Barrera Cutànea y DAC

2da Parte

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Barrera Cutánea

Partes de Estudio

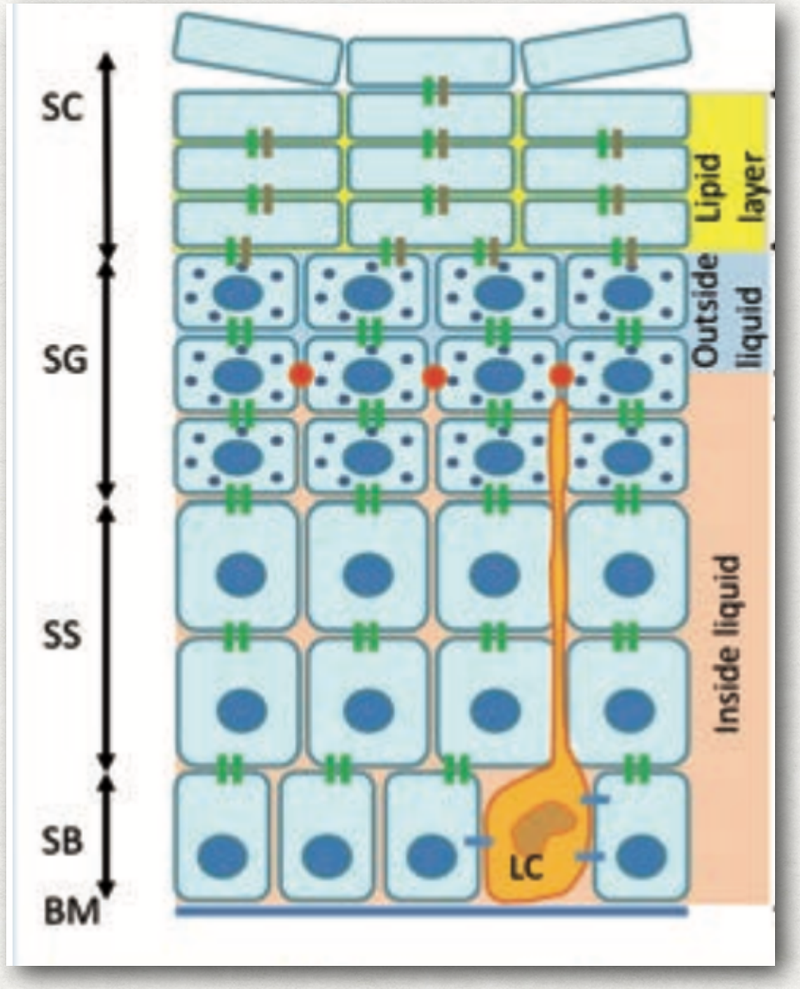
✓ Barrera Cutánea y Diferentes Enfermedades

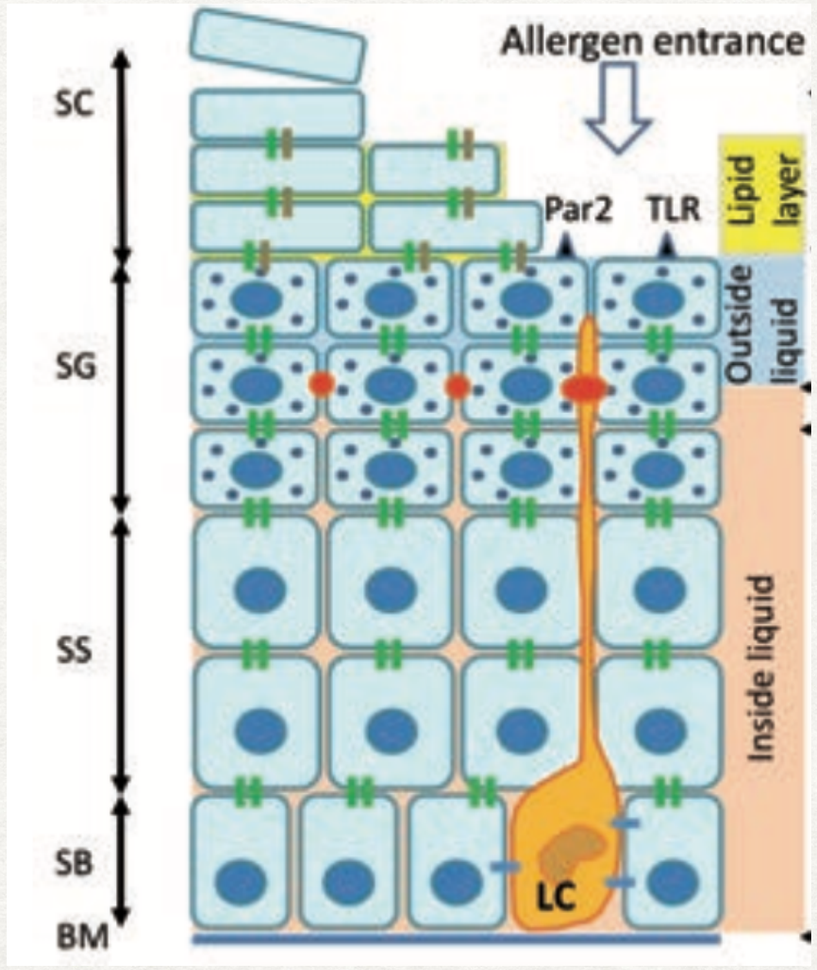
¿Qué ocurre cuando la Barrera Cutánea se daña?

Barrera Cutánea

Partes de Estudio

✓ Barrera Cutánea y Diferentes Enfermedades

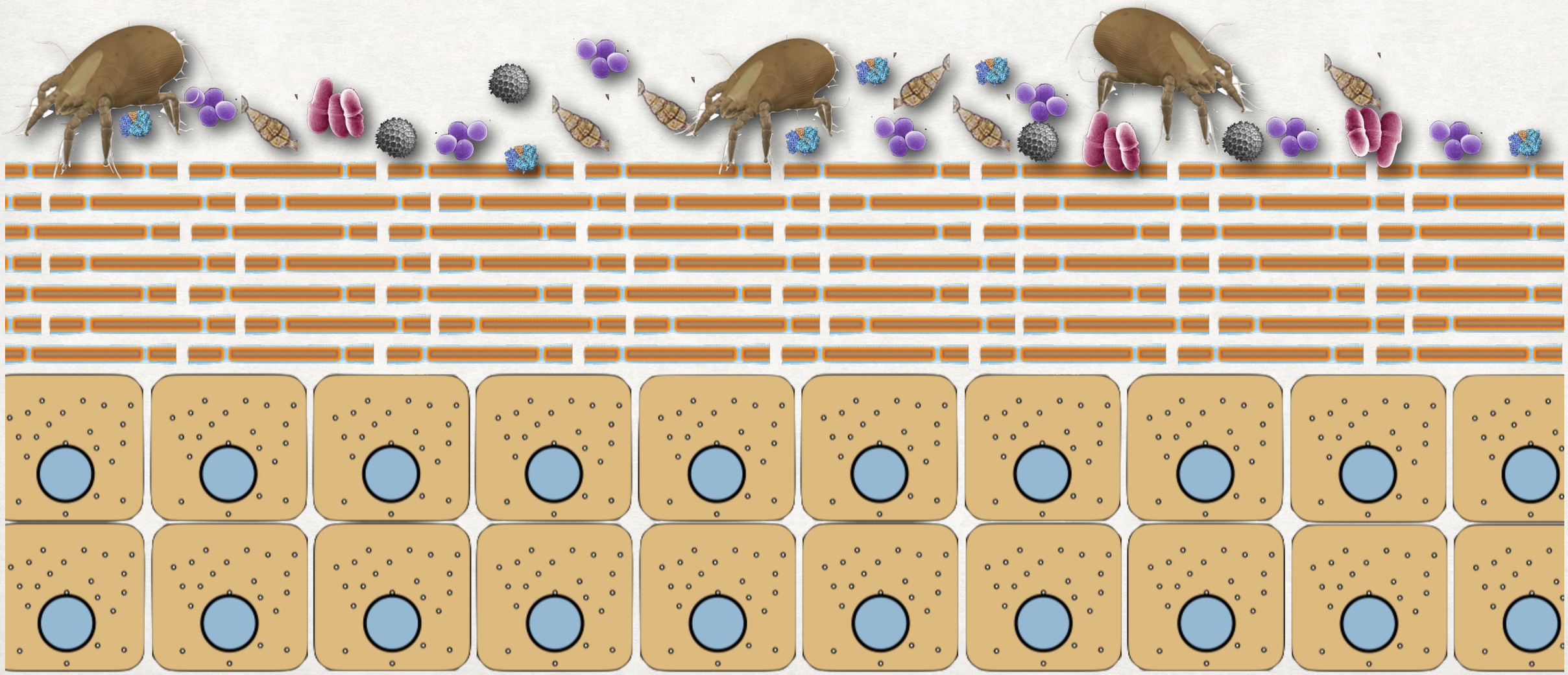




Barrera Cutánea

Partes de Estudio

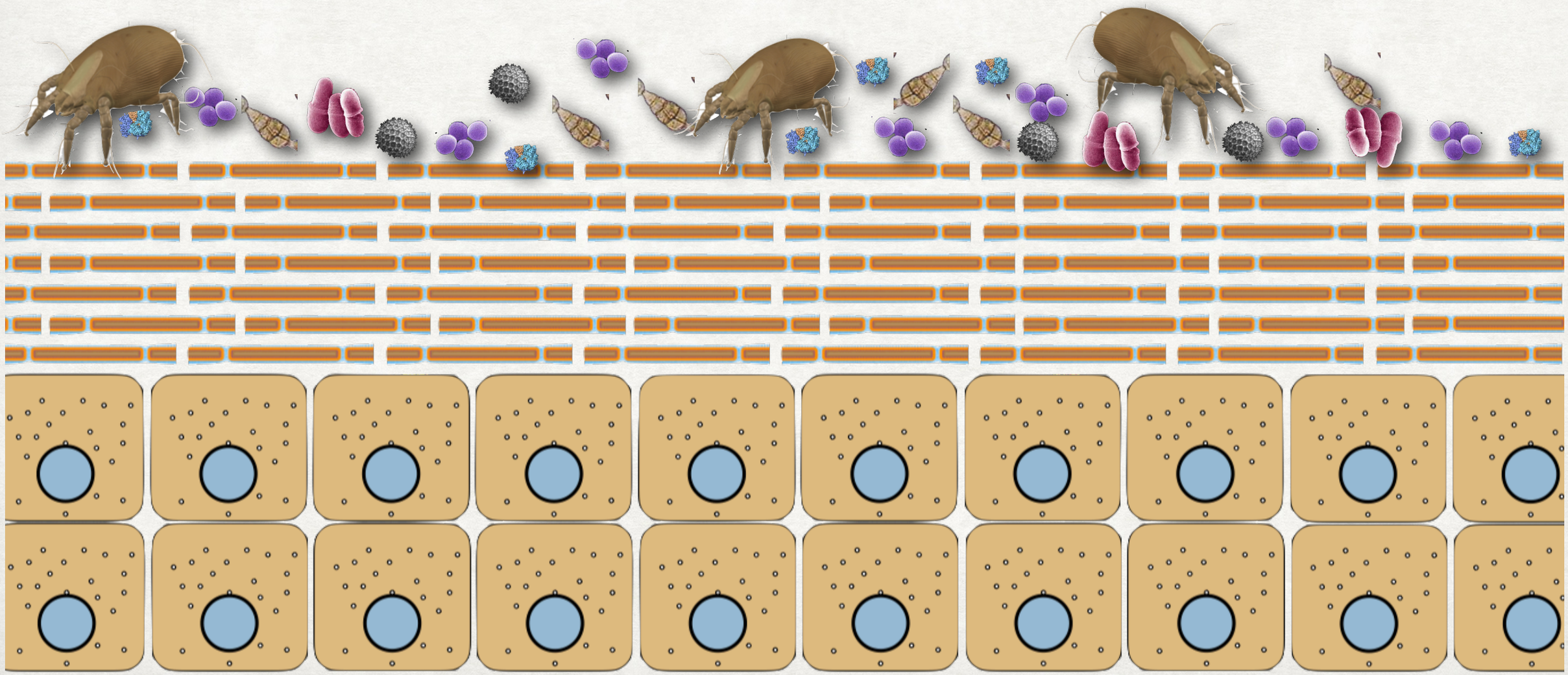
✓ Barrera Cutánea y Diferentes Enfermedades



Barrera Cutánea

Partes de Estudio

✓ Barrera Cutánea y Diferentes Enfermedades



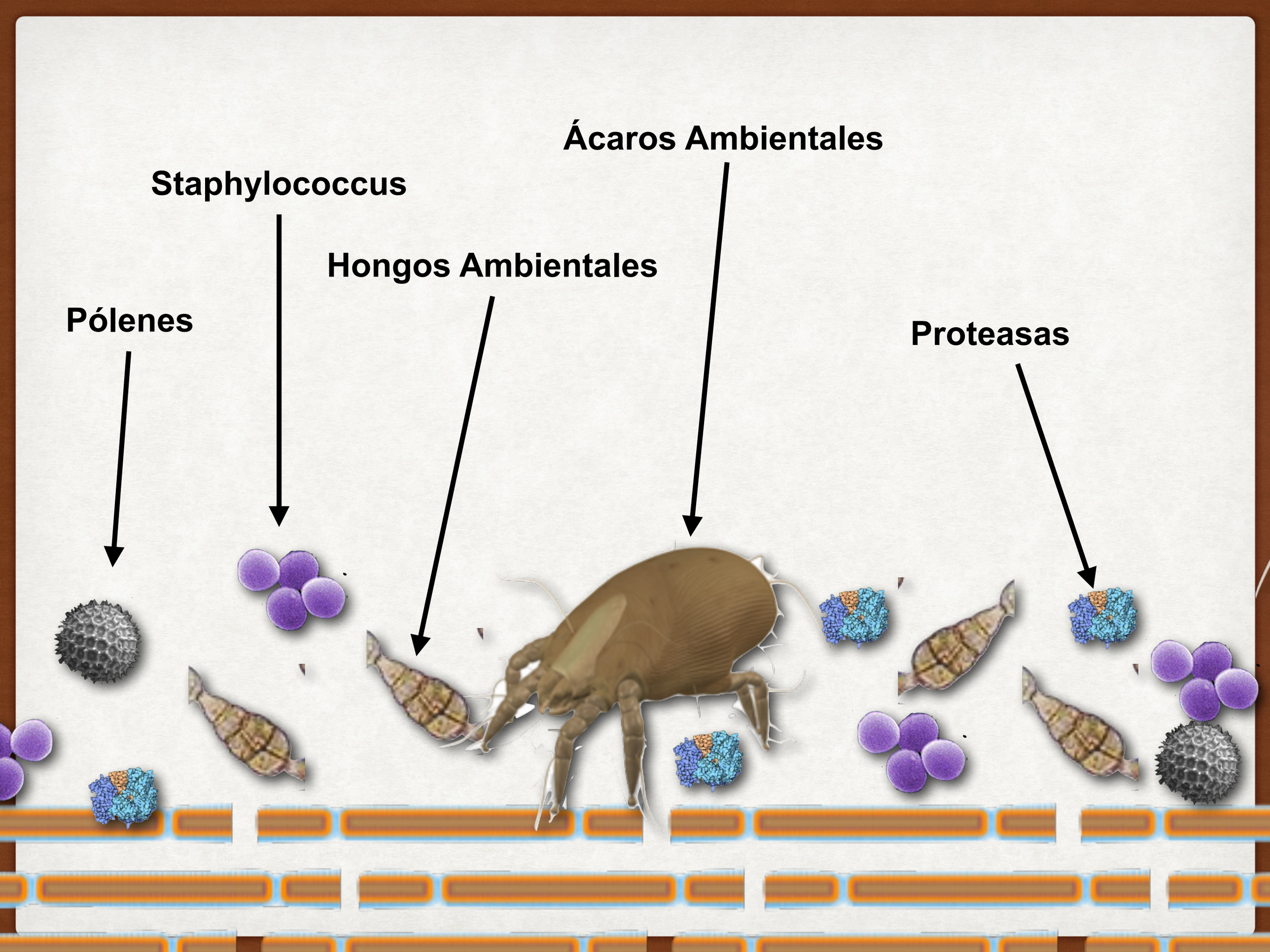
Ácaros Ambientales

Staphylococcus

Hongos Ambientales

Pólenes

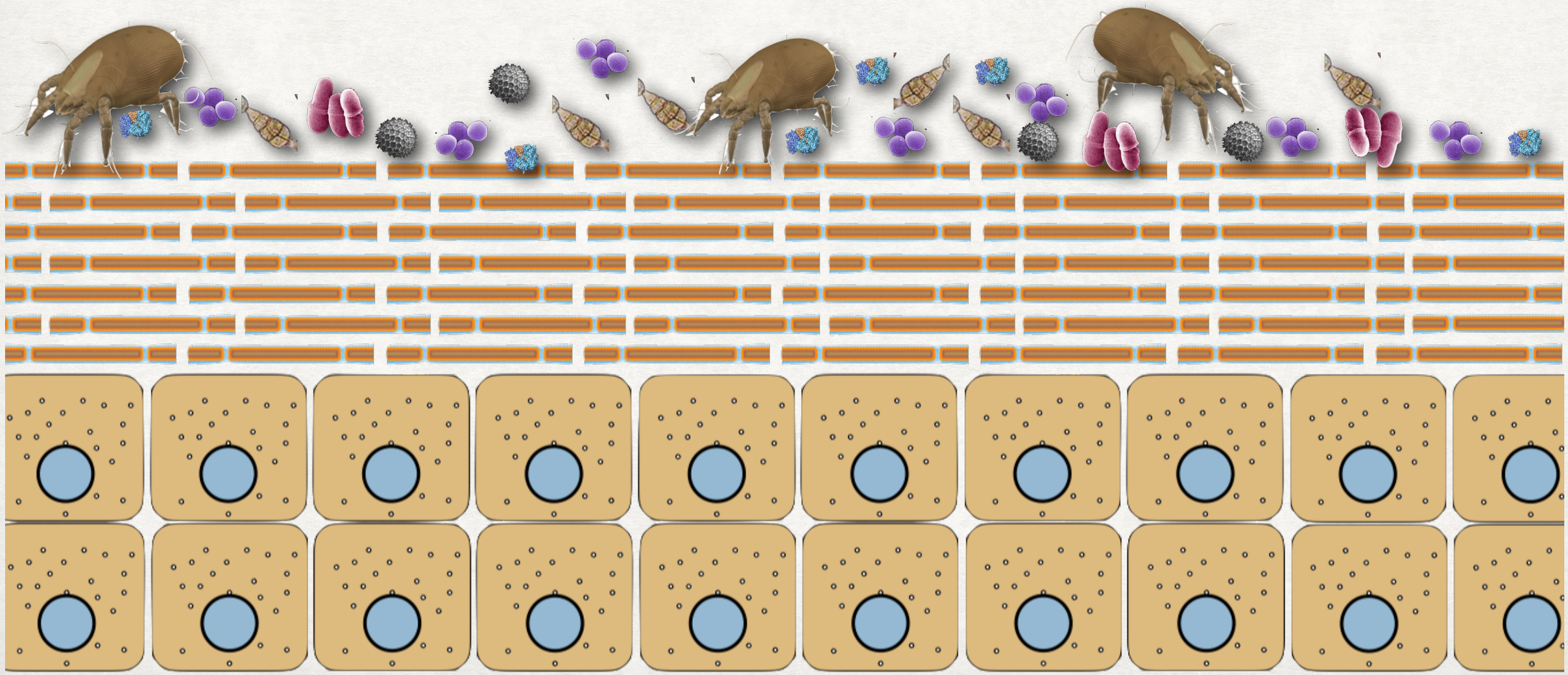
Proteasas



Barrera Cutánea

Partes de Estudio

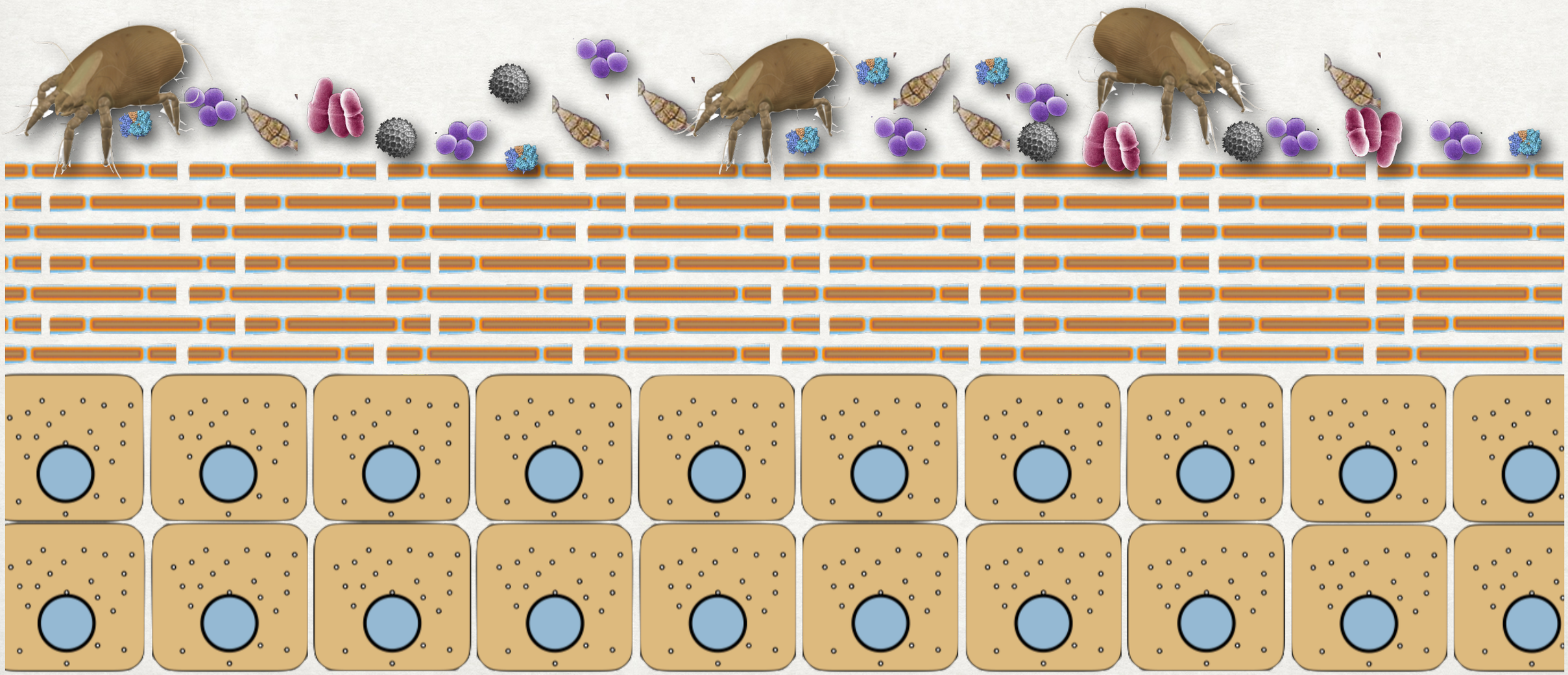
✓ Barrera Cutánea y Diferentes Enfermedades



Barrera Cutánea

Partes de Estudio

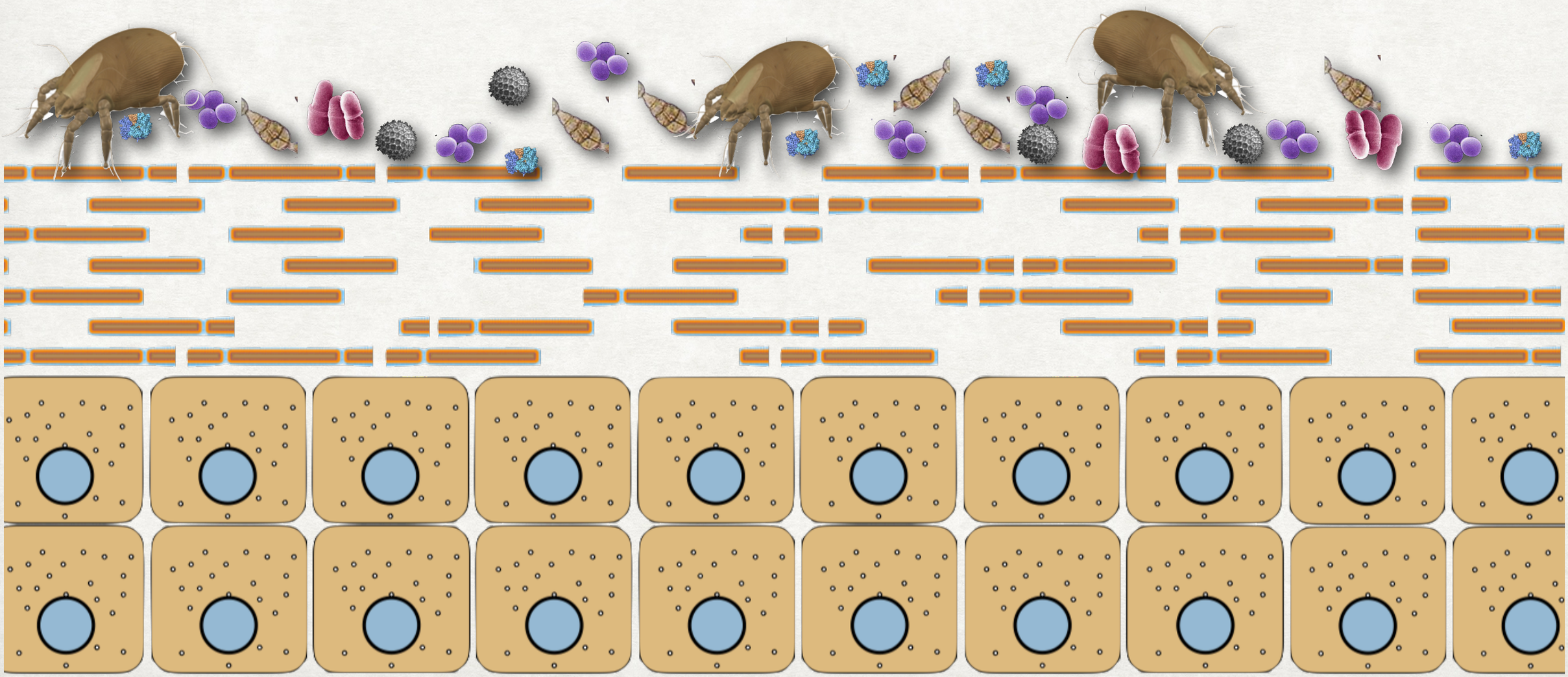
✓ Barrera Cutánea y Diferentes Enfermedades



Barrera Cutánea

Partes de Estudio

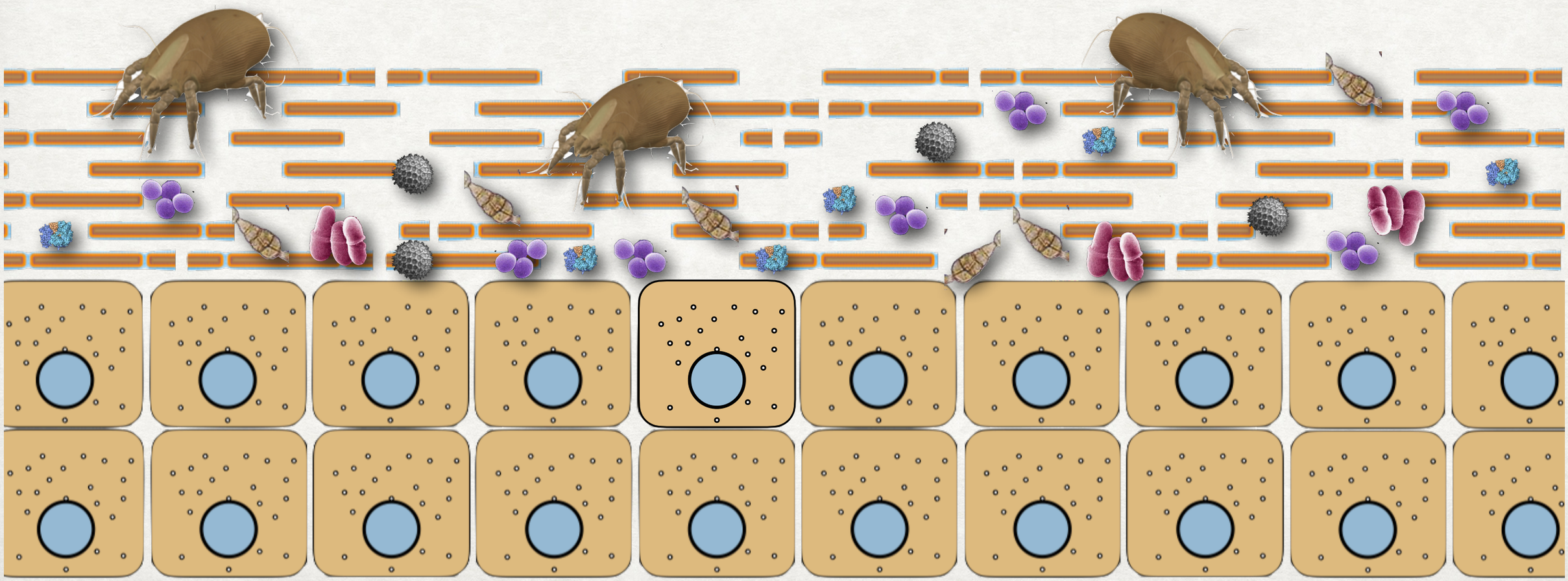
✓ Barrera Cutánea y Diferentes Enfermedades

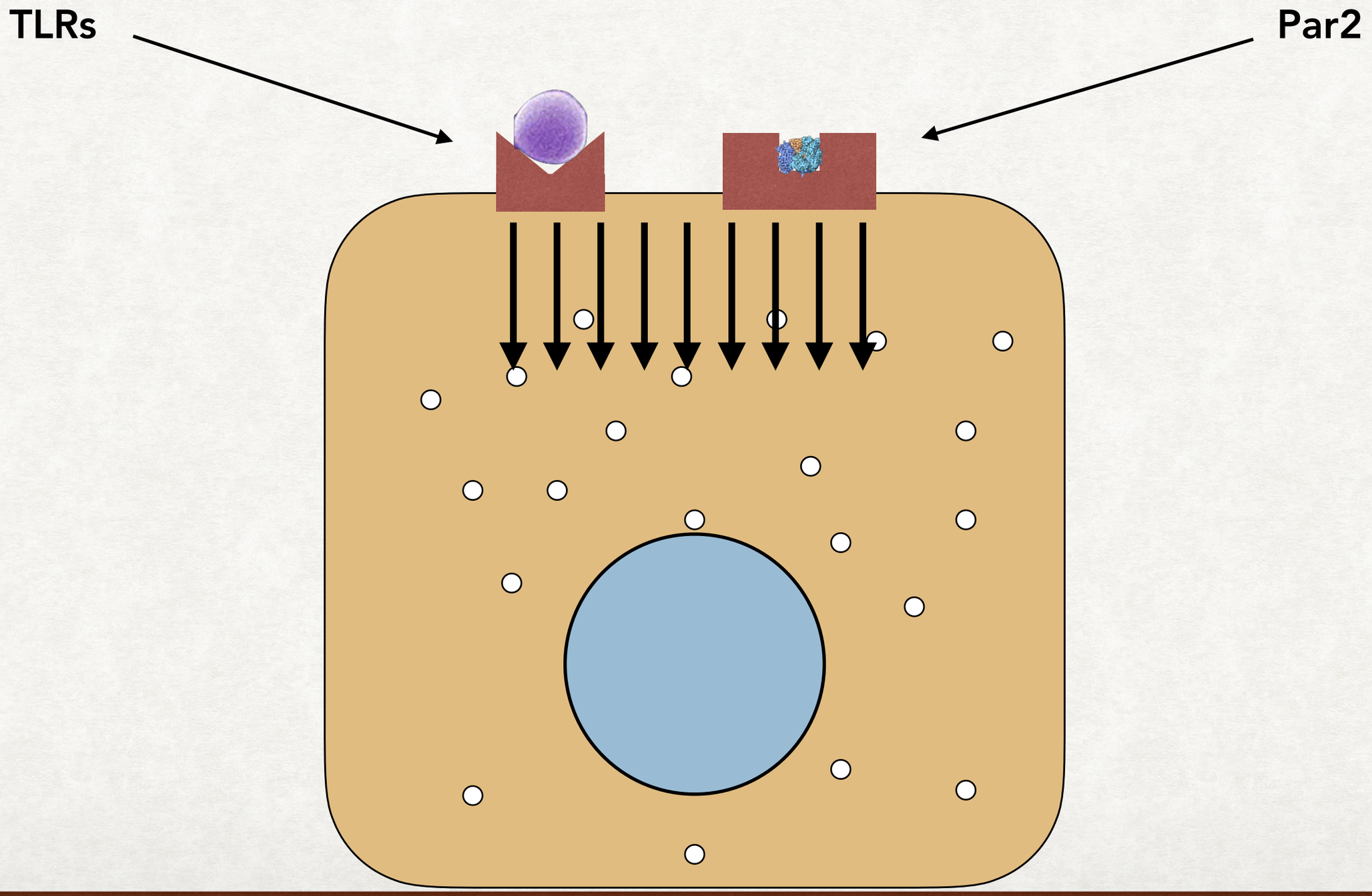


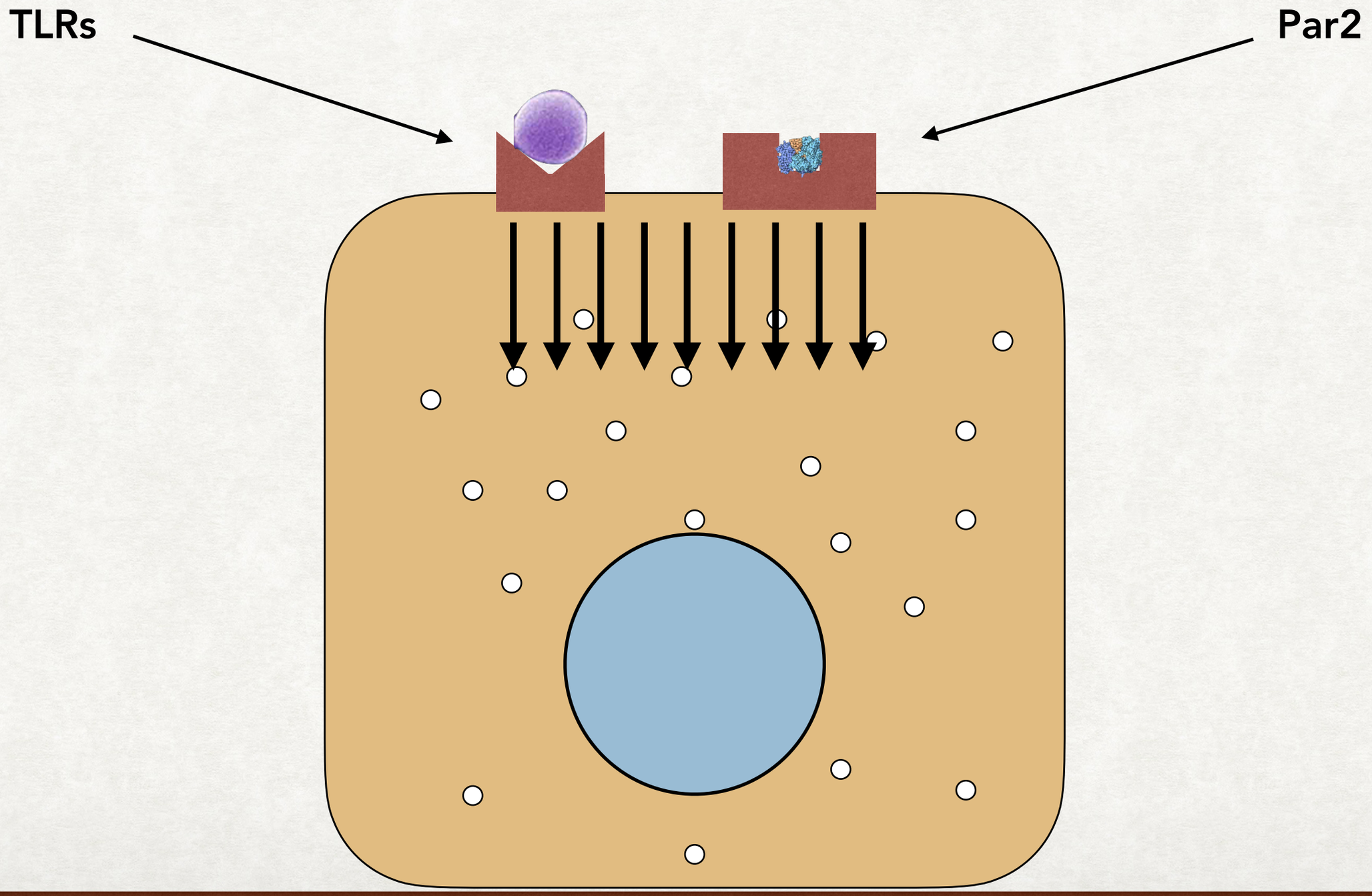
Barrera Cutánea

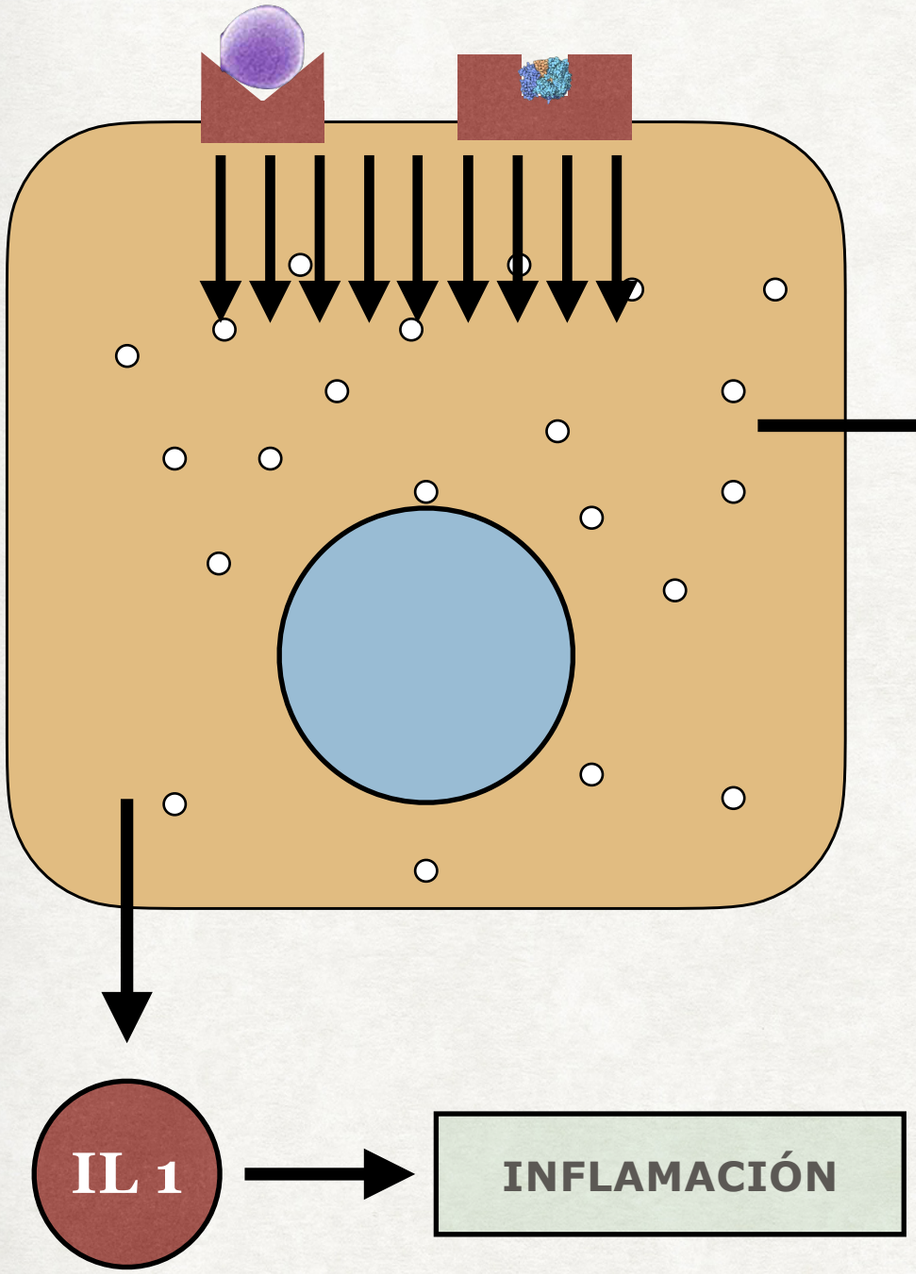
Partes de Estudio

- ✓ Barrera Cutánea y Diferentes Enfermedades

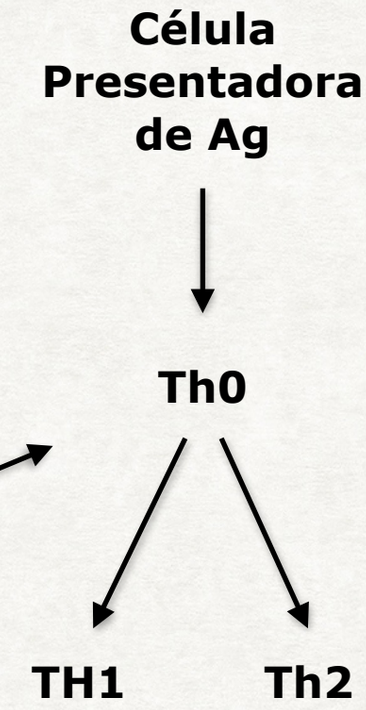



TLRs
Par2

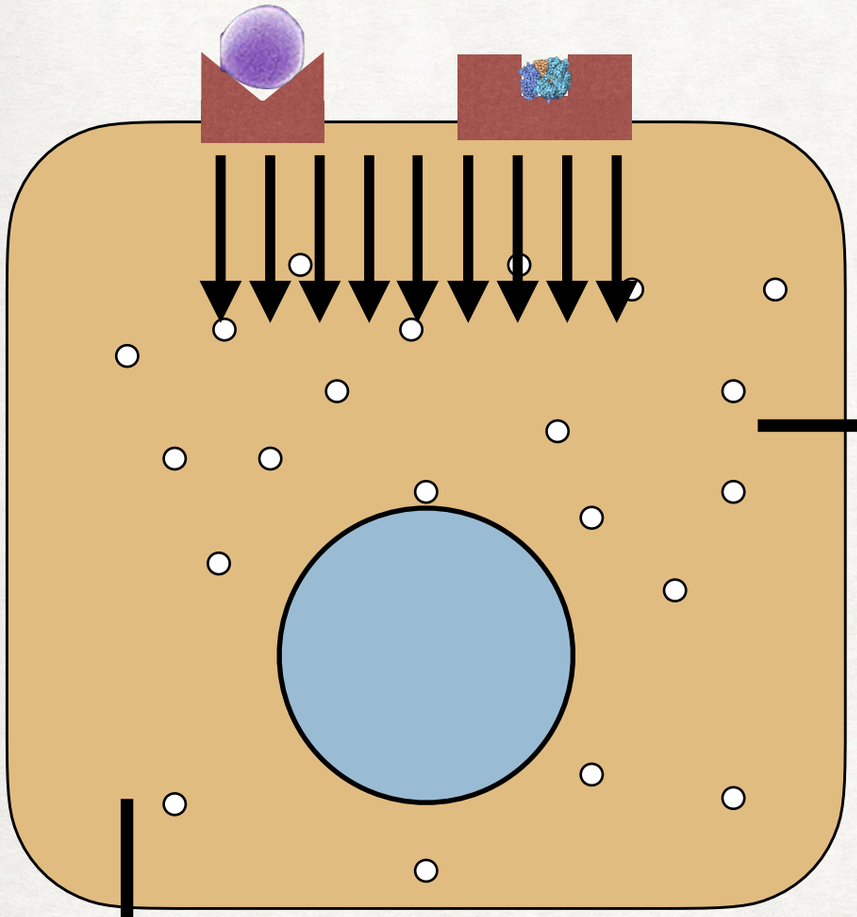

TLRs
Par2



TSLP


Célula
Presentadora
de Ag
Th0
TH1
Th2

IL 1
INFLAMACIÓN

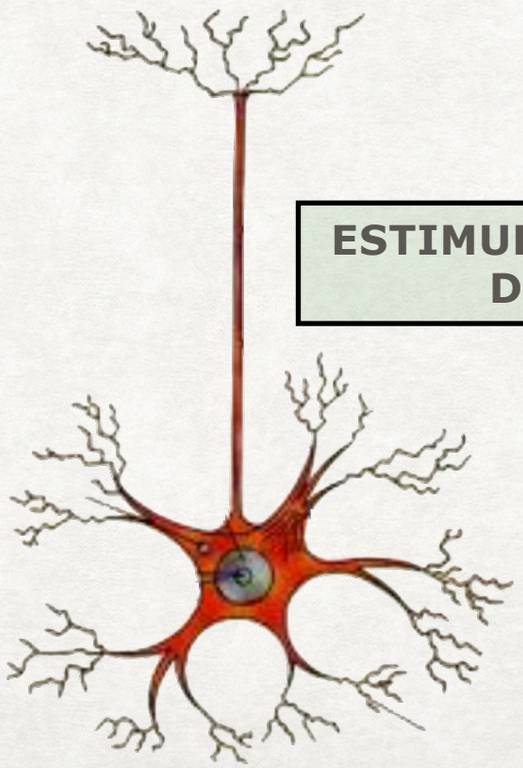


Célula Presentadora de Ag

Th0

TH1

Th2



ESTIMULACIÓN NEURONAL DEL PRURITO

INFLAMACIÓN

Veterinary Dermatology

Vet Dermatol 2013; **24**: 54–e14 DOI: 10.1111/j.1365-3164.2012.01096.x

Expression of thymic stromal lymphopoietin in canine atopic dermatitis

Jolanta Klukowska-Rötzler*, Ludovic Chervet†‡, Eliane J. Müller†§, Petra Roosje‡§, Eliane Marti*§ and Jozef Janda*

