



HRONISKU BRŪČU RAKSTUROJOŠIE IEKAISUMA MARĶIERI

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PROBLEMĀTIKA

- Diabēta pacientu skaits Eiropā:
 - Šodien: ~ 60 miljoni
 - 2030. gadā: ~ 72 miljoni
- Diabēta pacientu skaits Latvijā:
 - Šodien: ~ 95' 700
 - 6,17 % no populācijas
- Diabētiskā neiropātija ~ 50% pacientu
- Venozās čūlas ir iemesls ~85% amputāciju diabēta pacientiem
- Rietumeiropas valstīs čūlu ārstēšanai patērē 1-2% kopējā veselības aprūpes budžeta.



PROBLEMĀTIKA

Baktērijas

“Anti-microbial” peptīdi

Imūnšūnas

Endopeptidāzes

Citokīni



PROBLEMĀTIKA

<i>Cytokine^a</i>	<i>Initial level (range)</i>
Serum	
proMMP9, % std ^b	51.3 (7.2-449.9)
proMMP2, % std ^b	28.7 (0-114.7)
VEGF, pg/mL	165 (21.2-1315.0)
Wound fluid	
proMMP9, % std ^b	280.1 (33.4-829.1)
proMMP2, % std ^b	21.1 (2.7-193.4)
IL1 β , pg/mL	17,877 (864-85,848)
TNF α , pg/mL	767 (92-26,160)
BFGF, pg/mL	228 (65-1370)
VEGF, pg/mL	2950 (130-18580)
TGF β ₁ , pg/mL	114 (33-771)

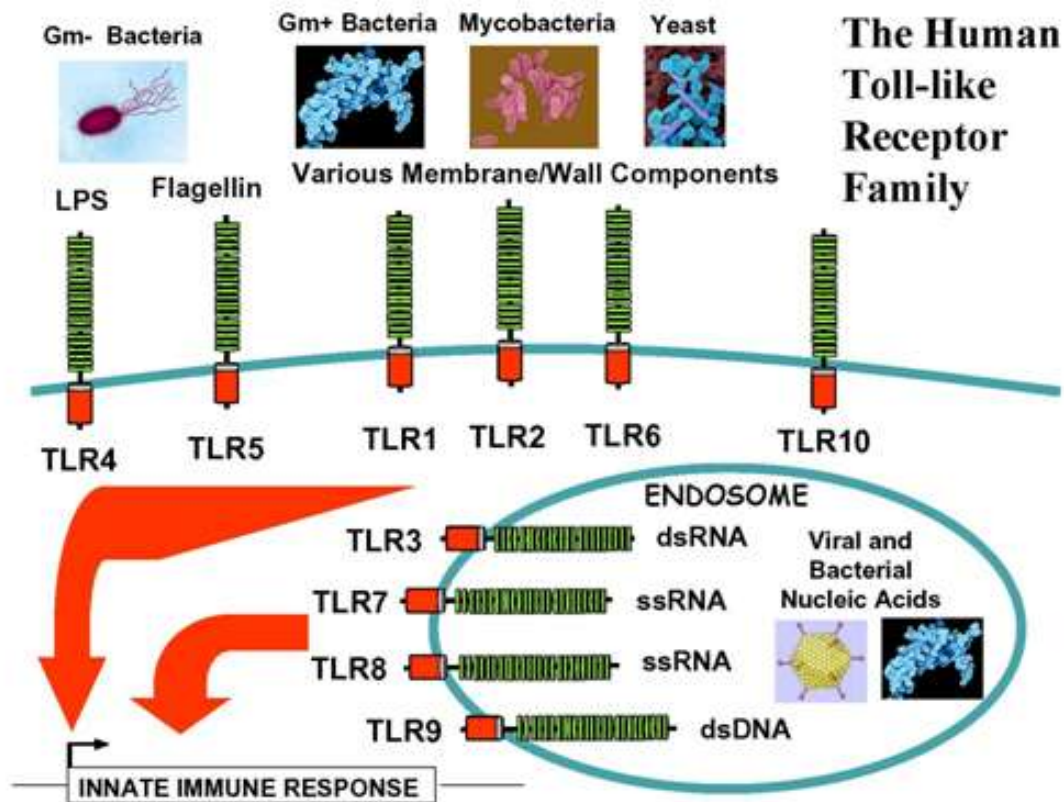
^aSee Table I for abbreviation expansions.

^bMMP concentrations expressed as a percentage of an MMP2 standard sample used for all assays.

