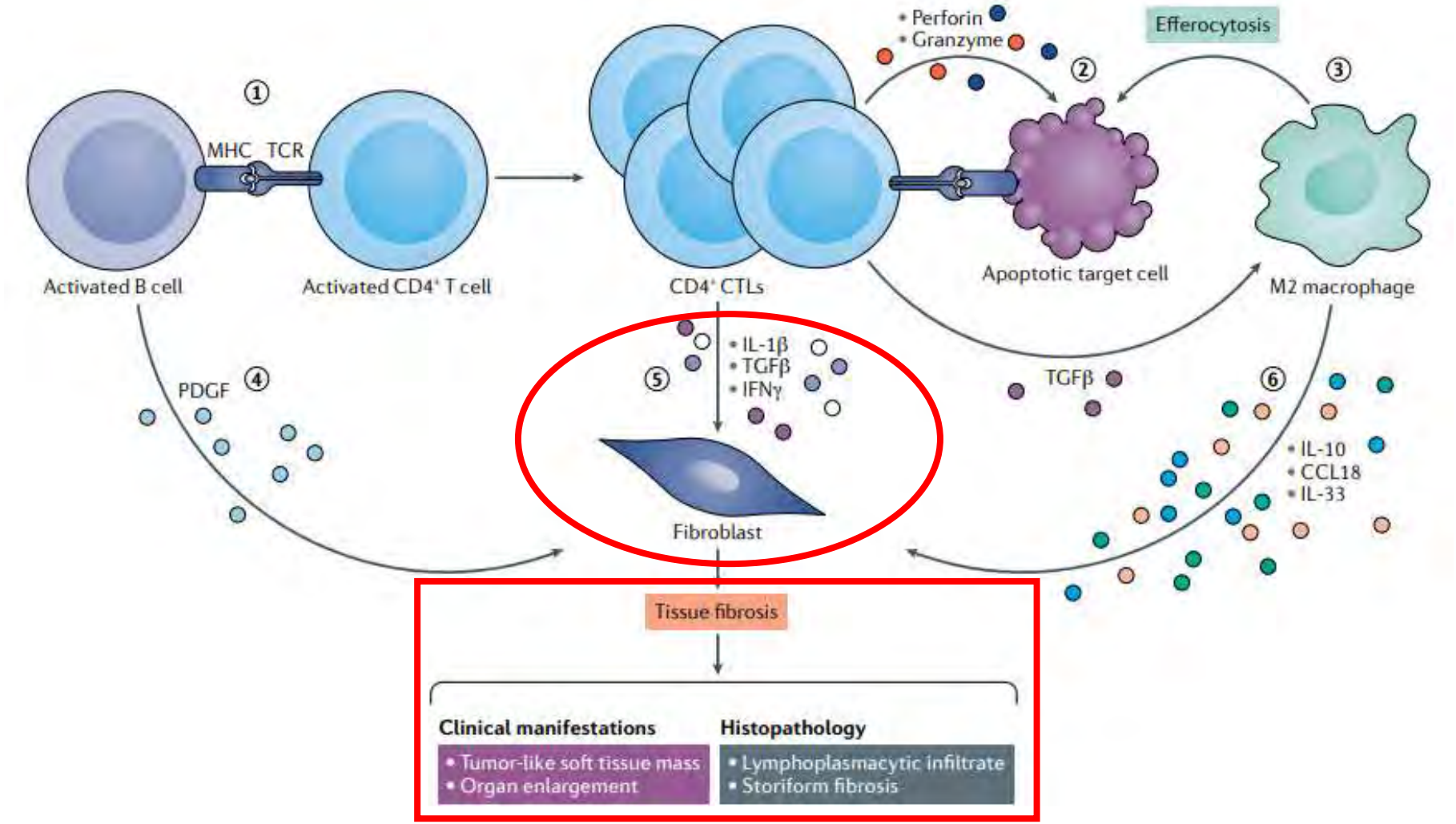




Nature Reviews Rheumatology **volume 16**, pages702–714 (2020)