Veterinary Dermatology

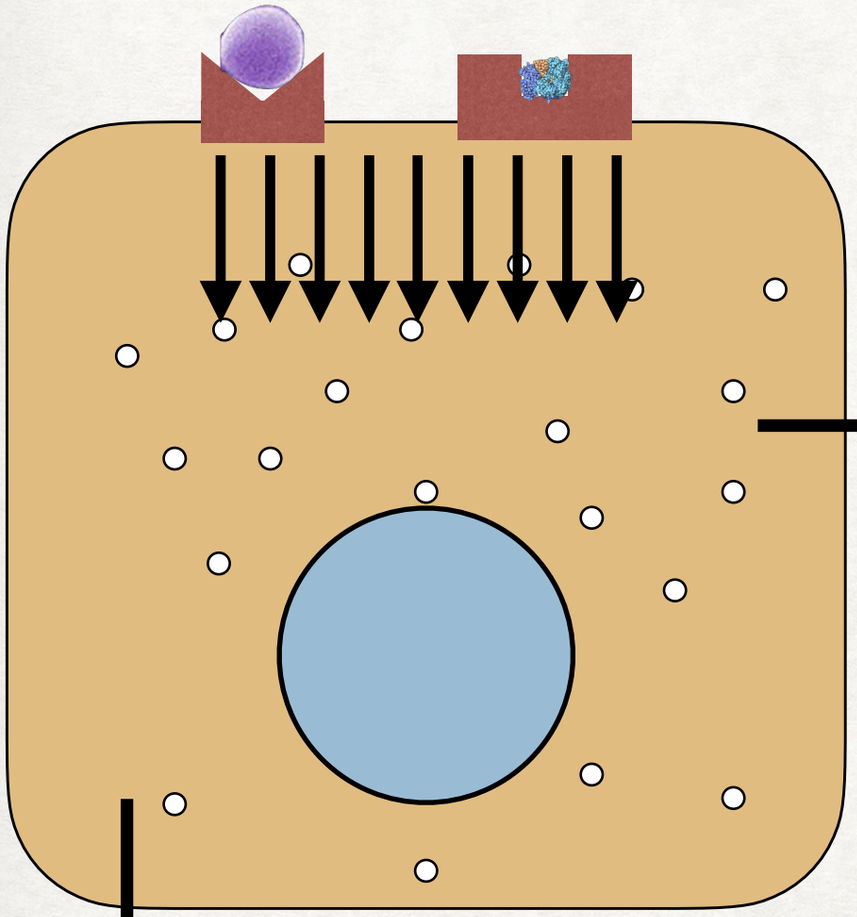
Vet Dermatol 2016; **27**: 184–e46 DOI: 10.1111/vde.12301

Transcription of thymic stromal lymphopoietin via Toll-like receptor 2 in canine keratinocytes: a possible association of *Staphylococcus* spp. in the deterioration of allergic inflammation in canine atopic dermatitis

Mayu Sakamoto, Ryota Asahina, Hiroaki Kamishina and Sadatoshi Maeda

Department of Veterinary Medicine, Faculty of Applied Biological Sciences, Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan

Correspondence: Sadatoshi Maeda, Department of Veterinary Medicine, Faculty of Applied Biological Sciences, Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan. E-mail: sadat@gifu-u.ac.jp

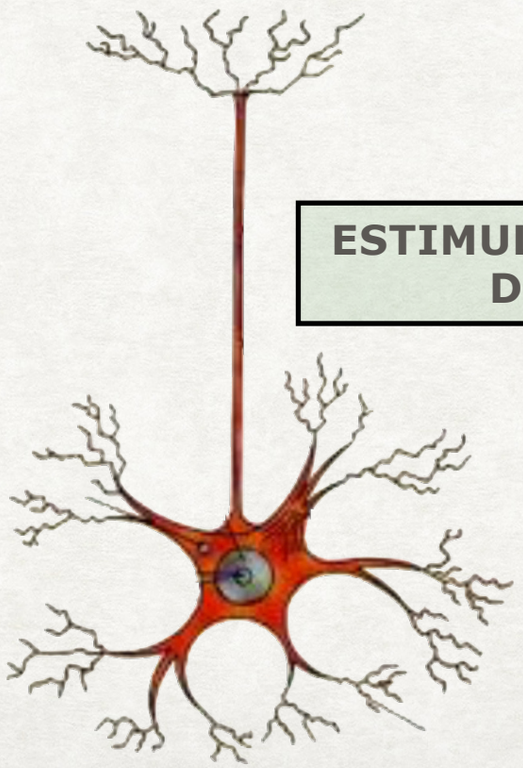


Célula Presentadora de Ag

Th0

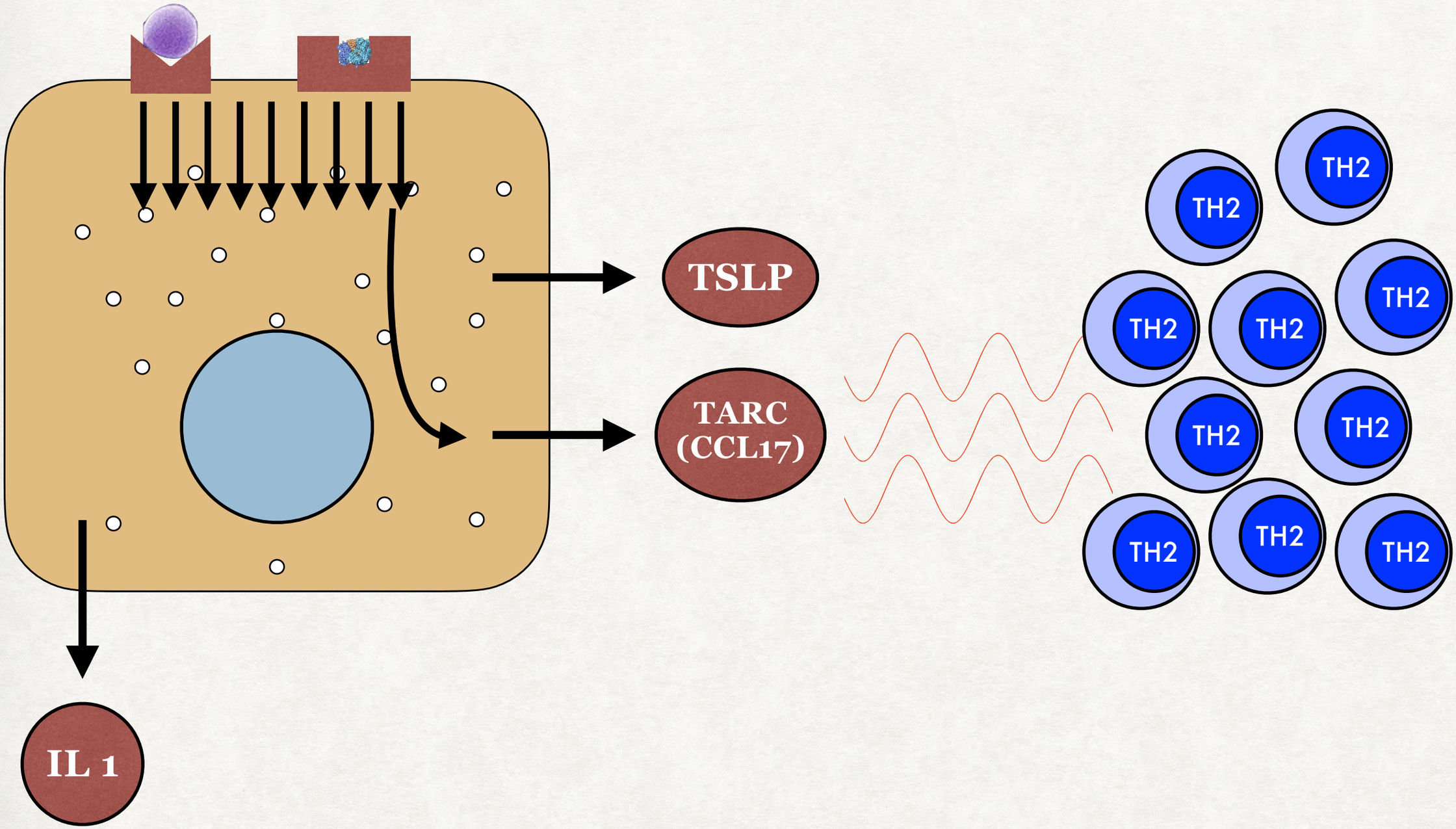
TH1

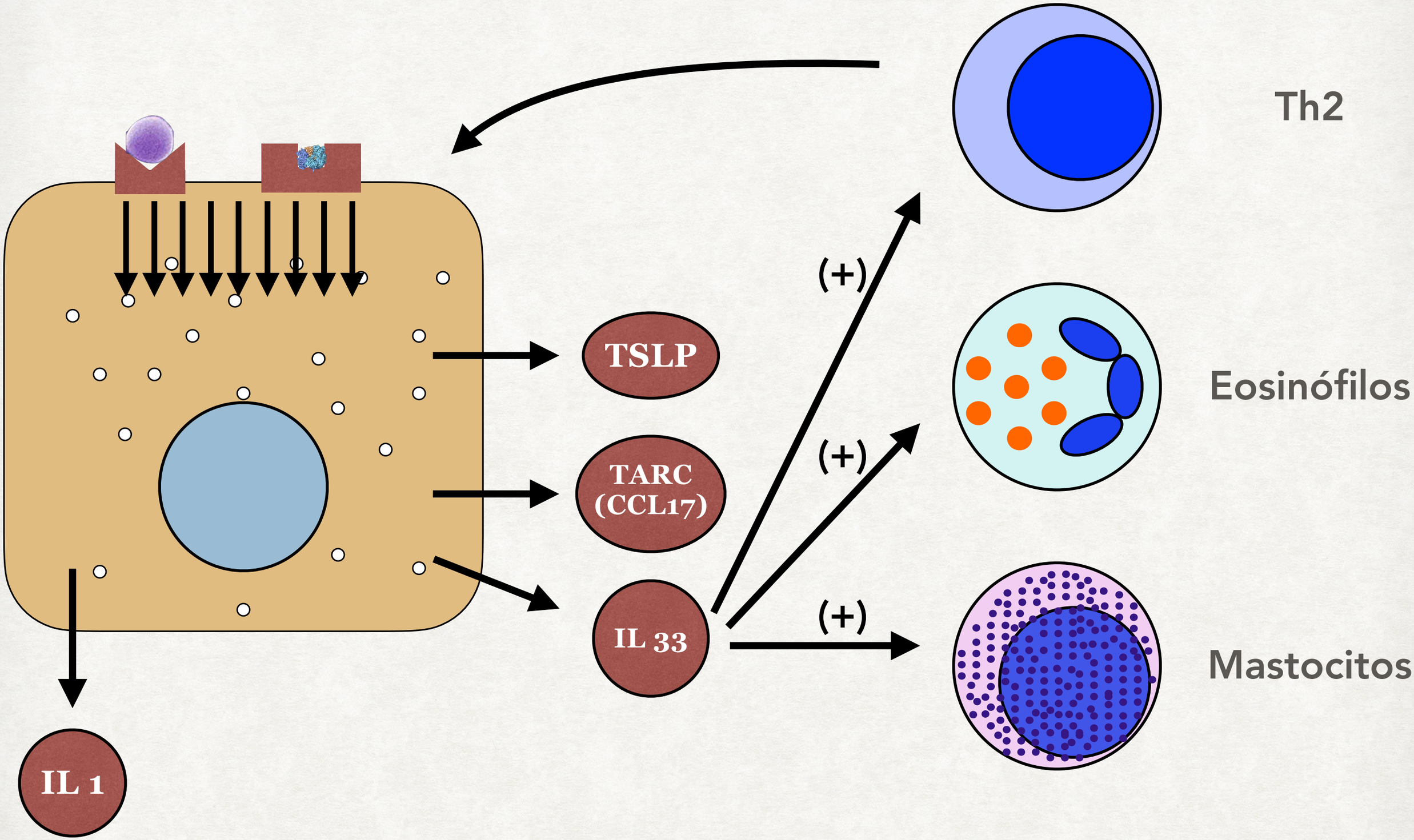
Th2

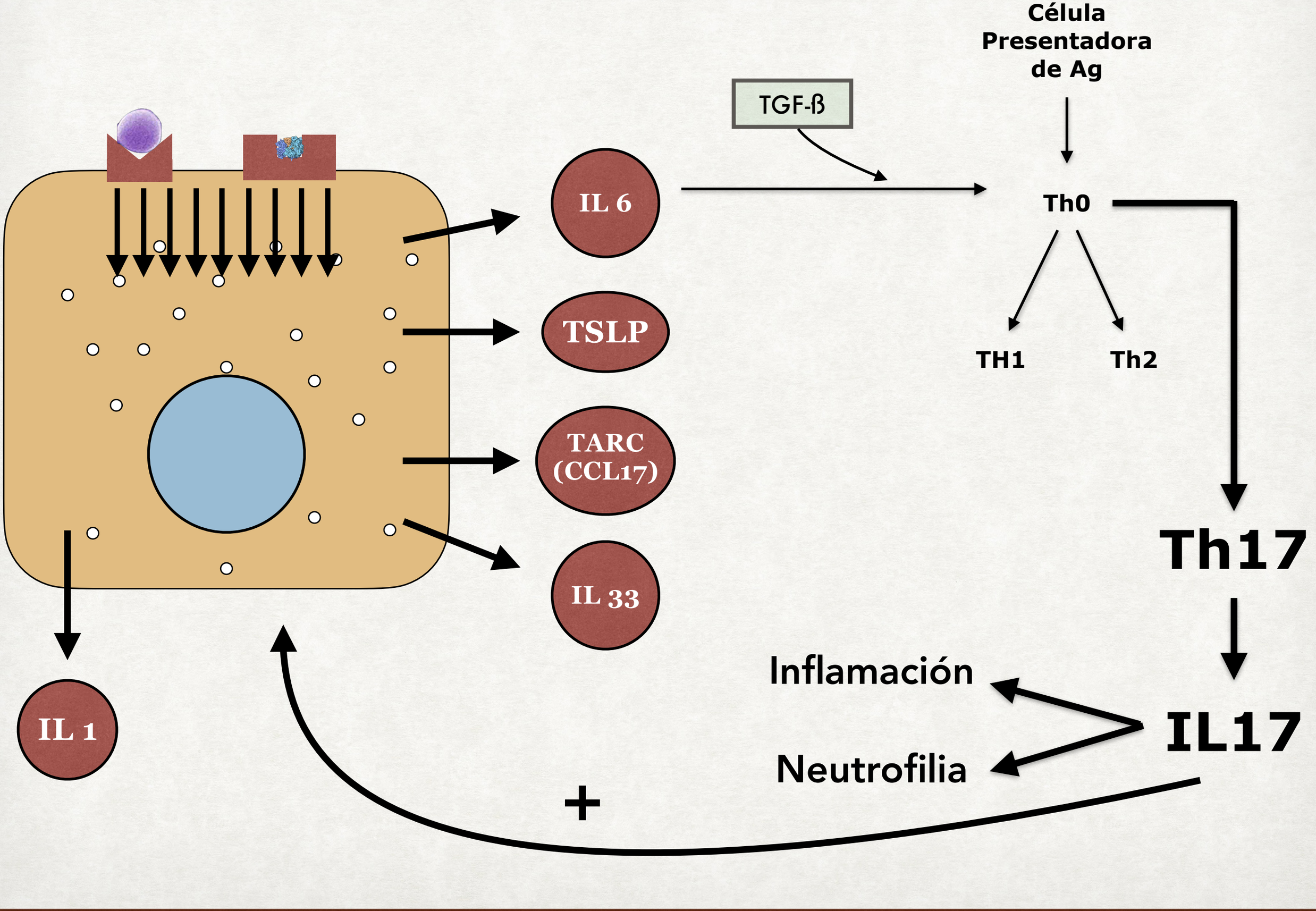


ESTIMULACIÓN NEURONAL DEL PRURITO

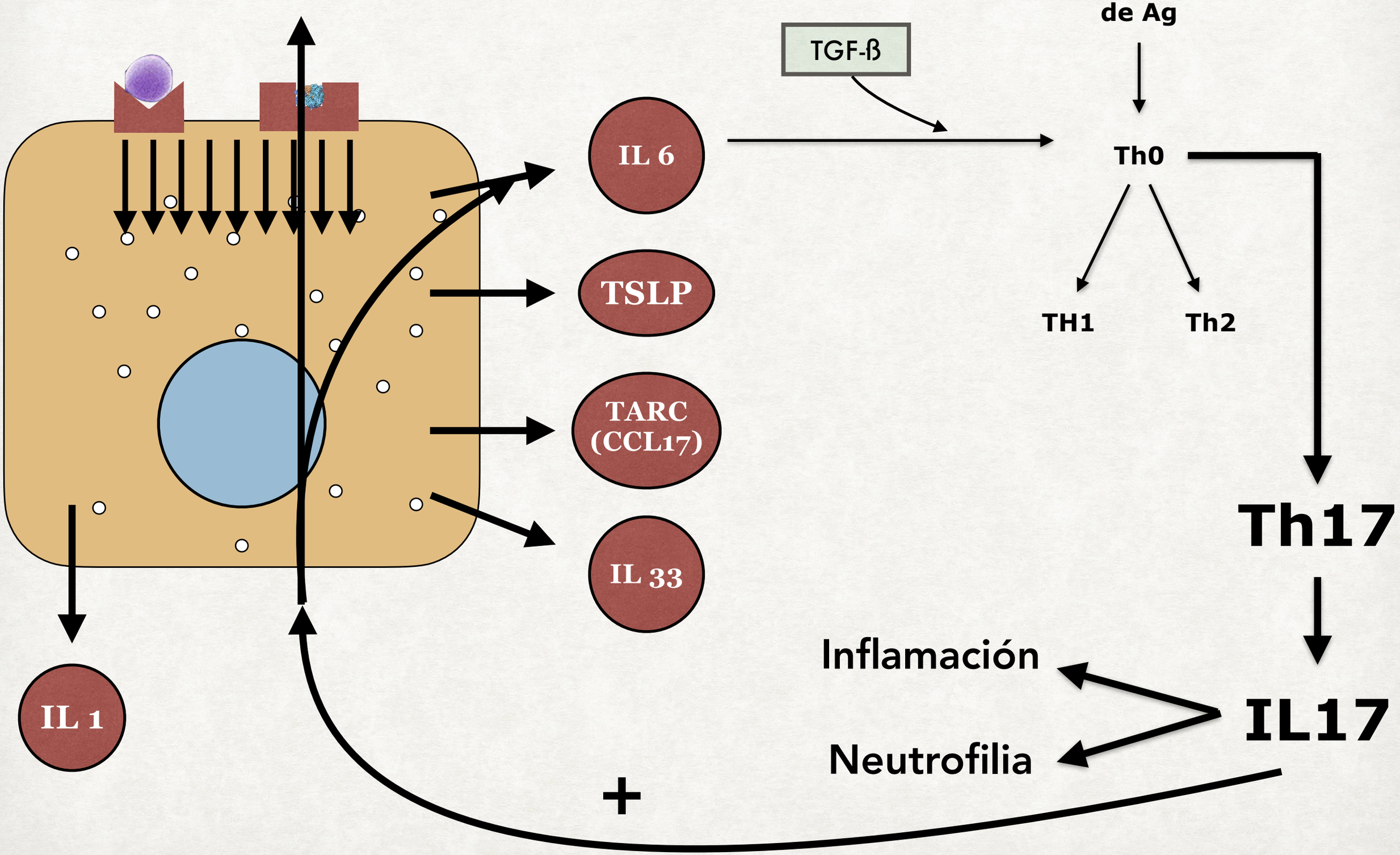
INFLAMACIÓN

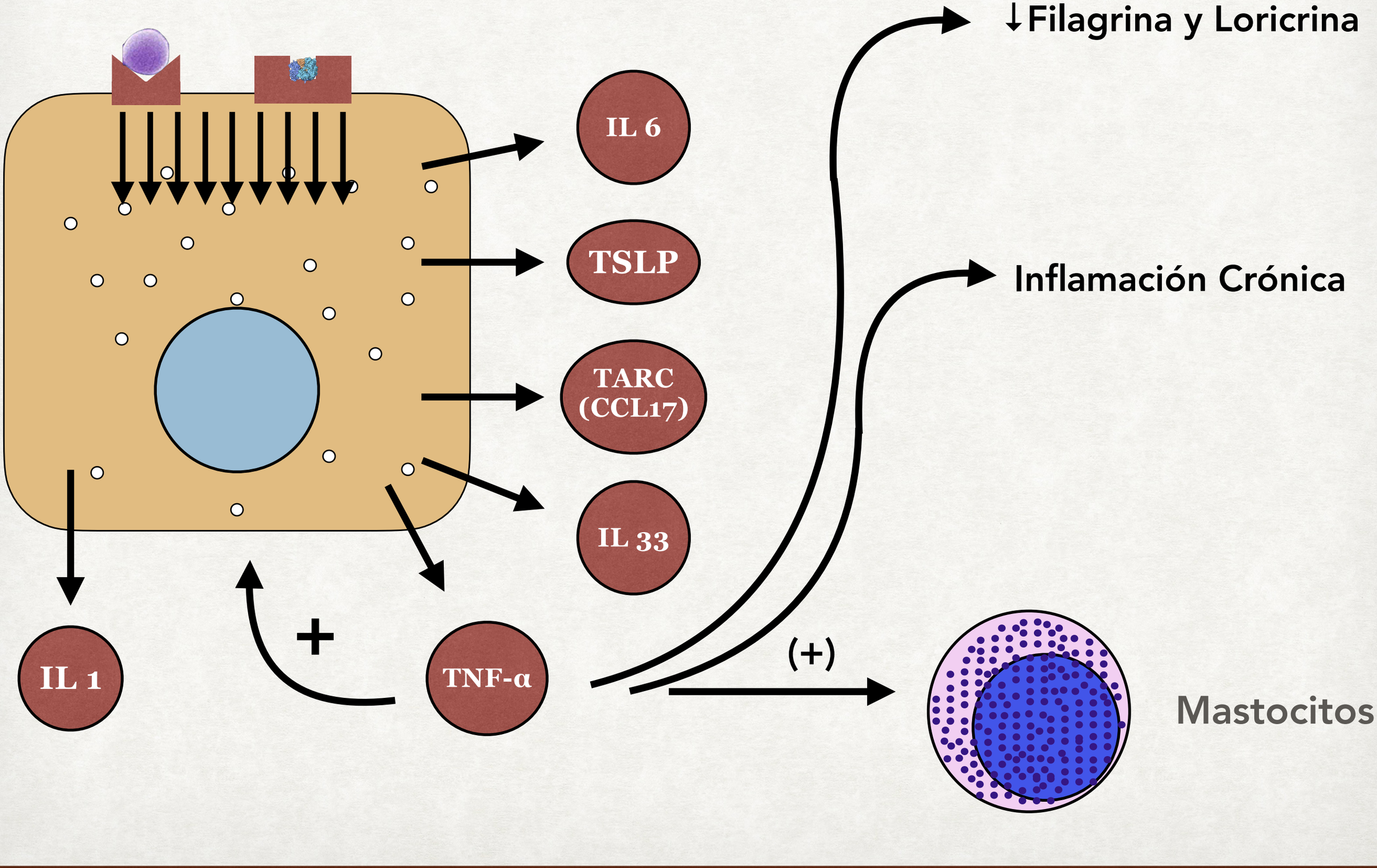

TSLP
TARC
(CCL17)
IL 1
TH2
TH2
TH2
TH2
TH2
TH2
TH2
TH2
TH2

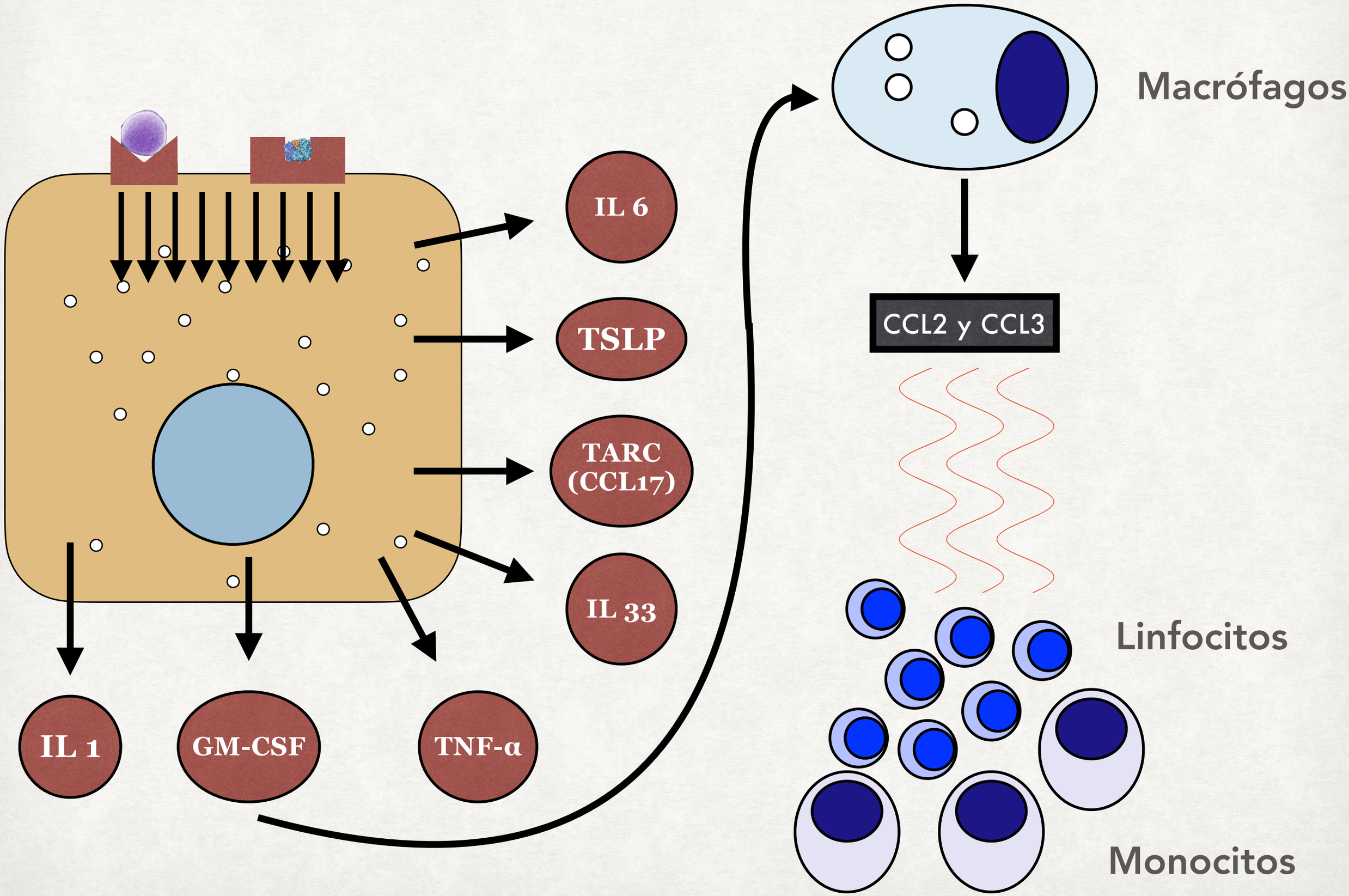

TSLP
TARC
(CCL17)
IL 33
IL 1
(+)
(+)
(+)
Th2
Eosinófilos
Mastocitos

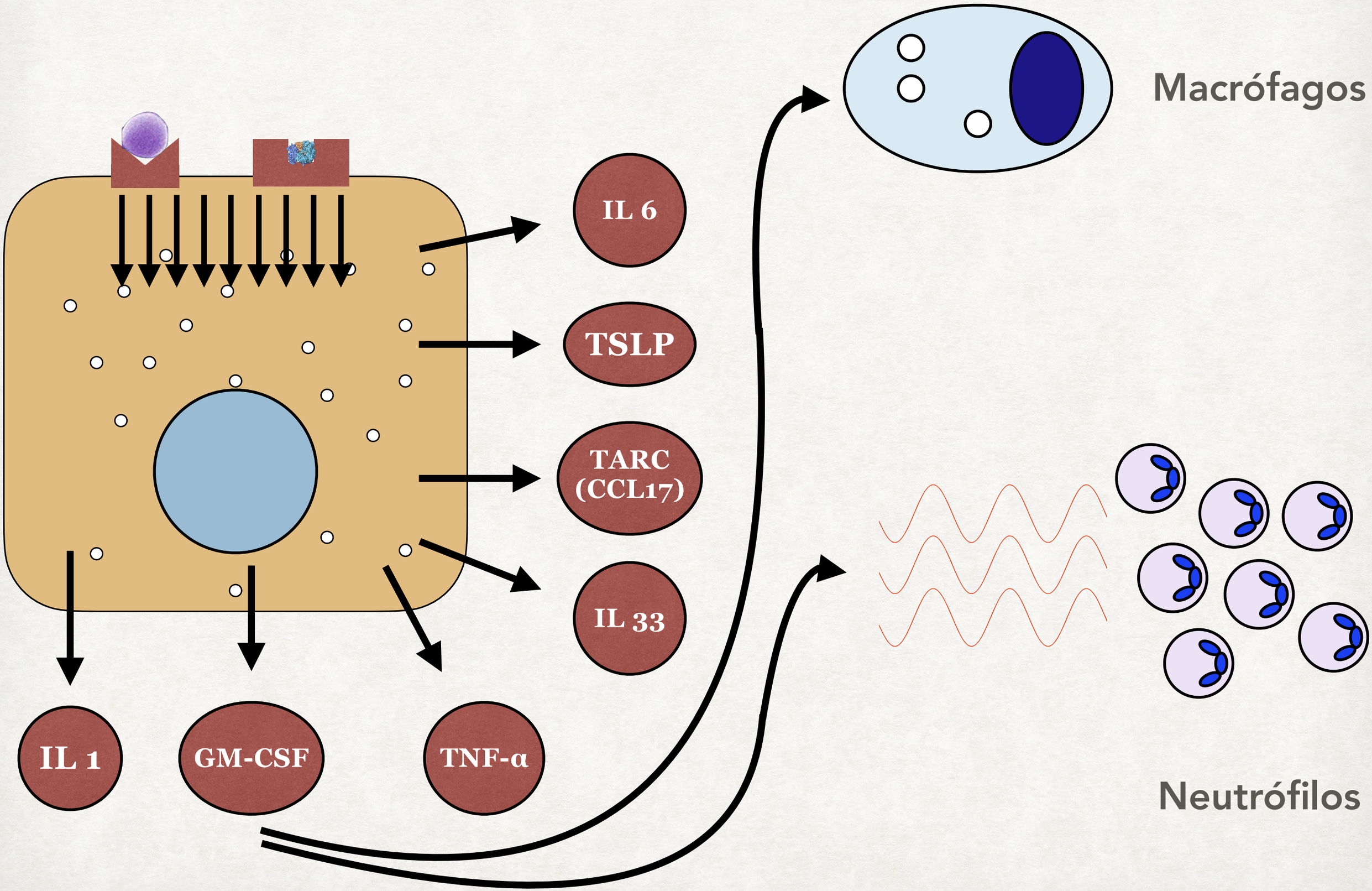

Célula Presentadora de Ag
TGF-ß
IL 6
TSLP
TARC (CCL17)
IL 33
IL 1
Th0
TH1
Th2
Th17
IL17
Inflamación
Neutrofilia
+

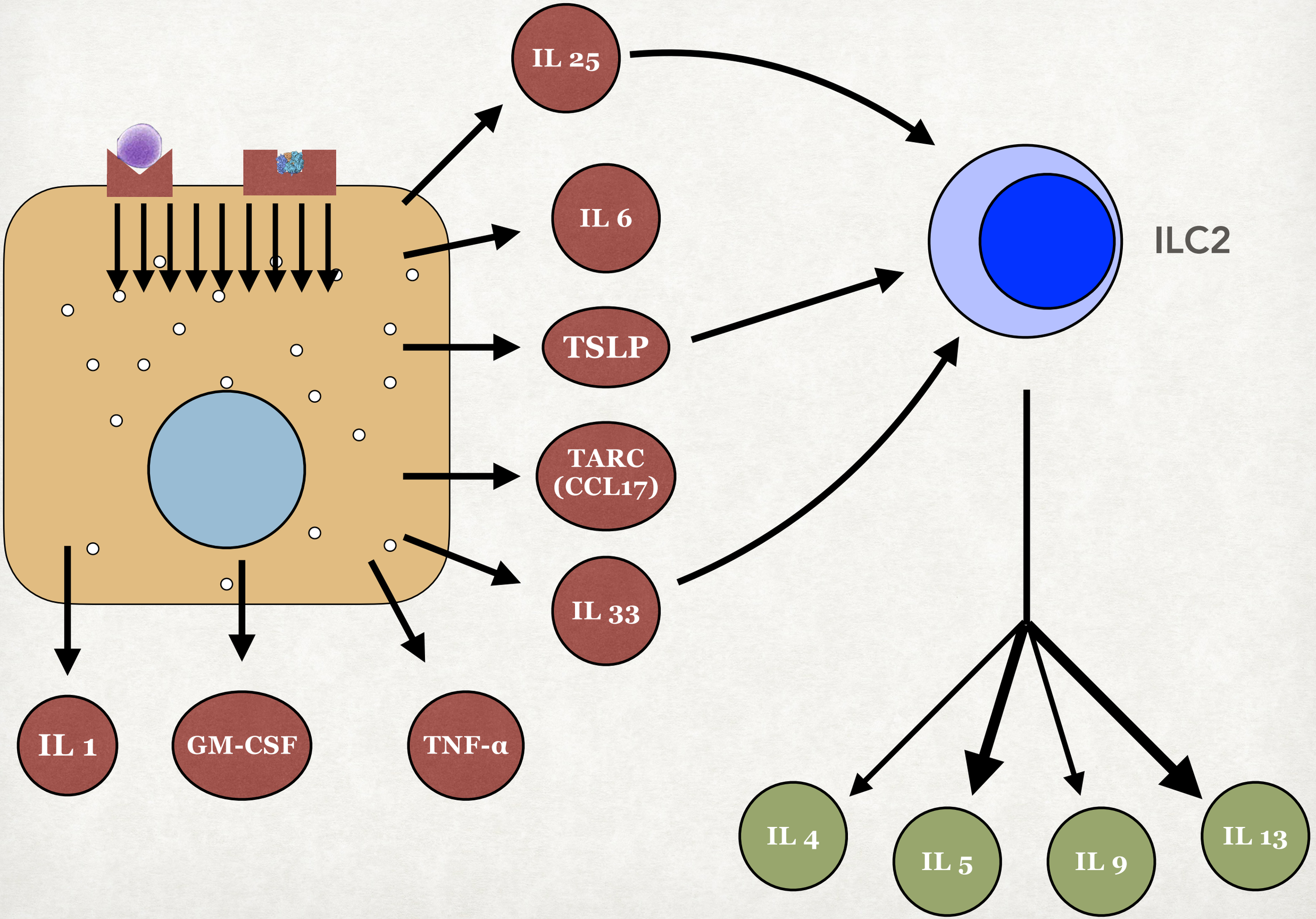
PÉPTIDOS ANTIMICROBIANOS

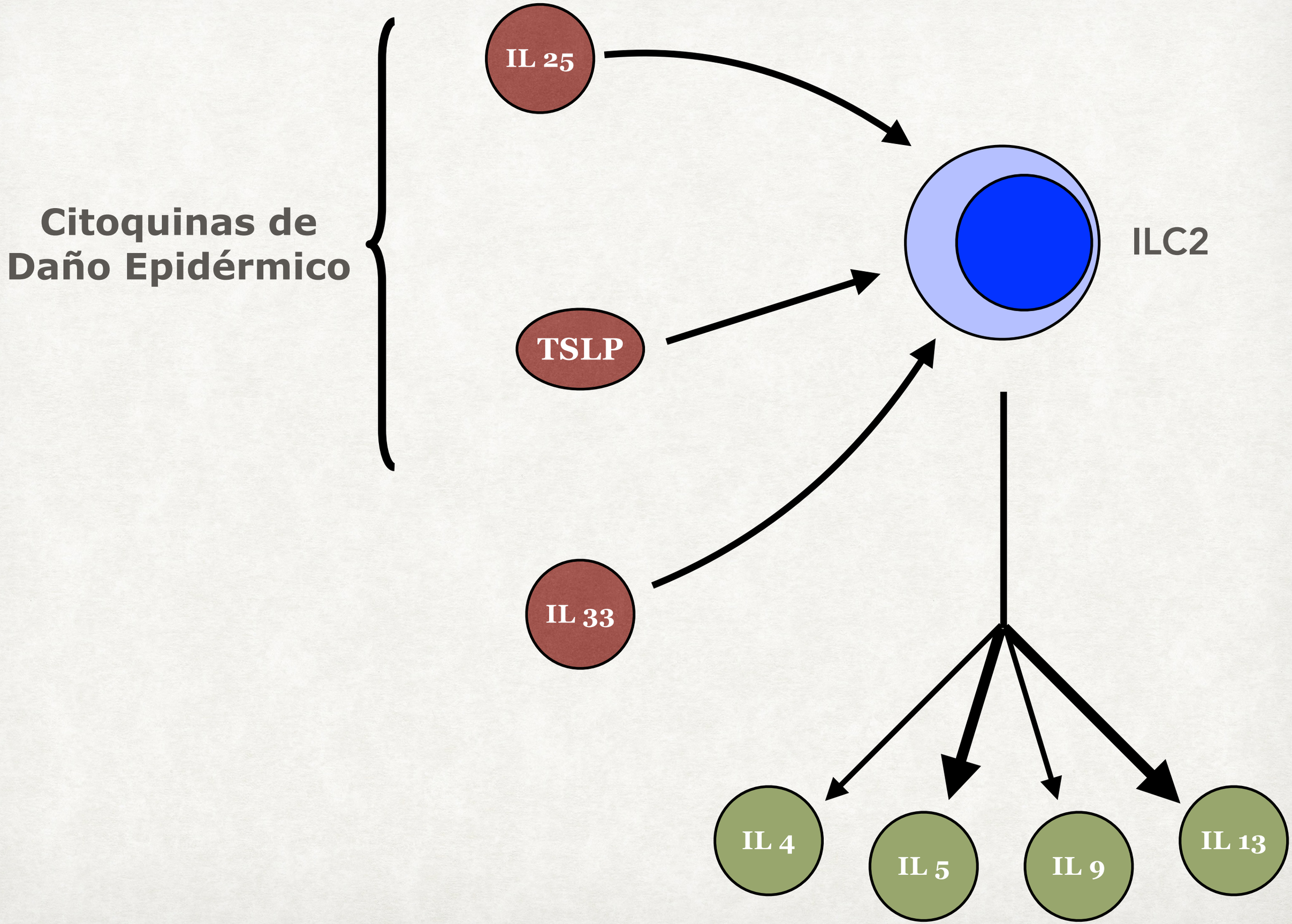


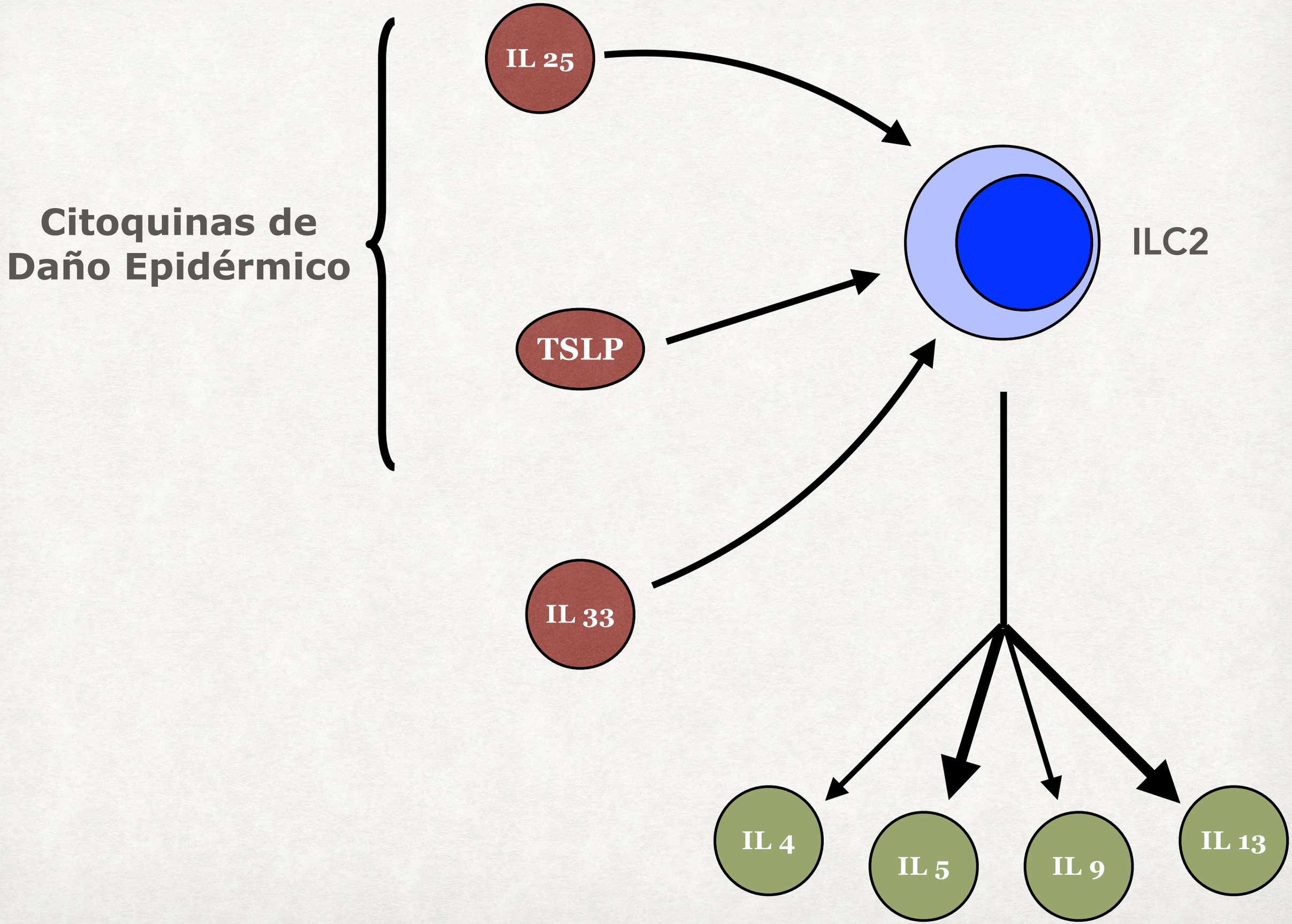

↓Filagrina y Loricrina
IL 6
TSLP
Inflamación Crónica
TARC
(CCL17)
IL 33
IL 1
+
TNF-α
(+)
Mastocitos