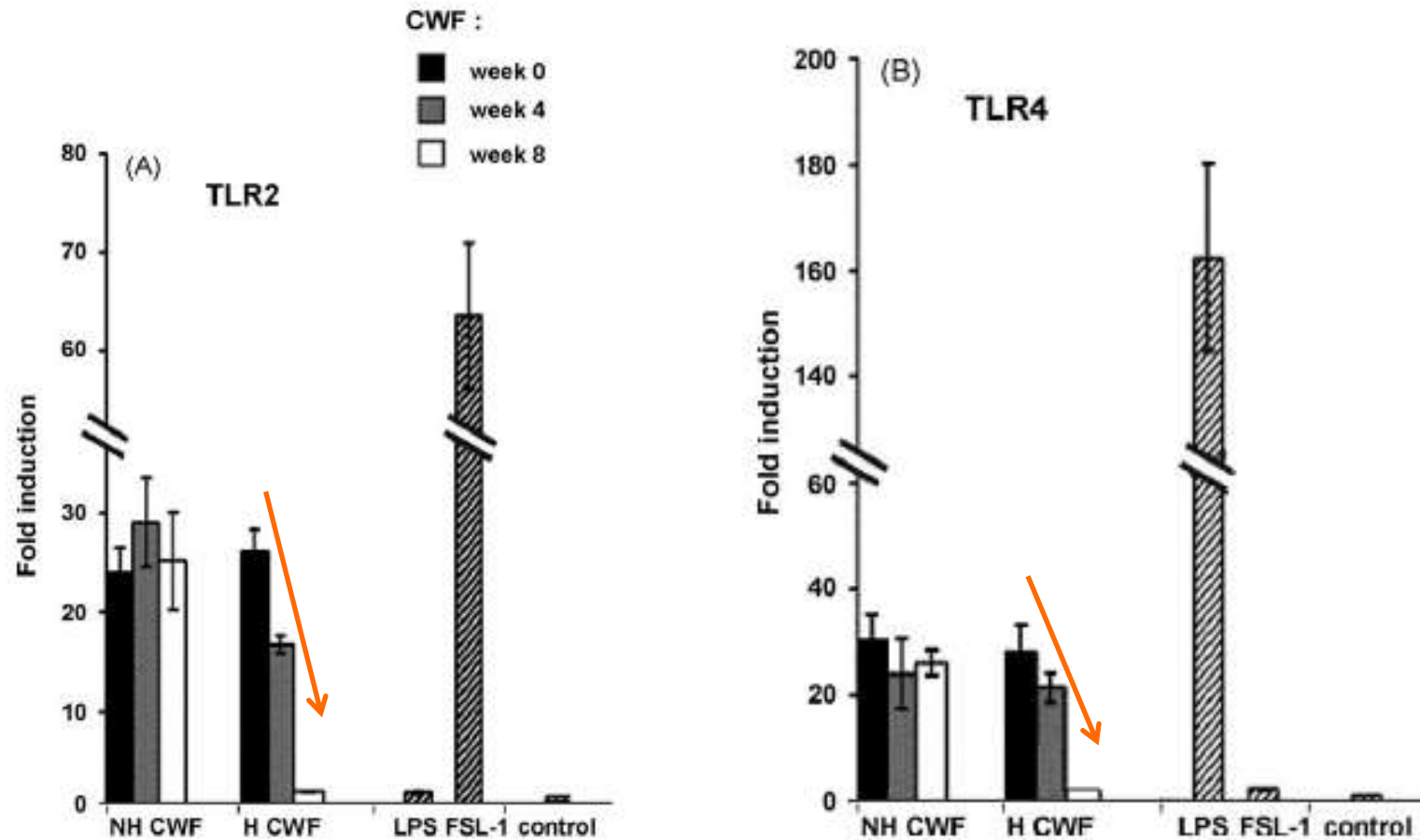


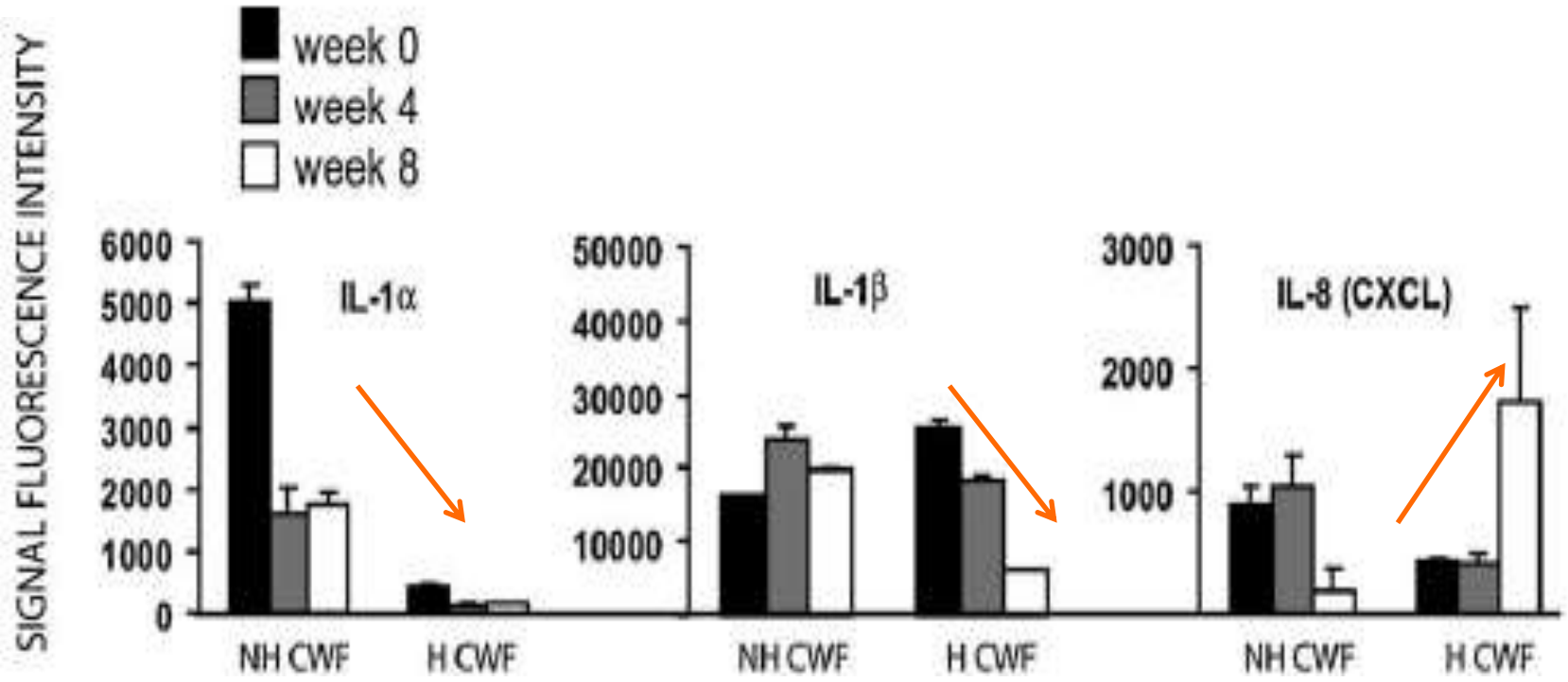
BAKTĒRIJAS

Gram +	Gram -
Staphylococcus aureus	Pseudomonas aeruginosa
Enterococcus	Esherichia coli
Diphtheroids	