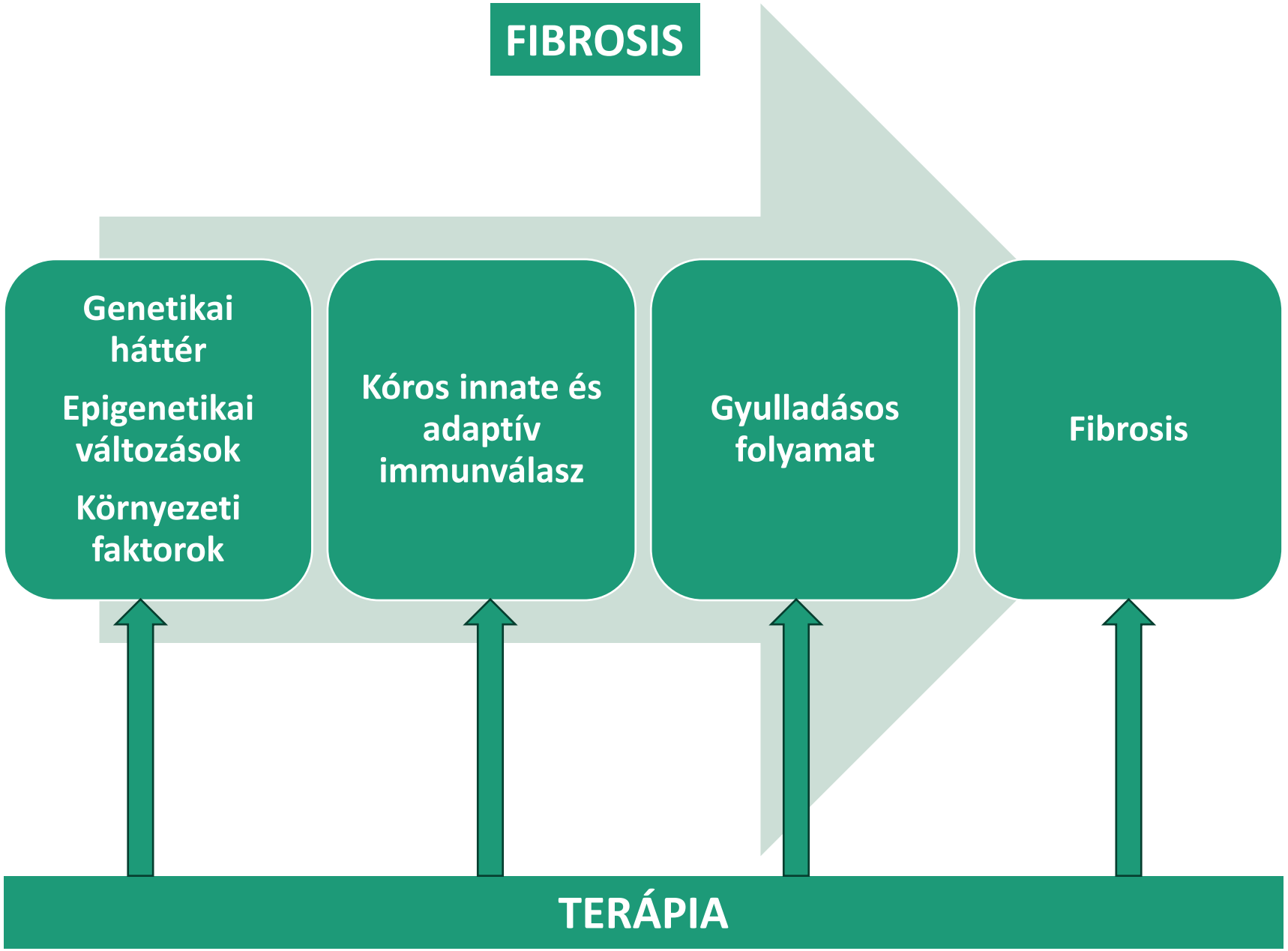
IgG4-related disease: an update on pathophysiology and implications for clinical care