IL 6
TSLP
TARC (CCL17)
IL 33
IL 1
GM-CSF
TNF-α
Macrófagos
CCL2 y CCL3
Linfocitos
Monocitos


IL 6
TSLP
TARC
(CCL17)
IL 33
IL 1
GM-CSF
TNF-α
Macrófagos
Neutrófilos

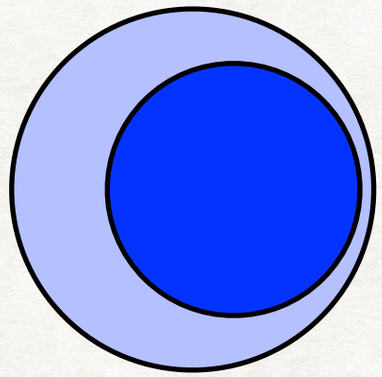

IL 25
IL 6
TSLP
TARC
(CCL17)
IL 33
ILC2
IL 1
GM-CSF
TNF-α
IL 4
IL 5
IL 9
IL 13


Citoquinas de Daño Epidérmico
IL 25
TSLP
IL 33
ILC2
IL 4
IL 5
IL 9
IL 13


Citoquinas de Daño Epidérmico
IL 25
TSLP
IL 33
ILC2
IL 4
IL 5
IL 9
IL 13

Citoquinas de Daño Epidérmico

- IL 25
- TSLP
- IL 33



ILC2

- IL 4
- IL 5
- IL 9
- IL 13

ILC2

FB

LB

Eotaxinas
(CCL11/24/26)

PLASM

IL 4

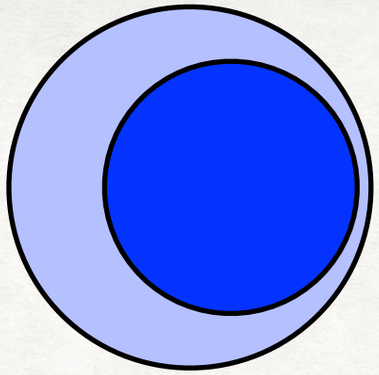
IL 5

IL 9

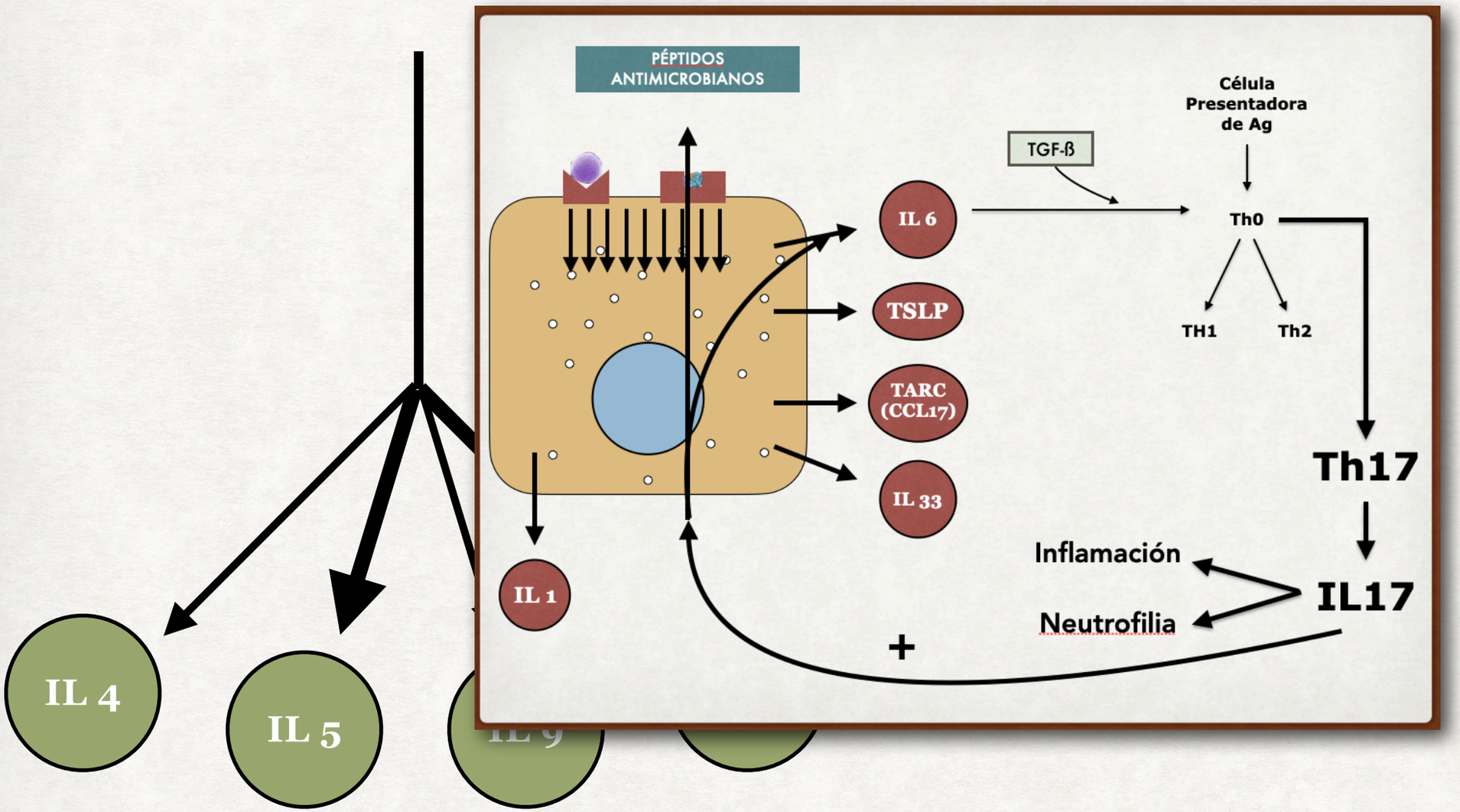
IL 13

(+)

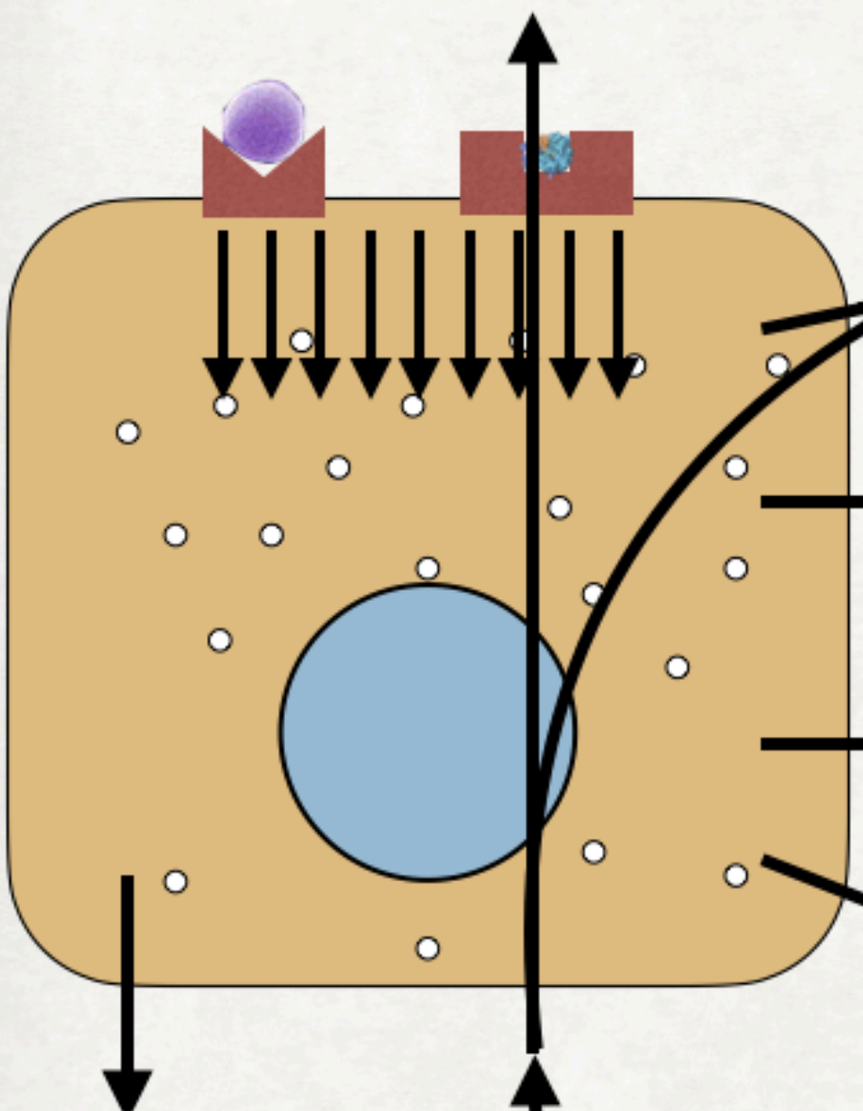
IgE



ILC2


PÉPTIDOS ANTIMICROBIANOS
IL 6
TSLP
TARC (CCL17)
IL 33
IL 1
TGF-ß
Célula Presentadora de Ag
Th0
TH1
Th2
Th17
IL17
Inflamación
Neutrofilia
+
IL 4
IL 5

PÉPTIDOS ANTIMICROBIANOS



IL 6

TSLP

TARC (CCL17)

IL 33

IL 1

TGF-ß

Célula Presentadora de Ag

Th0

TH1

Th2

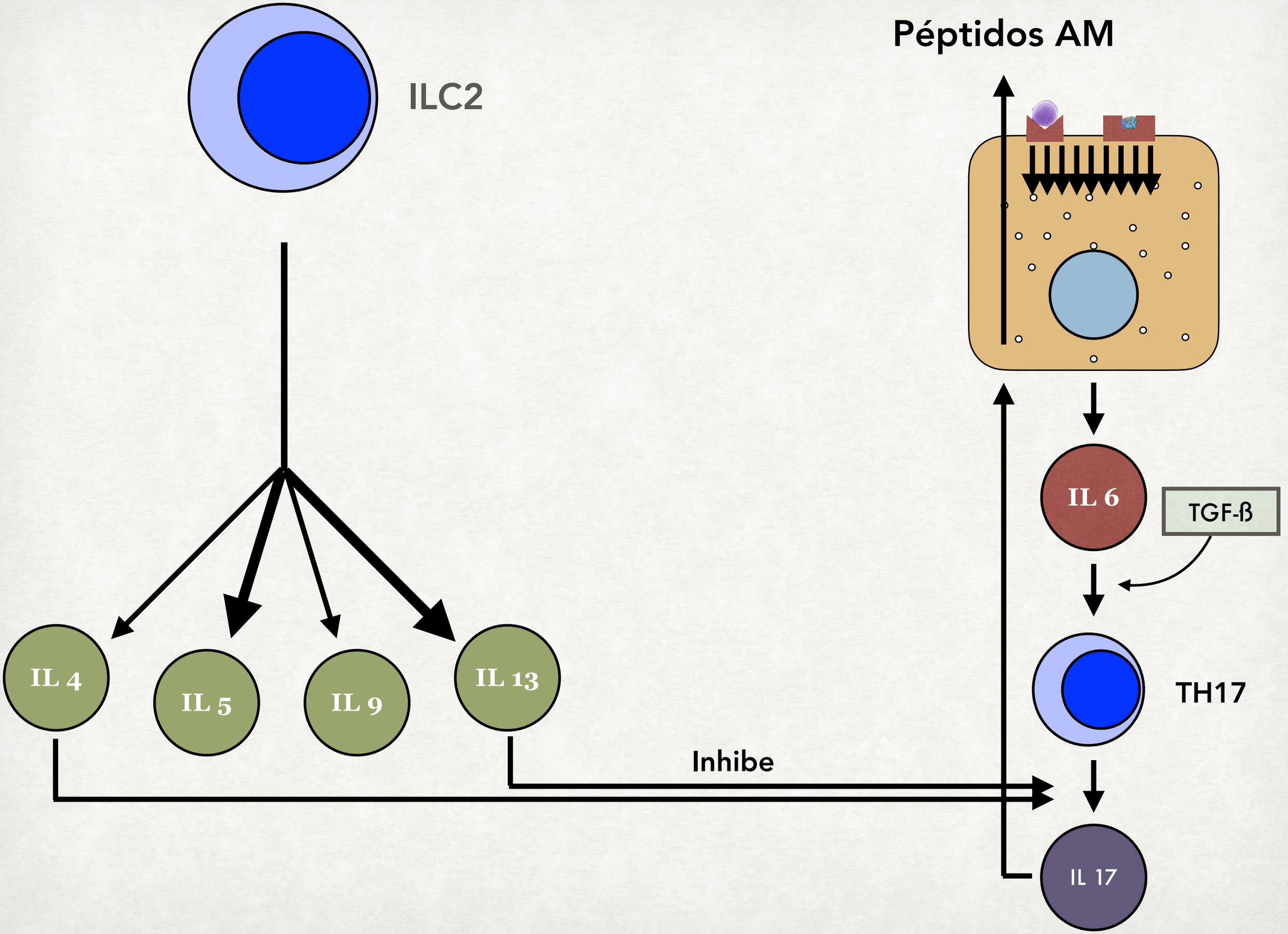
Th17

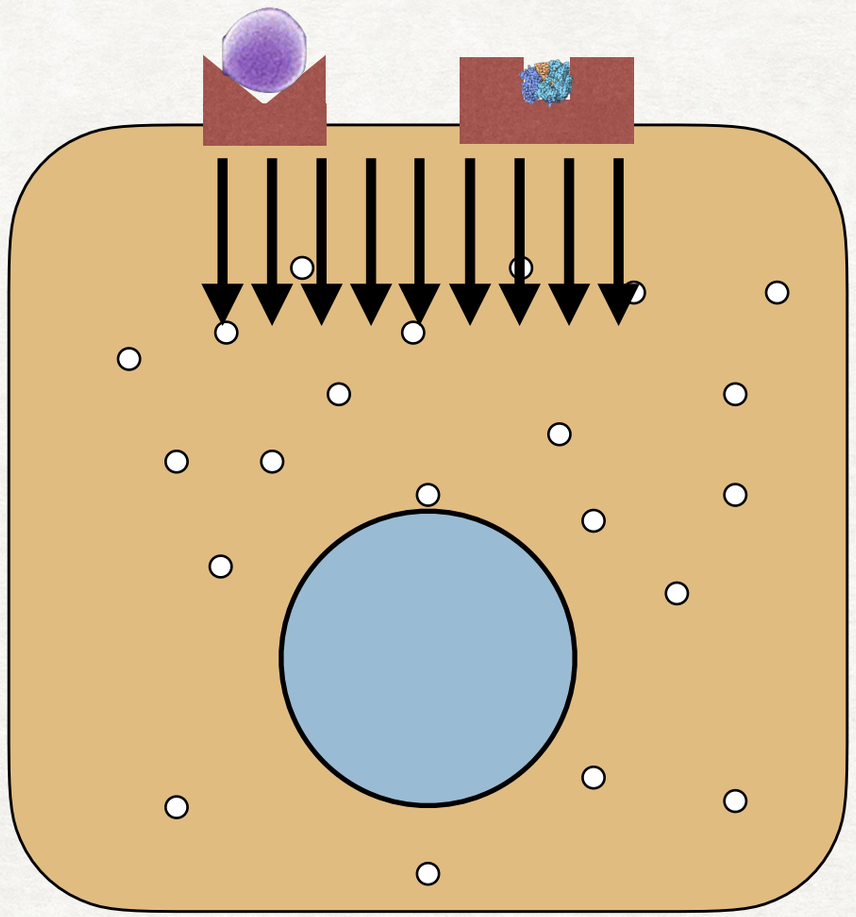
IL17

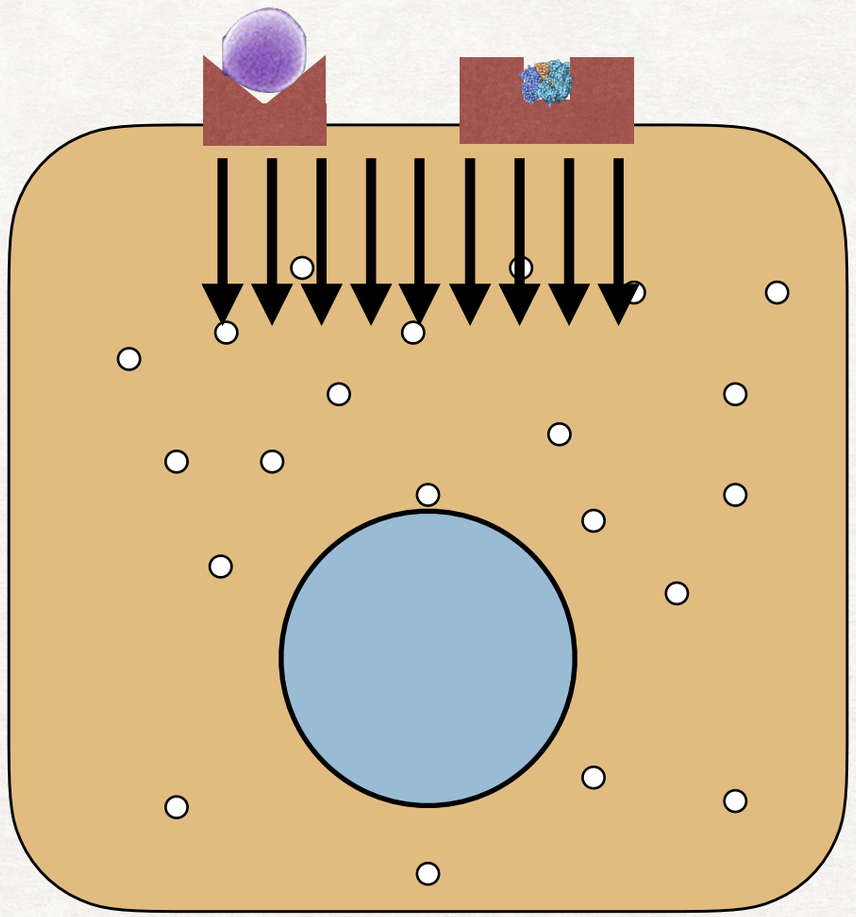
Inflamación

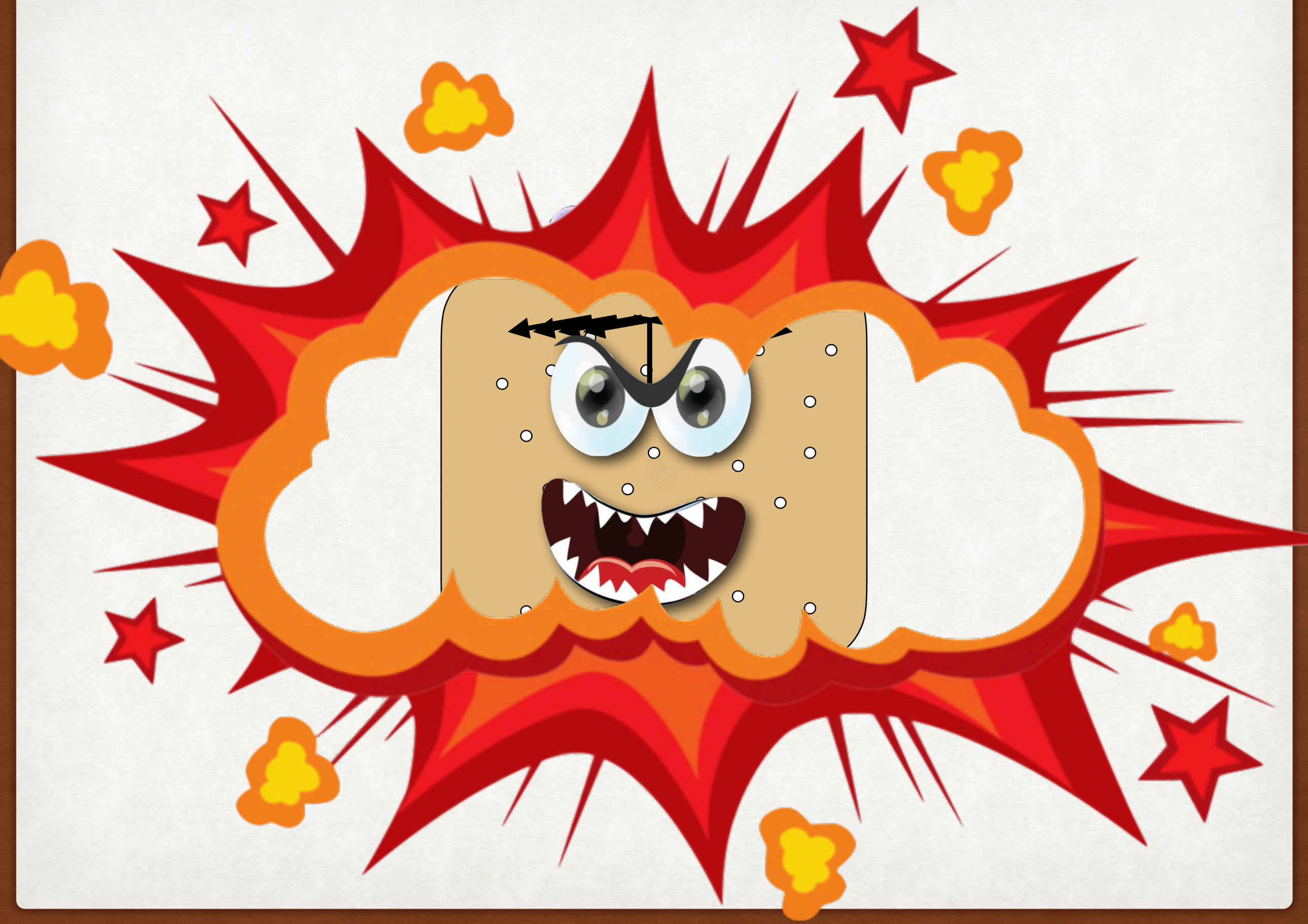
Neutrofilia

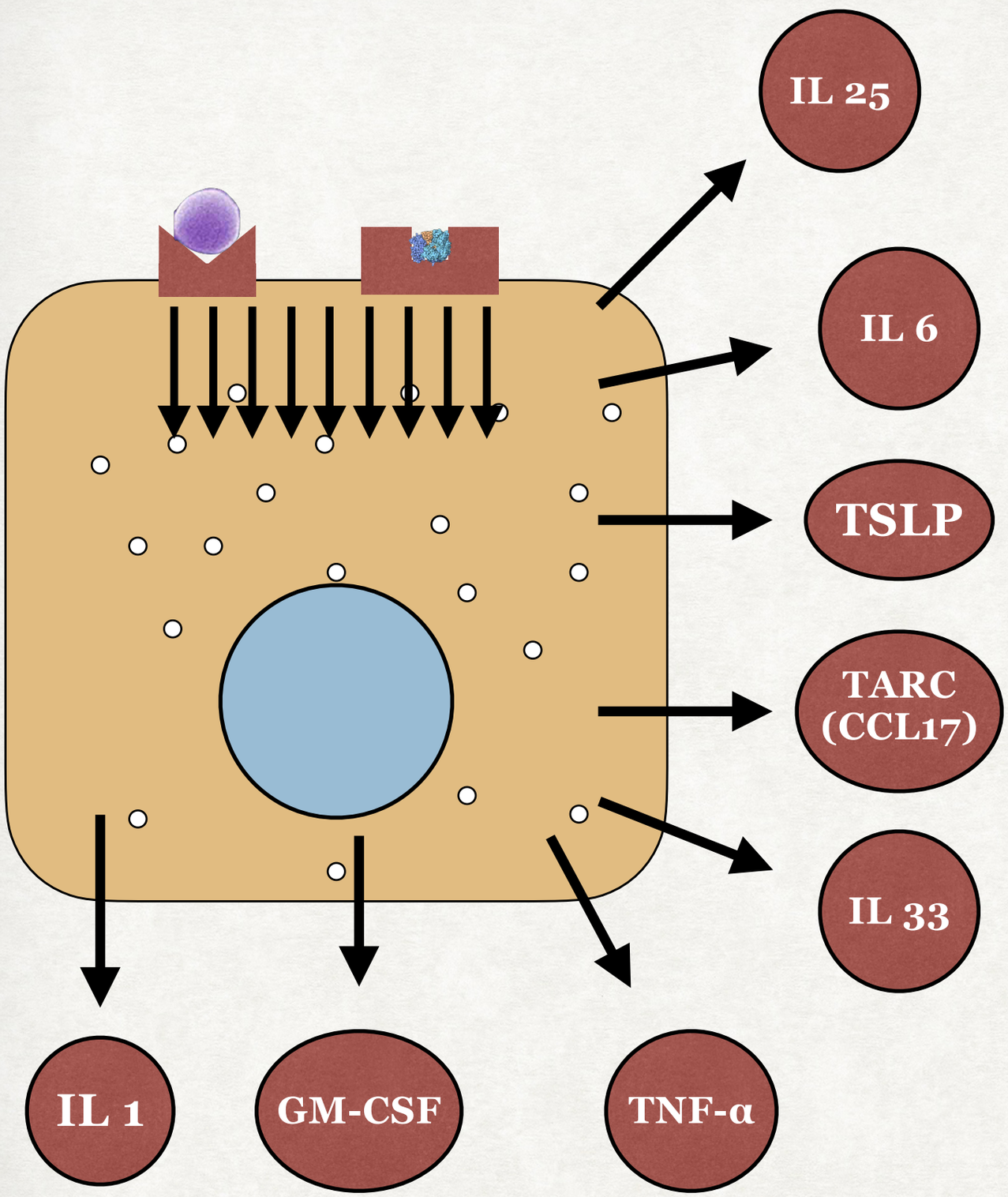
+


ILC2
IL 4
IL 5
IL 9
IL 13
Inhibe
Péptidos AM
IL 6
TGF-ß
TH17
IL 17

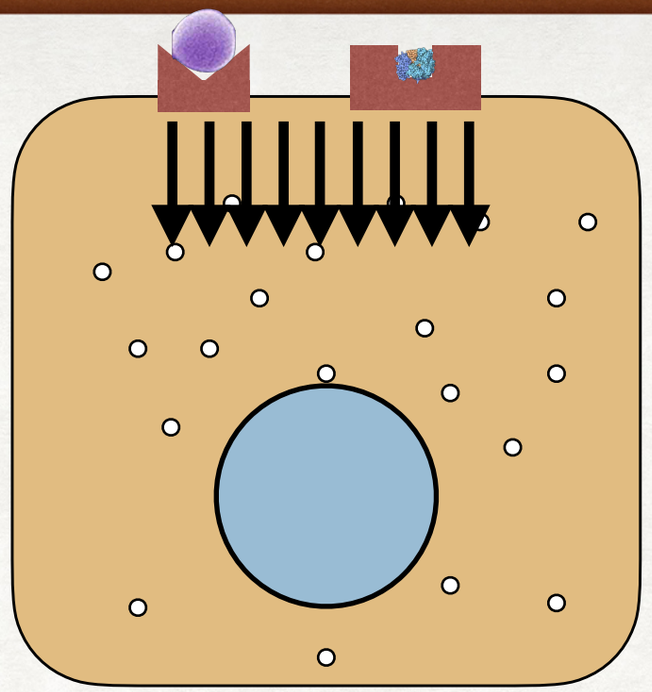






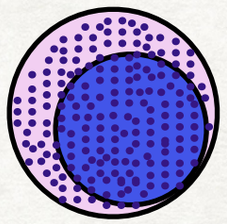

IL 25
IL 6
TSLP
TARC
(CCL17)
IL 33
IL 1
GM-CSF
TNF-α

ILC2
TH2
TH2
Eosinófilos
Mastocitos
Macrófagos
Neutrófilos



IL 6

IL 25

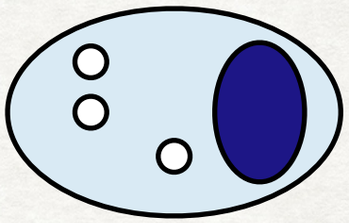


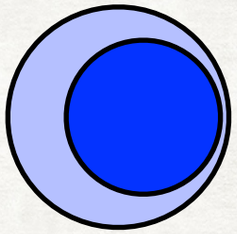
TARC (CCL17)

IL 1

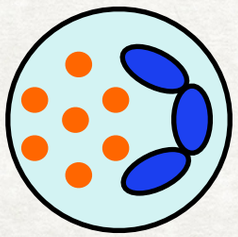
TNF-α

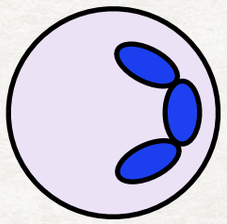
IL 33





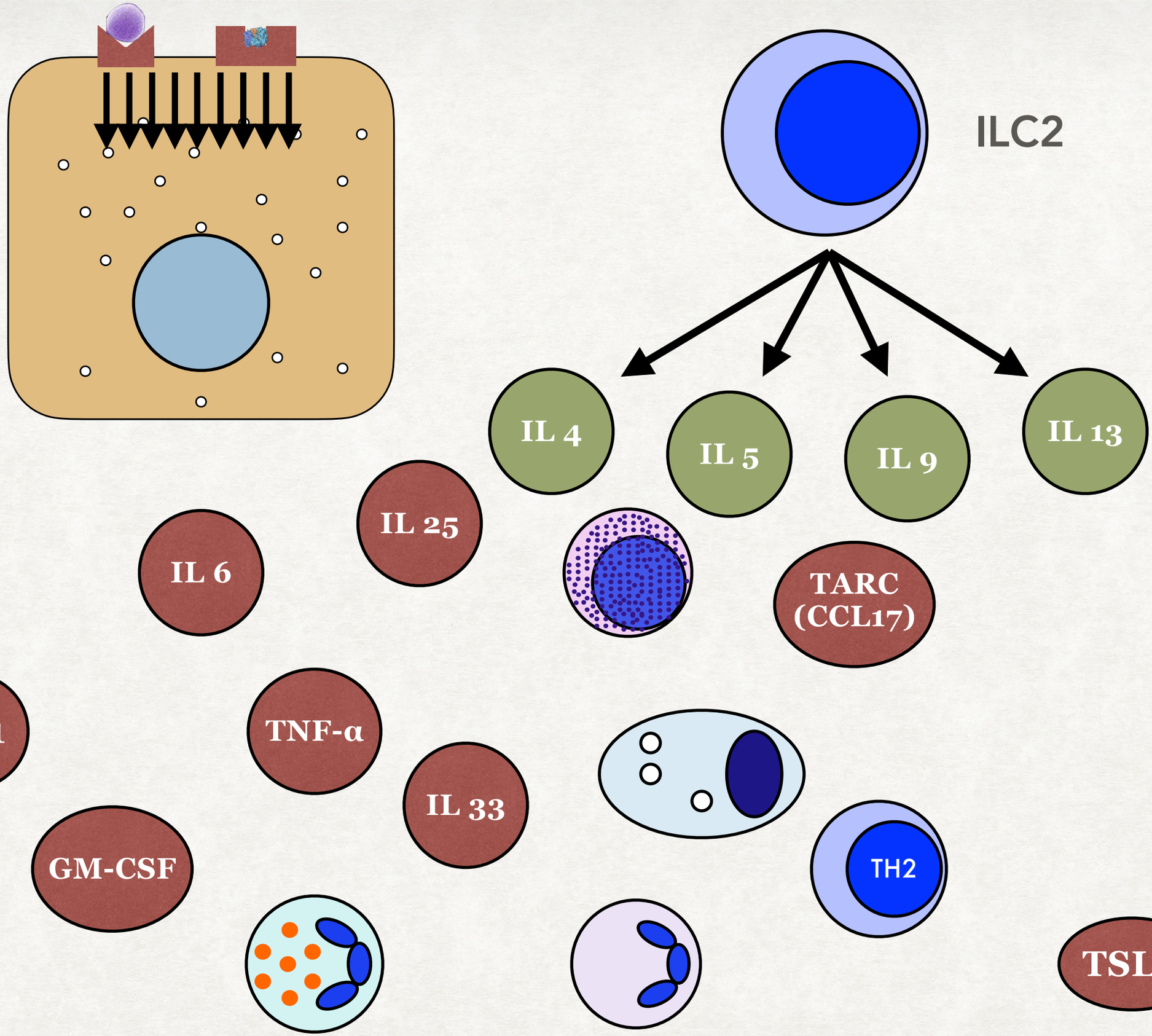
GM-CSF

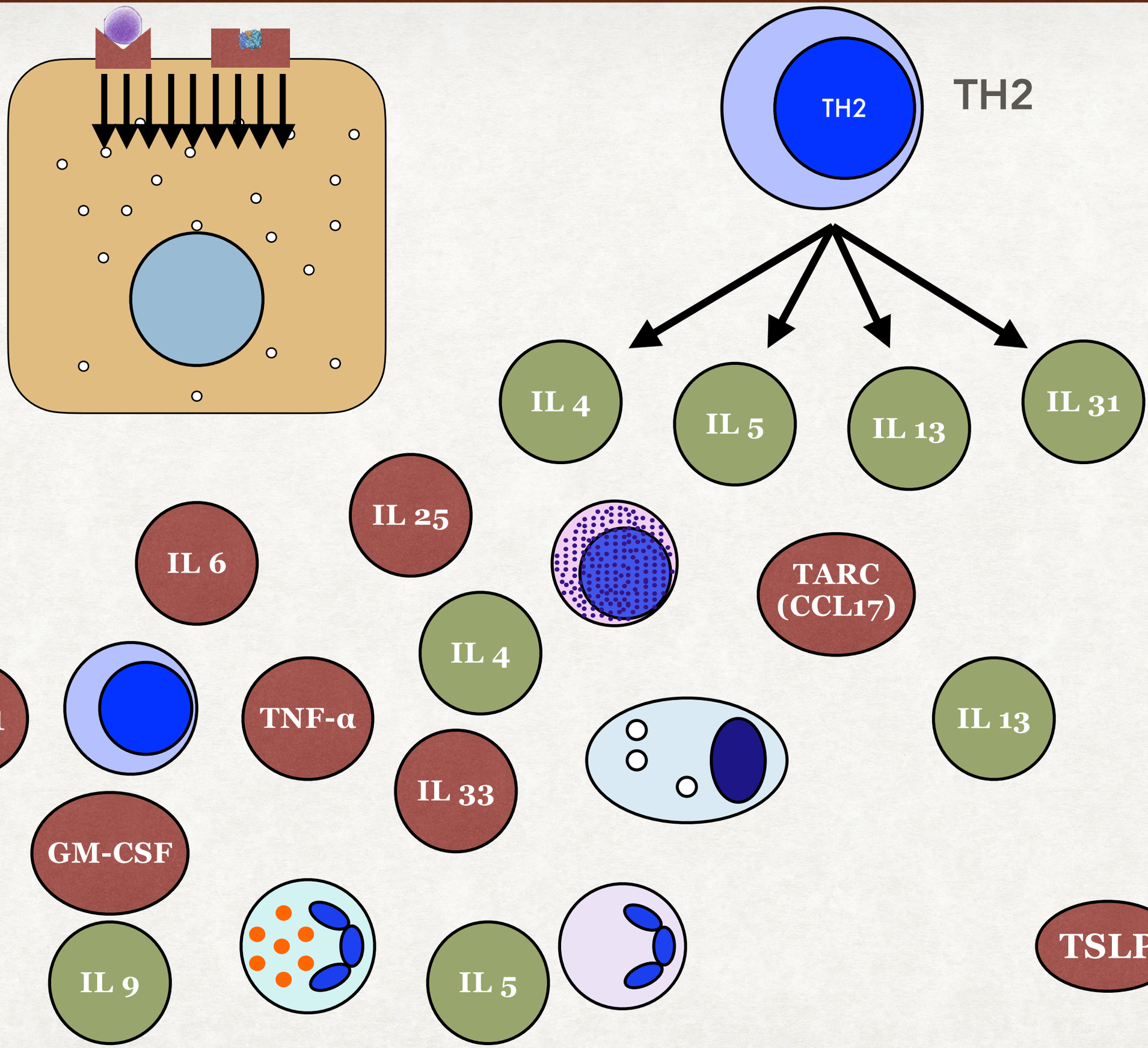




TH2

TSLP


ILC2
IL 4
IL 5
IL 9
IL 13
IL 25
IL 6
TARC
(CCL17)
IL 1
TNF-α
IL 33
GM-CSF
TH2
TSLP


TH2
TH2
IL 4
IL 5
IL 13
IL 31
IL 25
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(CCL17)
IL 4
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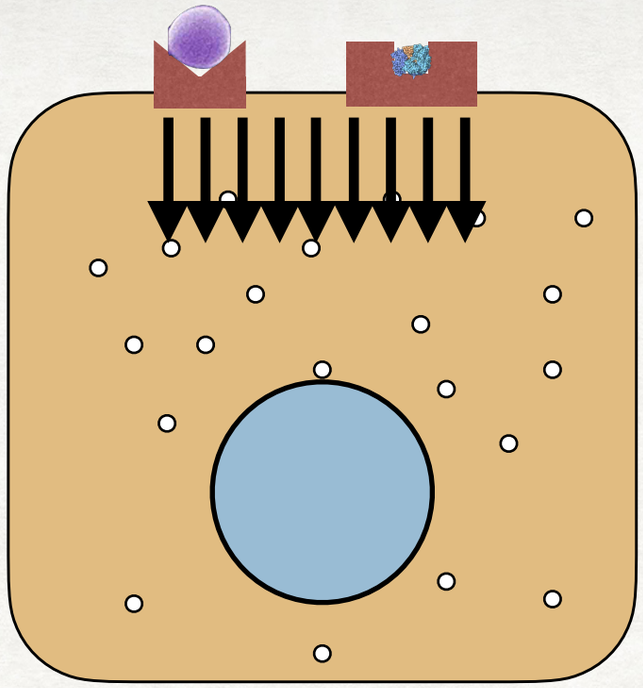
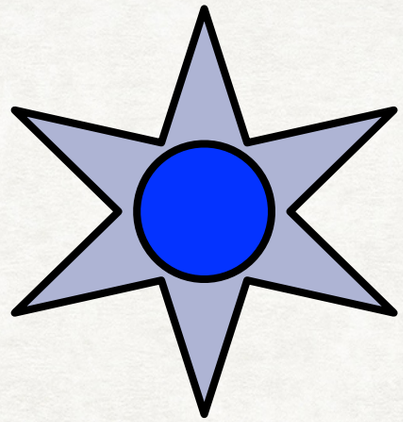
TNF-α
IL 13
IL 33
GM-CSF
IL 9
IL 5
TSLP



Célula Langerhans



IL 6

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TNF-α

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GM-CSF

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TARC (CCL17)

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TH2

IL 25

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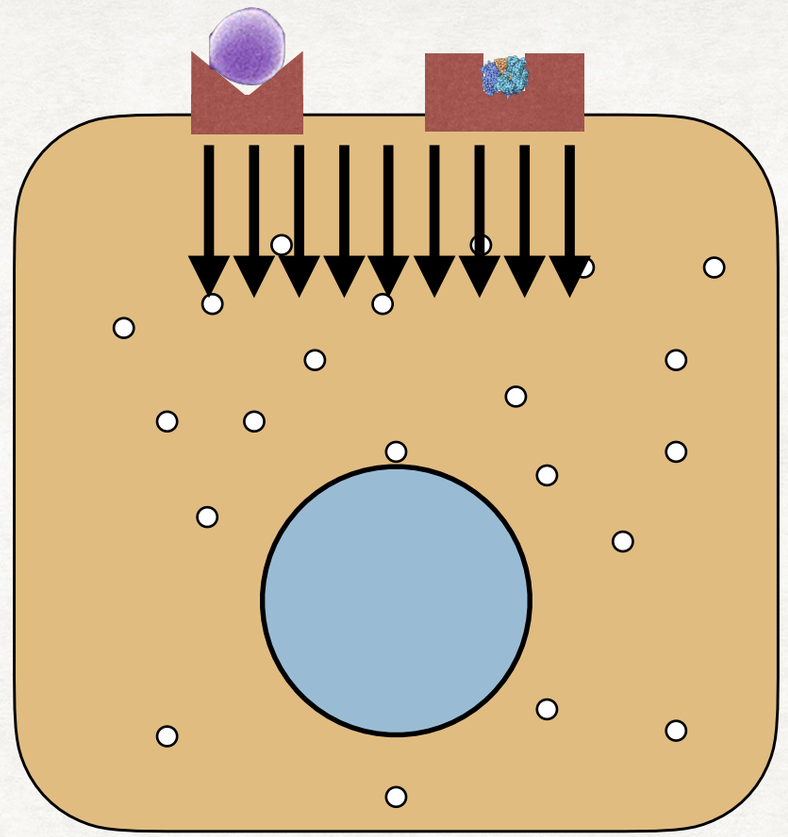