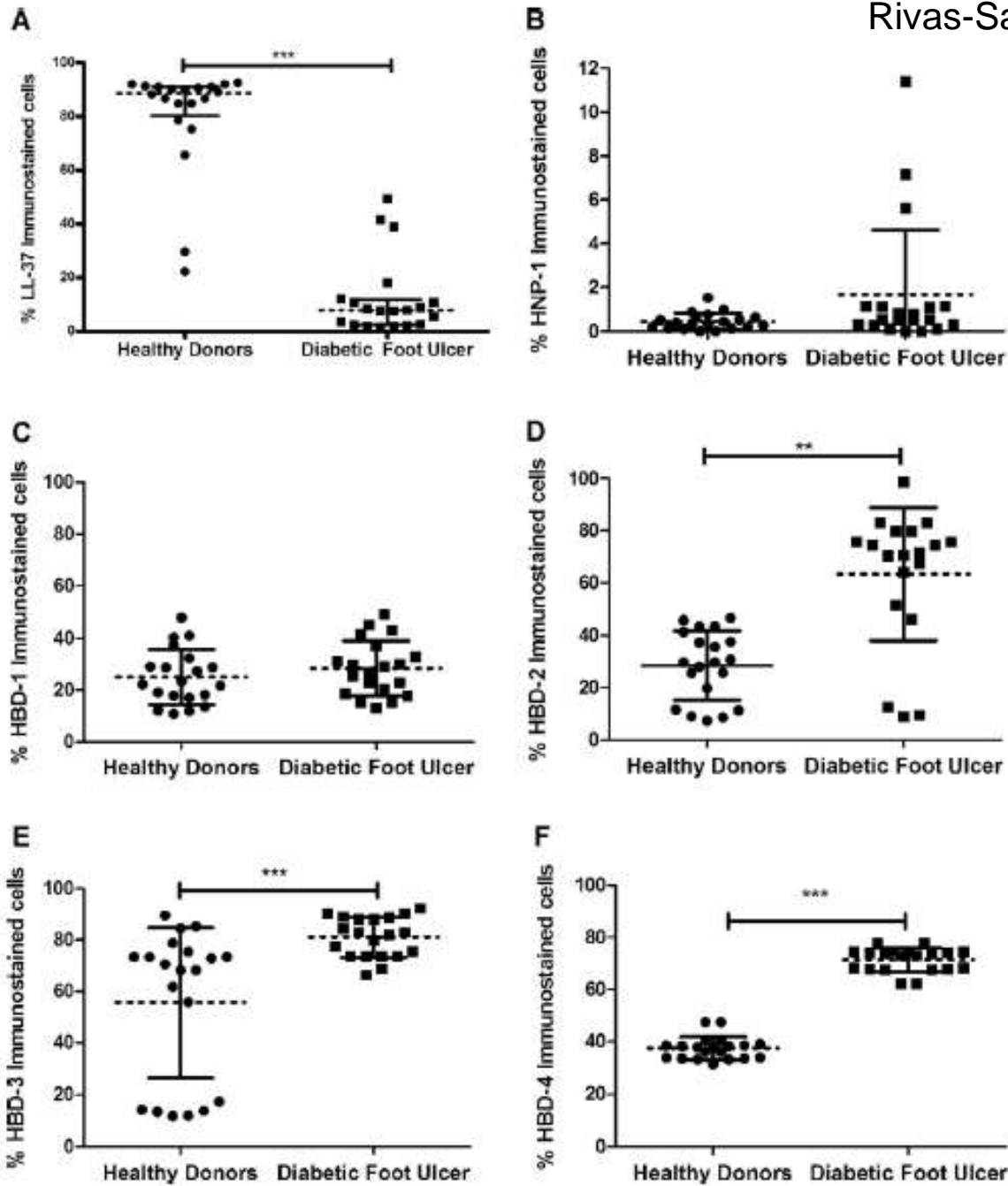


MONOCĪTU STIMULĀCIJA AR HRONISKU BRŪČU EKSDUDĀTU



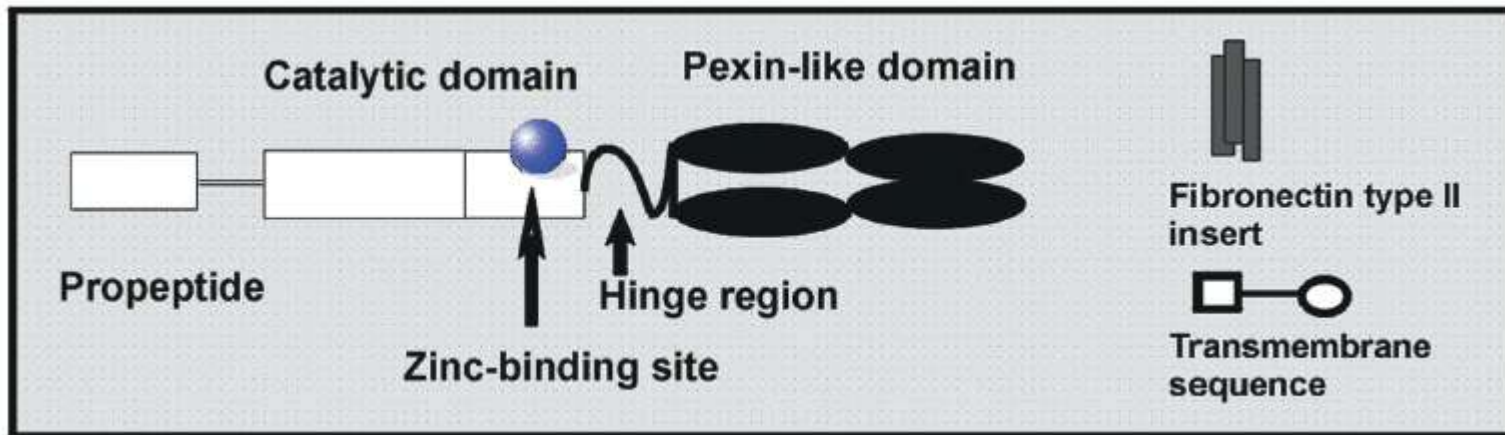
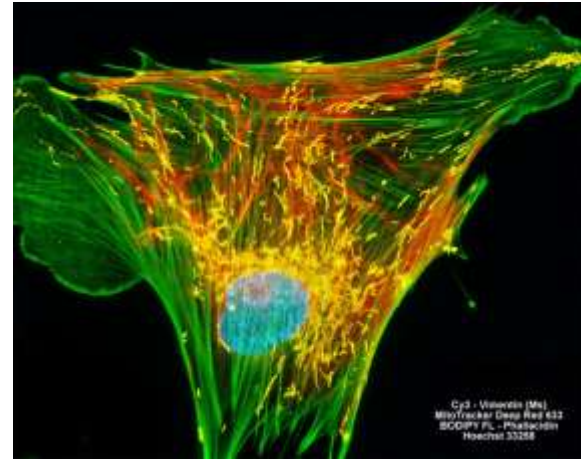


Anti-microbial peptides



MATRIKSA METALLOPROTEĀZES

- Imūnšūnas (neitrofīli, makrofāgi) un epitēlija, endotēlija šūnas, fibroblasti
- Cinku saturošas endopeptidāzes



MATRIKSA METALLOPROTEĀZES

- Funkcijas:
 - Degradē visas ekstracelulārā matricas komponentes
 - Veicina imūnšūnu migrāciju uz brūces centru
 - Pārveido *granulācijas* audus par rētaudiem
 - Regulē augšanas faktoros
 - Ietekmē angiogēnēzi



TABLE I

Subtype of MMPs	MMP No.	Substrates and function
Collagenase		
Interstitial collagenase	MMP-1	type I, II, III, VI, and X collagens, entactin, and aggrecan
Neutrophil-collagenase	MMP-8	type I, II, and III collagens, aggrecan
Collagenase-3	MMP-13	type I, II, and III collagens
Gelatinases		
Gelatinase A	MMP-2	type I, IV, V, VII, X, and XI collagens, fibronectin, laminin, aggrecan, elastin, tenascin C, and vitronektin
Gelatinase B	MMP-9	type IV, V, XIV collagens, aggrecan, elastin, entactin and vitronektin
Stromelysins		
Stromelysin-1	MMP-3	aggrecan, fibronectin, laminin, type III, IV, IX, and X collagens, tenascin C, and vitronektin
Stromelysin-2	MMP-10	aggrecan, fibronectin, and type IV collagen
Stromelysin-3	MMP-11	fibronectin, laminin, type IV collagen, aggrecan



Membrane-type MMPs		
MT1-MMP	MMP-14	activator of proMMP-2, type I, II, III collagens, fibronectin, laminin-1, and vitronectin
MT2-MMP	MMP-15	activator of proMMP-2, fibronectin, tenascin, aggrecan
MT3-MMP	MMP-16	activator of proMMP-2, type III collagen, fibronectin
MT4-MMP	MMP-17	unknown
MT5-MMP	MMP-24	activator of proMMP-2
MT6-MMP	MMP-25	type IV collagen, gelatin, fibronectin, fibrin

Other MMPs		
Matrilysin-1	MMP-7	aggrecan, fibronectin, laminin, type IV collagen, elastin, entactin, tenascin, and vitronectin
Matrilysin-2	MMP-26	type IV collagen, fibronectin, fibrinogen, and gelatin

Metalloelastase		
Metalloelastase	MMP-12	elastin, type IV collagen, fibronectin, laminin, vitronectin, proteoglycan
Enamelysin	MMP-20	aggrecan, cartilage oligomeric matrix protein (COMP)
Epilysin	MMP-28	unknown
No trivial name	MMP-19	aggrecan, cartilage oligomeric matrix protein (COMP)