Cory A. Perugino[1,2] and John H. Stone[1] ✉

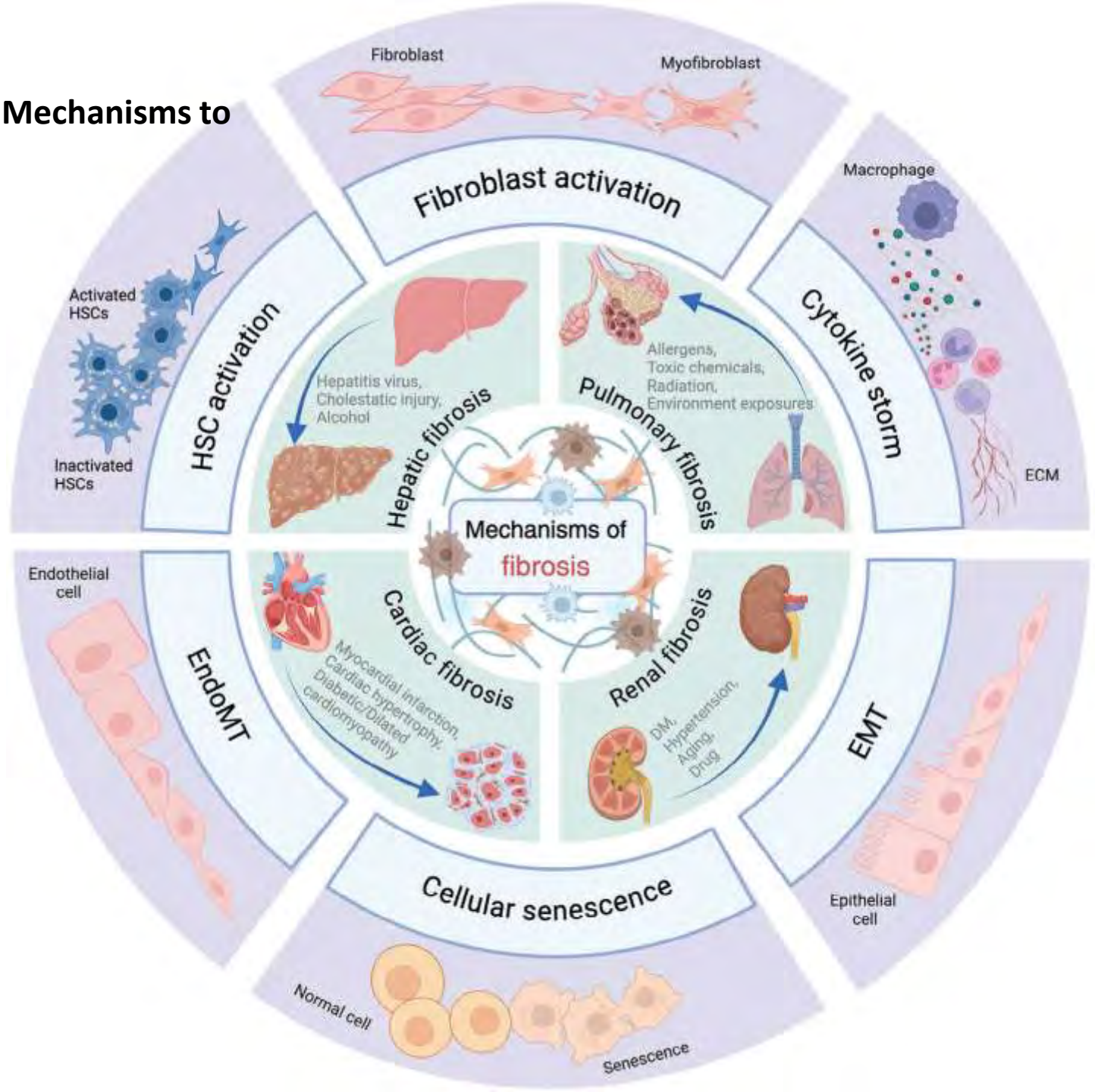


Nature Reviews Rheumatology **volume 16**, pages702–714 (2020)