IL 6
TNF-α
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TARC (CCL17)
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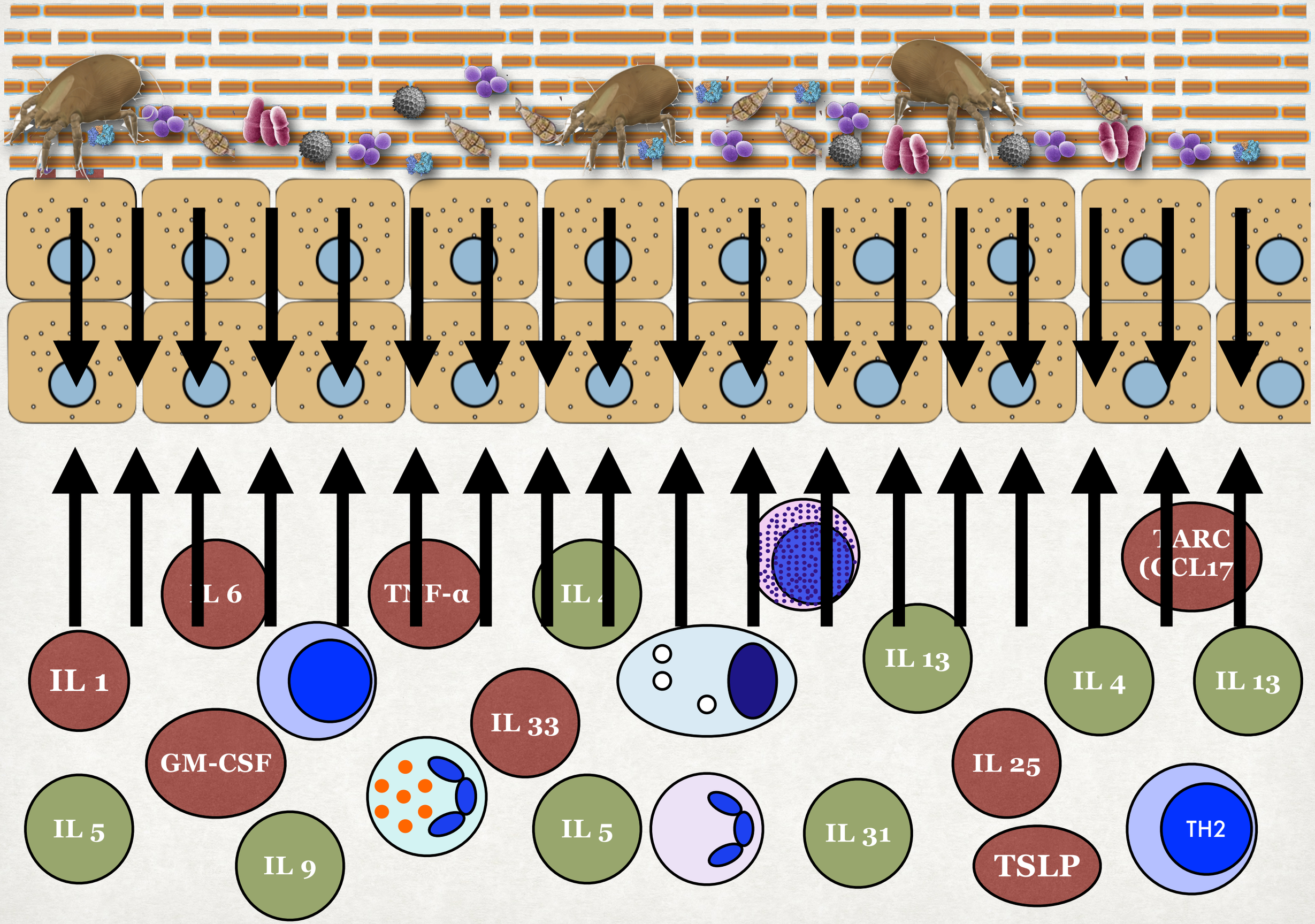
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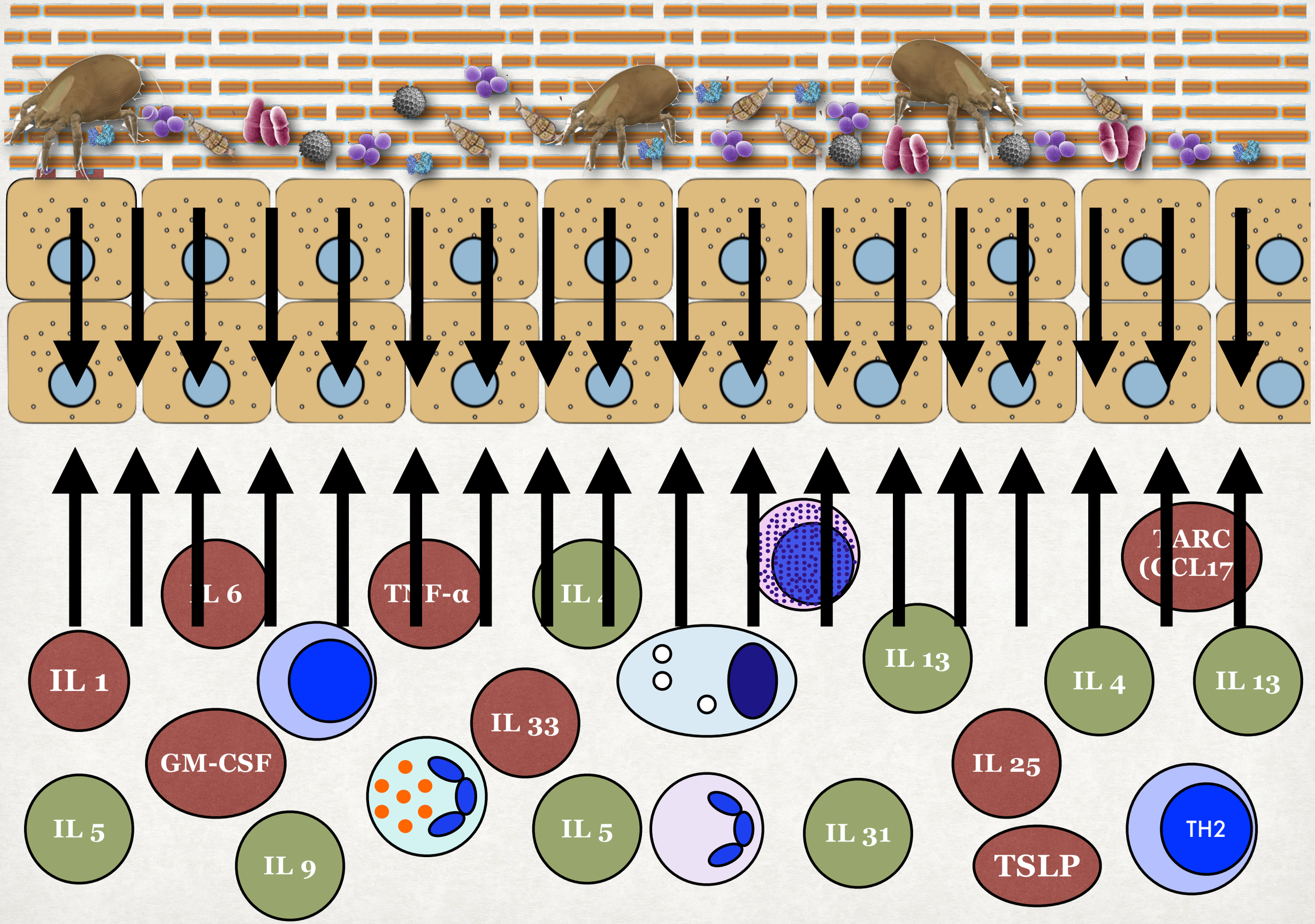
TH2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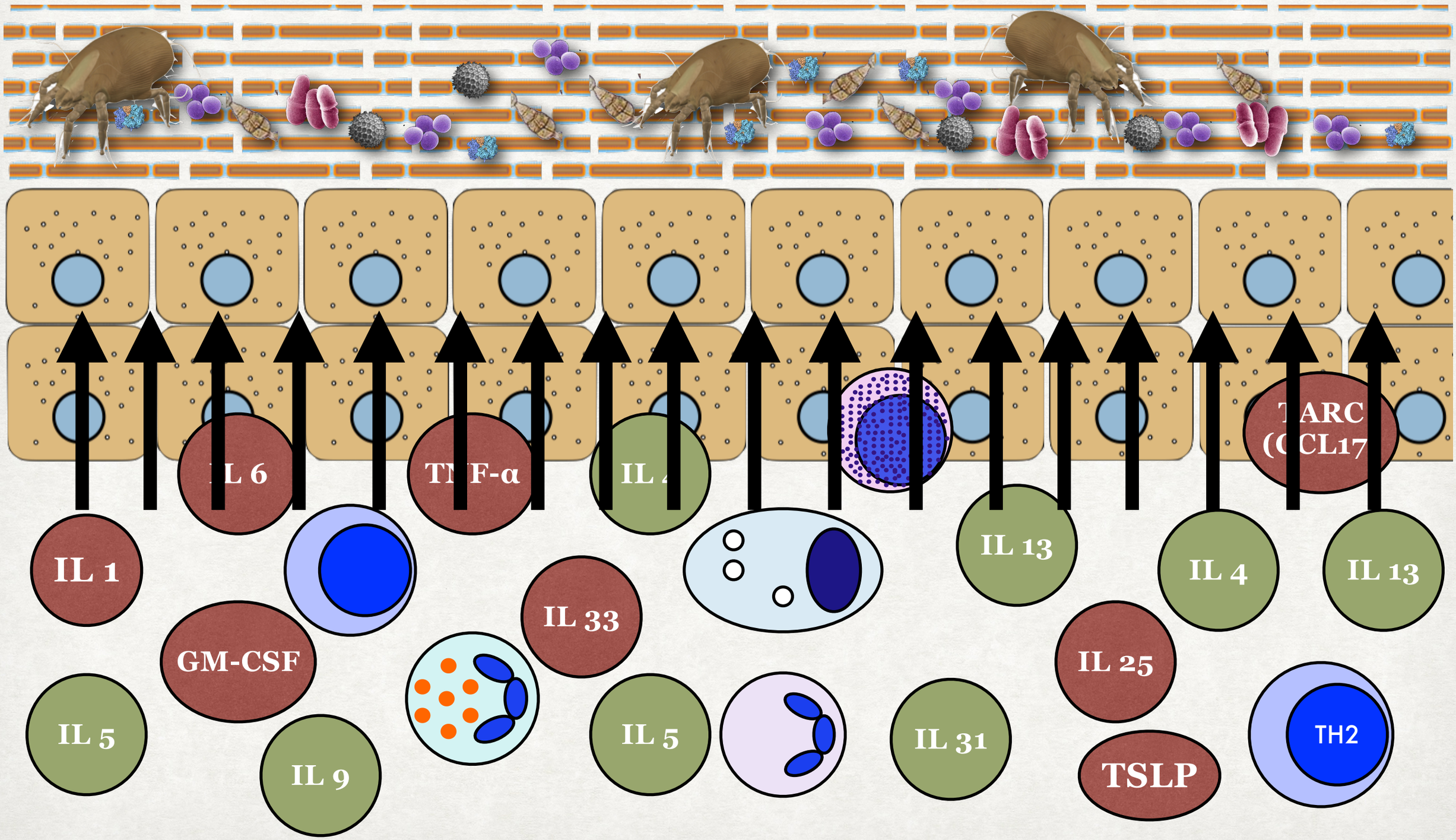
TH2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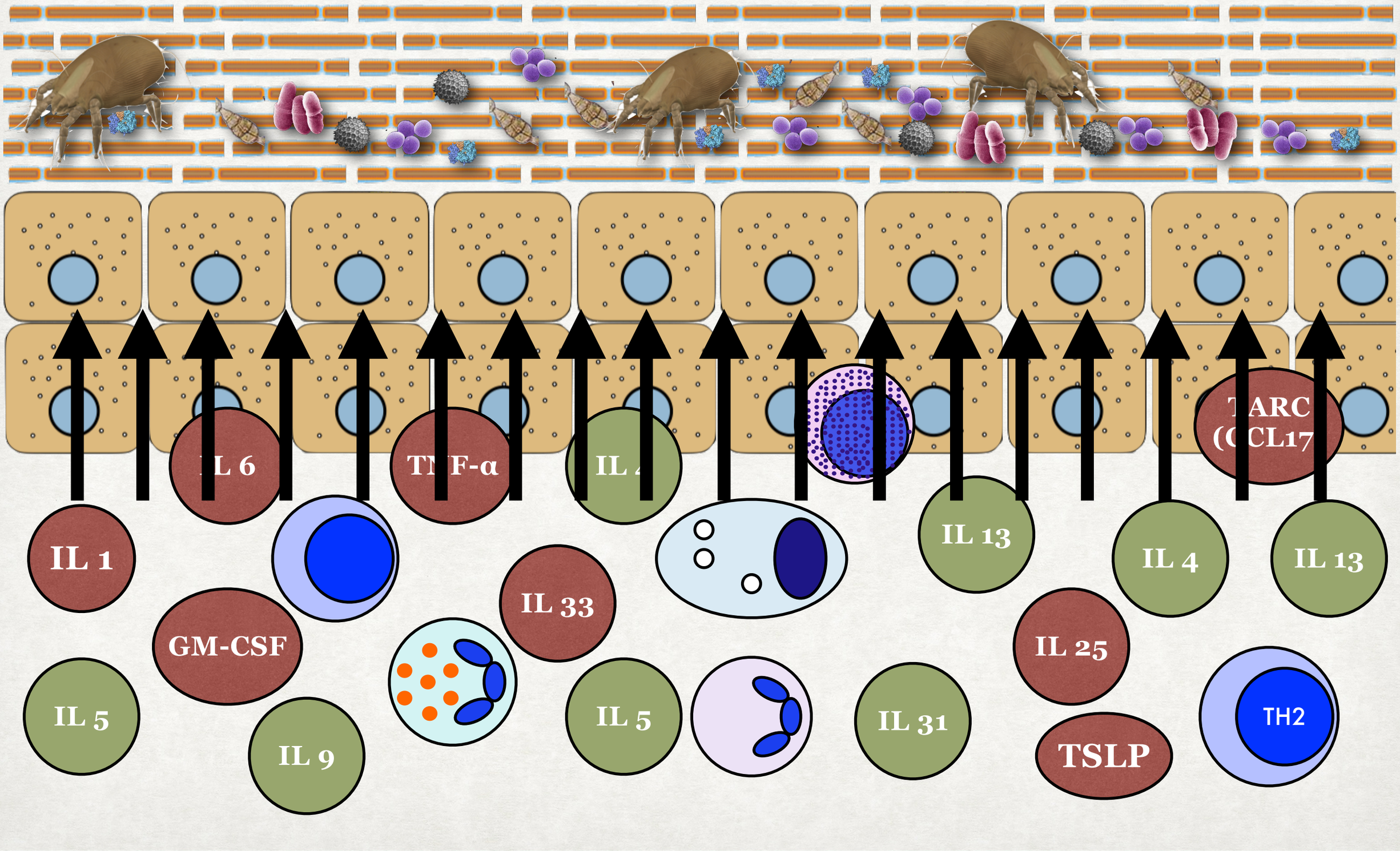
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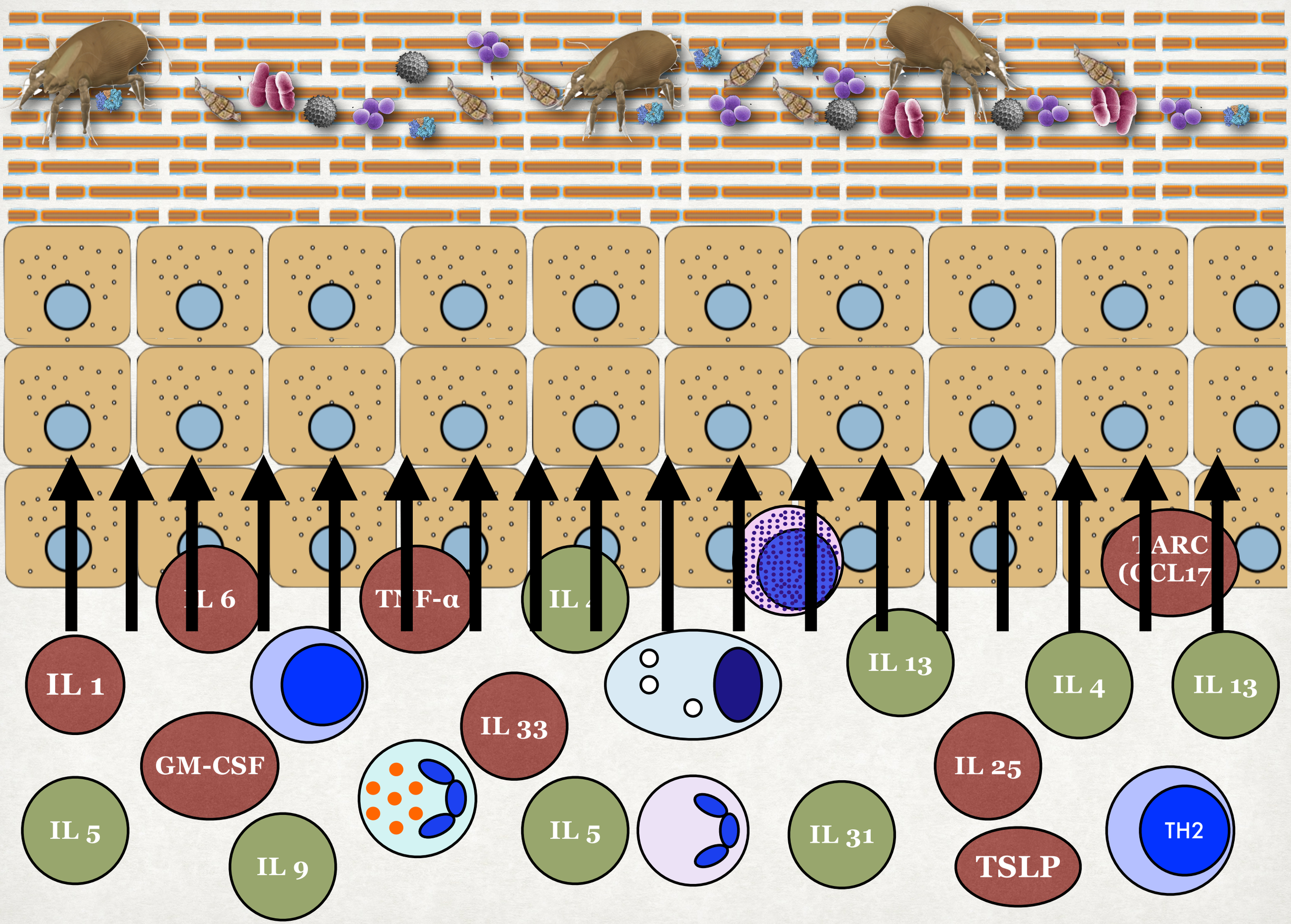
IL 6
TNF-α
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GM-CSF
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IL 25
TSLP
TH2

IL 6

TNF-α

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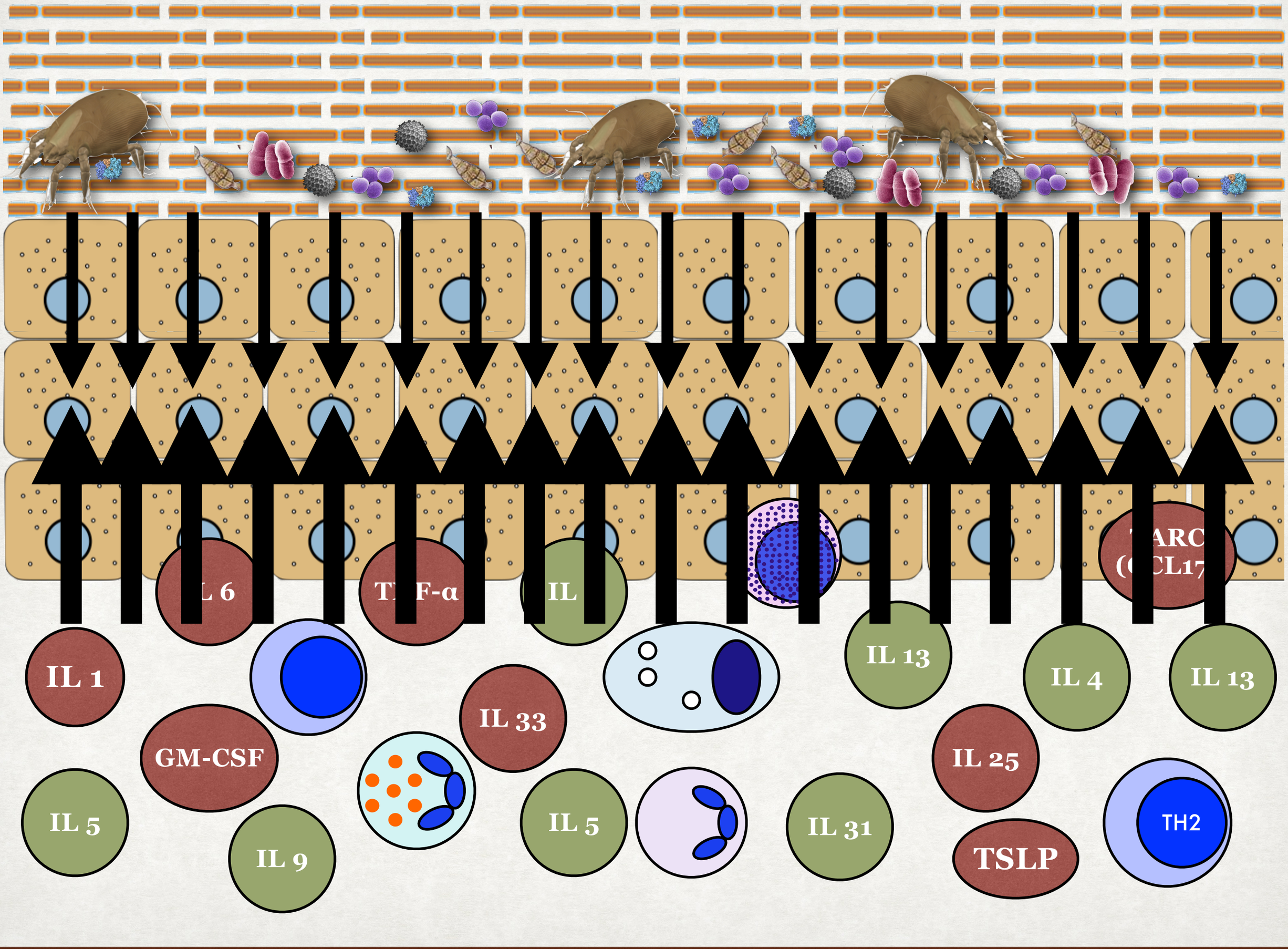
TSLP

TH2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ARC
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GM-CSF
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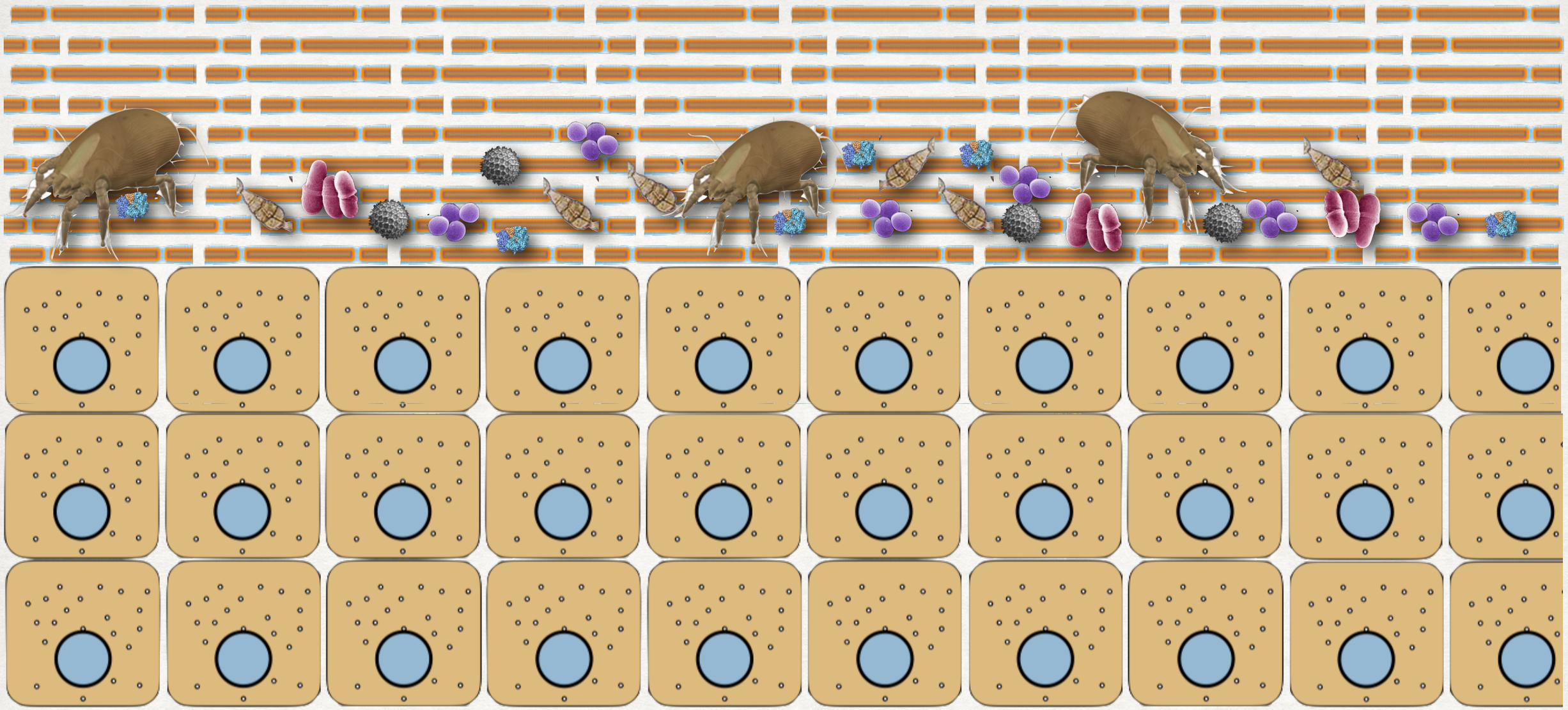
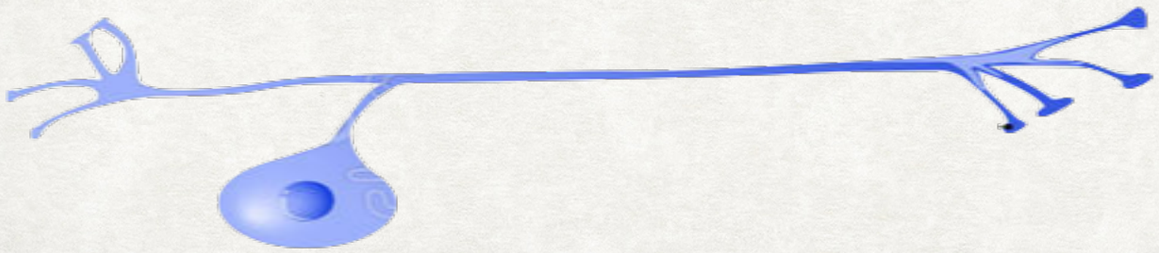
TSLP
TH2





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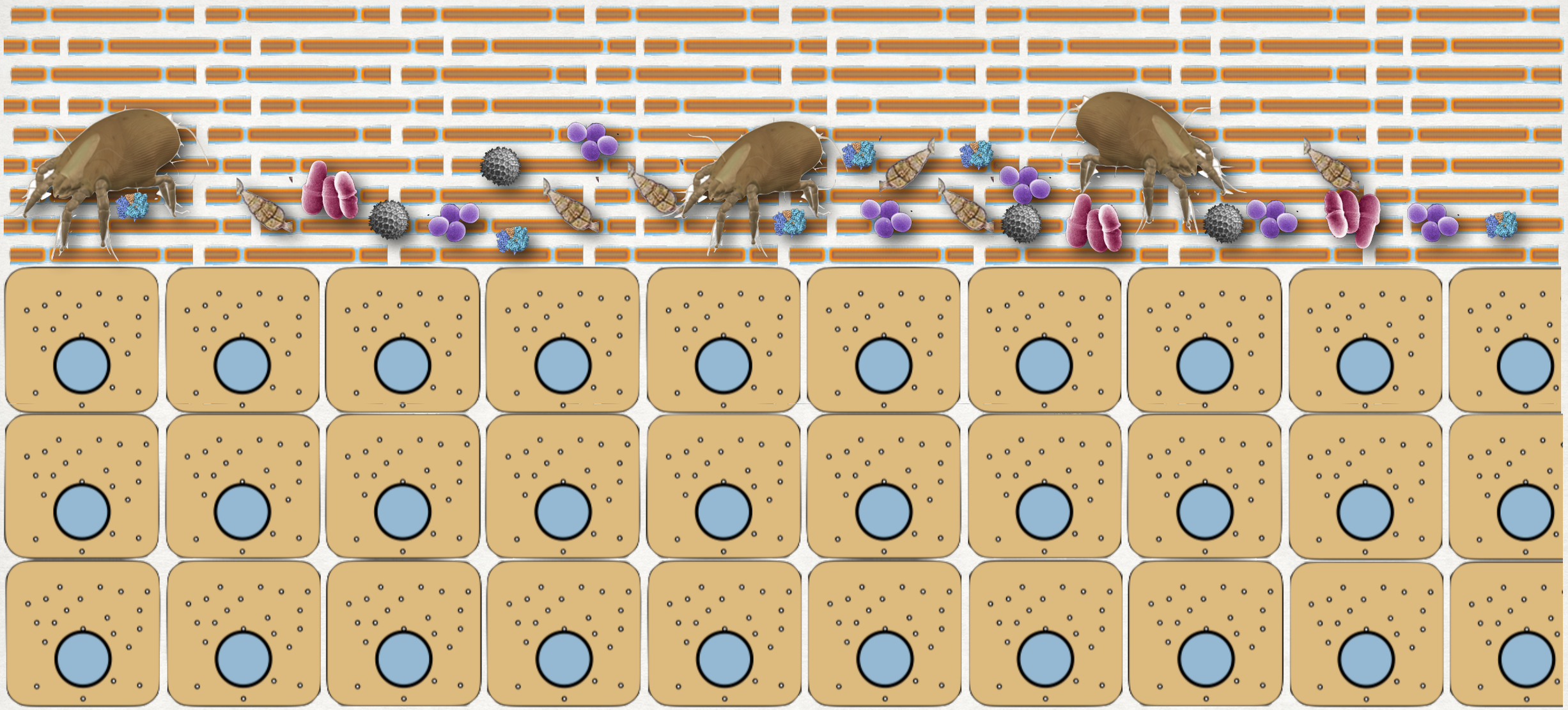

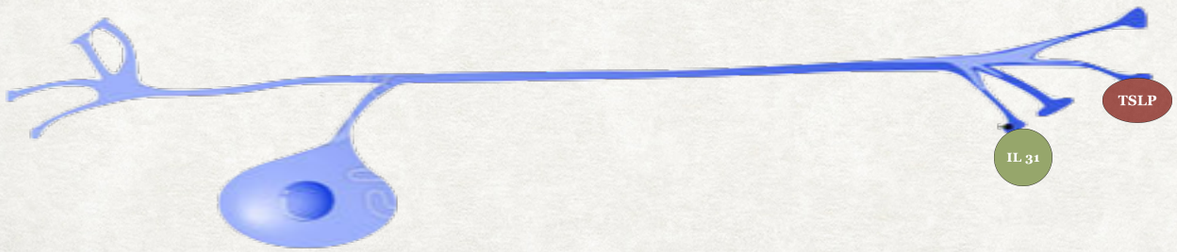
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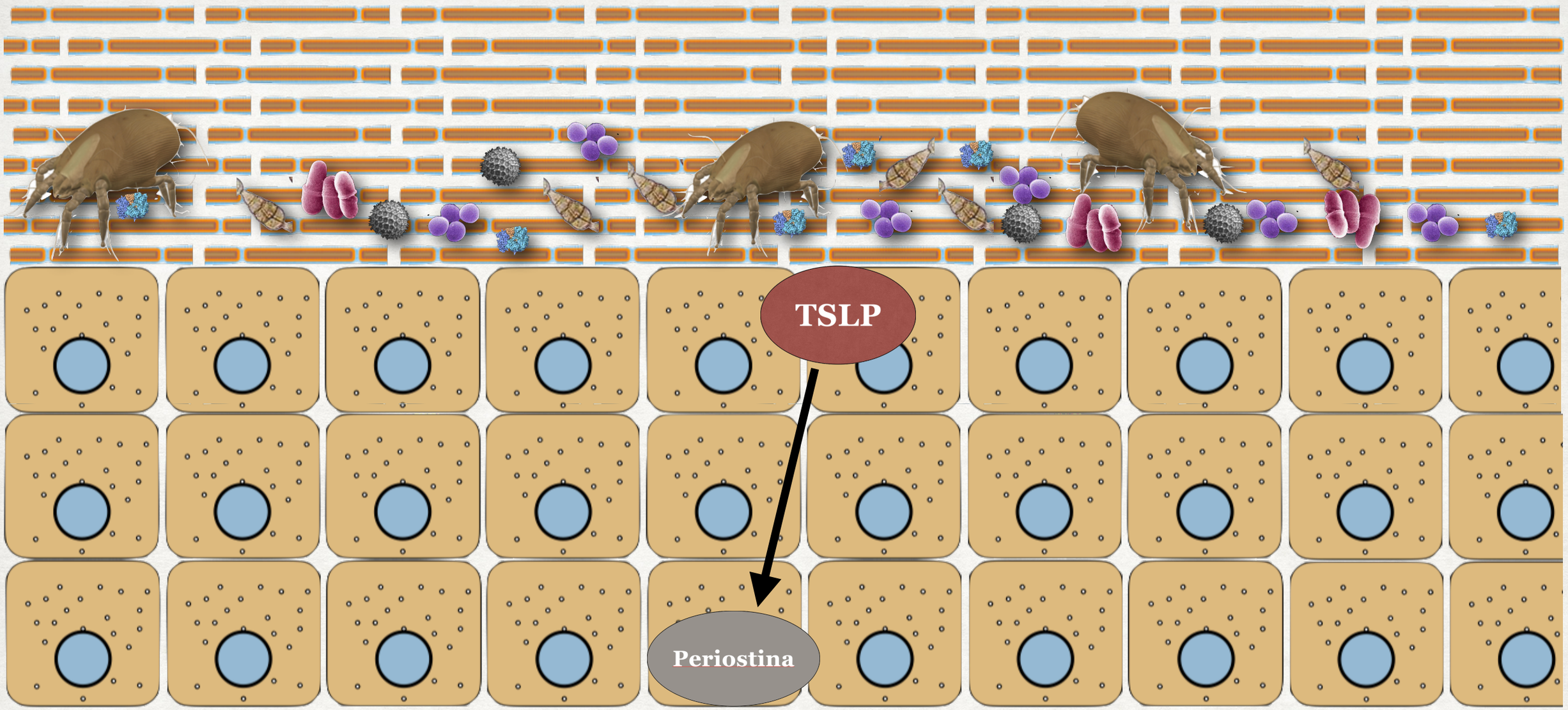
IL 31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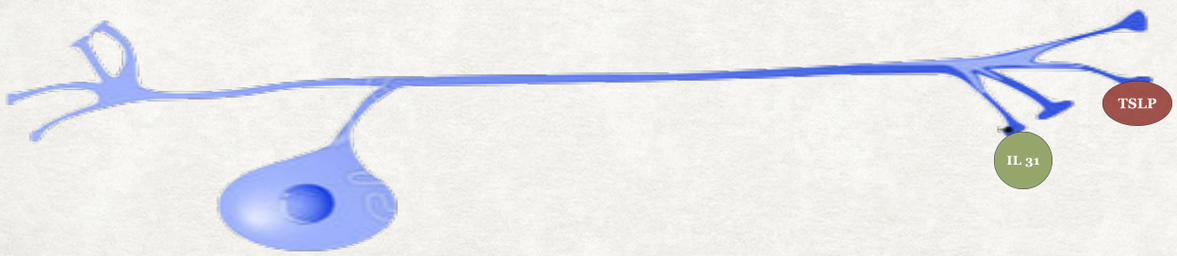
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IL 31

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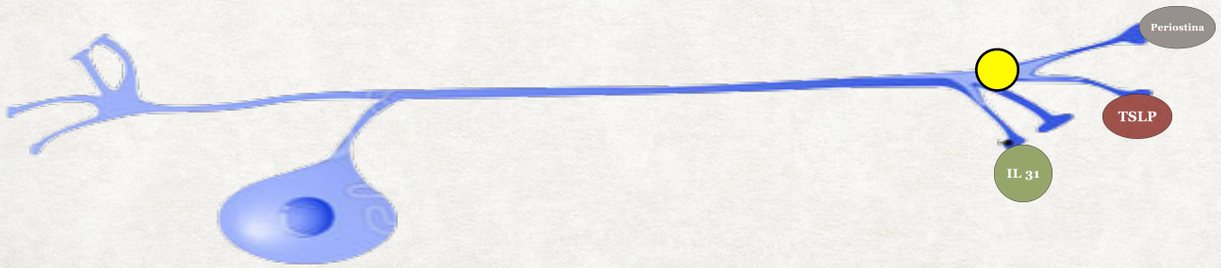

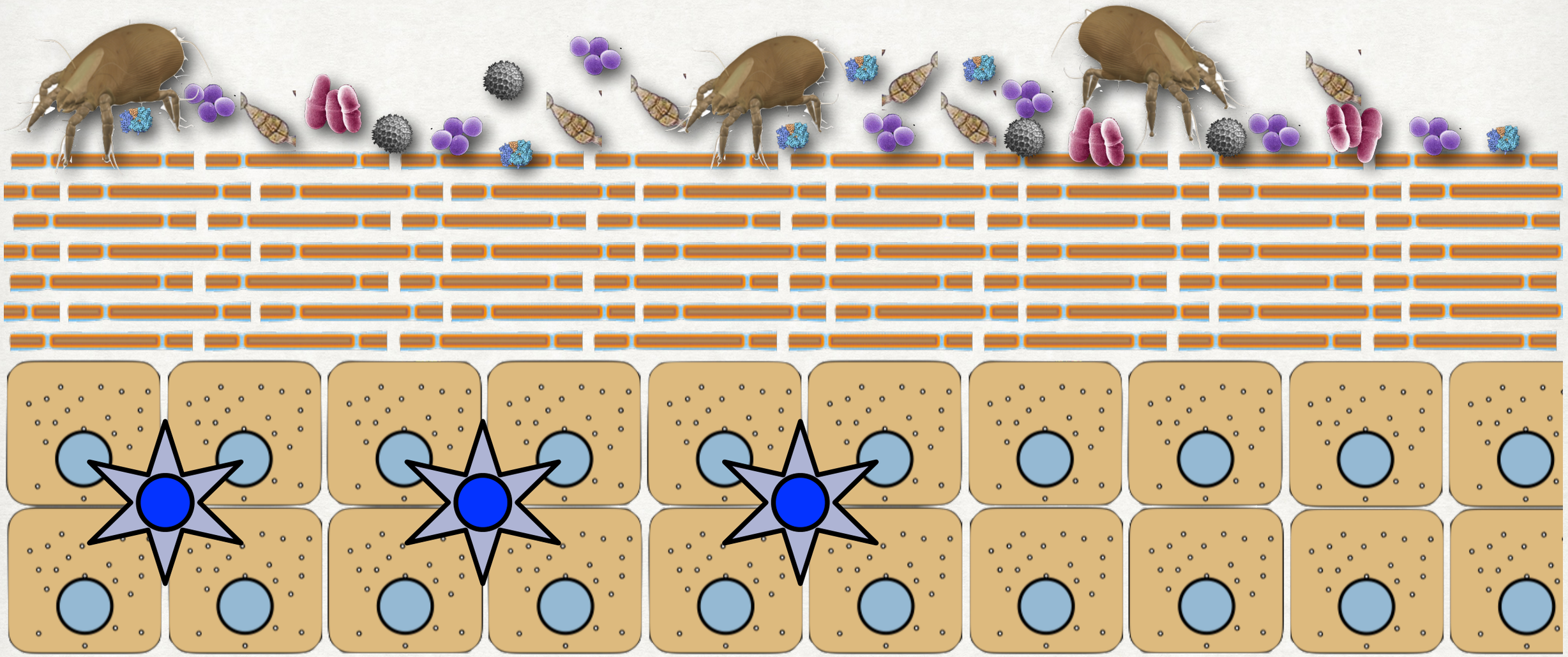

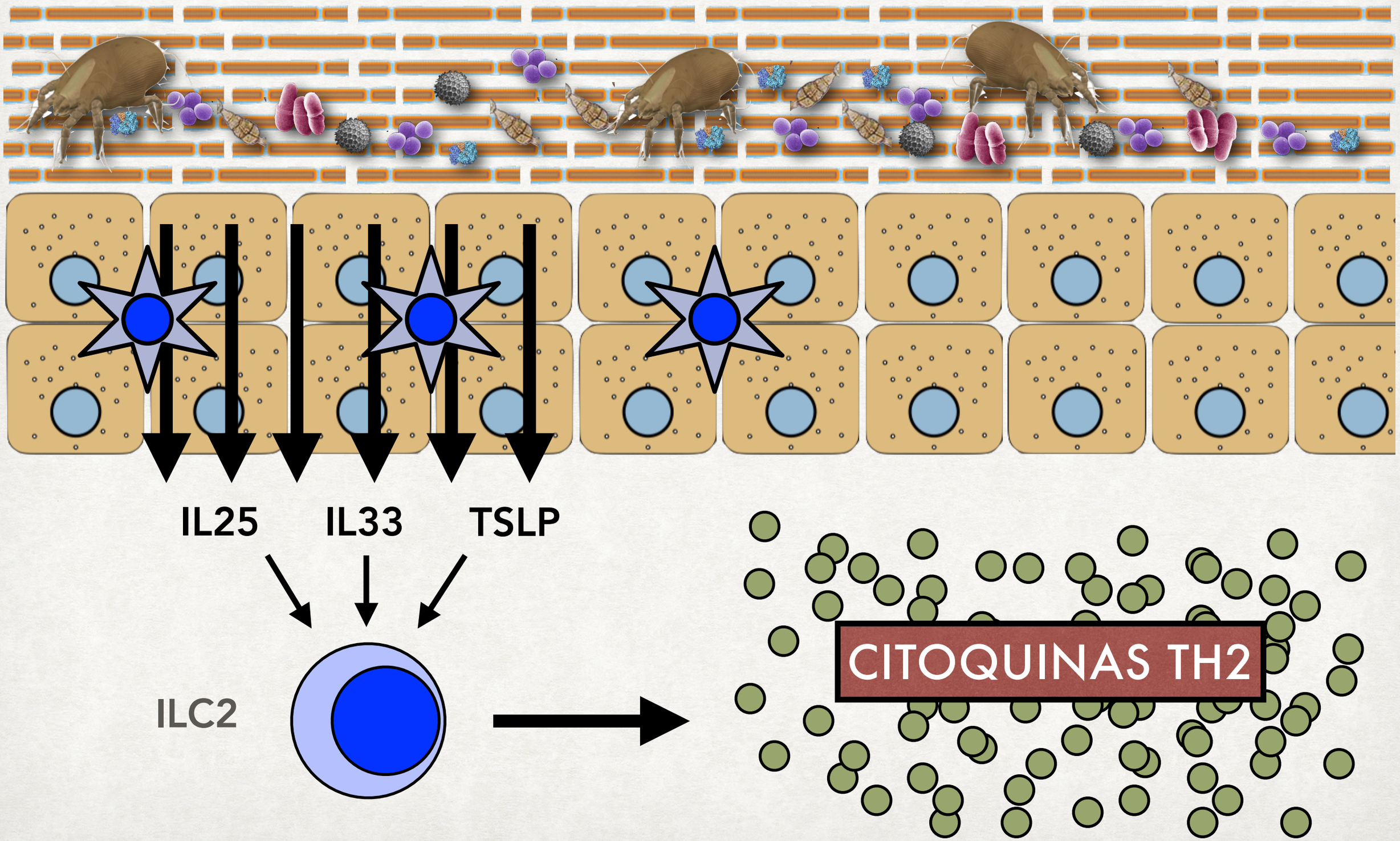
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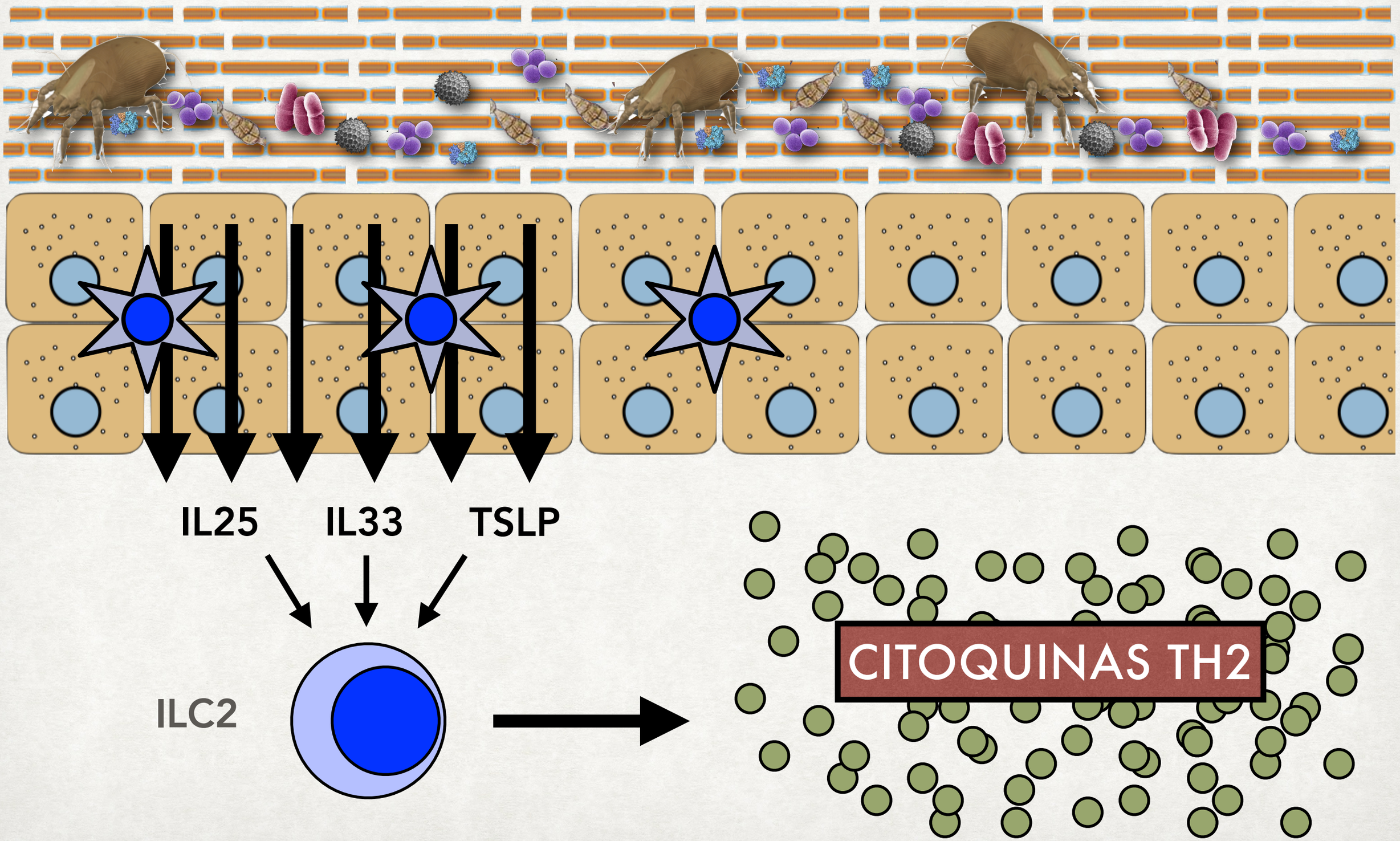
IL33
TSLP
ILC2
CITOQUINAS TH2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CITOQUINAS TH2