Iekaisums



Pārmērīga proteolītiskā aktivitāte



HRONISKS IEKAISUMS

Augšanas faktori

Šūnu virsmas receptori

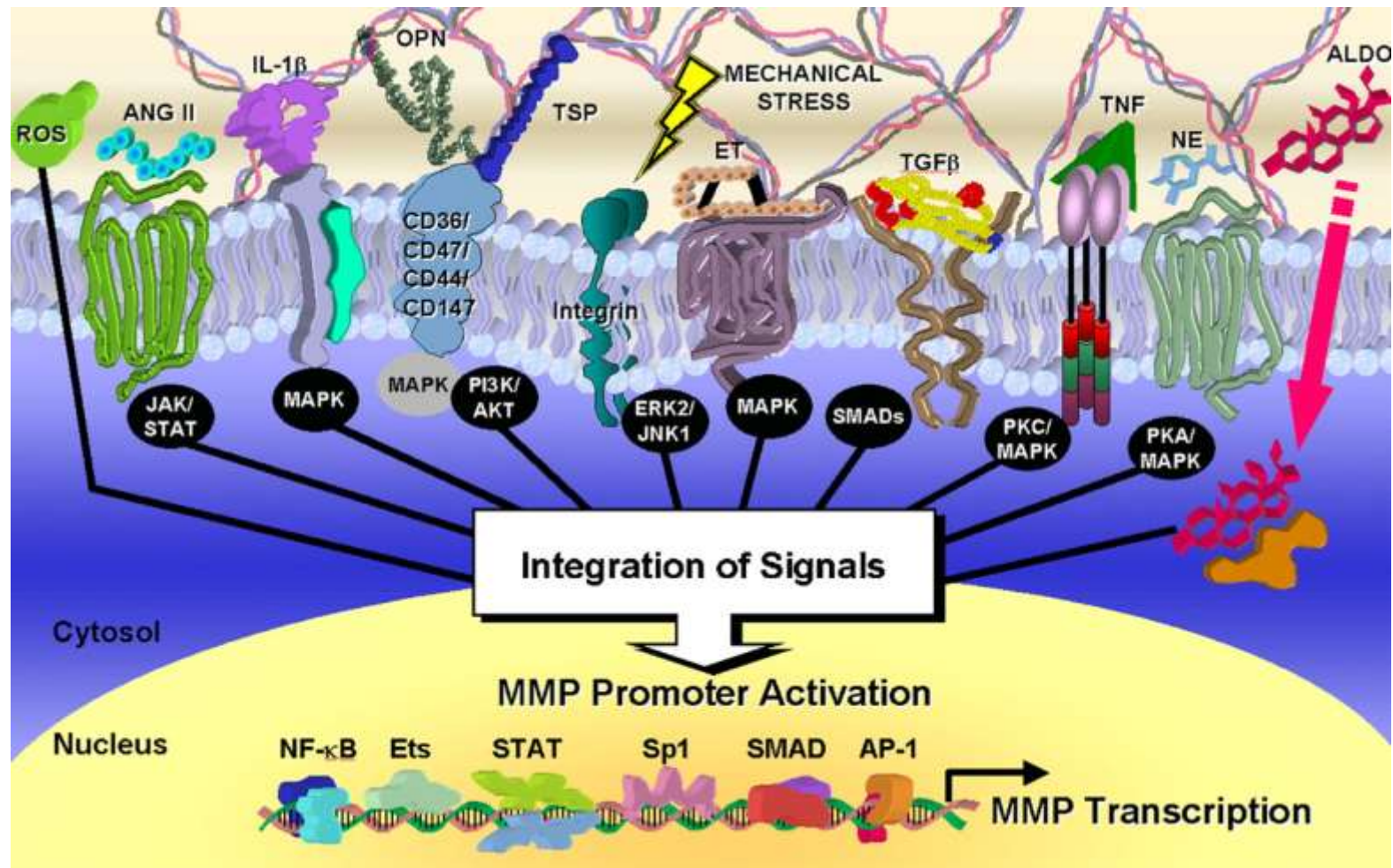
Citokīni

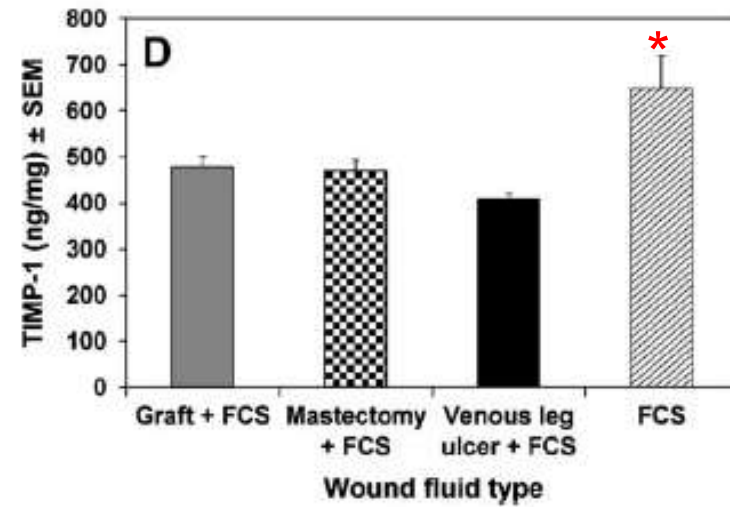
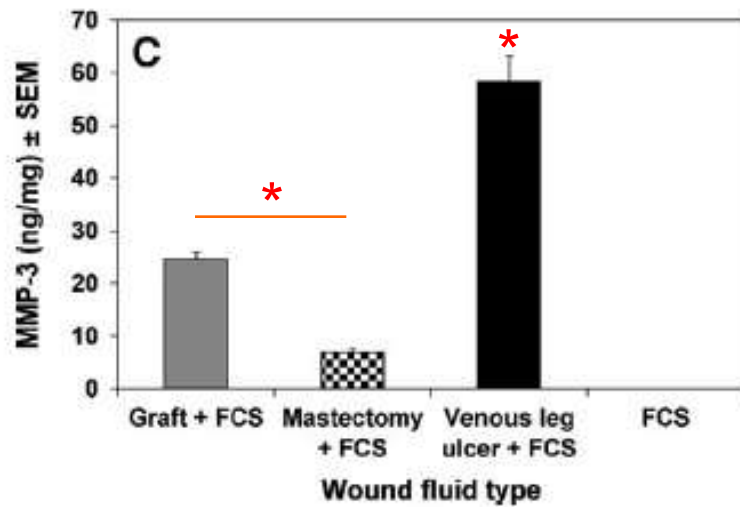
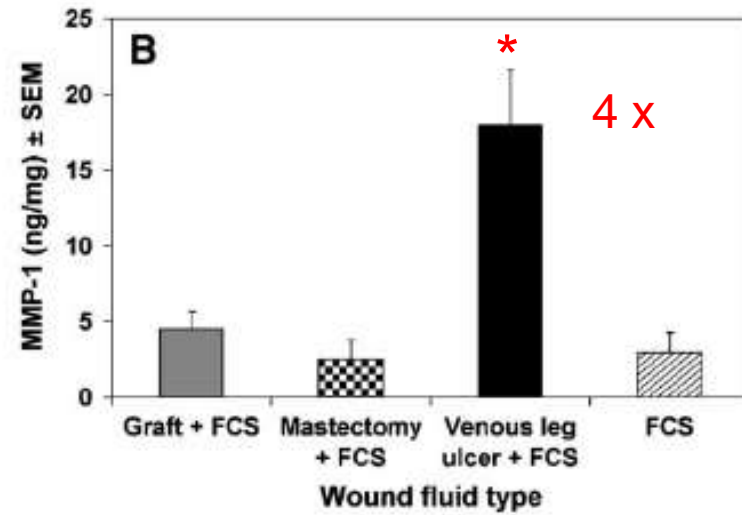
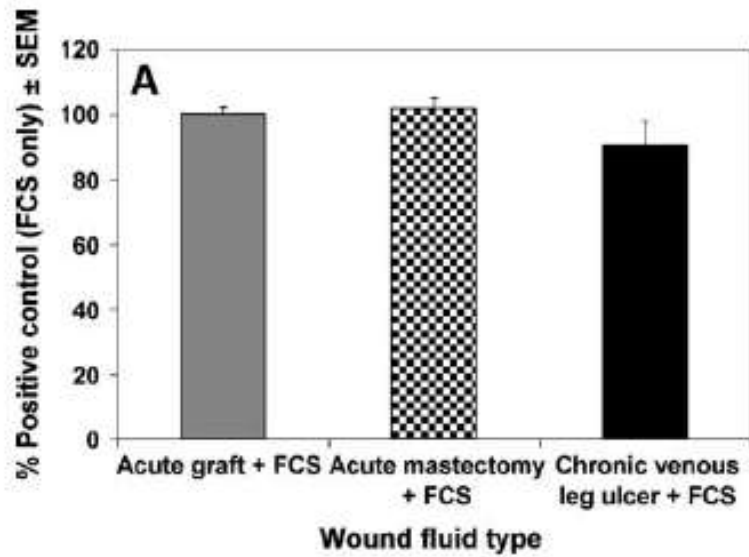
Ekstracelulārais matrikss