Fibrosissal járó kórképek kezelése

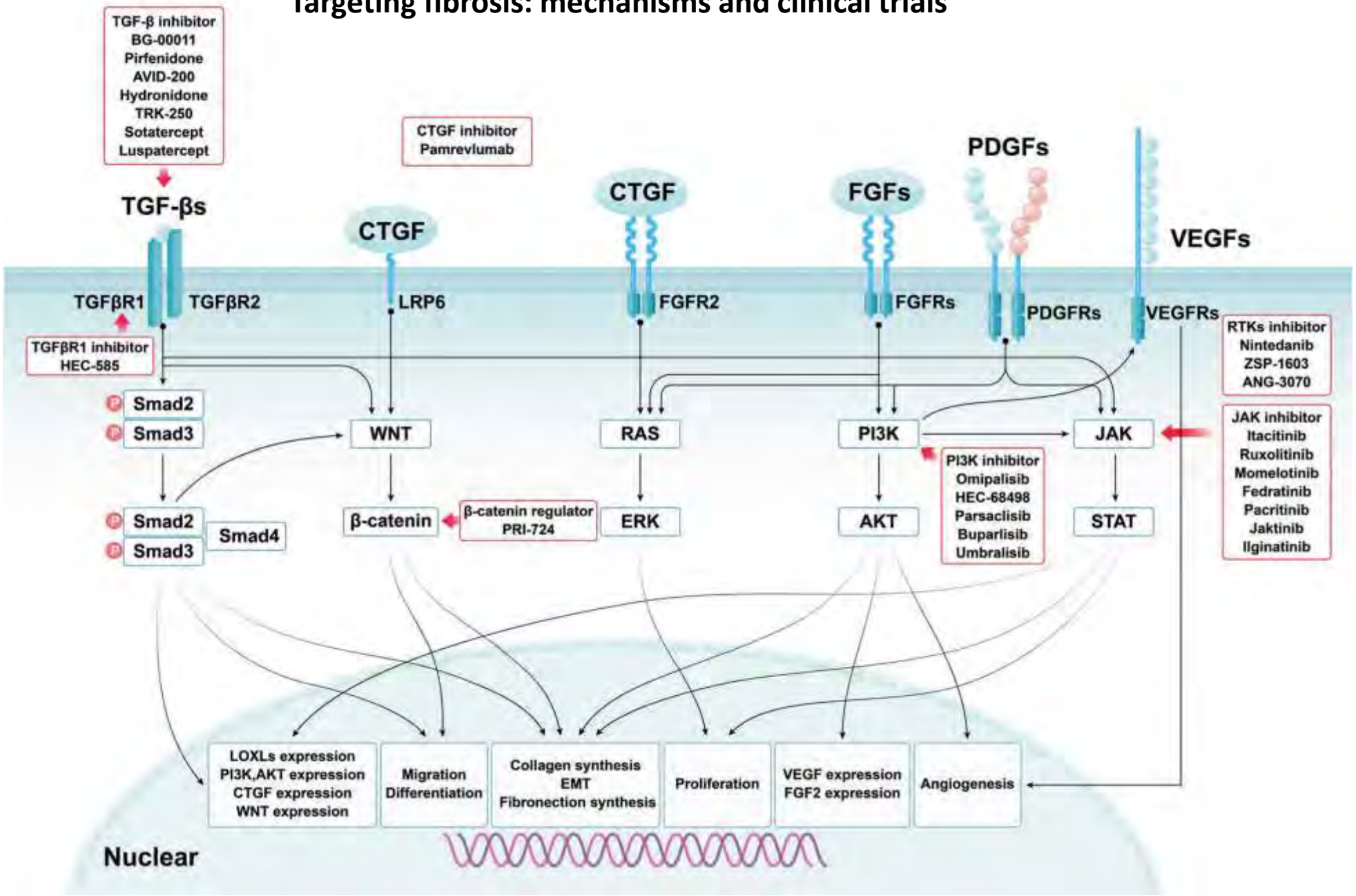

FIBROSIS
Genetikai háttér
Epigenetikai változások
Környezeti faktorok
Kóros innate és adaptív immunválasz
Gyulladásos folyamat
Fibrosis
TERÁPIA