IL25 IL33 TSLP

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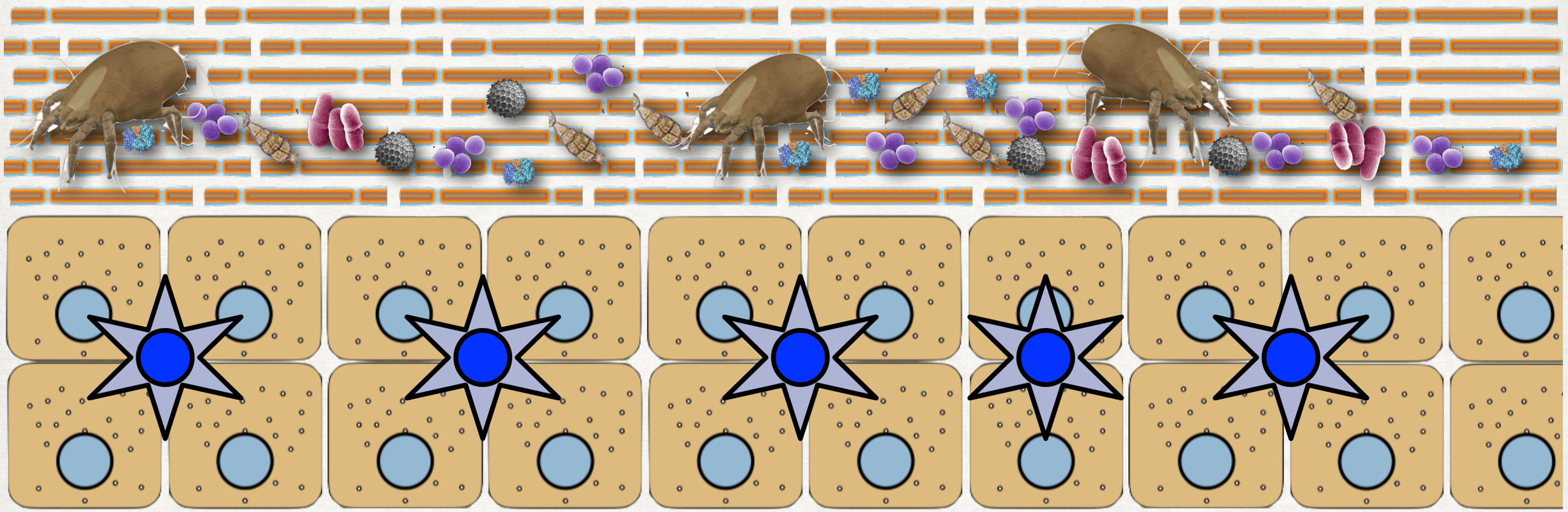
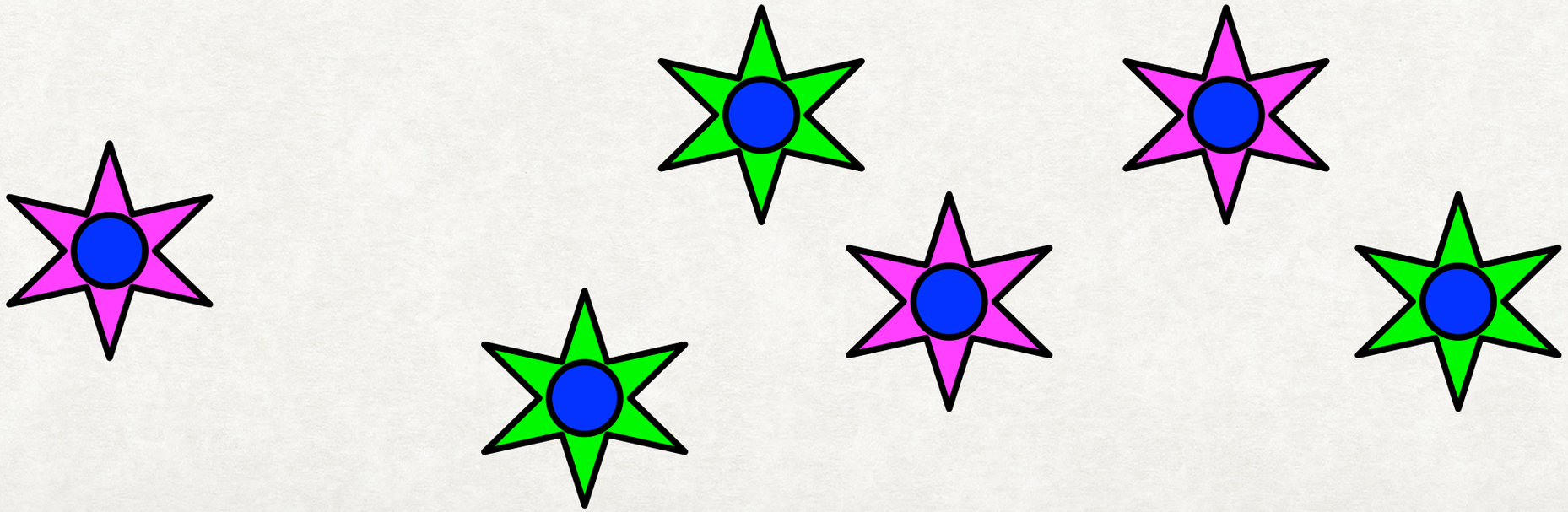




Otsuka, M., Egawa, G., & Kabashima, K. (2018). Uncovering the Mysteries of Langerhans Cells, Inflammatory Dendritic Epidermal Cells, and Monocyte-Derived Langerhans Cell-Like Cells in the Epidermis. Frontiers in Immunology, 9. doi:10.3389/fimmu.2018.01768

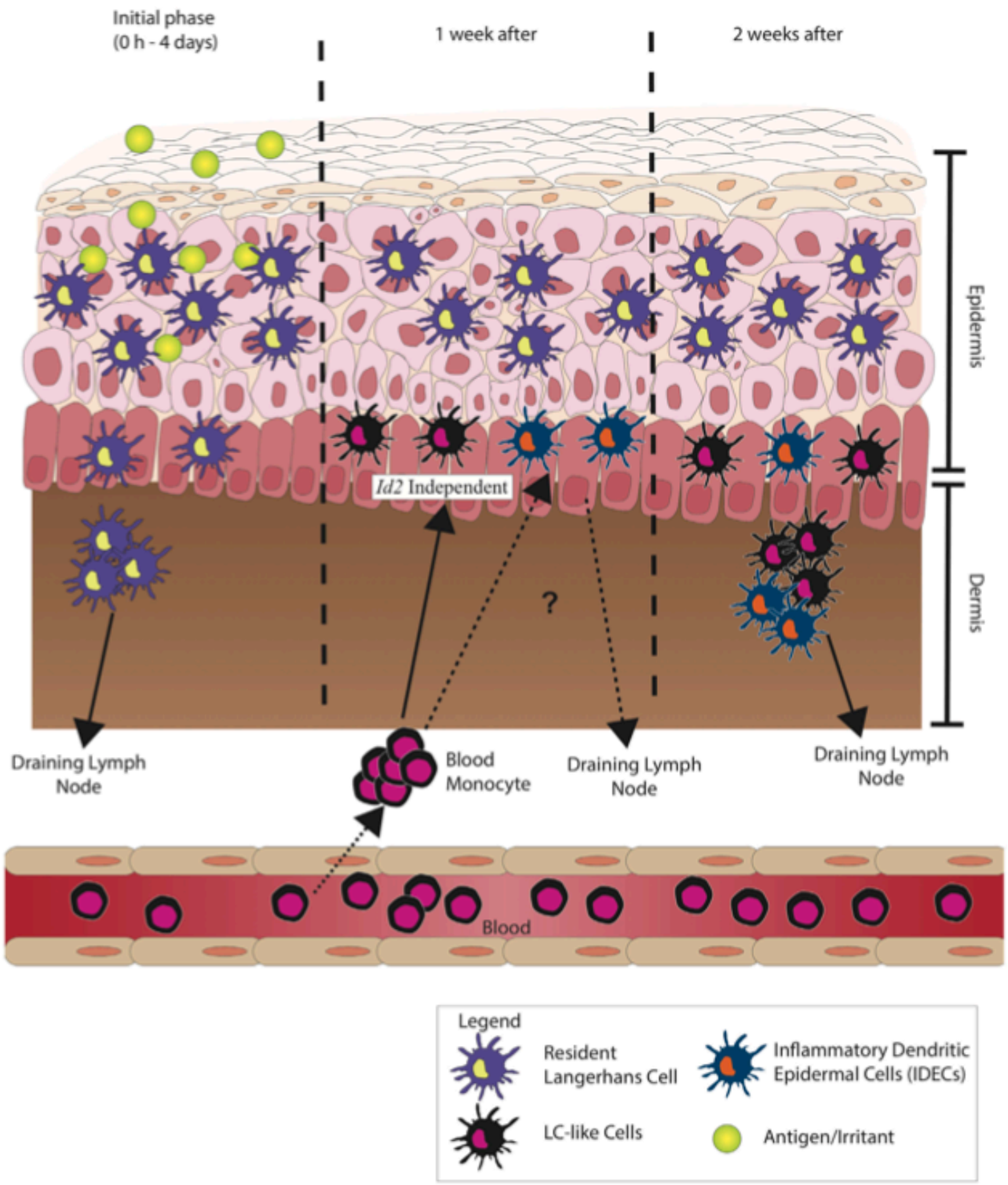
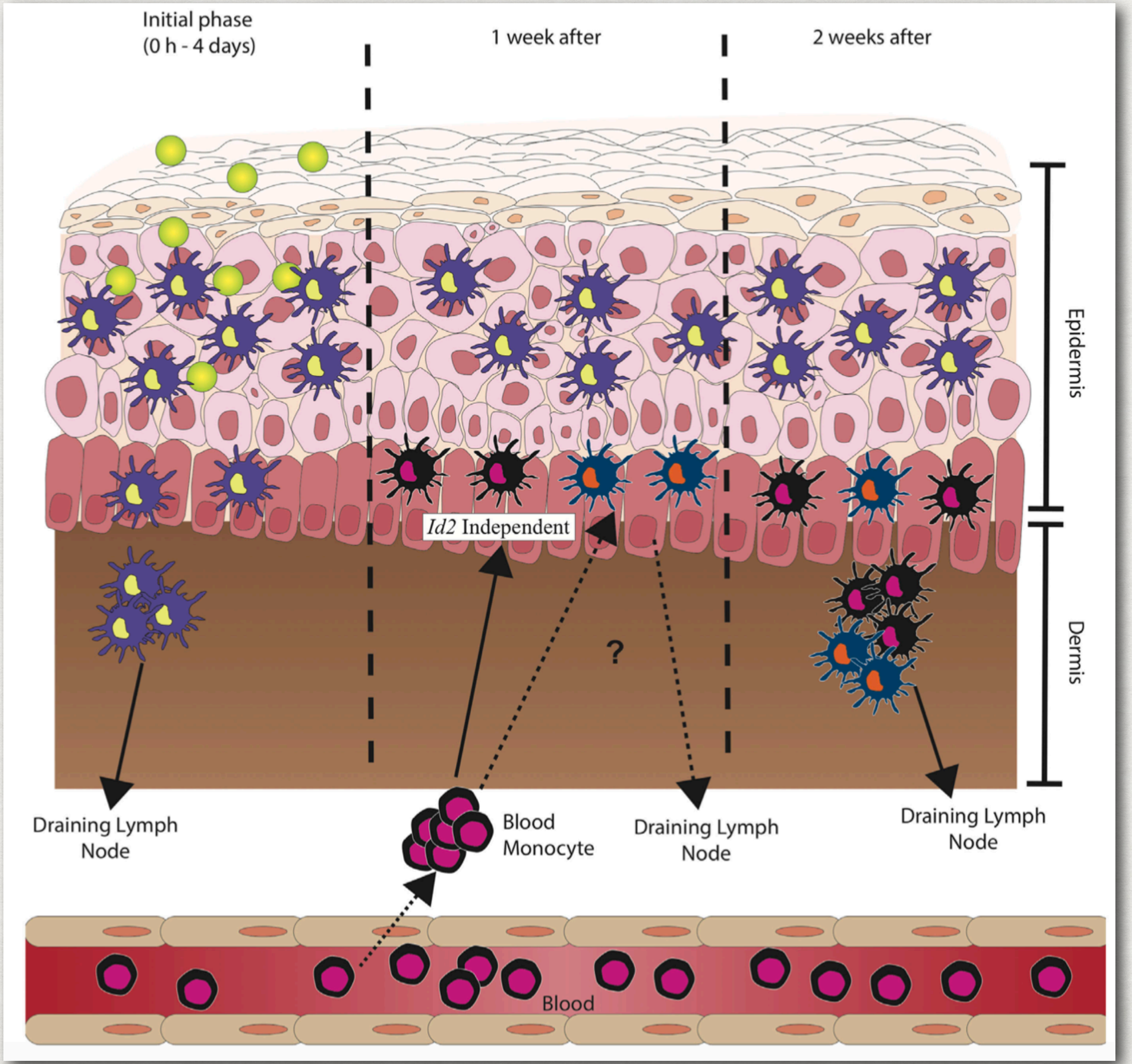
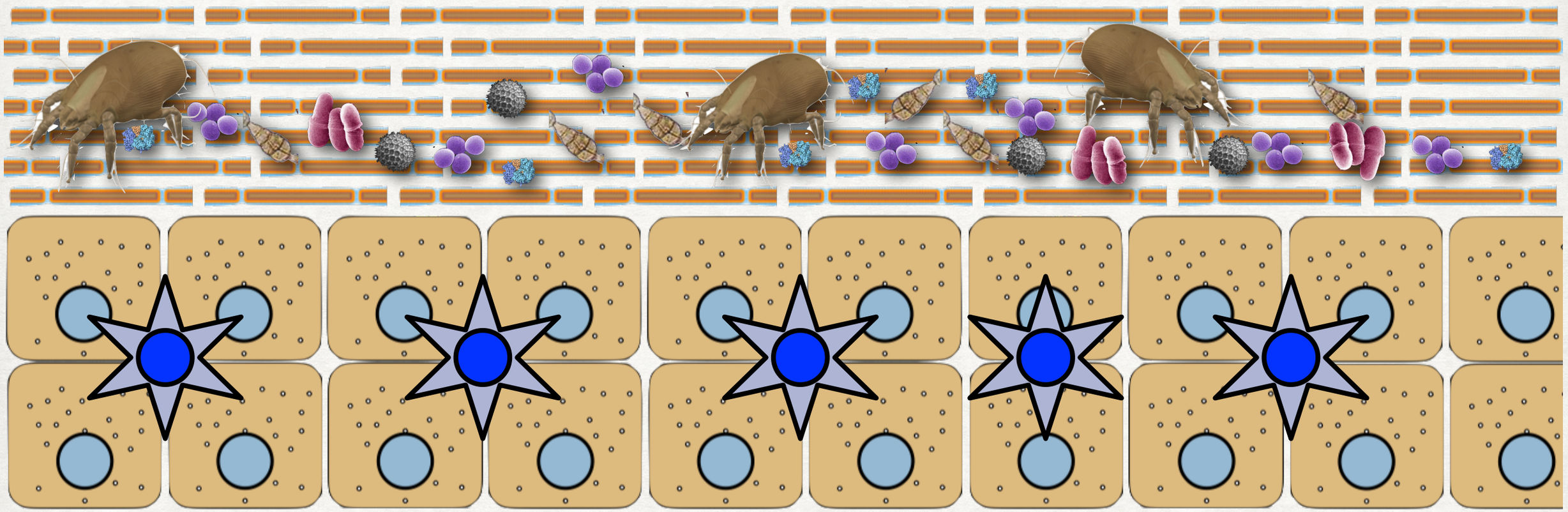
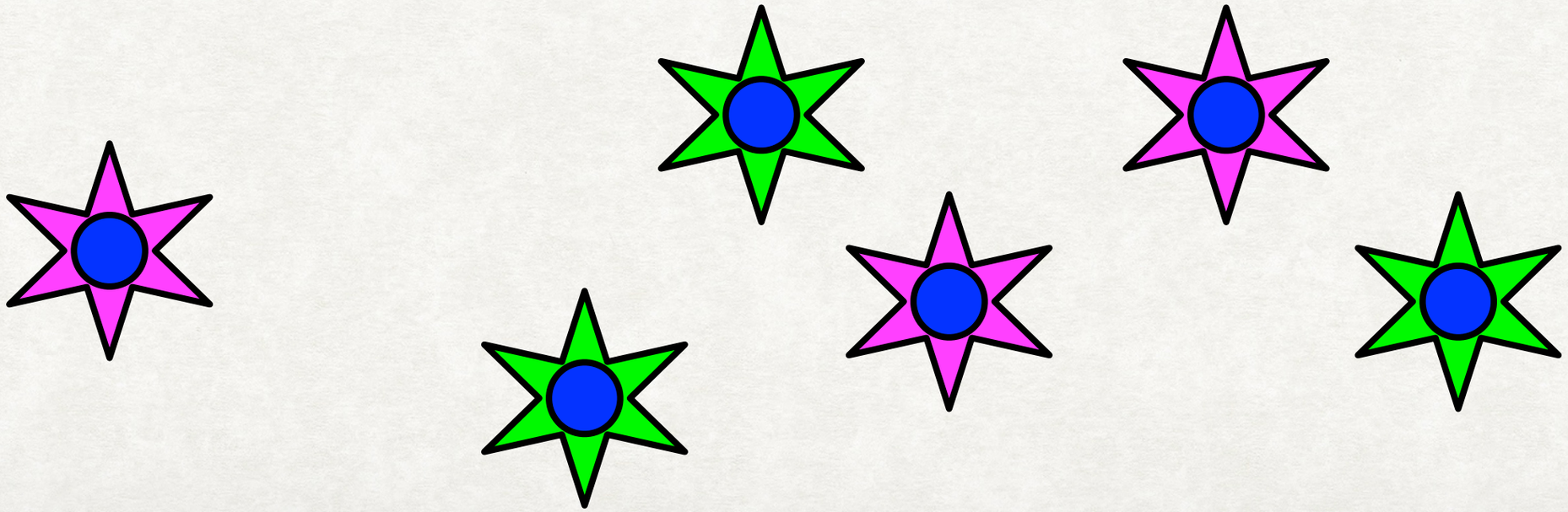
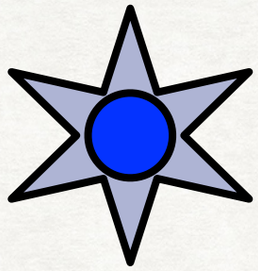


FIGURE 2 | Langerhans cells (LCs) during inflammation. During the initial phase of inflammation, LCs migrate to the draining lymph node, but unlike conventional/classical dendritic cells (cDCs), LCs are observed to peak in number at day 4 after initial sensitization to antigen. The migration of LCs has been observed to be much slower. After 1 week, it is believed that inflammatory dendritic epidermal cells (IDECs) increase in number. These circulating blood monocytes from the bone marrow differentiate to LC-like cells and do not depend on transforming growth factor-β (TGF-β) signaling pathway but are morphologically and phenotypically very similar to resident LCs. IDECs reside in the epidermal–dermal junction, and after 1 week of recruitment, they most likely migrate into the draining lymph node. These show the probable functional difference between LCs and IDECs as the kinetics of recruitment and migration between the two cells is different.


Initial phase
(0 h - 4 days)
1 week after
2 weeks after
Epidermis
Dermis
Id2 Independent
?
Draining Lymph Node
Blood Monocyte
Draining Lymph Node
Draining Lymph Node
Blood

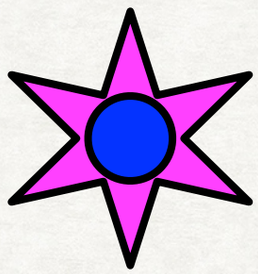






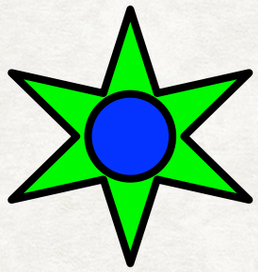
Célula de Langerhans

- Potencian Respuestas TH2 / TH22
- Estimulan Linfocitos Treg
- Dependen de TGF-**β**

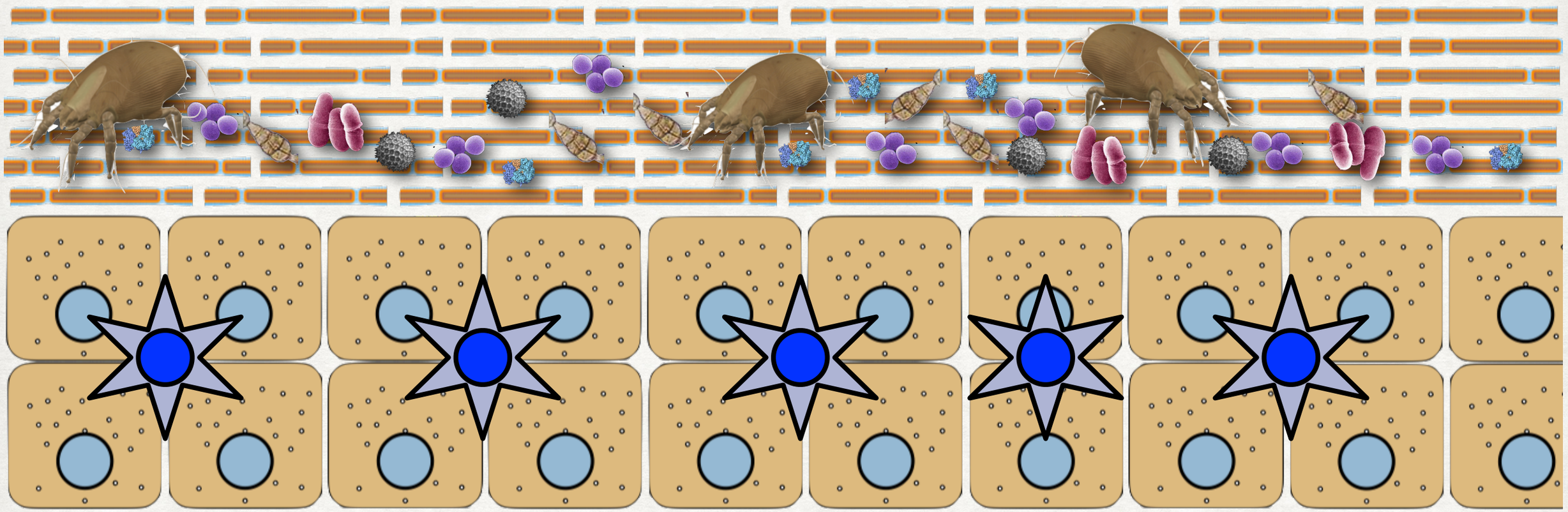


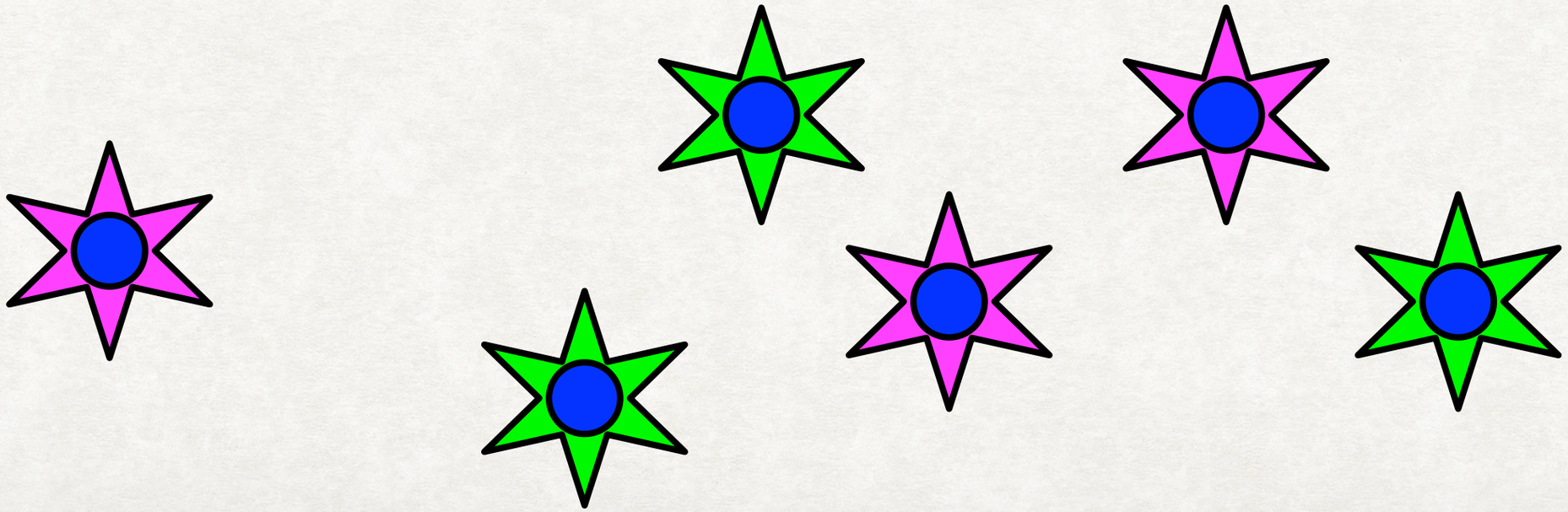
Célula Dendrítica Inflamatoria Epidérmica
(IDEC)

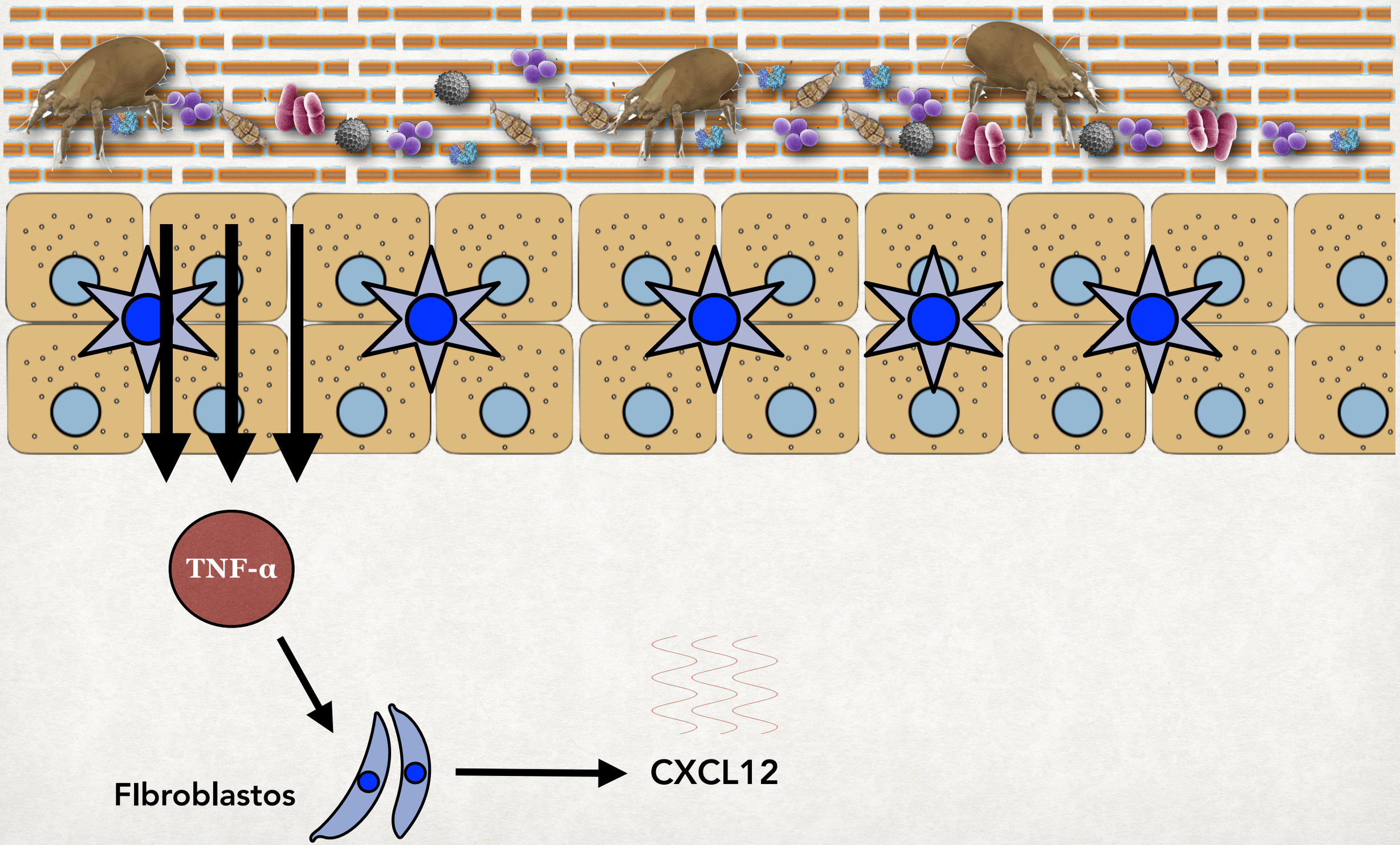
- Respuestas Variadas
- NO Dependen de TGF-**β**

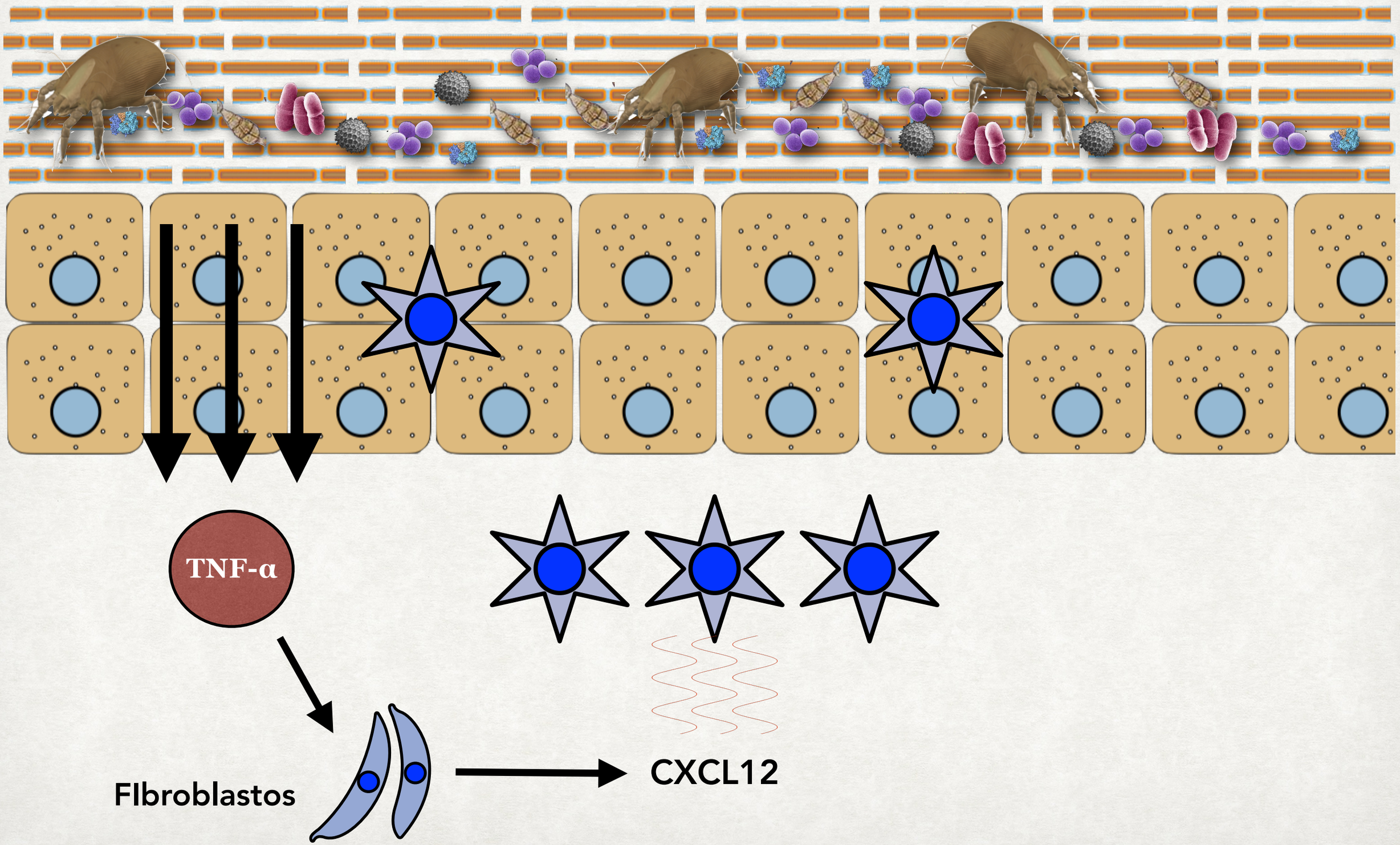


Célula de Langerhans Like
(Derivada de Monocitos)