↓ Brūces granulācija



MATRIKSA METALLOPROTEĀZES





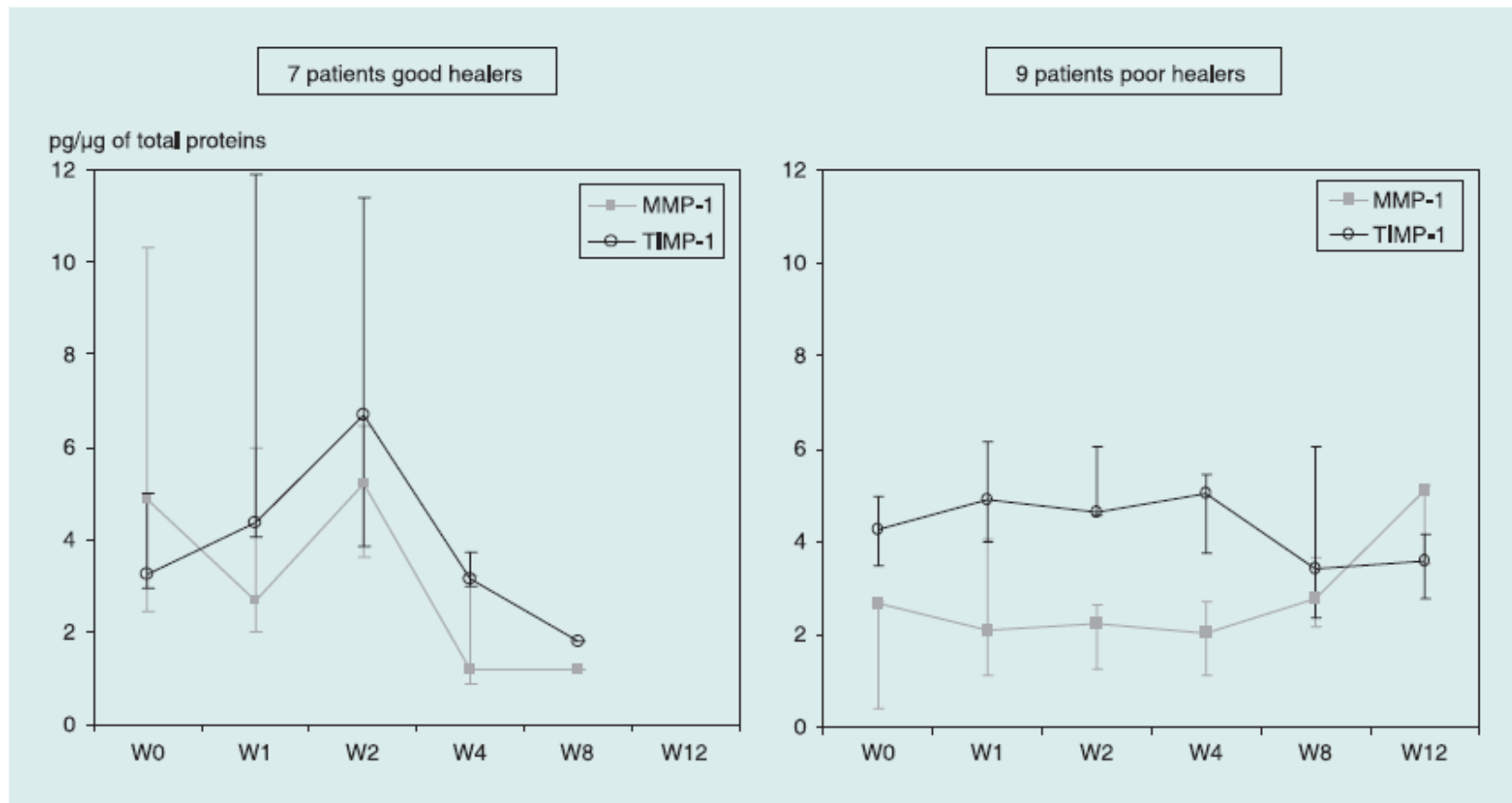


FIGURE 3 Levels of MMP-1 and TIMP-1 for good and poor healers during the 12-week follow-up period (results are expressed as medians with 25th and 75th percentiles).



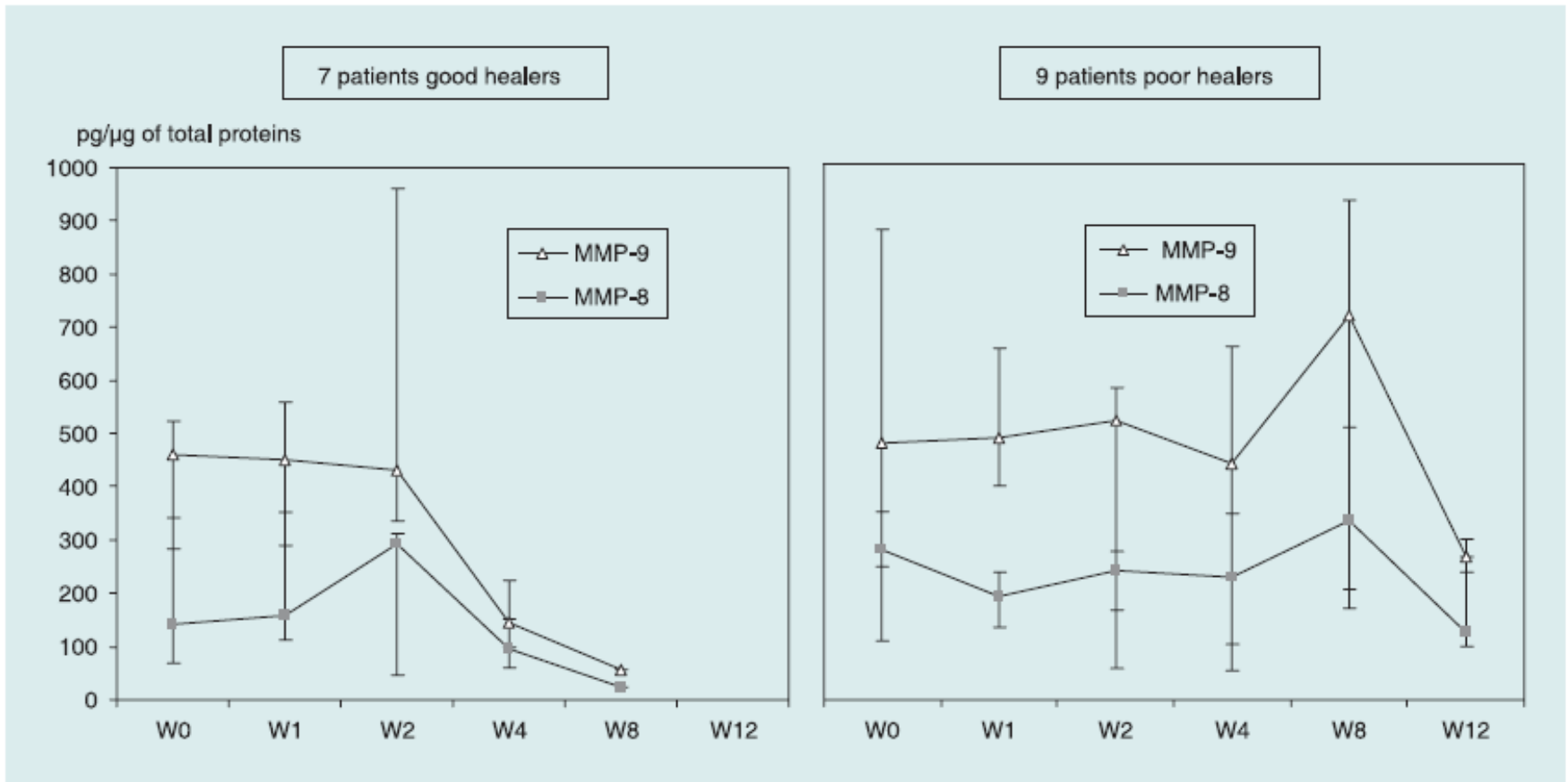
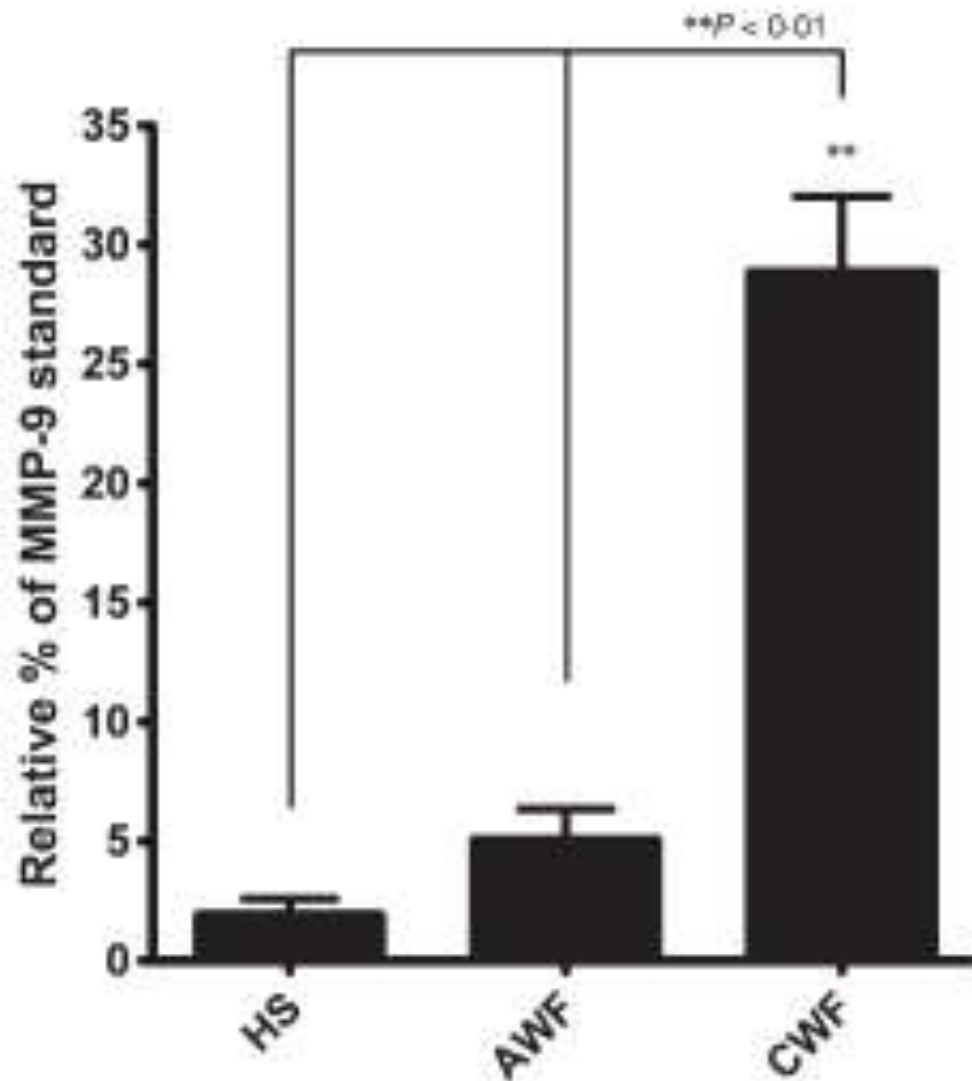