Targeting Fibrosis: From Molecular Mechanisms to Advanced Therapies



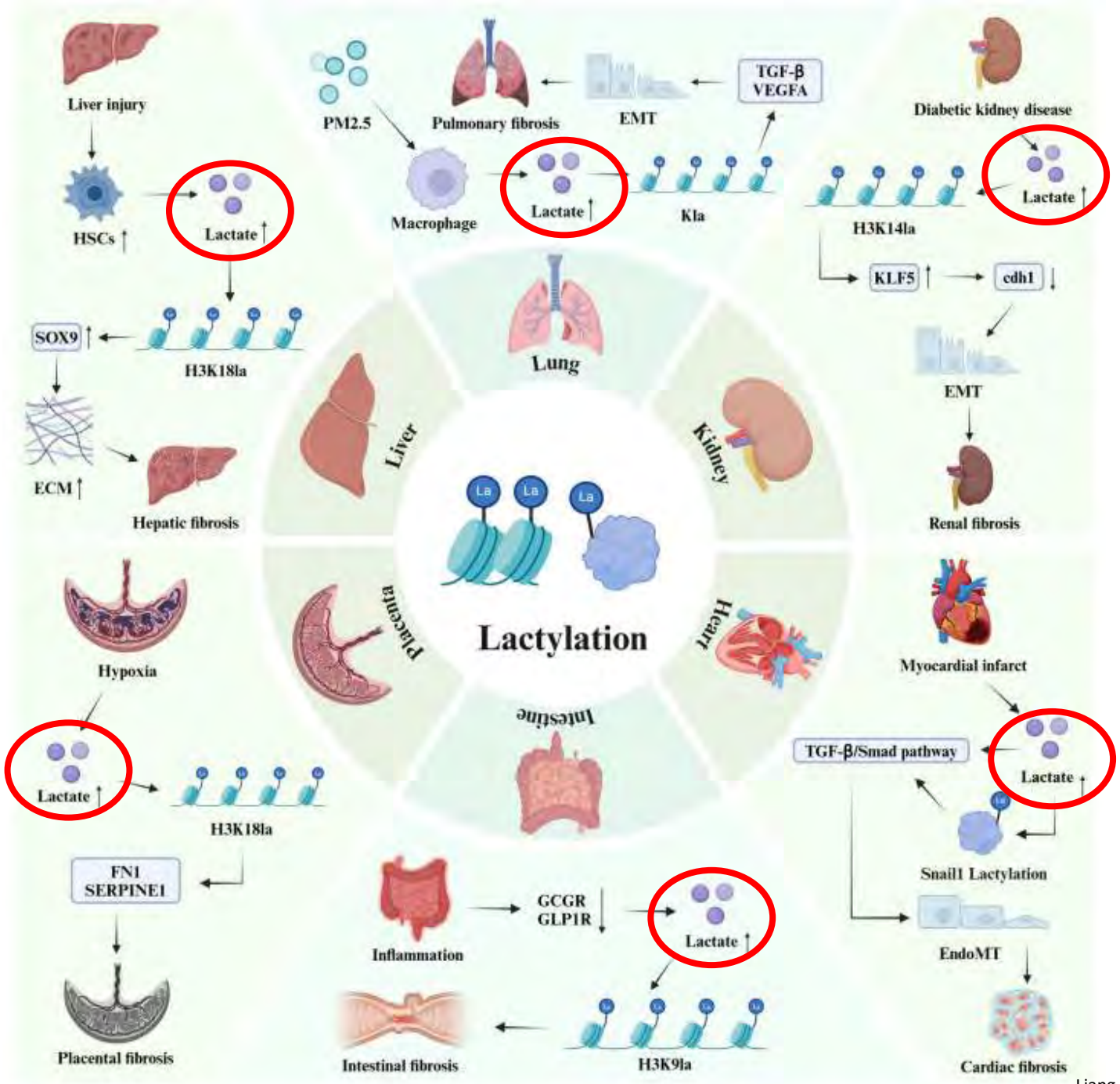
Adv. Sci. **2025**, *12*, 2410416

Targeting fibrosis: mechanisms and clinical trials



Zhao M et al. Signal Transduction and Targeted Therapy (2022) 7:206

Lactate and lactylation: novel perspectives on fibrosis pathogenesis and therapeutic directions



Liang et al. Journal of Translational Medicine (2025) 23:705

Fig. 3 Schematic diagram of the molecular mechanisms of lactylation modification in organ fibrosis. Emerging evidence highlights multiple Kla-related

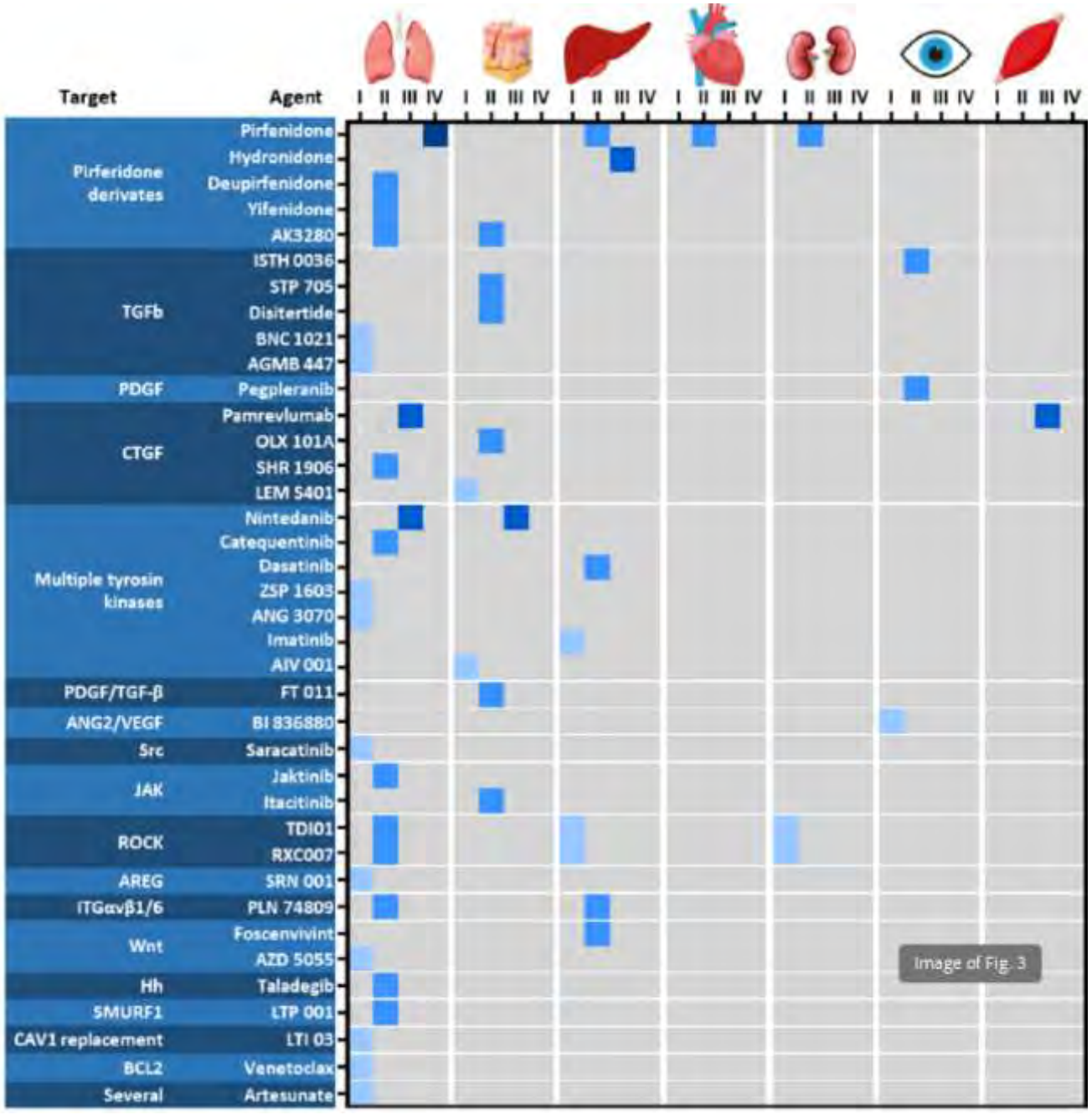
Senescence and tissue fibrosis: opportunities for therapeutic targeting