TNF-α
FIbroblastos
CXCL12


TNF-α
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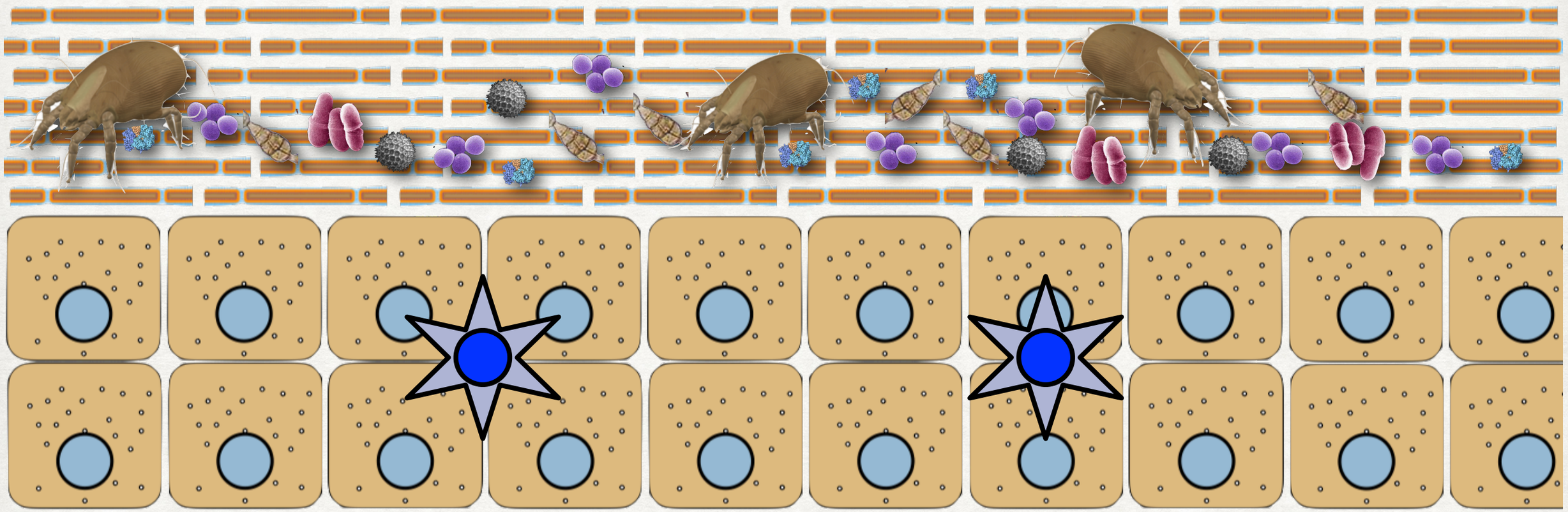
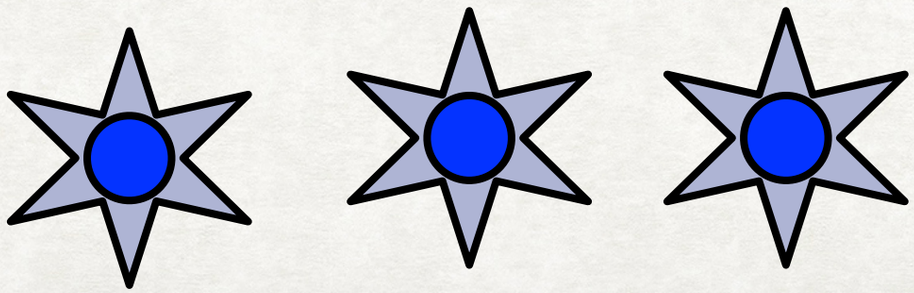
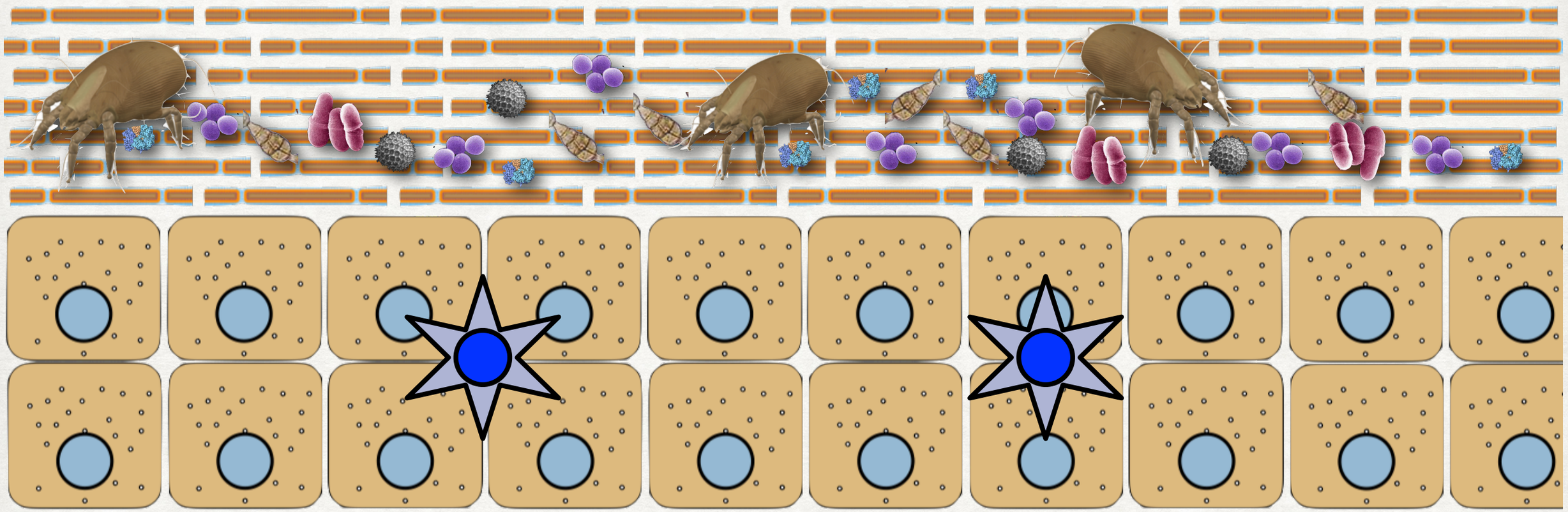
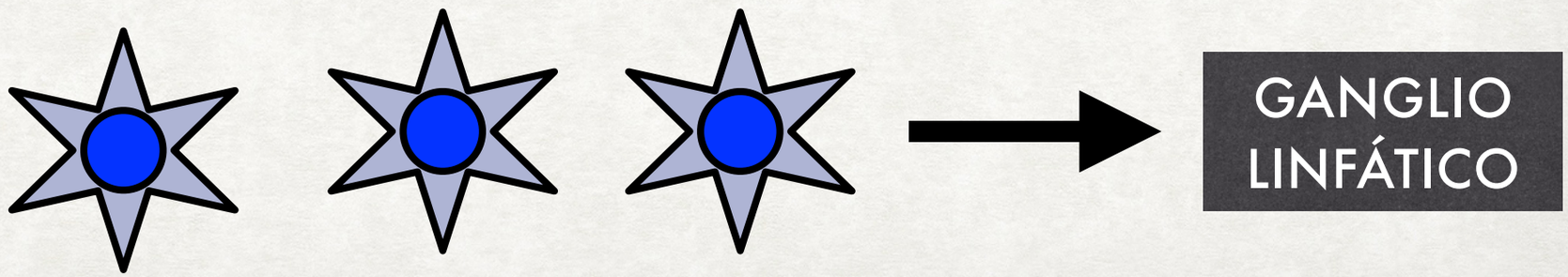
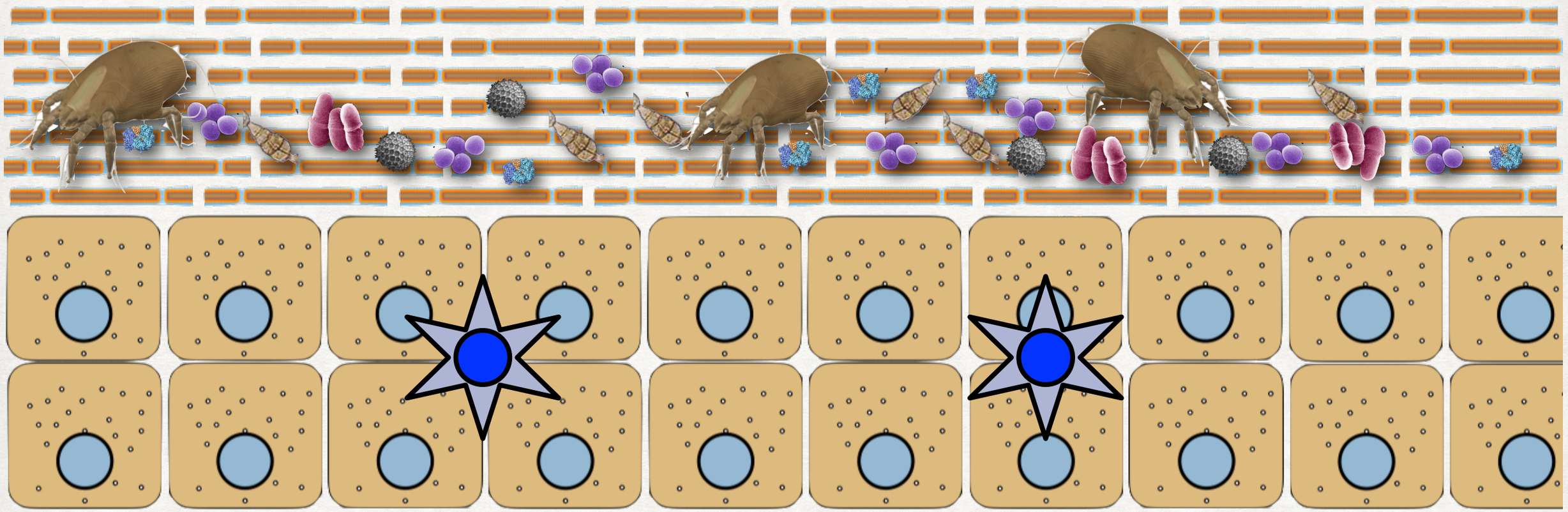
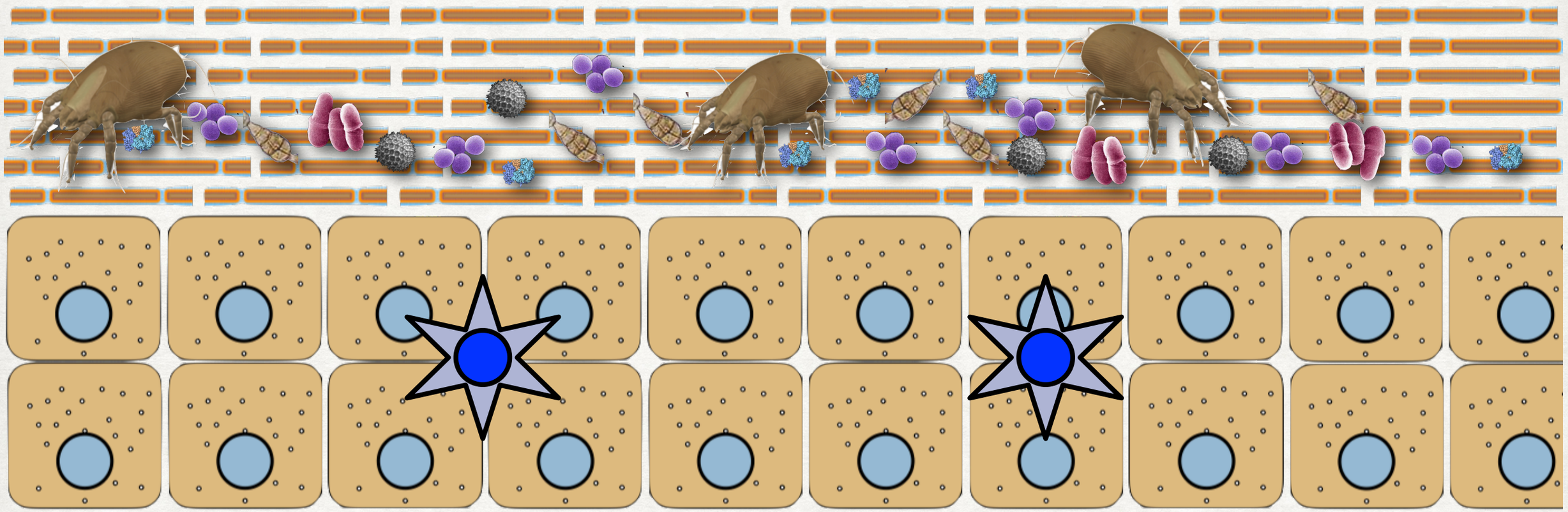


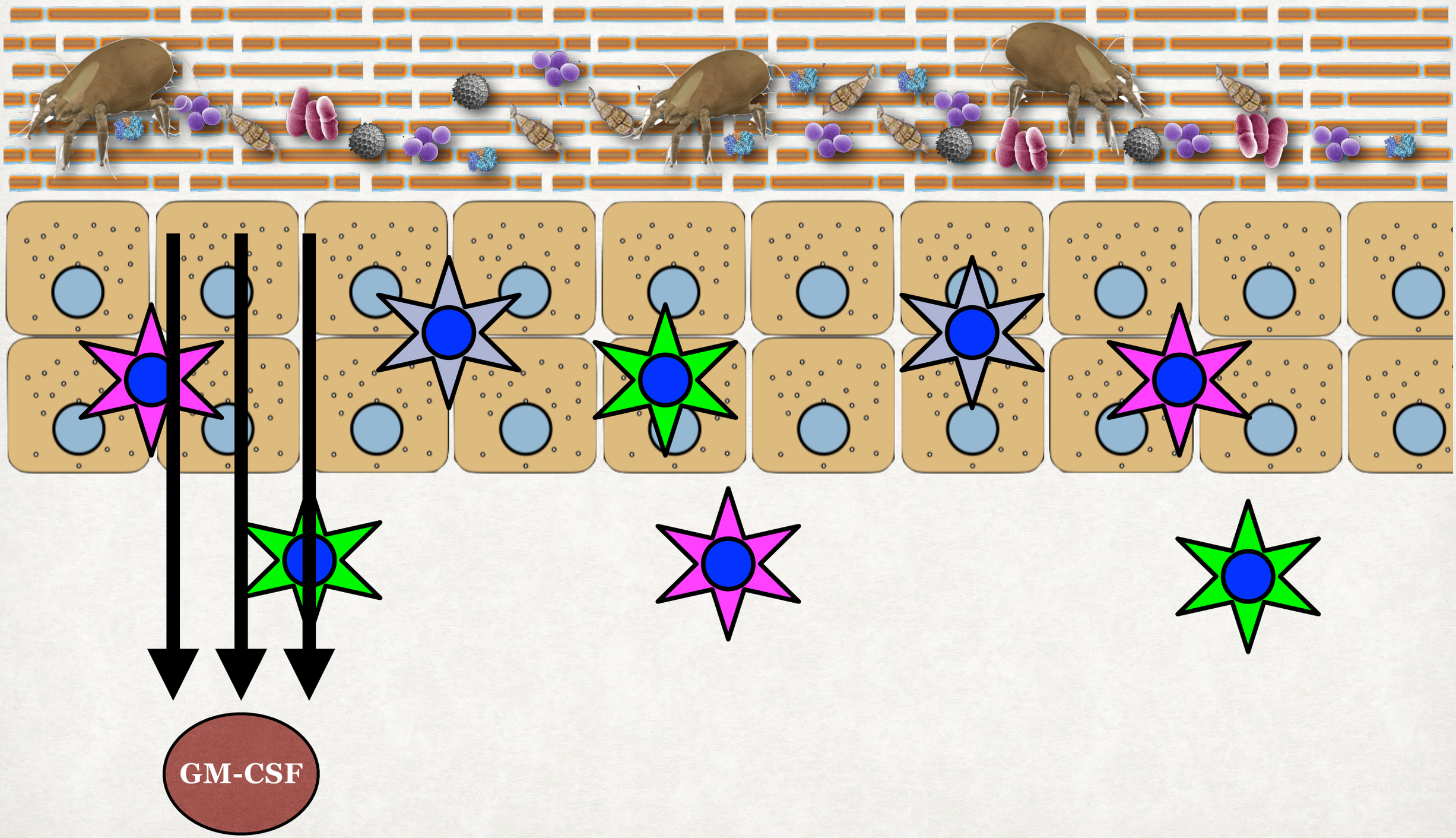





GANGLIO
LINFÁTICO






GM-CSF

NOTE *Internal Medicine*

Production of GM-CSF Mediated by Cysteine Protease of Der f in Canine Keratinocytes

Tsuyoshi KIMURA[1)], Machiko SEKIDO[2)], Naoki CHIMURA[1)], Sanae SHIBATA[2)], Naho KONDO[2)], Harumi KAMISHINA[2)], Hiroaki KAMISHINA[2)] and Sadatoshi MAEDA[2)]*

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ABSTRACT. House dust mite (HDM) allergens are the most common allergens for induction of IgE-mediated hypersensitivity. Recently, epicutaneous sensitization with HDM allergens has been emphasized in the development of atopic dermatitis (AD) by producing various soluble factors in keratinocytes. Among the soluble factors, GM-CSF is a key molecule that activates Langerhans cells, antigen-presenting cells in the epidermis. In the present study, we investigated the effects of *Dermatophagoides farinae* (Der f) on GM-CSF production in a canine keratinocyte cell line, CPEK. CPEKs were found to produce GM-CSF upon stimulation by Der f. The GM-CSF production was suppressed by addition of a cysteine protease inhibitor. The present results suggest that cysteine protease-derived Der f may be an initiator of allergic inflammation by inducing the production of GM-CSF in keratinocytes.

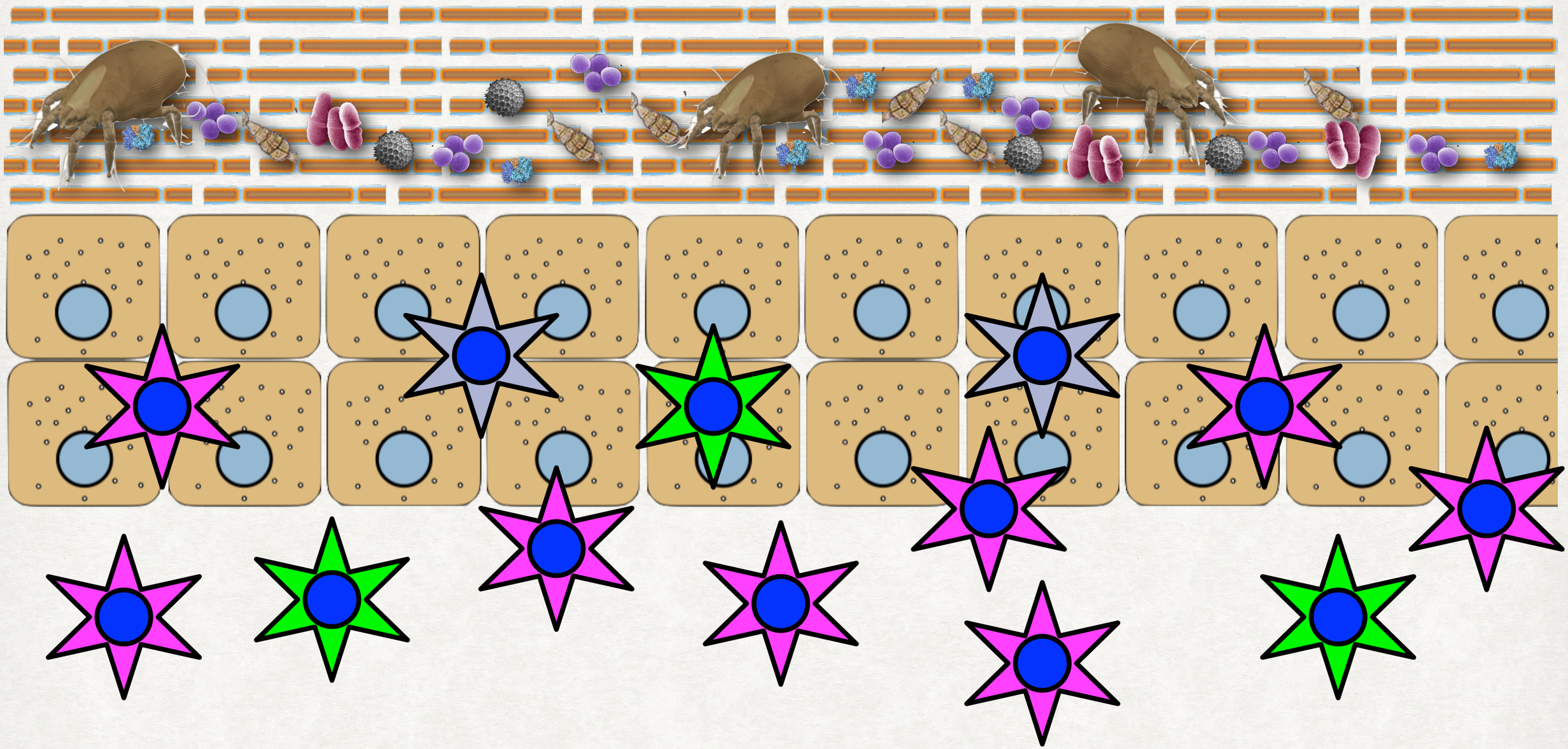
KEY WORDS: atopic dermatitis, canine, Der f, GM-CSF, keratinocytes.

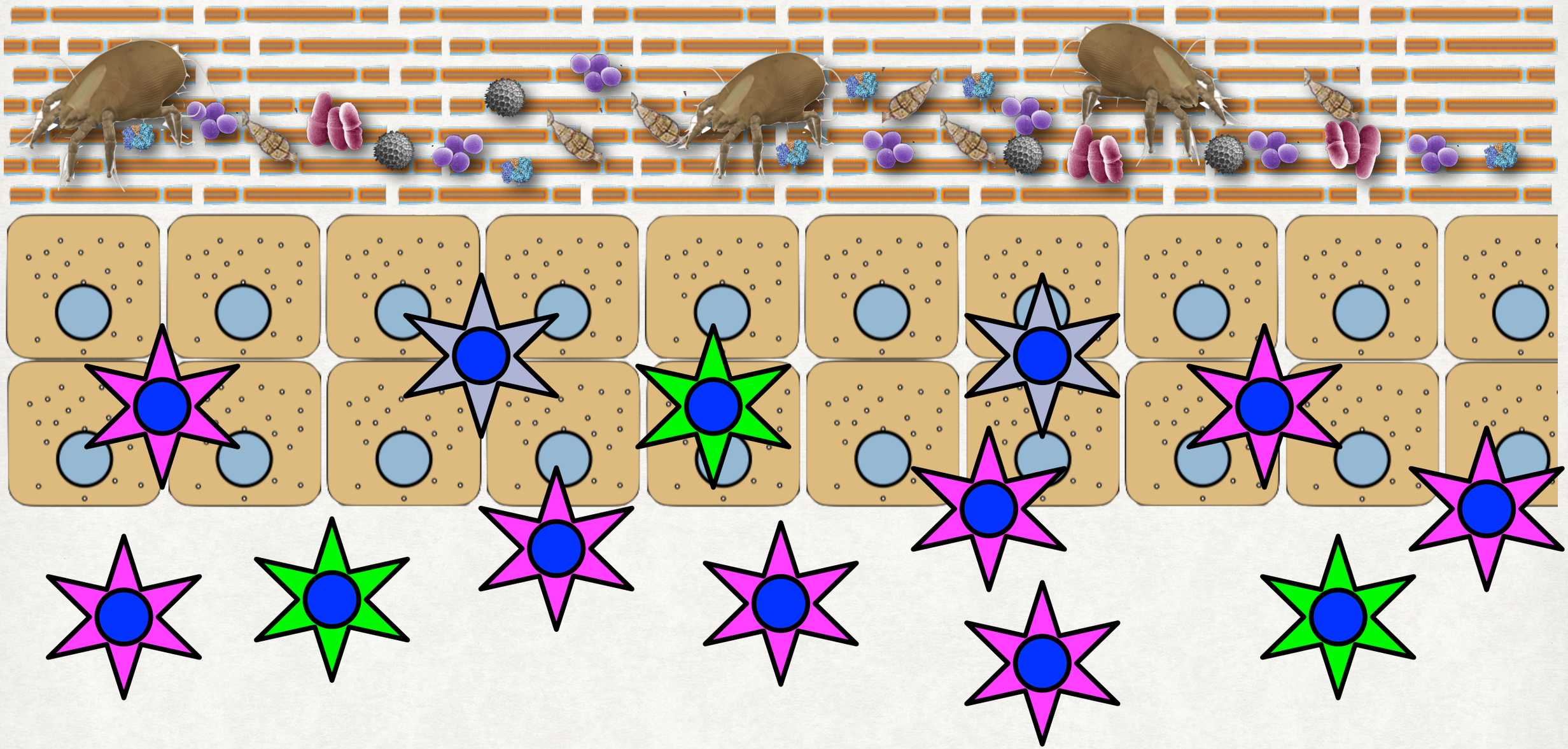
doi: 10.1292/jvms.11-0522; *J. Vet. Med. Sci.* 74(8): 1033–1036, 2012

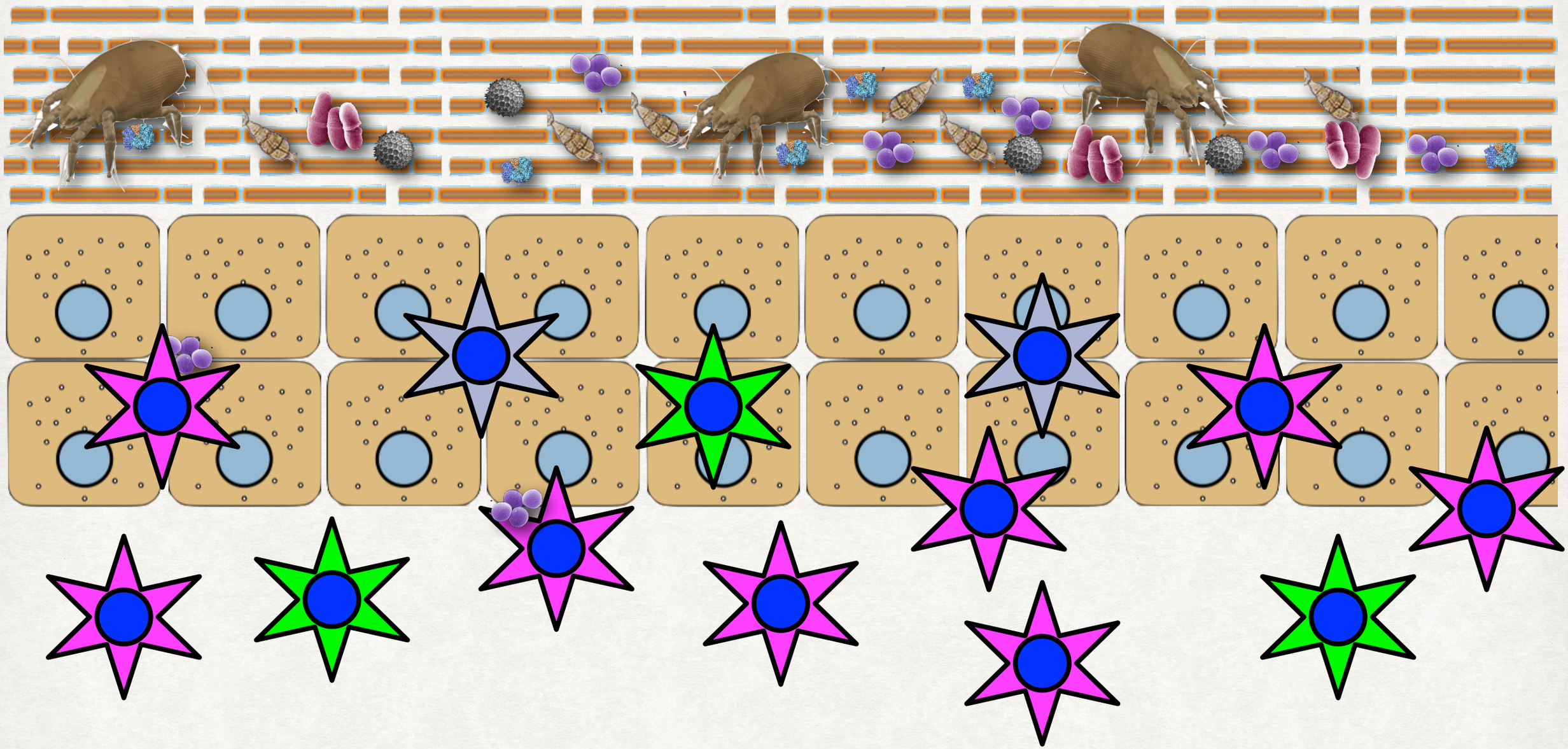
GM-CSF

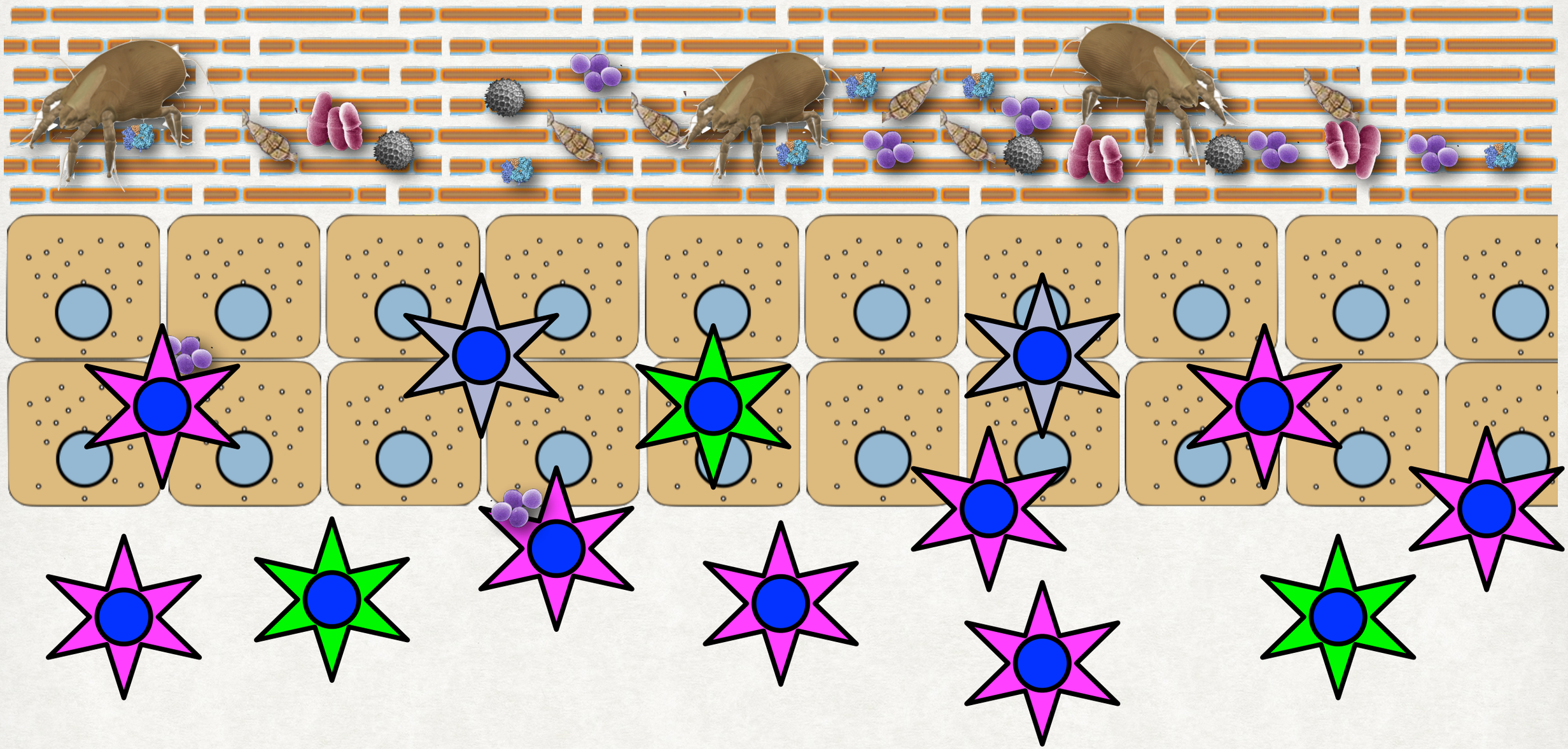
Macrófagos

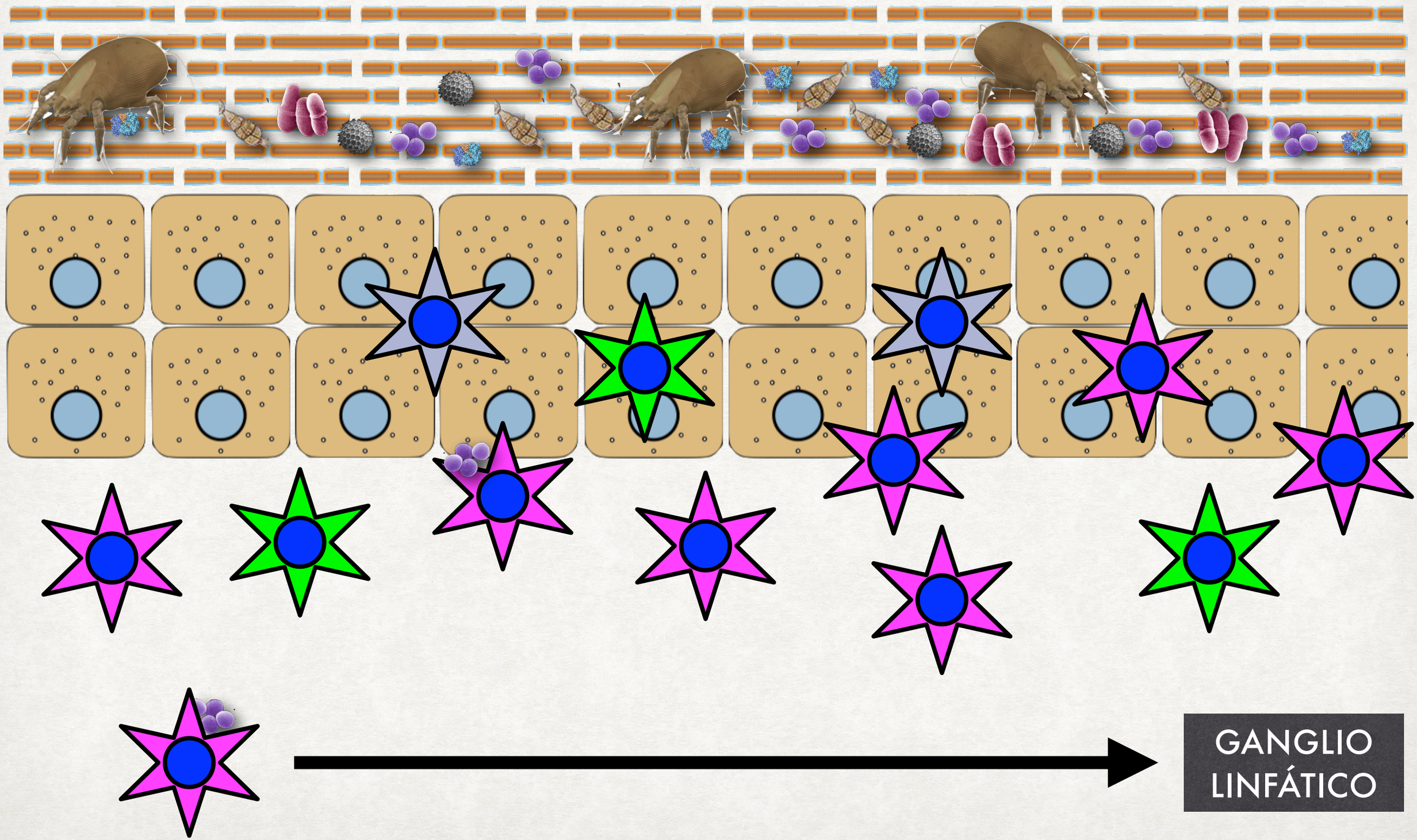
CCL2 y CCL3

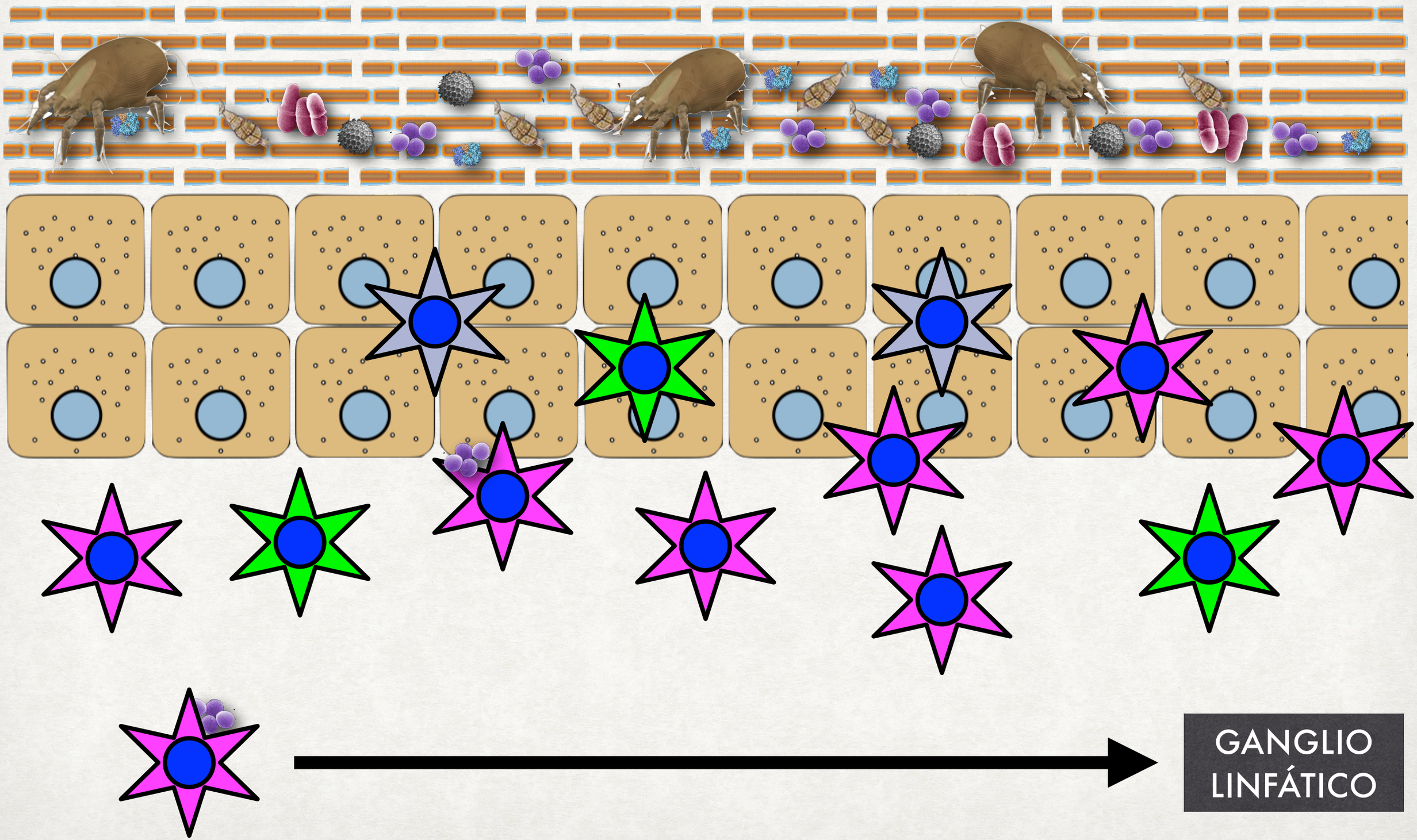









GANGLIO
LINFÁTICO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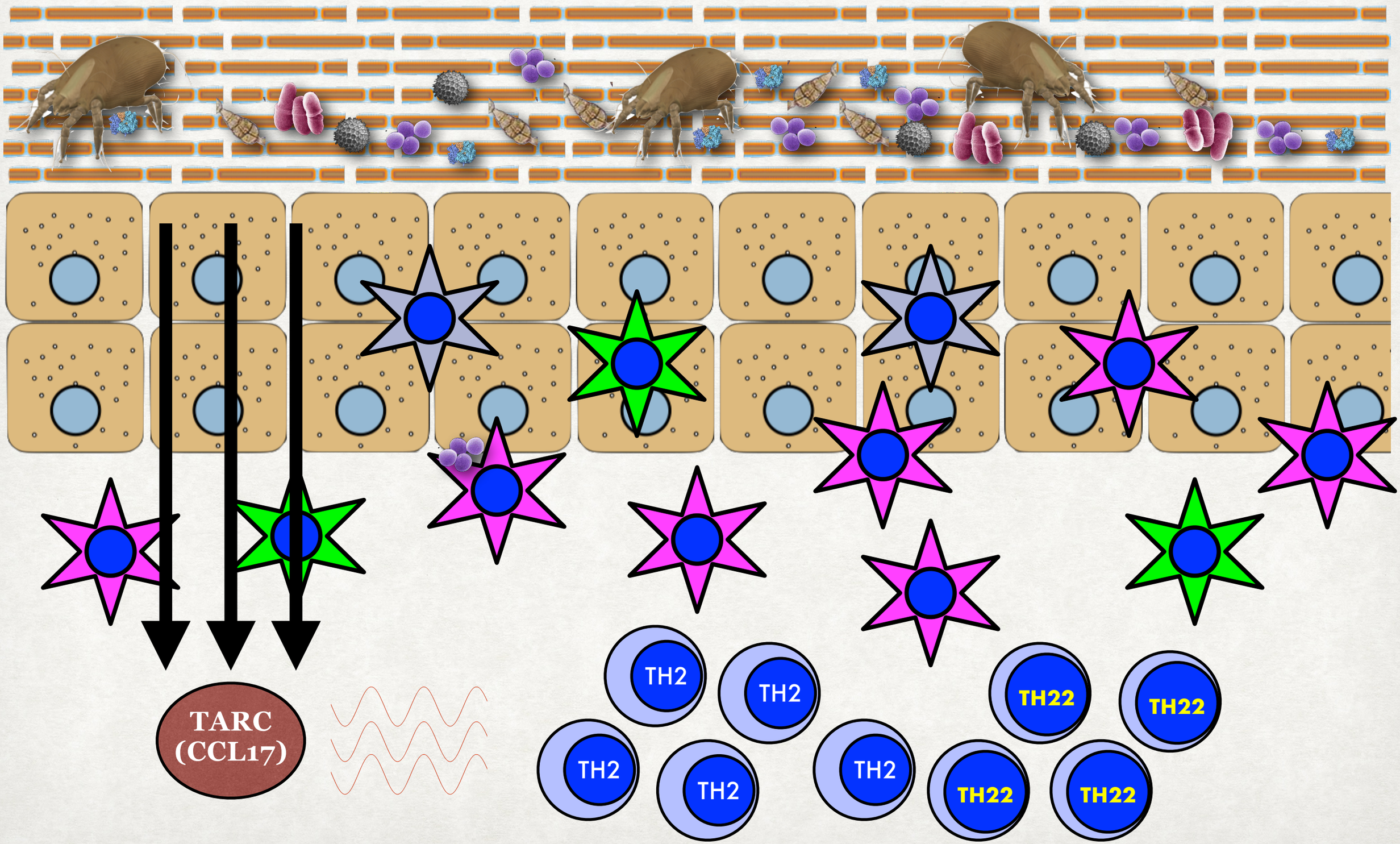
TARC
(CCL17)
TH2
TH2
TH2
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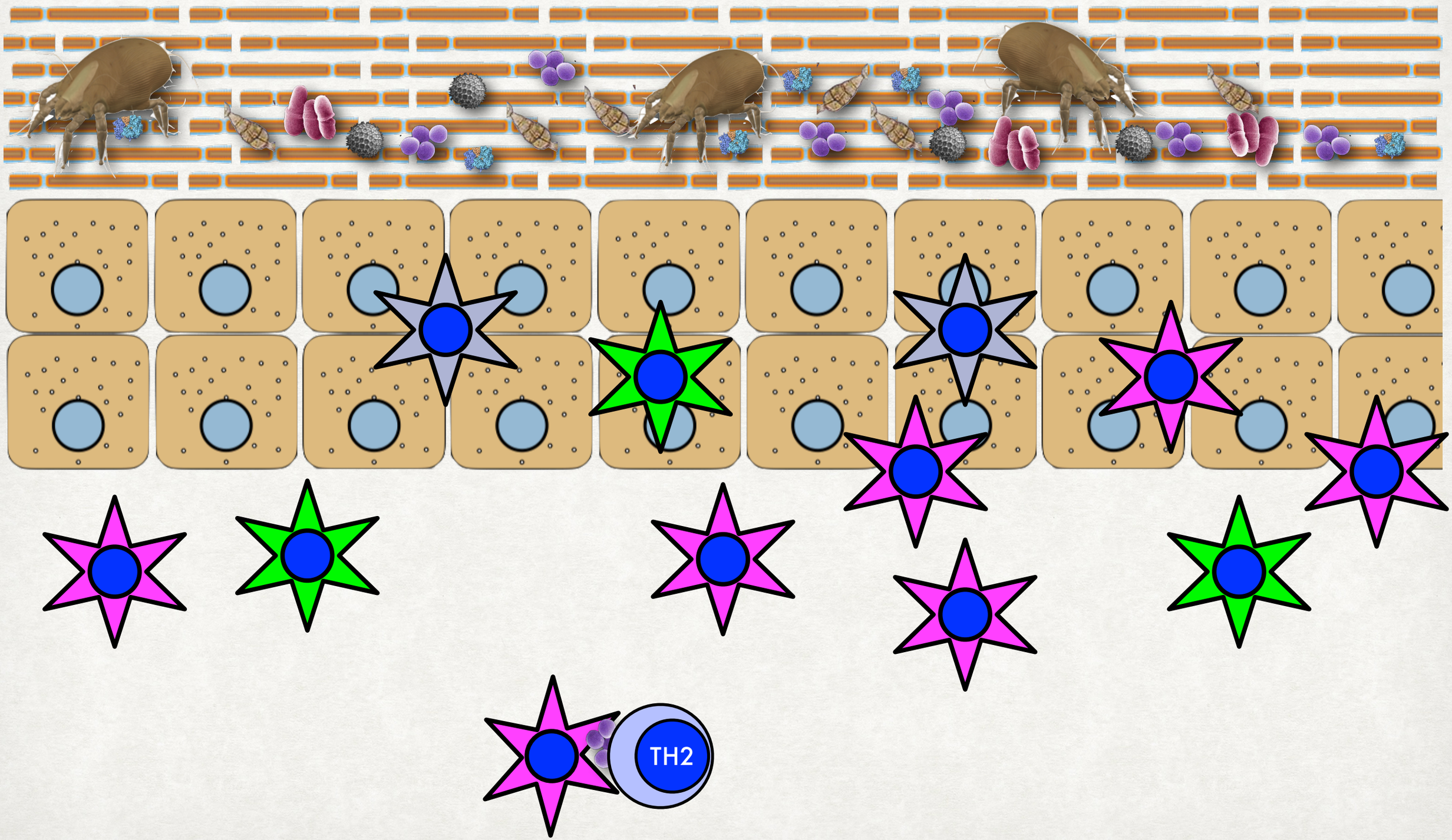
TH22
TH22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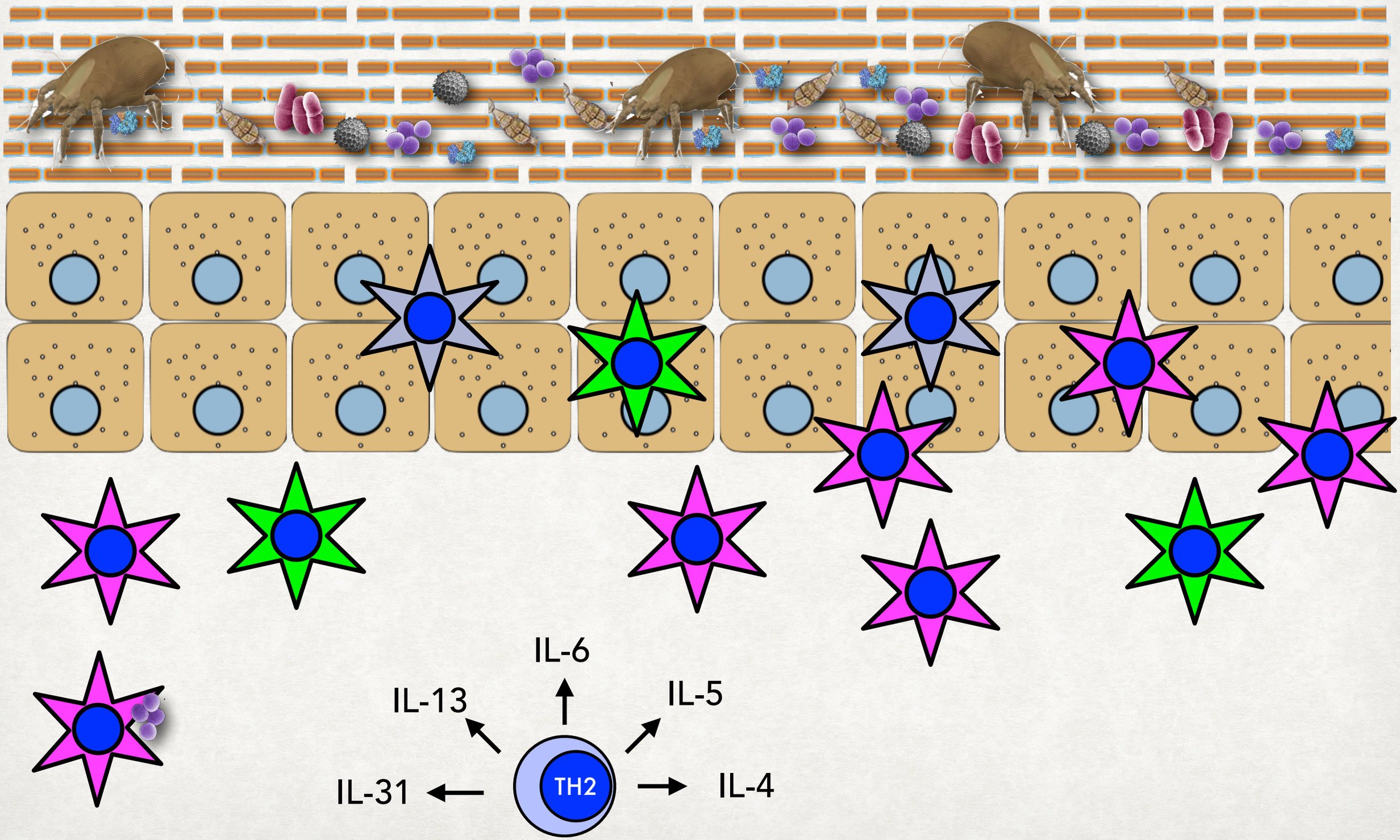