FIGURE 2 Levels of MMP-8 and MMP-9 for good and poor healers during the 12-week follow-up period (results are expressed as medians with 25th and 75th percentiles).





N=9





EIROPAS REĢIONĀLĀS
ATTĪSTĪBAS FONDS



EIROPAS SAVIENĪBA

IEGULDĪJUMS TAVĀ NĀKOTNĒ

HRONISKU BRŪČU DZĪŠANU VEICINOŠAS MEDICĪNAS IERĪCES IZSTRĀDE

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PROJEKTA MĒRĶIS

Hronisku brūču aprūpes un ārstēšanas galvenā problēma ir efektīvu, funkcionālu, brūču pārklājošu un vienlaicīgi iekaisumu regulējošu materiālu trūkums.

**Biodegradējams materiāls apvienots ar
imūnmodulējošu, reepitelizāciju stimulējošu
glikoproteīnu**



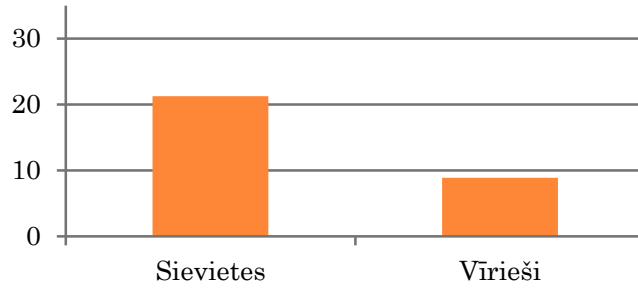
PĒTNIECĪBAS AKTIVITĀTES

- **Pacientu brūču eksudātu analīzes, lai identificētu pacientu grupas, kurām jauno medicīnas ierīci izmantot ar augstāko efektivitāti.**
- Biomateriāla, hialuronskābes atvasinājuma, funkcionalizēšana, kombinējot to ar imunomodulējošu glikoproteīnu.
- Jaunā materiāla un to komponentu *in vitro* novērtēšana.
- Jaunizveidotās medicīnas ierīces *in vivo* novērtēšana.

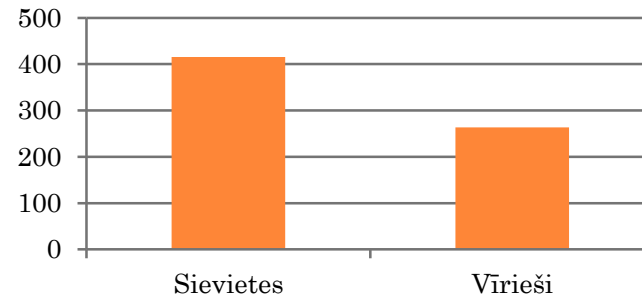


ATŠKIRĪBAS STARP DZIMUMIEM (S=16; V=20)