Trends in Molecular Medicine, December 2024, Vol. 30, No. 12

Table 1. Senescence in fibrosis *in vivo*

Target organ	Disease model	Senotherapeutic agent(s)	Outcomes	Refs
Cardiac fibrosis	Aged INK-ATTAC and C57BL/6J mice	ABT-263 (navitoclax)	Pharmacological or genetic clearance of senescent cells in mice alleviated myocardial hypertrophy and fibrosis	[93]
	Ischemia reperfusion model in C57BL/6J mice	ABT-263 (navitoclax)	Navitoclax reduced senescence and improved cardiac function by attenuating the profibrotic SASP, reducing scar, and enabling increased angiogenesis	[94]
	Human cardiac fibrosis on a chip model	Quercetin, dasatinib	The senolytic drugs led to an improvement in contractile function, reduced passive tension, and downregulated senescence-related gene expression in the tissue	[95]
Renal fibrosis	Renal artery stenosis in INK-ATTAC mice	Quercetin, dasatinib	Both p16-specific and quercetin–dasatinib improved renal function and structure	[96]
	C57BL/6J mice on high fat diet	Quercetin	Improved renal function indices and alleviated fibrosis	[97]
	Aged and/or kidney injury models in C57BL/6J mice	ABT-263 (navitoclax)	ABT-263 treatment resulted in improved functional recovery and reduced fibrosis	[44]
	Lupus nephritis in MRL/lpr mice	Fisetin	Fisetin treatment attenuated kidney fibrosis, reduced SASP expression, and increased tubular epithelial cell proliferation	[98]
Lung fibrosis	Bleomycin lung fibrosis in INK-ATTAC mice	Quercetin, dasatinib	Both p16-specific and quercetin–dasatinib improved renal function and structure	[93]
	Ex vivo fibrotic 3D lung tissue	Quercetin, dasatinib	Pharmacological treatment significantly eliminated senescent markers and the SASP	[99]
	Bleomycin lung fibrosis in C57BL/6J mice	Nintedanib	Nintedanib suppressed senescent cell survival through the JAK2/STAT3 signaling pathway in the lung fibrosis model	[100]
	Intratracheal γ-irradiated IMR90 cells in mice	Digoxin	Digoxin effectively eliminated senescence-induced lung fibrosis	[101]
	Bleomycin and crystalline silica-induced lung fibrosis in mice	ABT-263 (navitoclax)	ABT-263 induced fibroblast apoptosis, decreased fibroblast numbers, and reduced fibrosis	[67,102]
	Bleomycin-induced lung fibrosis in mice	Rapamycin	Rapamycin inhibited pulmonary fibrosis and epithelial–mesenchymal transition in mice	[103]
	Radiation-induced lung fibrosis in C57BL/6 mice	FOXO4-DRI	FOXO4-DRI alleviated pulmonary fibrosis by targeting senescence-like fibroblasts *in vivo*	[104]
	Senescent IMR90 cells-induced lung fibrosis in mice	ABT-263 (navitoclax)	Navitoclax significantly reduced collagen content in fibrotic lungs, comparable with the effect of nintedanib and pirfenidone	[105]
Liver fibrosis	CCl_4- or NASH-induced liver fibrosis in C57BL/6N mice	uPAR-specific CAR T cells	CAR T cells efficiently eliminated senescent cells, reduced fibrosis, and improved liver function in mice	[98]