IL-6
IL-13
IL-5
IL-31
TH2
IL-4

IL-6

IL-13

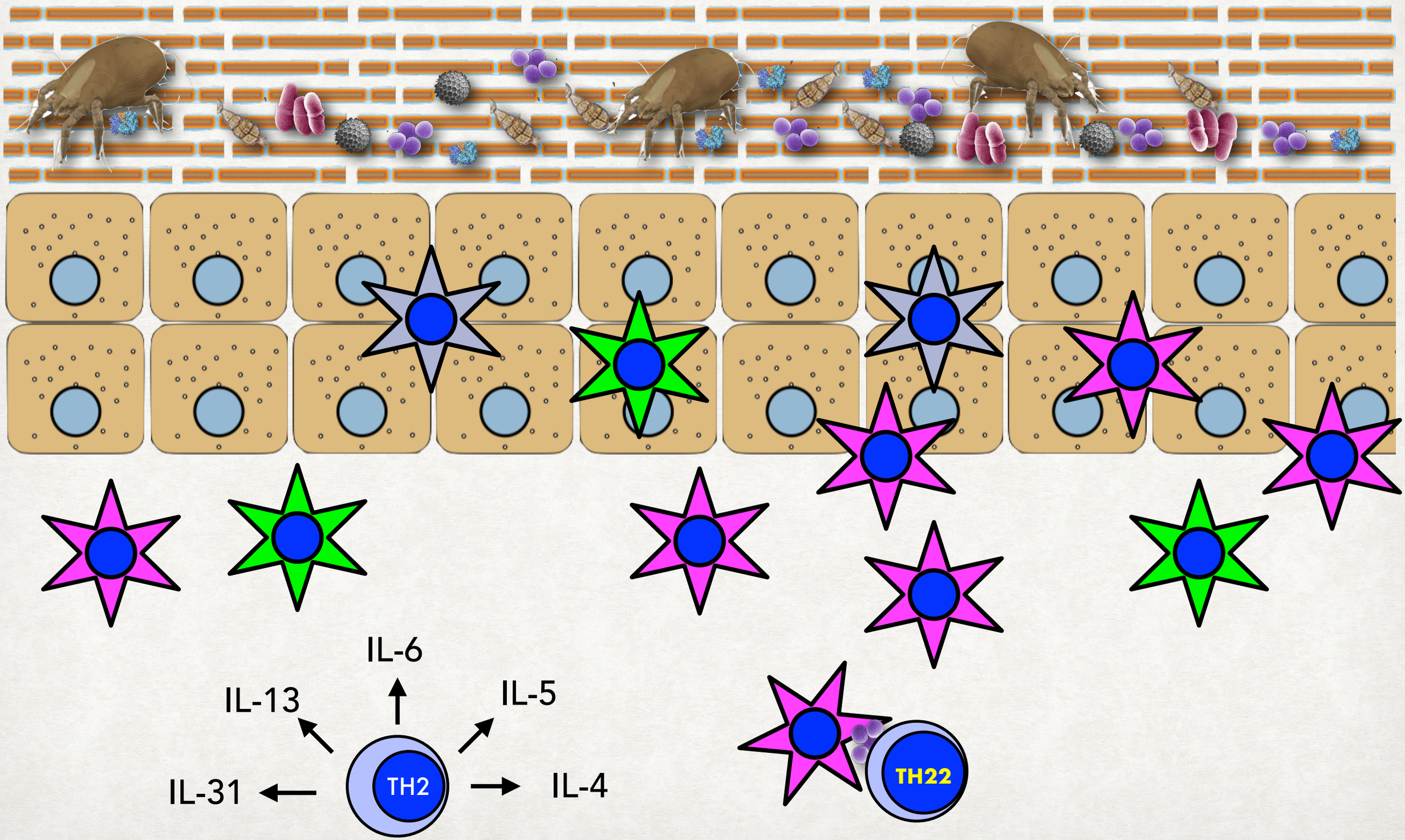
IL-5

IL-31

TH2

IL-4

TH22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IL-13
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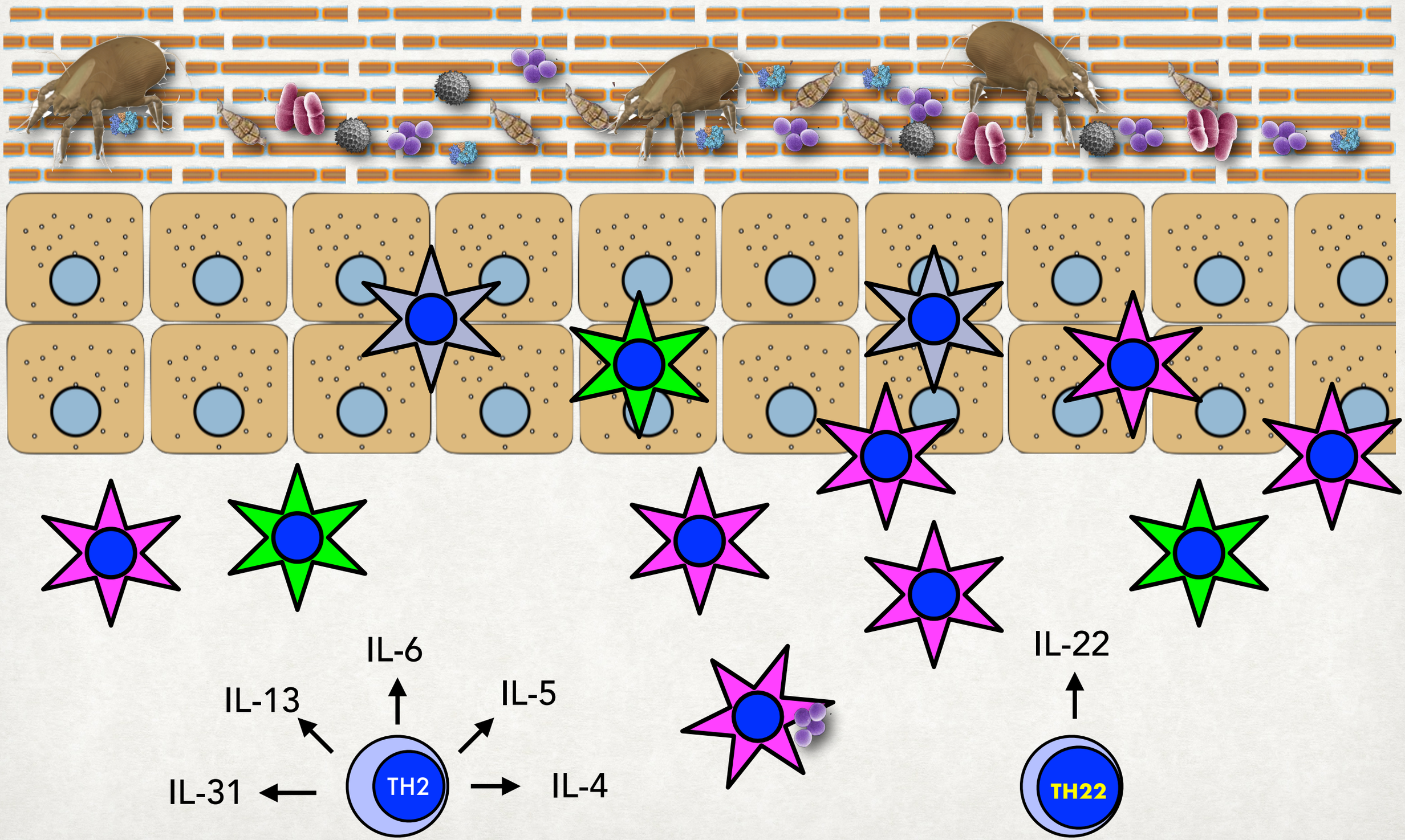
IL-31
TH2
IL-4
TH22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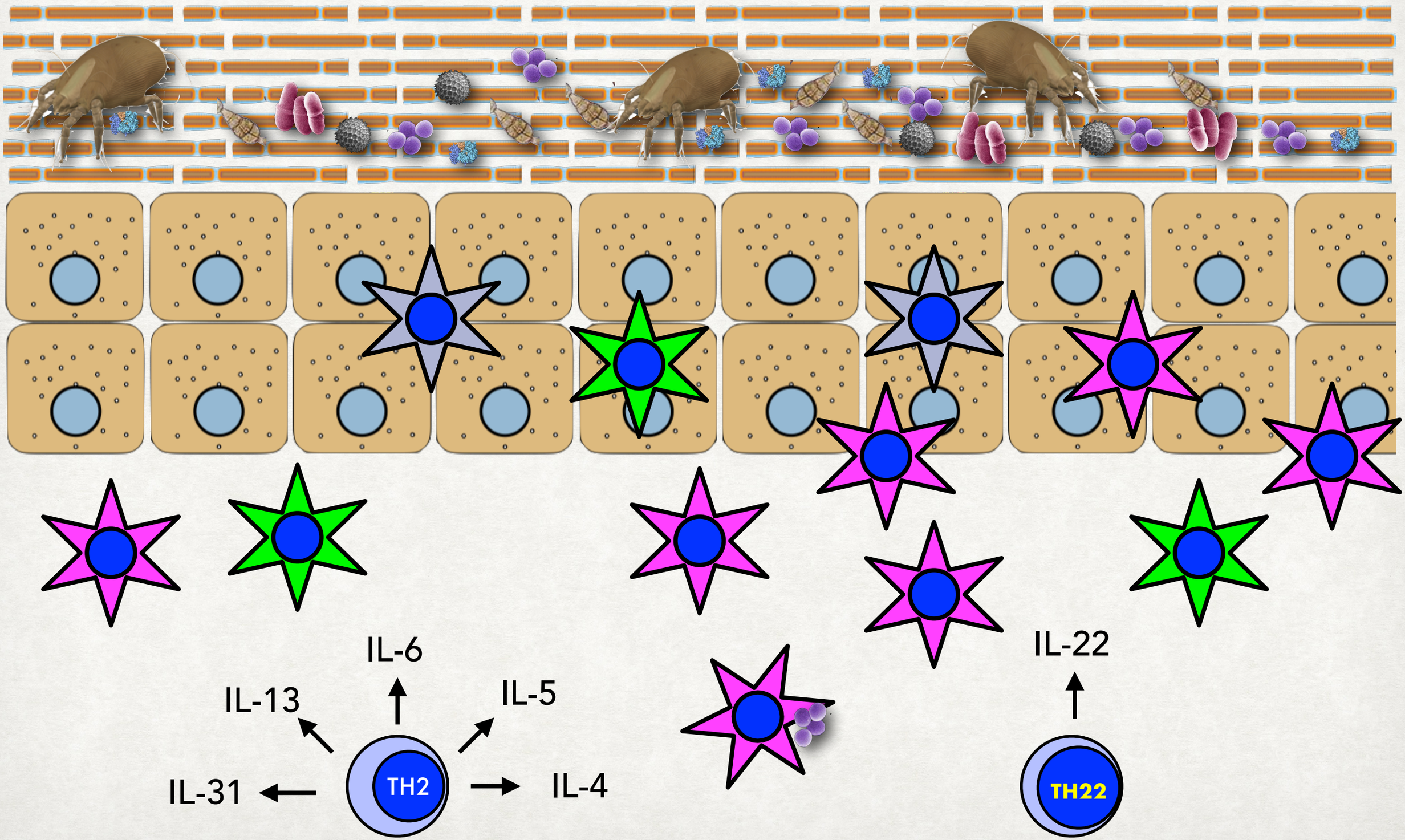
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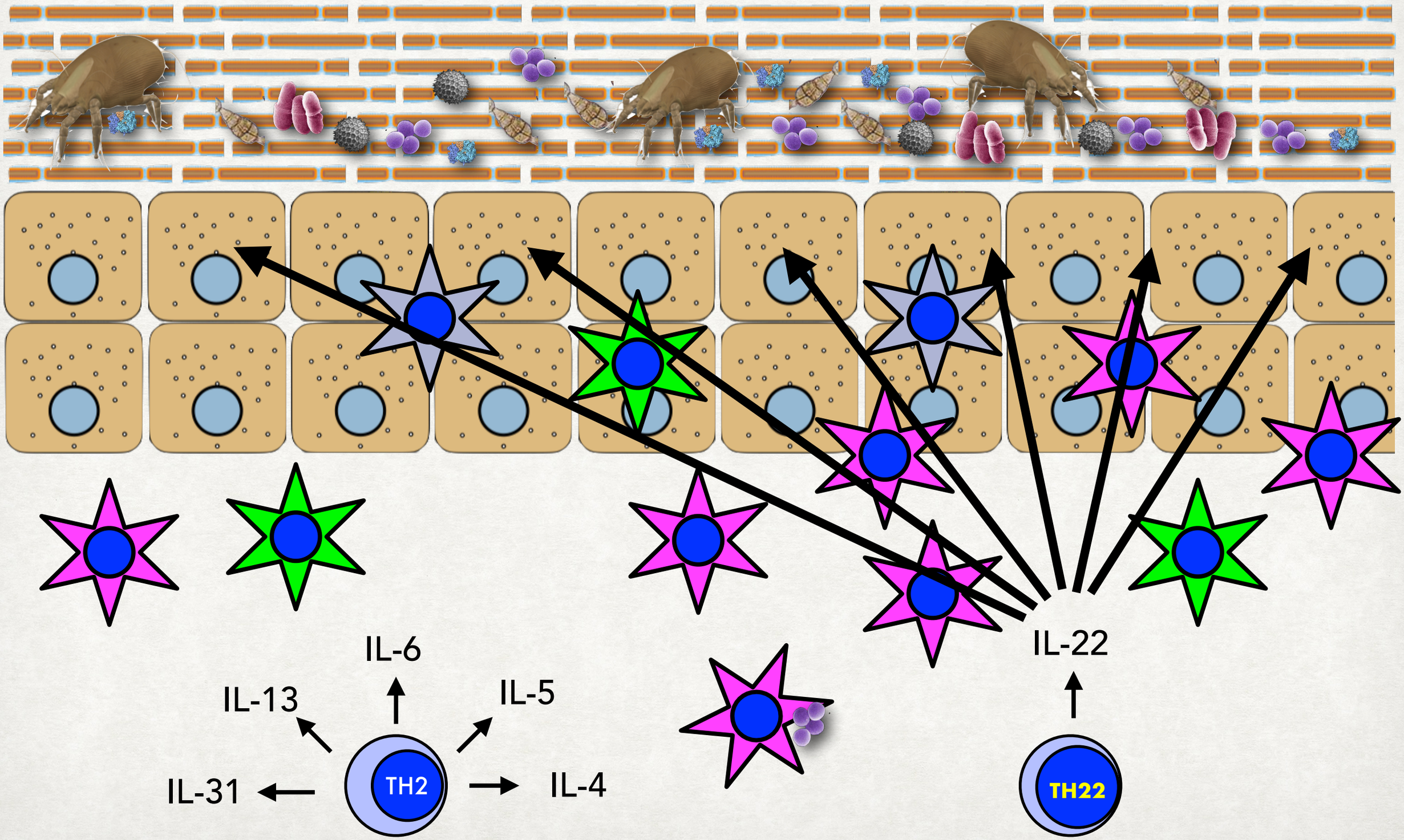
IL-6
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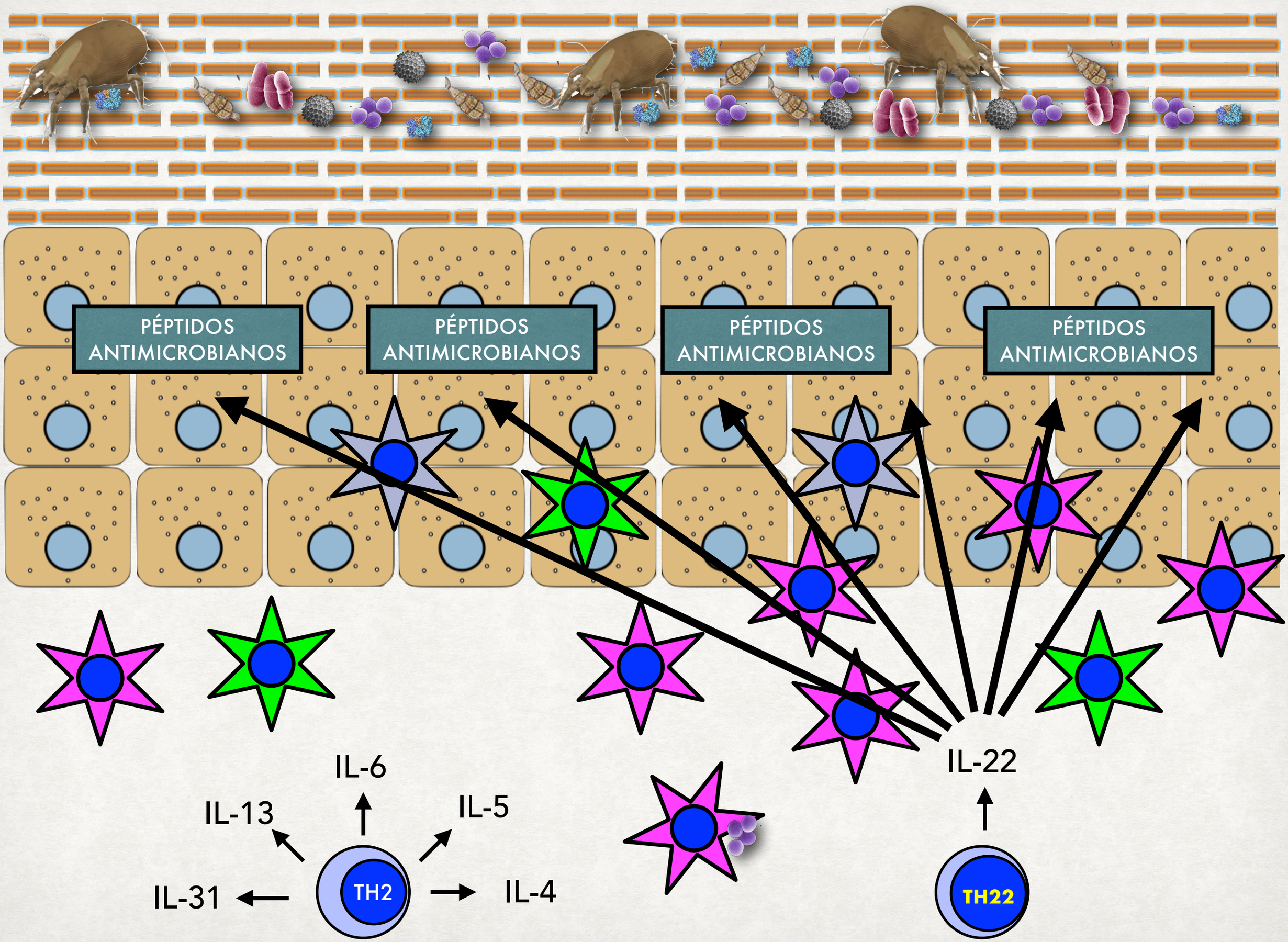
TH22


PÉPTIDOS ANTIMICROBIANOS
PÉPTIDOS ANTIMICROBIANOS
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PÉPTIDOS ANTIMICROBIANOS
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PÉPTIDOS ANTIMICROBIANOS

PÉPTIDOS ANTIMICROBIANOS

PÉPTIDOS ANTIMICROBIANOS

PÉPTIDOS ANTIMICROBIANOS

IL-6

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PÉPTIDOS ANTIMICROBIANOS

PÉPTIDOS ANTIMICROBIANOS

PÉPTIDOS ANTIMICROBIANOS

PÉPTIDOS ANTIMICROBIANOS

IL-6

IL-13

IL-5

IL-31

TH2

IL-4

IL-22

TH22

a

	HDM vs control at:		Fold Changes 6 h	24 h	48 h
Proinflammatory cytokines	*TNF*		1.1	-1.1	**1.4**
	LTB		1.1	**2.9**	**5.5**
	IL1A		-1.1	1.2	1.1
	IL1B		1.0	-1.0	1.2
	IL6		-1.5	3.0	**4.1**
	IL18		-1.4	1.7	**3.4**
Th1 cytokines	*IFNG*		1.1	1.0	1.0
	IL2		1.1	1.2	**1.4**
	IL12A		-1.2	-1.0	-1.0
	IL12B		-1.0	-1.0	-1.1
	IL27		-1.0	-1.1	-1.1
Th2/Th9 cytokines	*IL4*		1.2	1.3	**1.6**
	IL5	*	2.2	**5.9**	**9.0**
	IL9		-1.0	3.6	**9.9**
	IL13		1.6	**3.1**	**5.6**
	IL31	*	14.5	**41.6**	**96.2**
	IL33		-1.2	1.7	**2.6**
	TSLP	*	-3.1	**-9.9**	**-5.7**
Th17 cytokines	*IL17A*		1.1	1.0	1.1
	IL17B		-1.0	1.2	1.1
	IL17C		1.0	-1.1	1.0
	IL17F		1.0	1.1	1.2
	IL25	*	**-1.4**	**-1.8**	**-2.3**
Th22 cytokine	*IL22*	*	**2.1**	**5.2**	**4.7**
Regulatory cytokines	*TGFB1*		1.0	1.1	**1.5**
	IL10		1.1	1.0	1.2
CC Chemokines	*CCL5*	*	1.5	**4.9**	**9.0**
	CCL8		1.2	**1.8**	**3.4**
	CCL13		1.1	**1.9**	**2.1**
	CCL17	*	2.4	**35.8**	**185.5**
	CCL19		-1.8	**2.7**	**4.7**
	CCL22	*	1.1	**1.4**	**3.2**
	CCL24		2.0	**3.6**	**5.7**
	CCL27	*	1.0	**1.6**	1.4
	CCL28		-1.0	1.2	**1.5**
CXC Chemokines	*CXCL8*		-1.7	1.6	2.7
	CXCL10		-1.0	**3.6**	2.1
	CXCL11	*	-1.5	1.8	1.0
	CXCL13		1.1	-1.1	2.0

b

	HDM vs control at:		Fold Changes 6 h	24 h	48 h	
	cathepsin C	*CTSC*	1.1	**1.9**	**3.7**	*Proteases and receptors*
	cathepsin E	*CTSE*	1.0	-1.1	1.0	
	cathepsin S	*CTSS* *	1.2	**1.4**	**2.3**	
	matrix metalloproteinase 7	*MMP7*	-1.6	**1.6**	**3.5**	
	chymase	*CMA1*	1.4	**1.7**	**3.1**	
	tryptase	*LOC100049001*	1.2	1.4	**1.9**	
	mastin	*LOC448801*	1.4	**2.5**	**4.7**	
	coagulation factor II (thrombin) receptor-like 1 (PAR2)	*F2RL1* *	-1.1	1.1	1.1	
	coagulation factor II (thrombin) receptor-like 3 (PAR4)	*F2RL3* *	-1.1	-1.1	-1.0	
	tachykinin precursor 1 (substance P)	*TAC1*	-1.0	1.1	1.1	*Substance P and receptors*
	tachykinin receptor 1 (NK1R)	*TACR1*	-1.1	-1.1	-1.1	
	MAS-related GPR, member X2	*MRGPRX2*	-1.1	1.1	-1.0	
	endothelin 1	*EDN1*	1.1	-1.1	1.0	*Endothelin and receptors*
	endothelin receptor type A	*EDNRA*	-1.1	1.2	1.3	
	endothelin receptor type B	*EDNRB*	-1.3	-1.1	-1.3	
	neuromedin B	*NMB* *	1.1	**2.0**	**3.2**	*Bombesins and receptors*
	neuromedin B receptor	*NMBR*	1.0	1.0	-1.1	
	gastrin-releasing peptide	*GRP*	1.1	-1.1	-1.1	
	gastrin-releasing peptide receptor	*GRPR*	-1.0	-1.1	-1.2	
	histidine decarboxylase	*HDC*	-1.1	1.3	**1.6**	*Histamine and receptor*
	histamine N-methyltransferase	*HNMT*	1.3	1.4	**1.7**	
	histamine receptor H1	*HRH1*	1.1	1.1	**1.2**	
	tryptophan hydroxylase 1	*TPH1*	-1.0	1.0	1.1	*Serotonin and receptor*
	dopa decarboxylase (aromatic L-amino acid decarboxylase)	*DDC*	1.2	-1.1	-1.2	
	5-hydroxytryptamine (serotonin) receptor 7	*HTR7*	-1.1	1.2	1.3	
	nerve growth factor	*NGF*	**1.7**	-1.2	**-1.8**	*Neurotrophin and receptor*
	neurotrophic tyrosine kinase, receptor 1 (TrkA)	*NTRK1*	-1.1	**2.3**	**3.0**	
	arachidonate 5-lipoxygenase (5-LO)	*ALOX5* *	**1.8**	**1.4**	**1.5**	*Leukotrienes and receptors*
	arachidonate 5-lipoxygenase-activating protein (FLAP)	*ALOX5AP* *	**1.5**	**1.7**	**2.7**	
	leukotriene A4 hydrolase	*LTA4H*	1.1	1.3	**1.6**	
	leukotriene B4 receptor	*LTB4R*	-1.0	1.1	1.1	
	leukotriene B4 receptor 2	*LTB4R2*	1.0	1.0	-1.0	
	cysteinyl leukotriene receptor 1	*CYSLTR1*	1.0	1.1	**1.6**	
	cysteinyl leukotriene receptor 2	*CYSLTR2*	1.1	1.0	1.1	

bold = P ≤ 0.05

Olivry, T., Mayhew, D., Paps, J. S., Linder, K. E., Peredo, C., Rajpal, D., … Cote-Sierra, J. (2016). Early Activation of Th2/Th22 Inflammatory and Pruritogenic Pathways in Acute Canine Atopic Dermatitis Skin Lesions. Journal of Investigative Dermatology, 136(10), 1961–1969.

	IL17A		1.1	1.0	1.1
	IL17B		-1.0	1.2	1.1
Th17 cytokines	*IL17C*		1.0	-1.1	1.0
	IL17F		1.0	1.1	1.2
	IL25	*	**-1.4**	**-1.8**	**-2.3**
Th22 cytokine	*IL22*	*	**2.1**	**5.2**	**4.7**
Regulatory cytokines	*TGFB1*		1.0	1.1	**1.5**
	IL10		1.1	1.0	1.2
	CCL5	*	1.5	**4.9**	**9.0**
	CCL8		1.2	**1.8**	**3.4**
	CCL13		1.1	1.9	2.1
	CCL17	*	2.4	**35.8**	**185.5**
CC Chemokines	*CCL19*		-1.8	2.7	4.7
	CCL22	*	1.1	**1.4**	**3.2**
	CCL24		2.0	**3.6**	**5.7**
	CCL27	*	1.0	**1.6**	1.4
	CCL28		-1.0	1.2	**1.5**

TARC

dopa decarb

arachic

Th22 cytokine	*IL22*	*	**2.1**	**5.2**	**4.7**
Regulatory cytokines	*TGFB1*		1.0	1.1	**1.5**
	IL10		1.1	1.0	1.2
CC Chemokines	*CCL5*	*	1.5	**4.9**	**9.0**
	CCL8		1.2	**1.8**	**3.4**
	CCL13		1.1	**1.9**	**2.1**
	CCL17	*	2.4	**35.8**	**185.5**
	CCL19		-1.8	**2.7**	**4.7**
	CCL22	*	1.1	**1.4**	**3.2**
	CCL24		2.0	**3.6**	**5.7**
	CCL27	*	1.0	**1.6**	1.4
	CCL28		-1.0	1.2	**1.5**
CXC Chemokines	*CXCL8*		-1.7	1.6	2.7
	CXCL10		-1.0	**3.6**	2.1
	CXCL11	*	-1.5	1.8	1.0
	CXCL13		1.1	-1.1	2.0

dopa deca

arach

Eotaxina

Th1 cytokines	*IL12A*		-1.2	-1.0	-1.0
	IL12B		-1.0	-1.0	-1.1
	IL27		-1.0	-1.1	-1.1
Th2/Th9 cytokines	*IL4*		1.2	1.3	**1.6**
	IL5	*	2.2	**5.9**	**9.0**
	IL9		-1.0	3.6	**9.9**
	IL13		1.6	**3.1**	**5.6**
	IL31	*	**14.5**	**41.6**	**96.2**
	IL33		-1.2	1.7	**2.6**
	TSLP	*	-3.1	**-9.9**	**-5.7**
Th17 cytokines	*IL17A*		1.1	1.0	1.1
	IL17B		-1.0	1.2	1.1
	IL17C		1.0	-1.1	1.0
	IL17F		1.0	1.1	1.2
	IL25	*	**-1.4**	**-1.8**	**-2.3**
Th22 cytokine	*IL22*	*	**2.1**	**5.2**	**4.7**
Regulatory	*TGFB1*		1.0	1.1	**1.5**

Daño Epidérmico

??

Coagula

dopa decarbo

Table 1. Differential Expression of TSLP Isoforms in Barrier Surface Diseases

Pathology	Short TSLP	Long TSLP
Asthma	-	↑↑
Crohn's disease	↓↓	-
Ulcerative colitis	-	↑
Celiac disease	↓↓	↓↓
Atopic dermatitis	↓↓	↑
Psoriasis	-	↓↓

-, unchanged; ↑↑, upregulated; ↓↓, downregulated.

Tsilingiri, K., Fornasa, G., & Rescigno, M. (2017). Thymic Stromal Lymphopoietin: To Cut a Long Story Short. Cellular and Molecular Gastroenterology and Hepatology, 3(2), 174–182.

Th2/Th9 cytokines	IL13	1.6	3.1	5.6
	IL31 *	14.5	41.6	96.2
	IL33	-1.2	1.7	2.6
	TSLP *	-3.1	-9.9	-5.7
Th17 cytokines	IL17A	1.1	1.0	1.1
	IL17B	-1.0	1.2	1.1
	IL17C	1.0	-1.1	1.0

Daño Epidérmico

??

	IL18	-1.4	1.7	**3.4**	
	IFNG	1.1	1.0	1.0	
	IL2	1.1	1.2	**1.4**	coagulati
Th1 cytokines	*IL12A*	-1.2	-1.0	-1.0	coagulati
	IL12B	-1.0	-1.0	-1.1	
	IL27	-1.0	-1.1	-1.1	
	IL4	1.2	1.3	**1.6**	
	IL5 *	2.2	**5.9**	**9.0**	
	IL9	-1.0	3.6	**9.9**	
Th2/Th9 cytokines	*IL13*	1.6	**3.1**	**5.6**	
	IL31 *	14.5	**41.6**	**96.2**	
	IL33	-1.2	1.7	**2.6**	
	TSLP *	-3.1	**-9.9**	**-5.7**	
	IL17A	1.1	1.0	1.1	
	IL17B	-1.0	1.2	1.1	
Th17 cytokines	*IL17C*	1.0	**-1.1**	1.0	
	IL17F	1.0	1.1	1.2	

TH2

Barrera Cutánea

Partes de Estudio

✓ Barrera Cutánea y Diferentes Enfermedades

▸ **Barrera Cutánea y Dermatitis Atópica**

1- Disminución en cantidad y organización de Ceramidas

2- Disminución en la Cantidad de Filagrina

Estrato Corneo y Dermatitis Atópica

✓ Corneocitos no perfectamente formados

✓ Menor hidratación superficial

✓ pH del estrato corneo mas elevado

✓ Menor cantidad de Esfingosina y Pépitidos Antimicrobianos

✓ Mayor penetración de Alergenos, Proteasas Ambientales y MO

Estrato Corneo y Dermatitis Atópica

- ✓ Corneocitos no perfectamente formados
- ✓ Menor hidratación superficial
- ✓ pH del estrato corneo mas elevado
- ✓ Menor cantidad de Esfingosina y Pépitidos Antimicrobianos
- ✓ Mayor penetración de Alergenos, Proteasas Ambientales y MO

Menor cantidad de Esfingosina y Pépitidos Antimicrobianos

Incremento de Staph en la Superficie

Mayor penetración de Alergenos, Proteasas Ambientales y MO

Mayor activación de Queratinocitos y Células MCHII

Incremento de Citoquinas de los Queratinocitos (TARC - TSLP - Il-1 - otras)

Inflamación polarizada hacia TH2 y TH22

Inflamación crónica mixta TH1, TH2 y TH22

Menor síntesis de Ceramidas Filigrana y Peptidos AB

Mayor llegada de Ag a cel. presentadora

Potenciación de Respuesta Inmune Adaptativa - Inflamación

Estrato Corneo y Dermatitis Atópica

- ✓ Corneocitos no perfectamente formados
- ✓ Menor hidratación superficial
- ✓ pH del estrato corneo mas elevado
- ✓ Menor cantidad de Esfingosina y Pépitidos Antimicrobianos
- ✓ Mayor penetración de Alergenos, Proteasas Ambientales y MO

Menor cantidad de Esfingosina y Pépitidos Antimicrobianos

Incremento de Staph en la Superficie

Mayor penetración de Alergenos, Proteasas Ambientales y MO

Mayor activación de Queratinocitos y Células MCHII

Mayor llegada de Ag a cel. presentadora

Incremento de Citoquinas de los Queratinocitos (TARC - TSLP - Il-1 - otras)

Potenciación de Respuesta Inmune Adaptativa - Inflamación

Inflamación polarizada hacia TH2 y TH22

Menor síntesis de Ceramidas Filigrana y Peptidos AB

Inflamación crónica mixta TH1, TH2 y TH22

Inflamación

Daño del Estrato Corneo

Prurito

Il-31

Citoquinas TH2

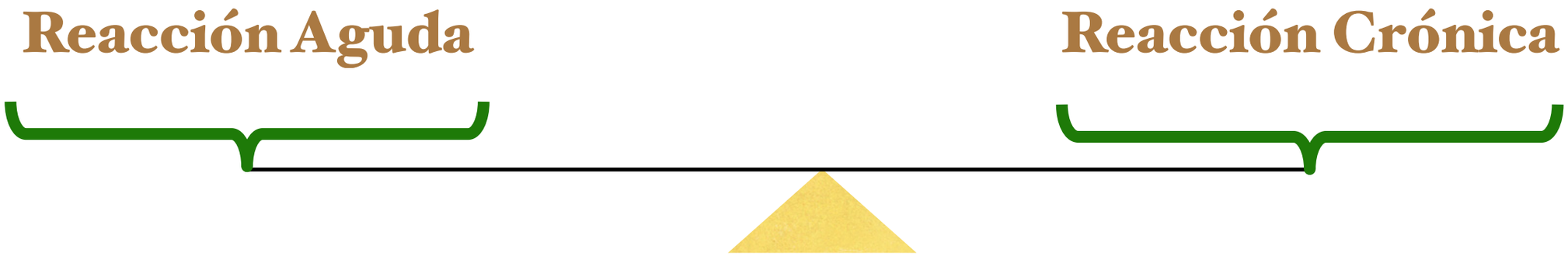
TSLP

Citoquinas de Queratinocitos

Proceso Inflamatorio en DA

Inmunidad Adaptativa

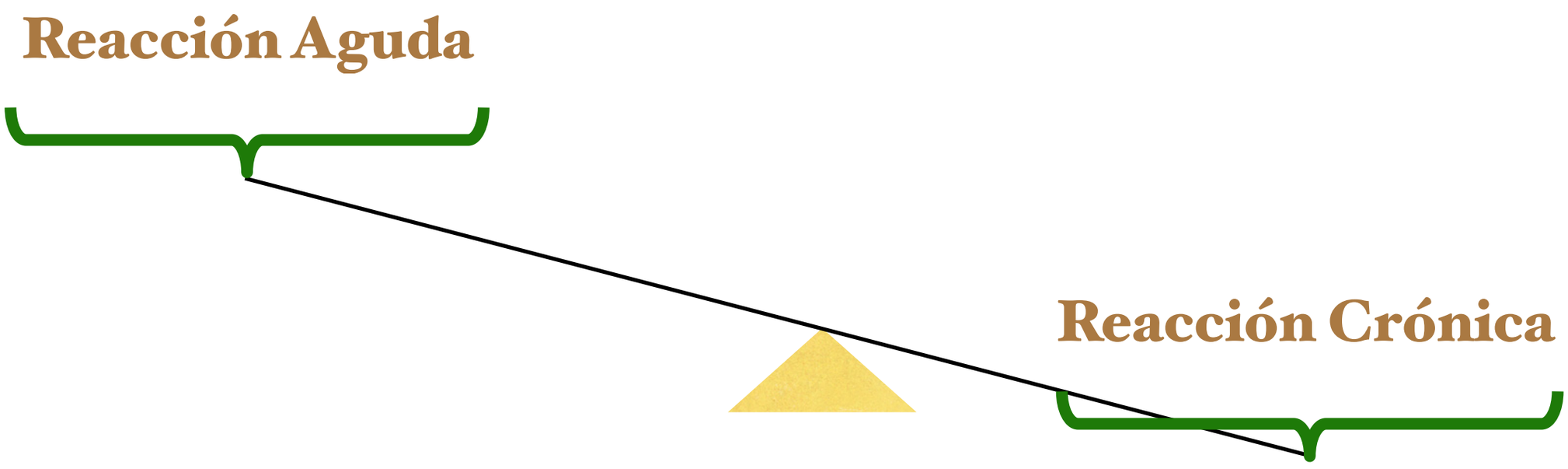
Queratinocito



Proceso Inflamatorio en DA

Inmunidad Adaptativa

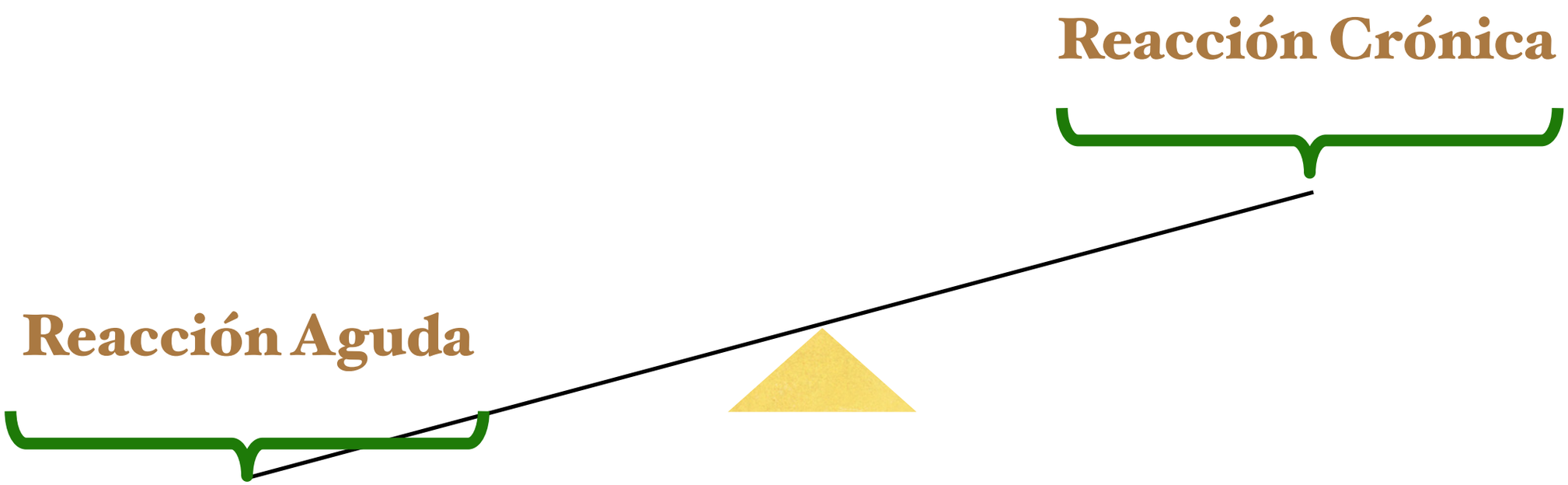
Queratinocito



Proceso Inflamatorio en DA

Inmunidad Adaptativa

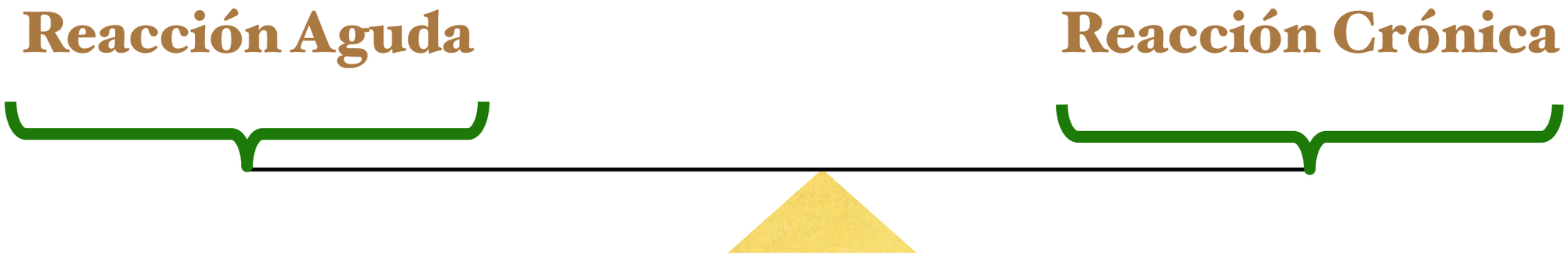
Queratinocito



Proceso Inflamatorio en DA

Inmunidad Adaptativa

Queratinocito



FENOTIPO AGUDO

FENOTIPO CRÓNICO

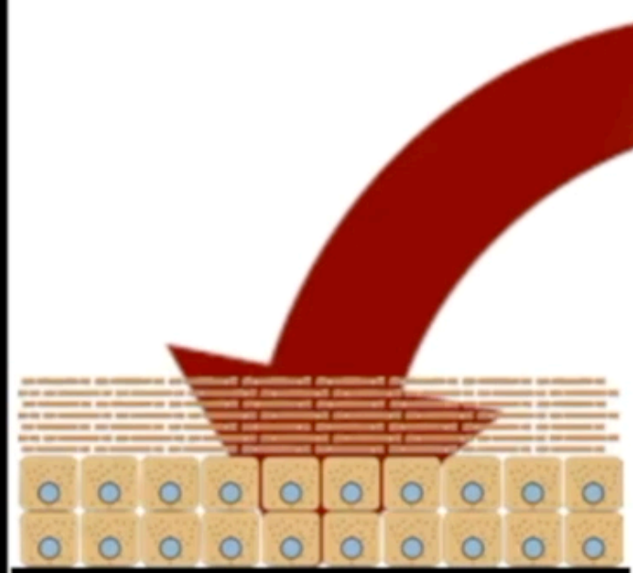
FENOTIPO AGUDO

FENOTIPO CRÓNICO

FENOTIPO AGUDO

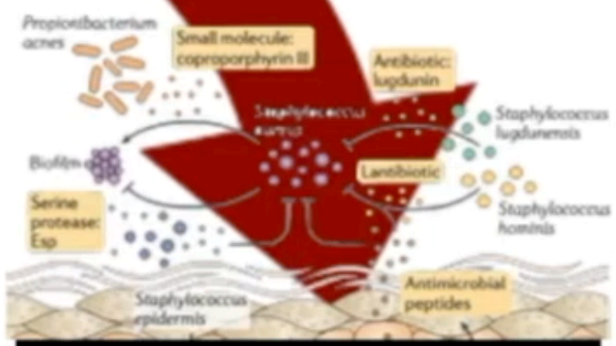
FENOTIPO CRÓNICO

Dermatitis Atópica



Daño en la Barrera Cutánea

Inflamación



Disbiosis Superficial

Citoquinas de Daño Epidérmico

Staph. Malassezia

Alergenos Ambientales

Alergenos Alimentarios

Ectoparásitos

Irritantes

Proteasas

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

1- Mucho componente es SECUNDARIO INFLAMATORIO

doi: 10.1111/cea.12023

Clinical & Experimental Allergy, **43**, 586–598

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REVIEW

Cytokine regulation of the epidermal barrier

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Clinical & Experimental Allergy

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Summary

Studies published in recent years have highlighted the role of epidermal barrier defects in both atopic skin disease and the development of broader allergic manifestations. While genetic determinants of barrier function are important, it is clear that local acquired effects are also involved in disease pathogenesis. In this review, we aimed to summarize the known influences of cytokines abundantly expressed during atopic skin disease on components of epidermal barrier integrity and function.