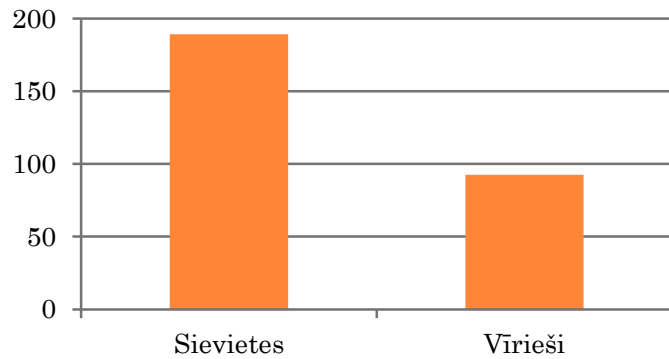
TNF-a



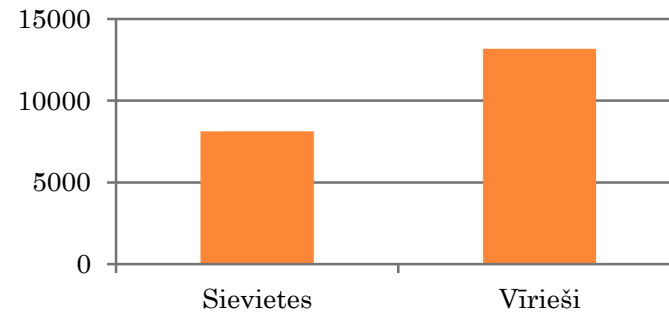
IL-6



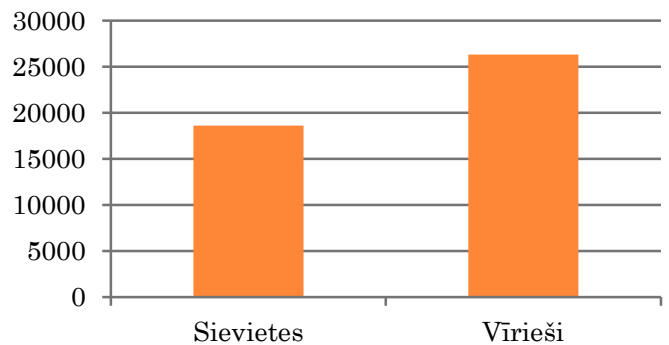
IL-1b



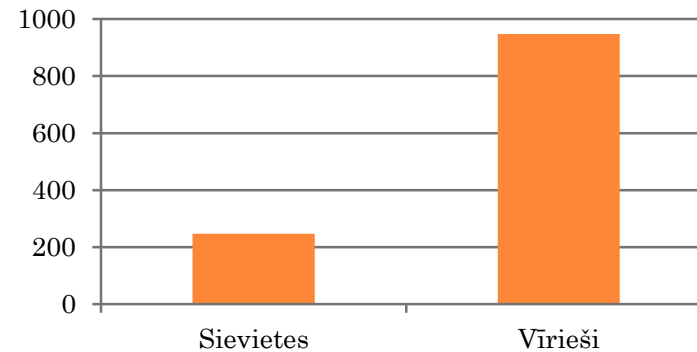
MMP-1



MMP-2



MMP-10 *

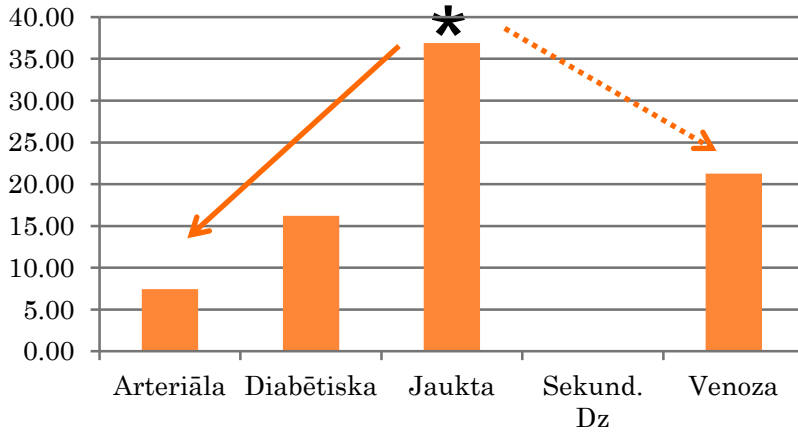


PILLOT-DATI

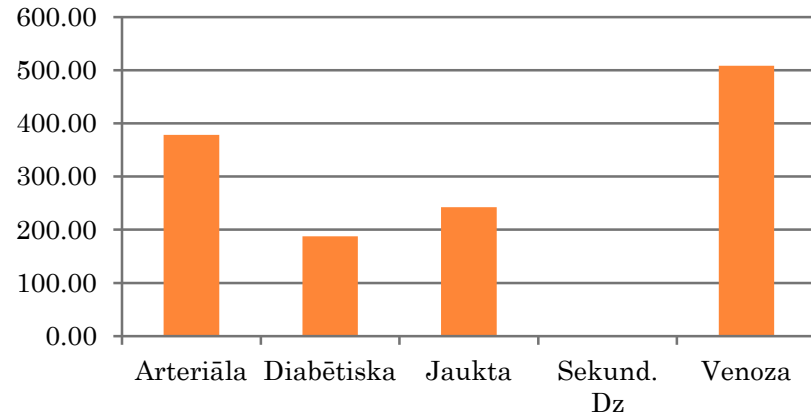


ČŪLAS TIPI (A=7; D=2; J=7; S=0; V=18)

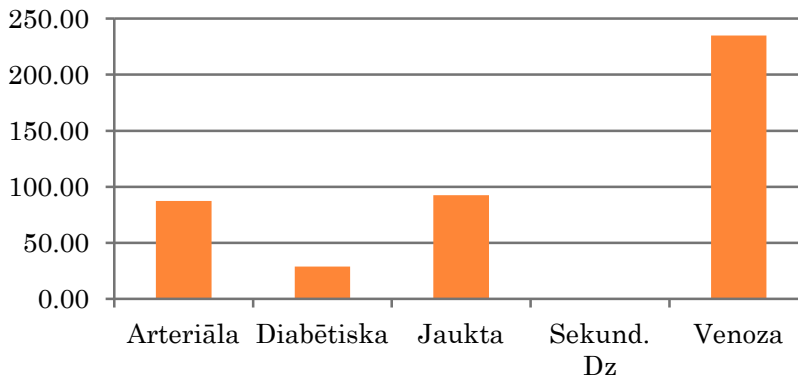
TNF-a



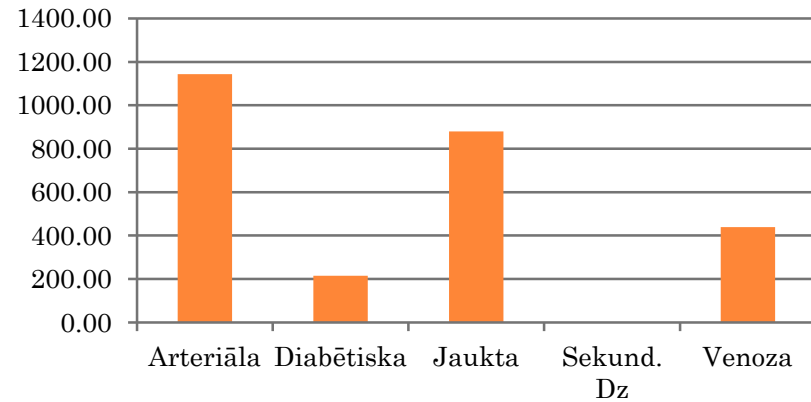
IL-6



IL-1b



MMP-10

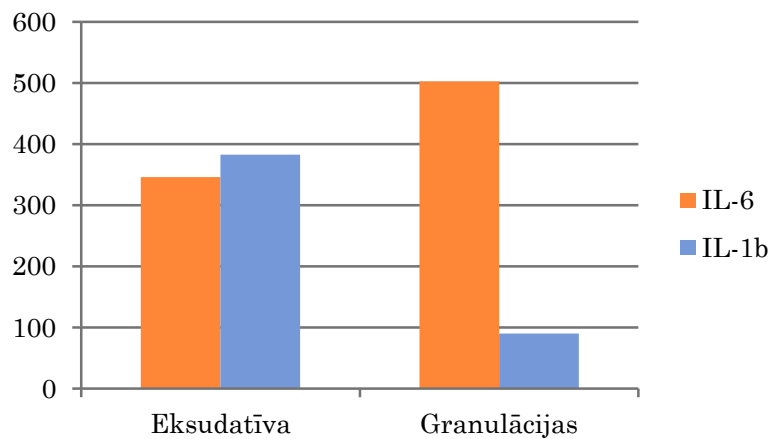
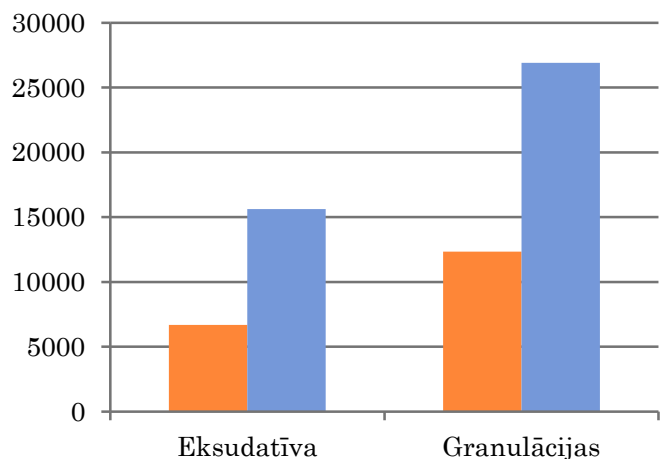
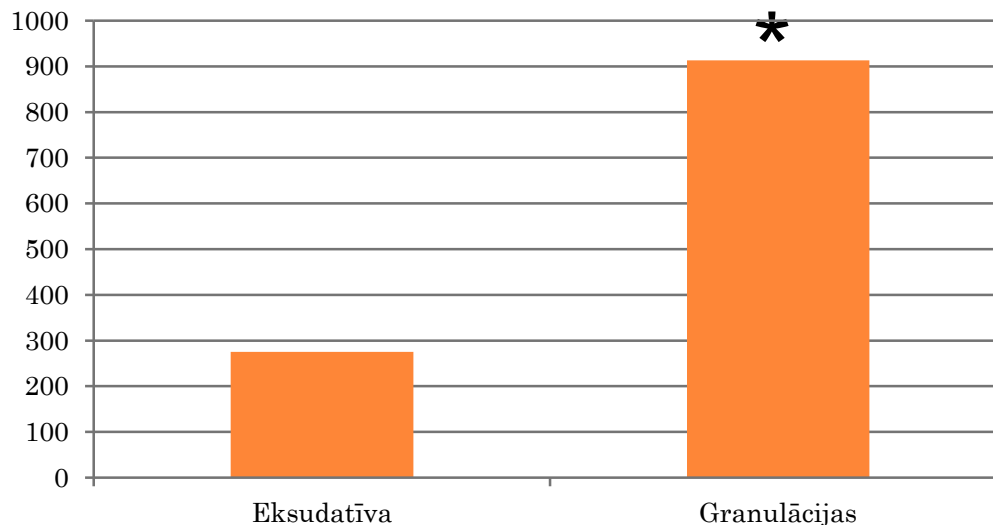


PILLOT-DATI



ČŪLAS ATTĪSTĪBAS FĀZE (E=17; G=16)