Új fibrosisgátló kezelési lehetőségek



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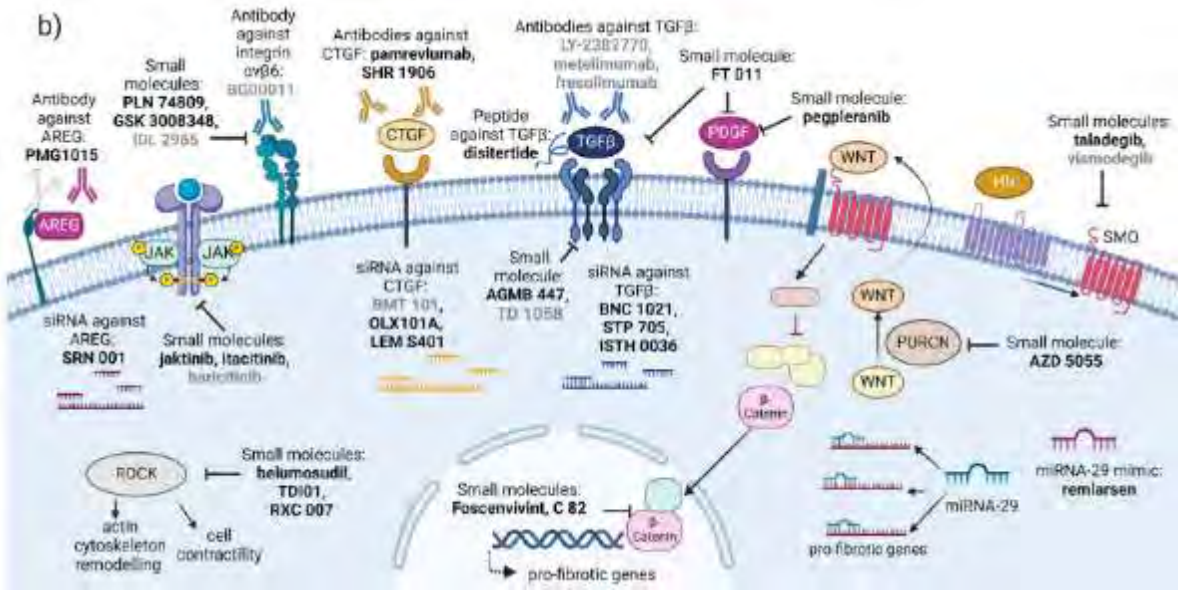
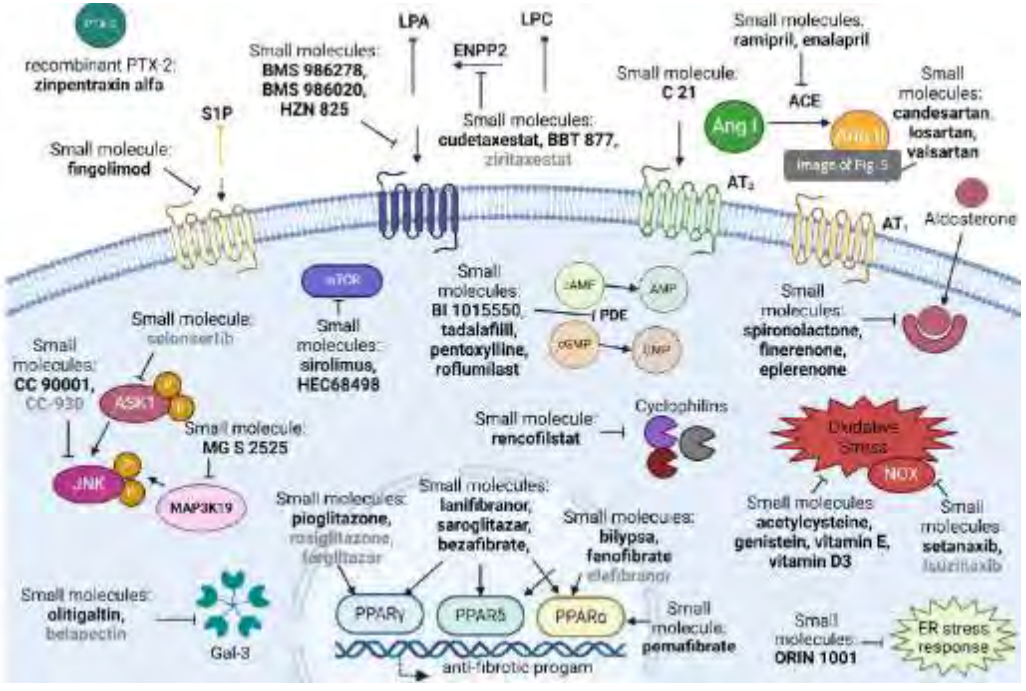
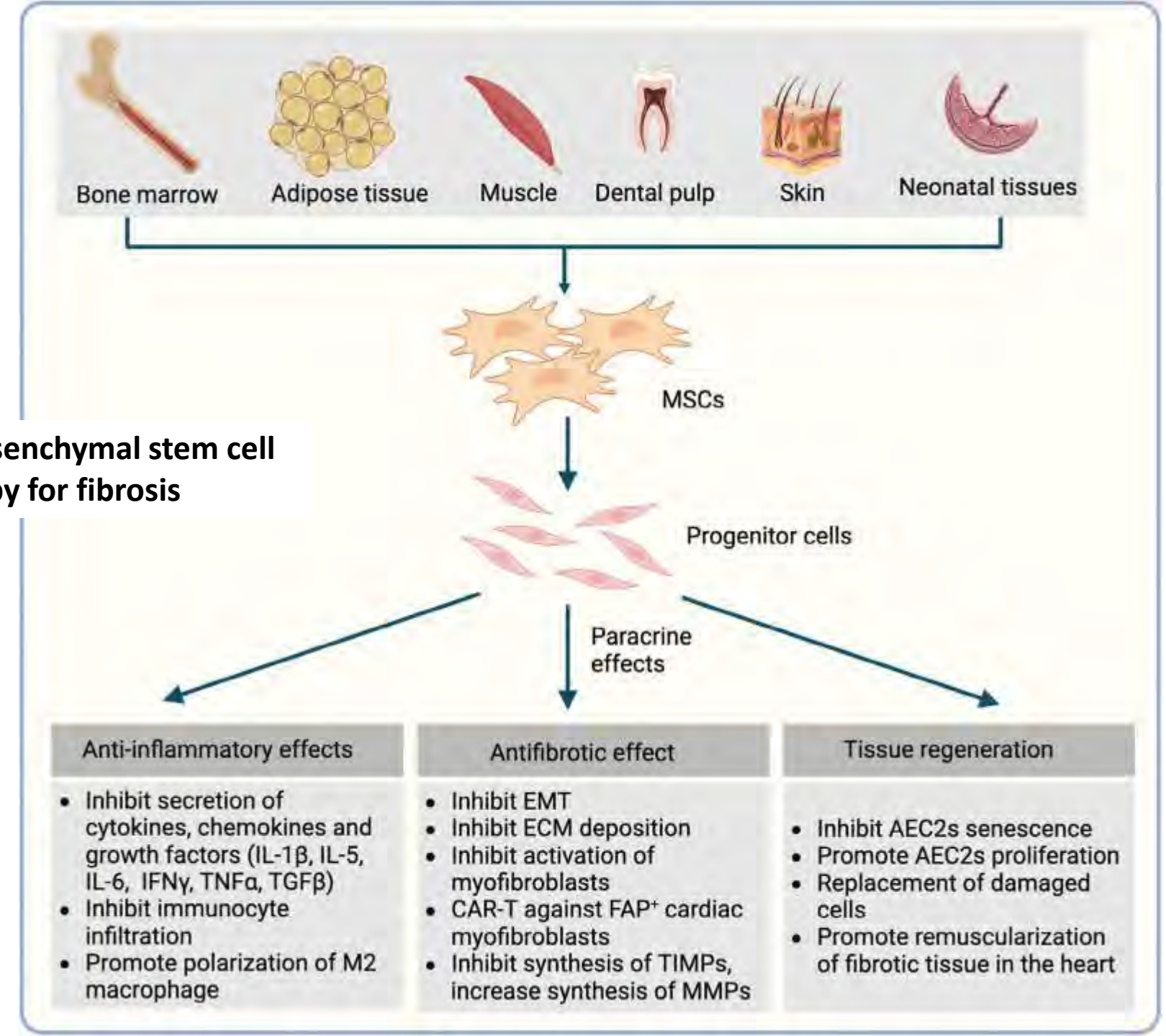




Mechanisms of mesenchymal stem cell (MSC)-based therapy for fibrosis



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ORIGINAL RESEARCH

CAR-Macrophage Therapy Alleviates Myocardial Ischemia-Reperfusion Injury

Jiawan Wang,* Heng Du,* Wanrun Xie,* Jinmiao Bi,* Hao Zhang, Xu Liu, Yuhan Wang, Shaolong Zhang, Anhua Lei, Chuting He, Hailong Yuan, Jiahe Zhang, Yujing Li, Pengfei Xu, Siqi Liu, Yanan Zhou, Jianghua Shen, Jingdong Wu, Yihong Cai, Chaofan Yang, Zeya Li, Yingxin Liang, Yang Zhao, Jin Zhang, Moshi Song

Circulation Research. 2024;135:1161–1174

Cell

Article

Allogeneic CD19-targeted CAR-T therapy in patients with severe myositis and systemic sclerosis

Cell 187, 4890–4904, September 5, 2024

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