MMP-10

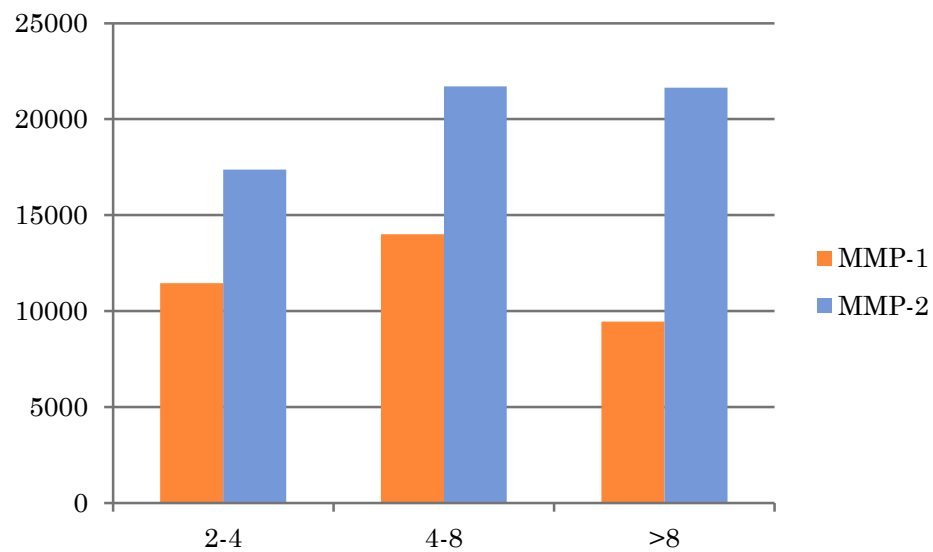
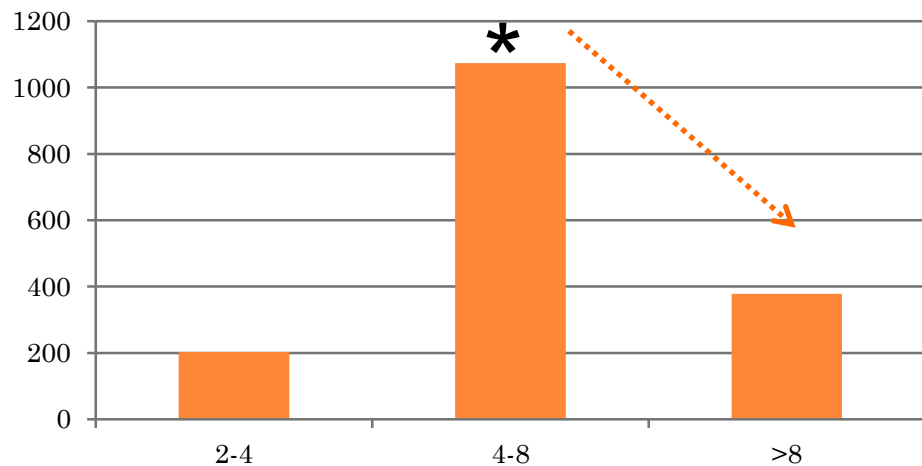


PILOT-DATI



ČŪLAS VECUMS (2-4=5; 4-8=8; >8=23)

IL-6

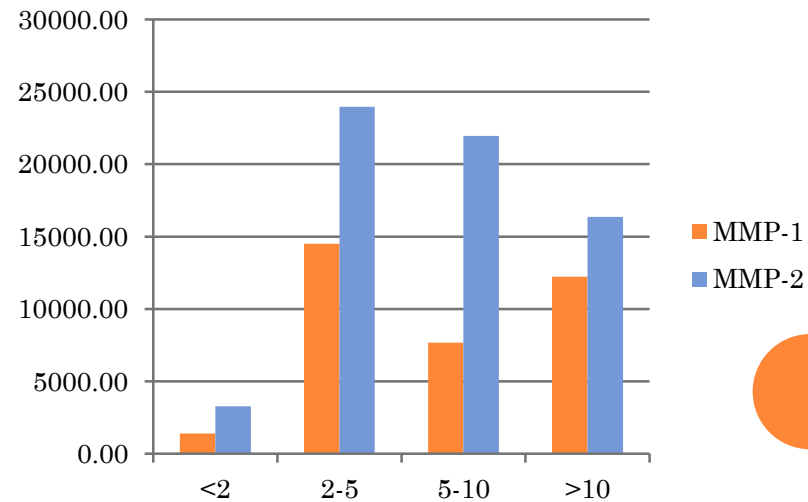
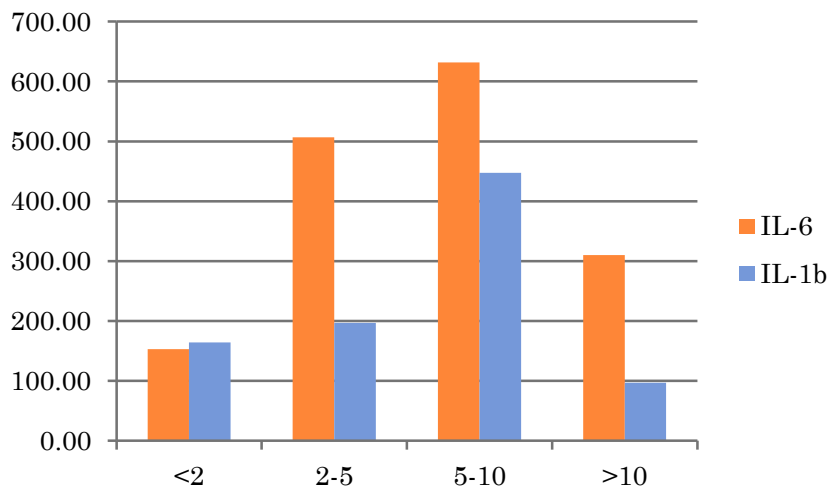
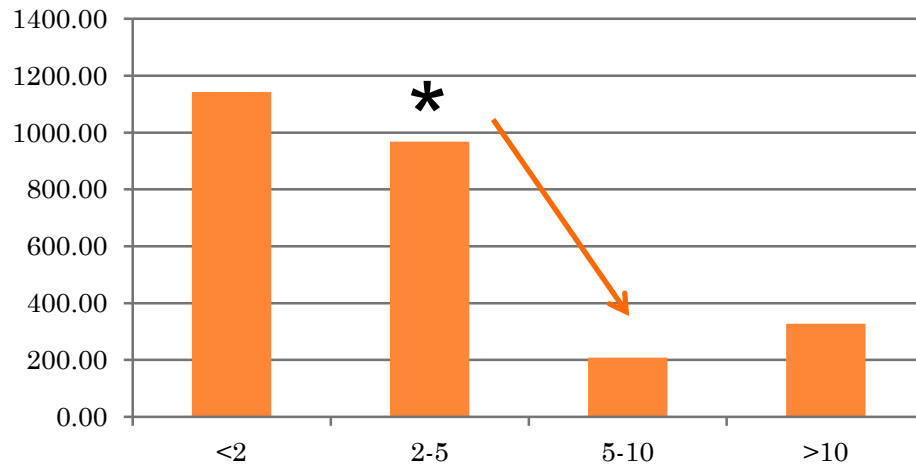


PILOT-DATI



ČŪLAS IZMĒRS (<2=3; 2-5=13; 5-10=12; >10=8)

MMP-10



PILOT-DATI



KORELĀCIJAS

Cell Contents:

Correlation Coefficient

P Value

Number of Samples

	IL-6	IL-1beta	MMP-1	MMP-2	MMP-10
TNF-alpha	0.257 0.141 34	0.377 0.0368 31	0.0742 0.679 33	0.112 0.531 33	0.0221 0.902 33
IL-6		0.0385 0.833 32	0.674 0.00000526 35	0.506 0.00206 35	0.317 0.0635 35
IL-1beta			-0.172 0.345 32	-0.348 0.0512 32	-0.190 0.294 32
MMP-1				0.761 0.000000200 35	0.489 0.00303 35
MMP-2					0.410 0.0146 35

PILLOT-DATI





EIROPAS REĢIONĀLĀS
ATTĪSTĪBAS FONDS



EIROPAS SAVIENĪBA

IEGULDĪJUMS TAVĀ NĀKOTNĒ

HRONISKU BRŪČU DZĪŠANU VEICINOŠAS MEDICĪNAS IERĪCES IZSTRĀDE

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