Las citoquinas alteran la estructura de la Barrera Cutánea

Journal of Dermatological Science 68 (2012) 25–35

Contents lists available at SciVerse ScienceDirect

Journal of Dermatological Science

journal homepage: www.elsevier.com/jds

Th1 cytokines accentuate but Th2 cytokines attenuate ceramide production in the stratum corneum of human epidermal equivalents: An implication for the disrupted barrier mechanism in atopic dermatitis

Eri Sawada [a,1], Naoki Yoshida [a,b,1], Ayumi Sugiura [a], Genji Imokawa [a,c,*]

[a] School of Bioscience and Biotechnology, Tokyo University of Technology, Japan
[b] Department of R&D Center, Ikeda Mohando Co., Ltd., Japan
[c] Research Institute for Biological Functions, Chubu University, Japan

Citoquinas H2 (Il-4 - Il-6) disminuyen Esfigomielinasa acida, β-Glucocerebrosidasa y Serina-Palmitoil Transferasa (Sintesis de Ceramida)

Cytokine modulation of atopic dermatitis filaggrin skin expression

Michael D. Howell, PhD,[a]* Byung Eui Kim, MD, PhD,[a,b]* Peisong Gao, PhD,[c] Audrey V. Grant, ScM,[c] Mark Boguniewicz, MD,[a] Anna DeBenedetto, PhD,[d] Lynda Schneider, MD,[e] Lisa A. Beck, MD,[d] Kathleen C. Barnes, PhD,[c] and Donald Y. M. Leung, MD, PhD[a] *Denver, Colo, Seoul, Korea, Baltimore, Md, Rochester, NY, and Boston, Mass*

Il 4 e Il 13 (Ambas Citoquinas H2) reducen expresión de Filigrana

DOI:10.1111/j.1600-0625.2010.01109.x
www.blackwellpublishing.com/EXD

Letter to the Editor

Missing C-terminal filaggrin expression, NFkappaB activation and hyperproliferation identify the dog as a putative model to study epidermal dysfunction in atopic dermatitis

Ludovic Chervet[1,4], Arnaud Galichet[1,4], W. H. Irwin McLean[2], Huijia Chen[2], Maja M. Suter[1,4], Petra J. Roosje[3,4*] and Eliane J. Müller[1,4*]

[1]Molecular Dermatology, Institute of Animal Pathology, Vetsuisse Faculty, University of Bern, Bern, Switzerland;
[2]Epithelial Genetics Group, Division of Molecular Medicine, Colleges of Life Sciences and Medicine, Dentistry & Nursing, University of Dundee, Dundee, Scotland;
[3]Division of Clinical Dermatology, Department of Clinical Veterinary Medicine, University of Bern, Bern, Switzerland;
[4]DermFocus, Vetsuisse Faculty, University of Bern, Bern, Switzerland
Correspondence: Eliane J. Müller, Molecular Dermatology, Institute of Animal Pathology, Vetsuisse Faculty, University of Bern, Bern, Switzerland, Länggass-Strasse 122, Postfach 8466, Bern CH-3001, Switzerland, Tel.: +41 31 631 24 03, Fax: +41 31 631 26 35, e-mail: eliane.mueller@itpa.unibe.ch
[*]*Equal contribution.*

Se identificaron alteraciones en la transcripción de Filagrinas de origen Genético (mutaciones) e Inflamatorio

ORIGINAL ARTICLE

TNF-α Downregulates Filaggrin and Loricrin through c-Jun N-terminal Kinase: Role for TNF-α Antagonists to Improve Skin Barrier

Byung Eui Kim[1], Michael D. Howell[1,2], Emma Guttman[3,4], Patricia M. Gilleaudeau[3], Irma R. Cardinale[3], Mark Boguniewicz[1,2], James G. Krueger[3] and Donald Y.M. Leung[1,2]

Filaggrin (*FLG*), loricrin (*LOR*), and involucrin are important epidermal barrier proteins. As psoriasis is characterized by overexpression of tumor necrosis factor-α (TNF-α) and impaired skin barrier, we investigated the expression of skin barrier proteins in psoriasis patients and whether their expression was modulated by TNF-α. The expression of *FLG* and *LOR* was found to be decreased in lesional and non-lesional skin of psoriasis patients. A correlation was found between the expression of TNF-α and epidermal barrier proteins in psoriasis. TNF-α was found to modulate the expression of *FLG* and *LOR* via a c-Jun N-terminal kinase-dependent pathway. Importantly, we report that clinical treatment of psoriasis patients with a TNF-α antagonist results in significant enhancement of epidermal barrier protein expression. Our current study suggests that TNF inhibits barrier protein expression, and TNF-α antagonists may contribute to clinical improvement in patients with psoriasis by improving barrier protein expression.

Journal of Investigative Dermatology (2011) **131,** 1272–1279; doi:10.1038/jid.2011.24; published online 24 February 2011

TNF-α disminuye Filagrinas y Loricrina

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

1- Mucho componente es SECUNDARIO INFLAMATORIO

2- ¿ Desinflamar la piel sería Util ?

A Prospective, Double-lbinded, Controlled Pilot Study to Evaluate the Effects of Cyclosporine (Atopica) on Skin Barrier Function in Canine Atopic Dermatitis by Measurement of Trans-Epidermal Water Loss

Feld D

Marsella R

Ahrens K

From the Department of Small Animal Clinical Sciences,
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University of Florida, Gainesville, Florida, USA
Corresponding author: Rosanna Marsella
Address: Department of Small Animal Clinical Sciences
2015 SW 16th Avenue
College of Veterinary Medicine
University of Florida
Gainesville, FL 32610-0126
Phone: 001-352-278 0742
Fax: 001- 352-392 6125
Email: Marsella@ufl.edu

Funding Source: Self funded
No conflicts to declare

Ni Glucocorticoides ni Ciclosporina mejoraron la TEWL en perros con Dermatitis Atópica (aunque SI mejoraron los dignos clínicos)

Barrera Cutánea

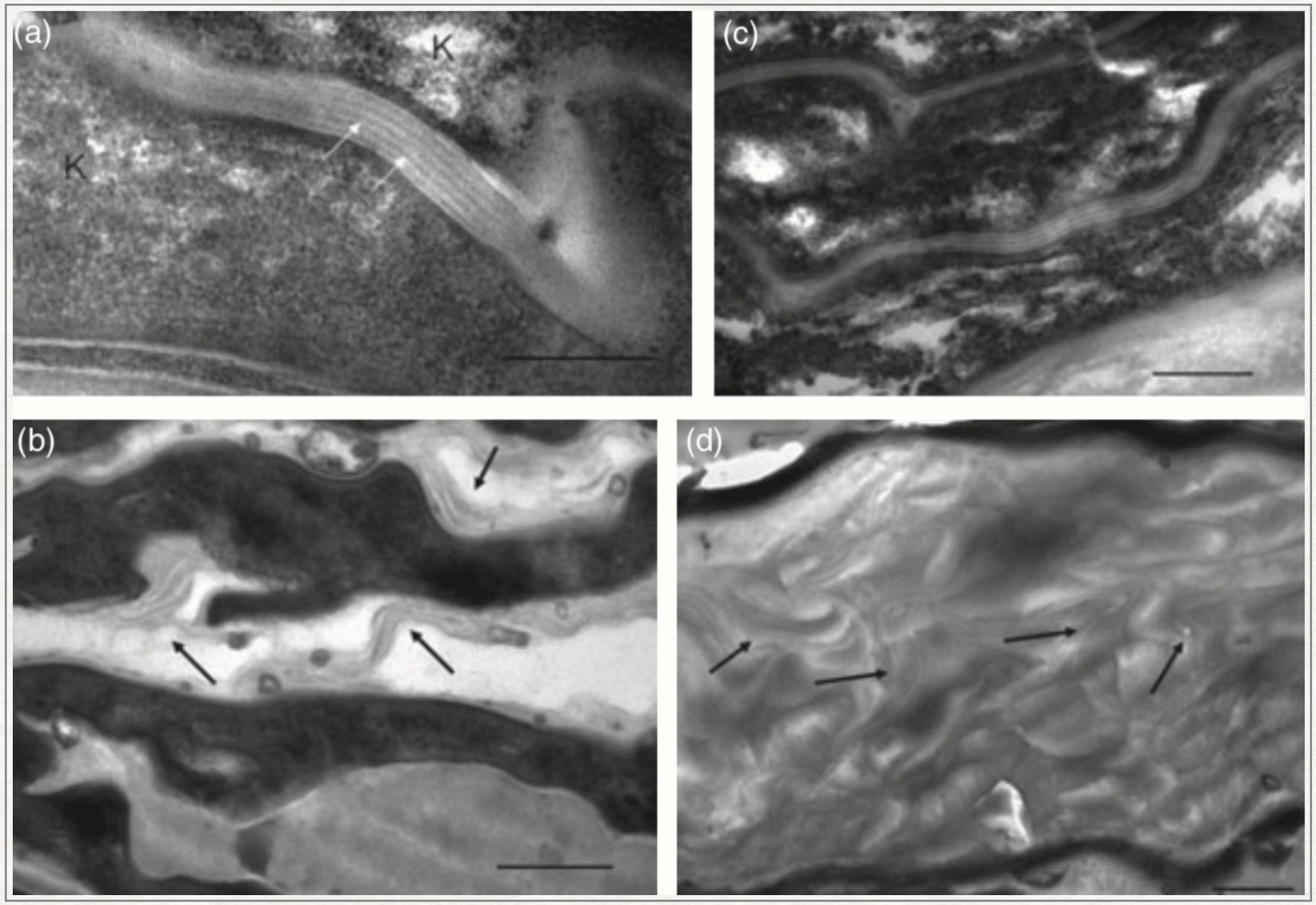
Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

1- Mucho componente es SECUNDARIO INFLAMATORIO

2- ¿ Desinflamar la piel sería Util ?

3- ¿ Si se Colocan Ceramidas es suficiente ?



Marsella, R., Samuelson, D., & Doerr, K. (2010). *Transmission electron microscopy studies in an experimental model of canine atopic dermatitis. Veterinary Dermatology, 21(1), 81–88.* doi:10.1111/j.1365-3164.2009.00802.x

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LUEGO DE APLICAR ALERGENO

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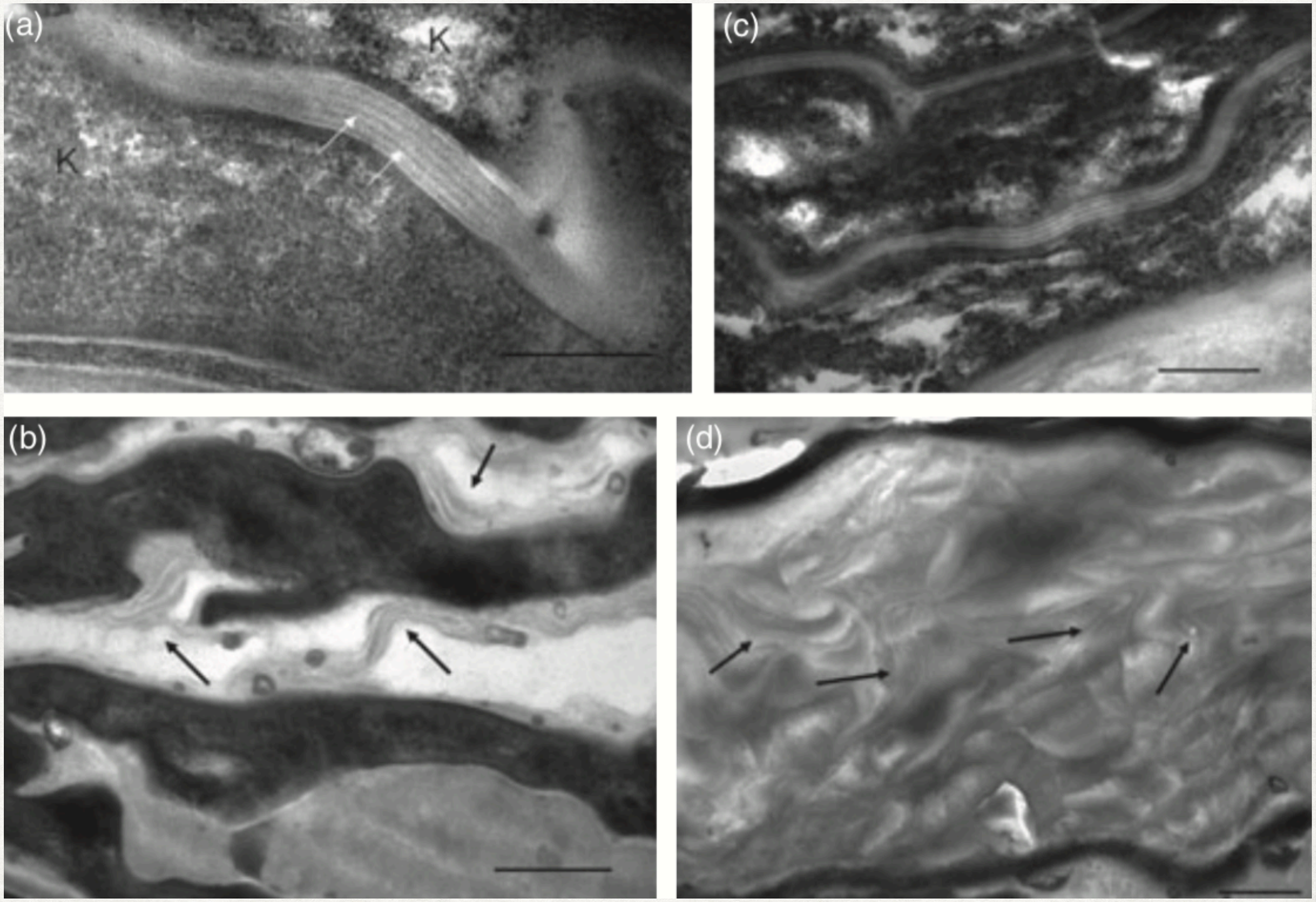

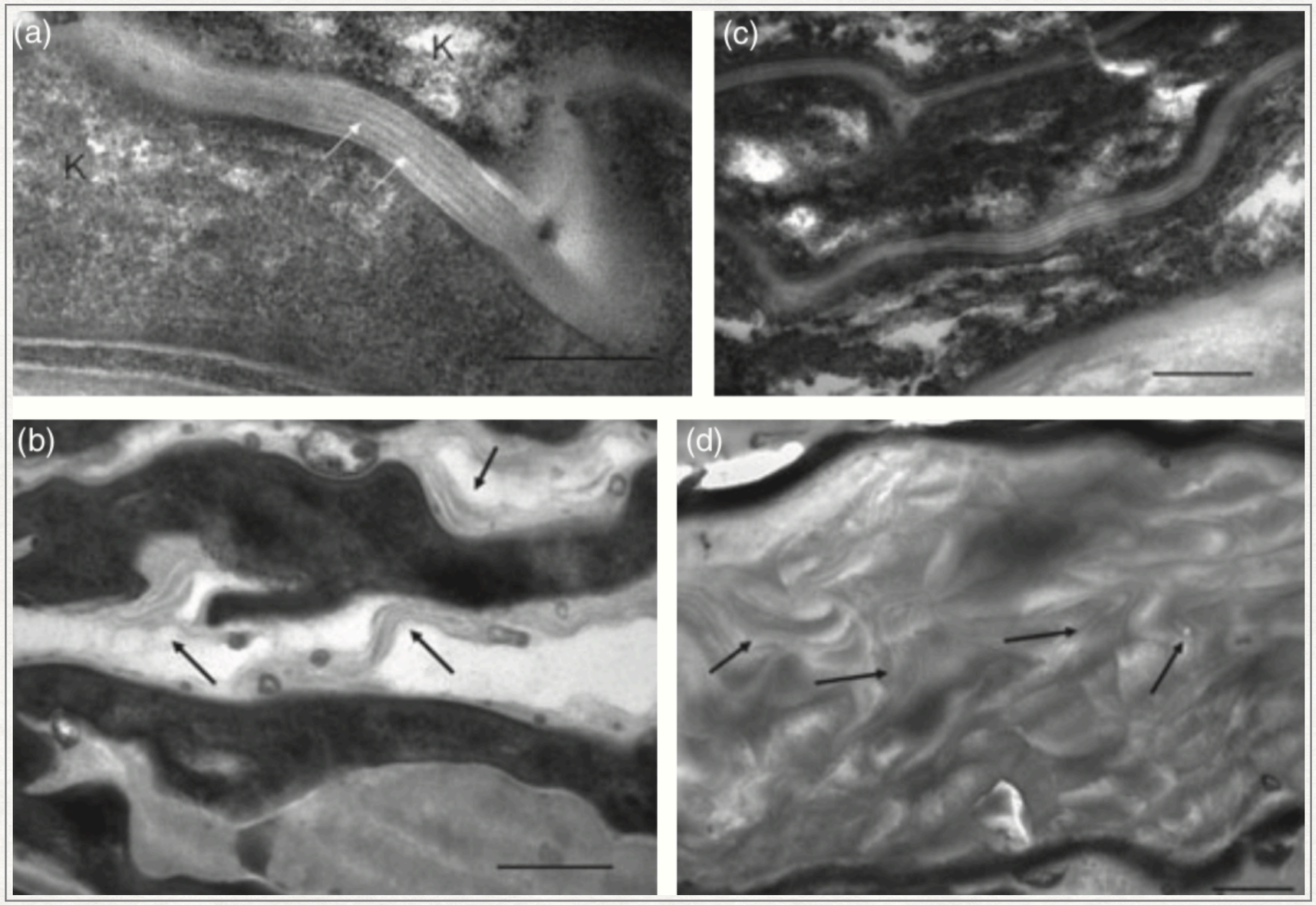

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PERRO CON AD

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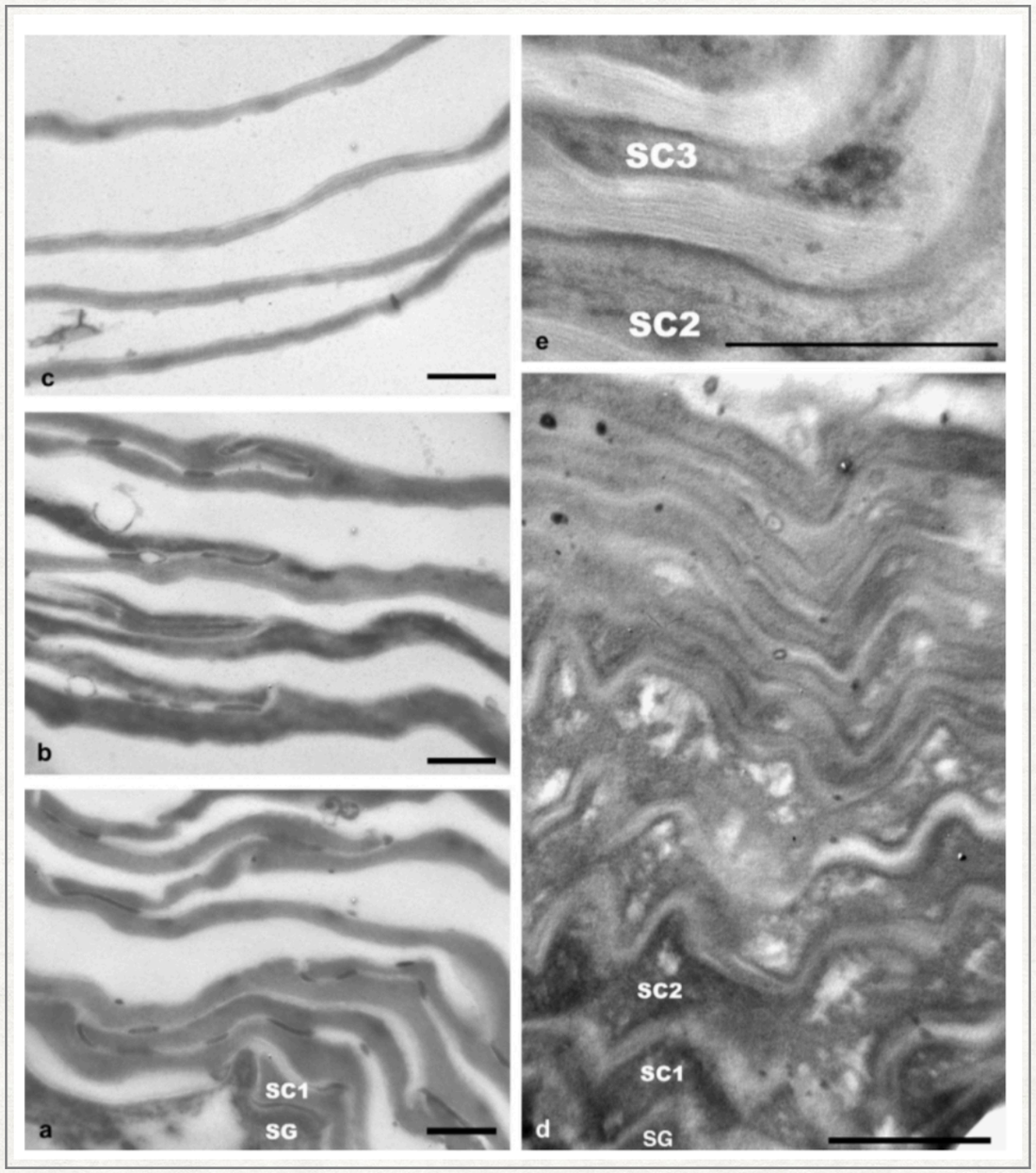
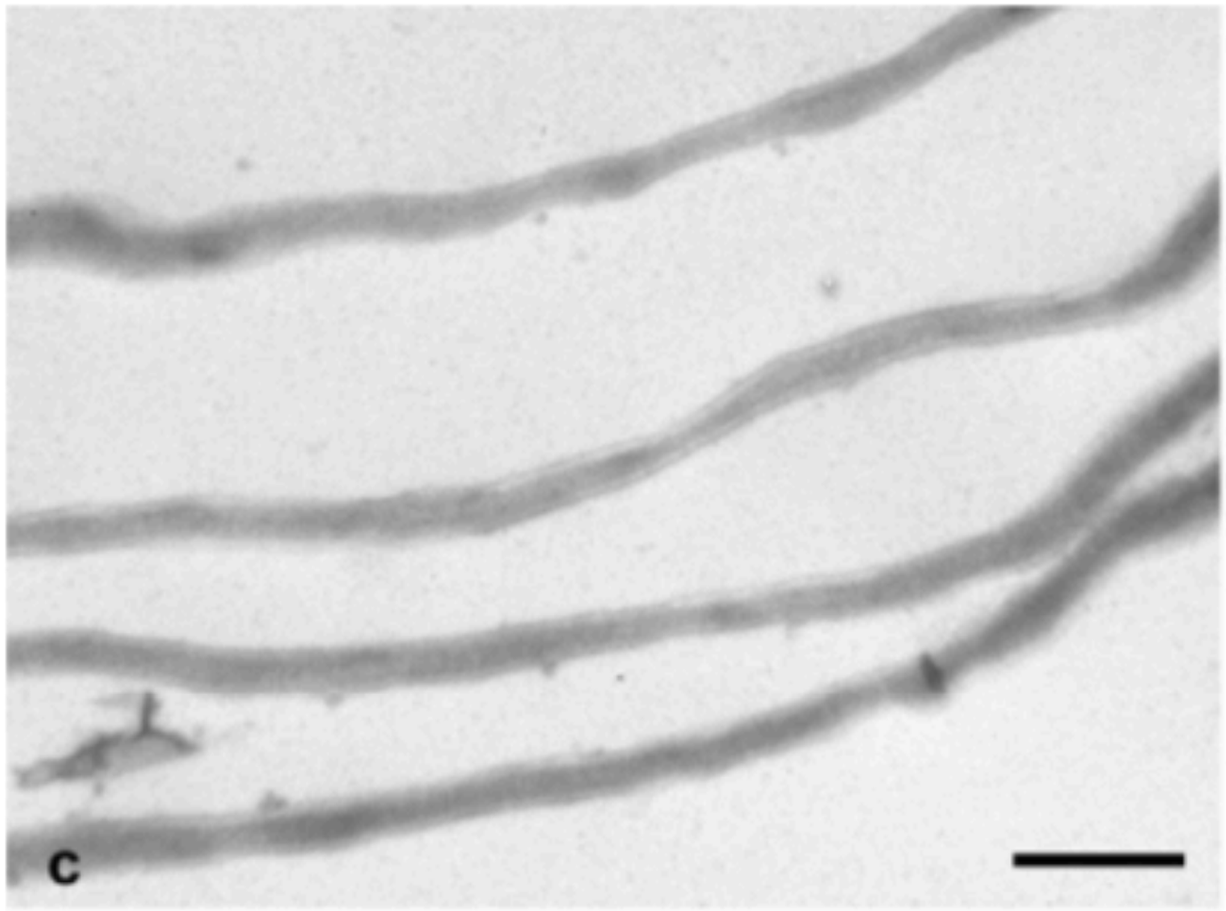


A. Piekutowska[*], D. Pin[†], C. A. Re`me[‡], H. Gatto[‡] and M. Haftek (2008) Effects of a Topically Applied Preparation of Epidermal Lipids on the Stratum Corneum Barrier of Atopic Dogs. J. Comp. Path. 2008, Vol. 138, 197e203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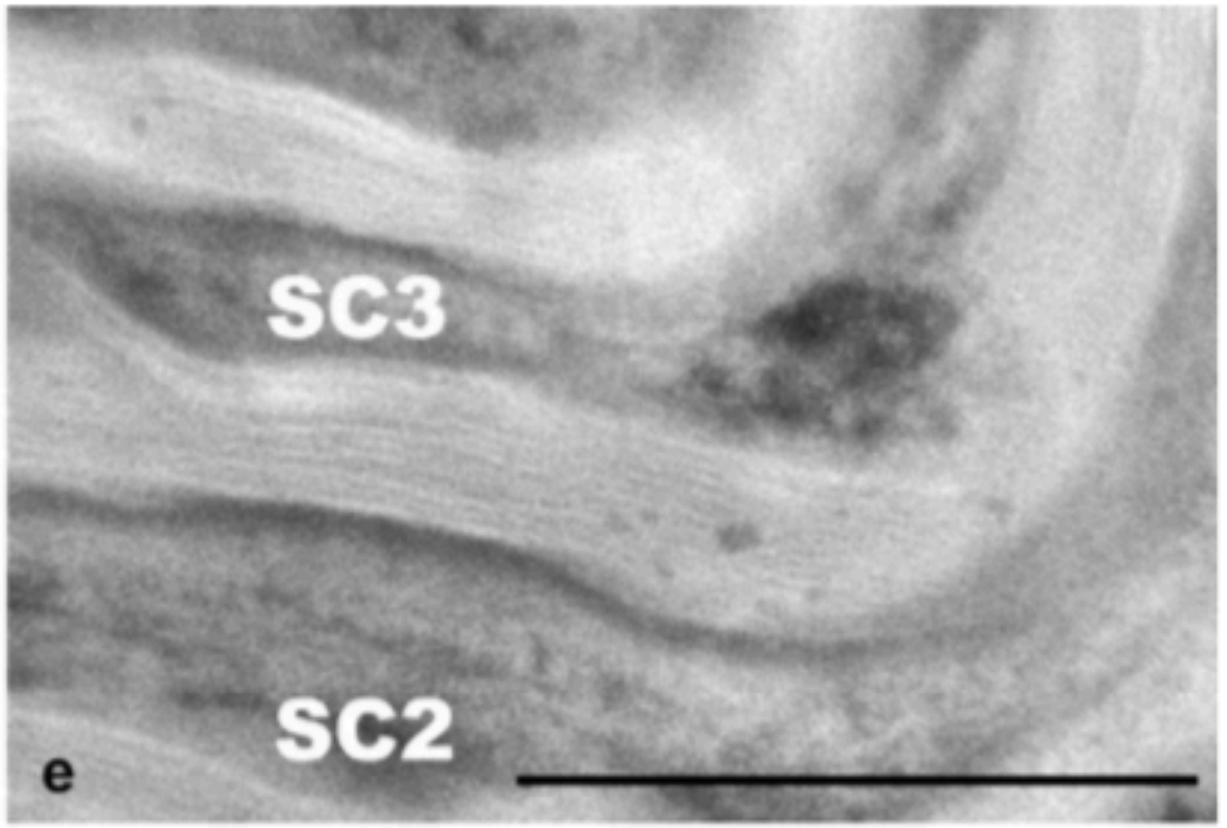
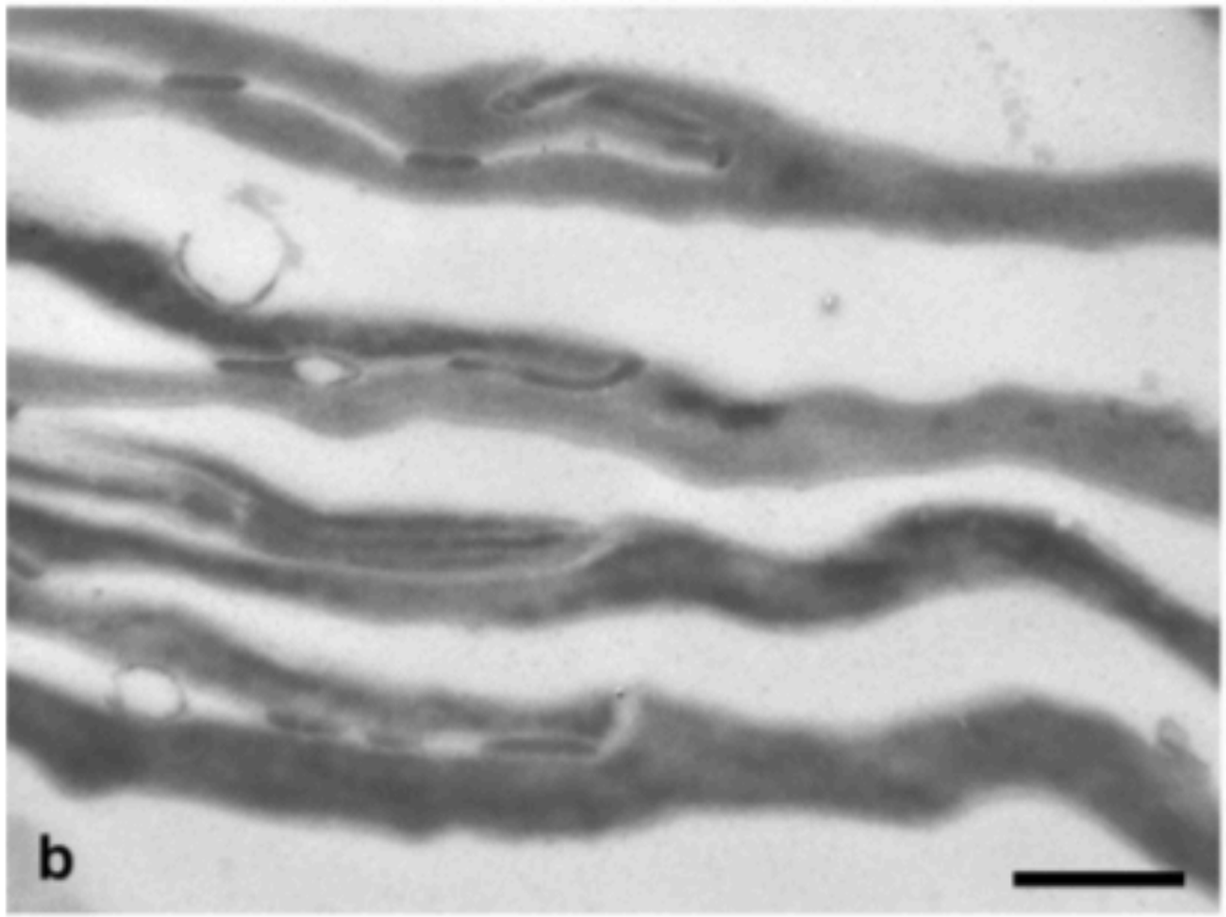

SC3
SC2
e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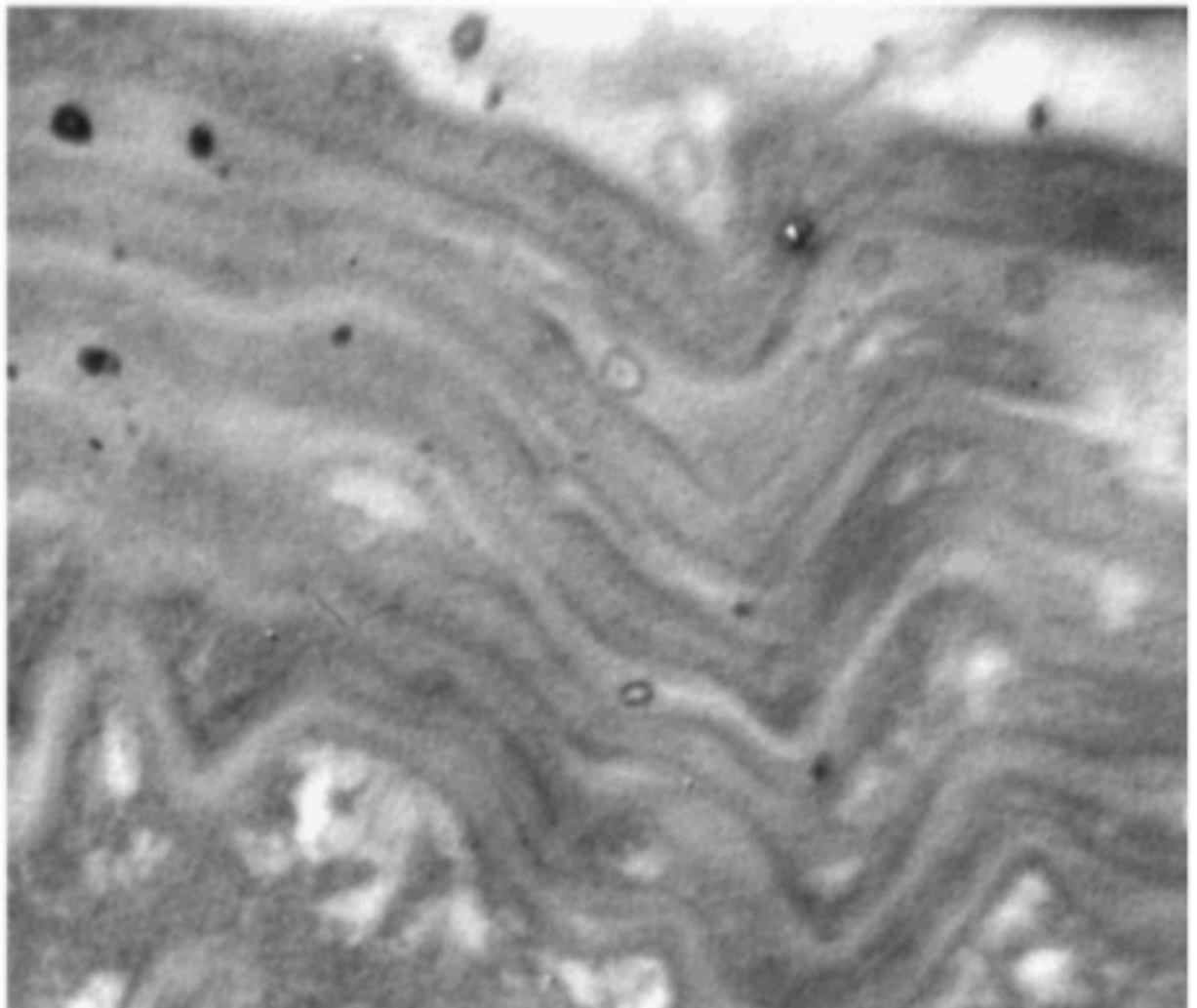

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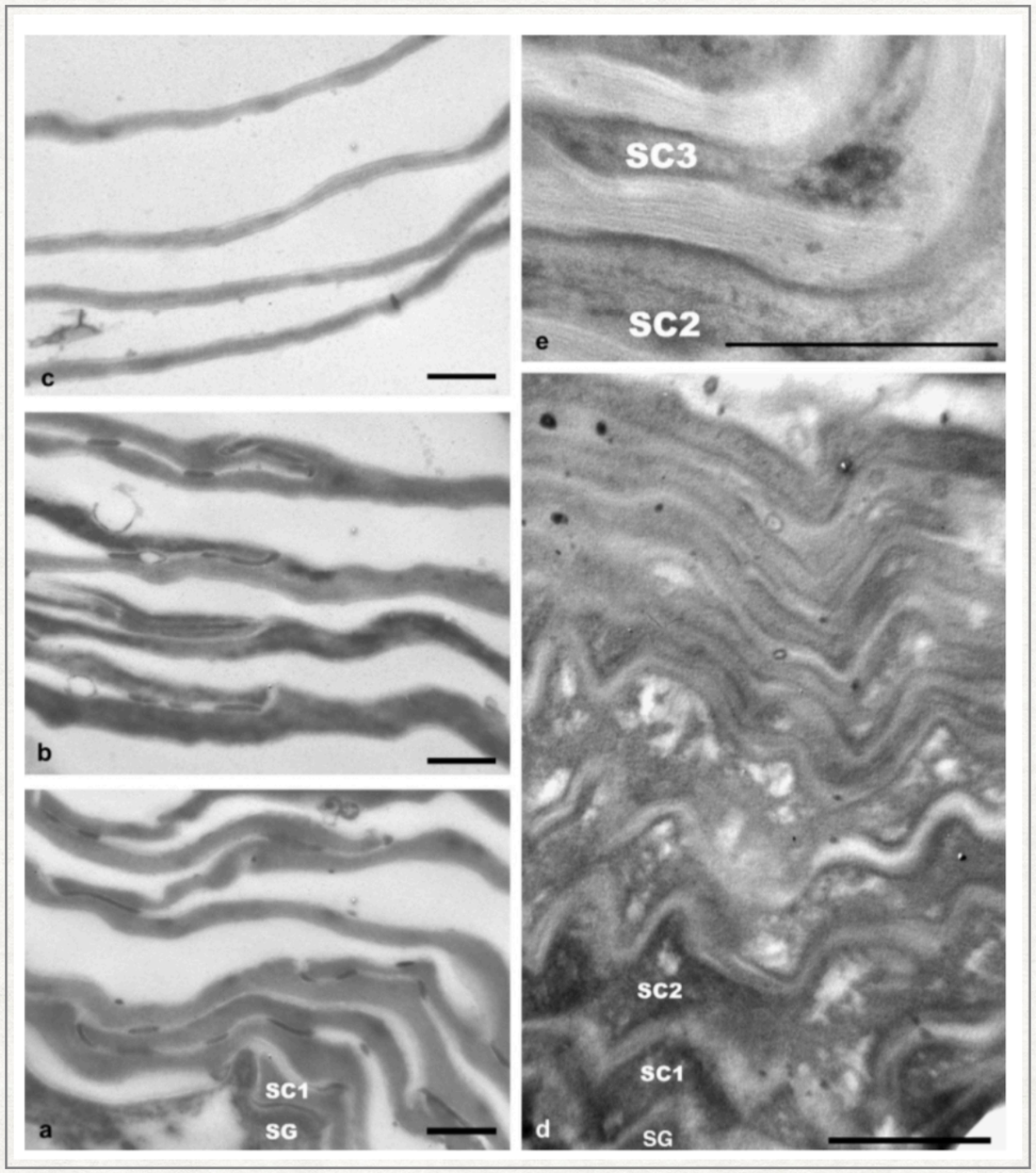

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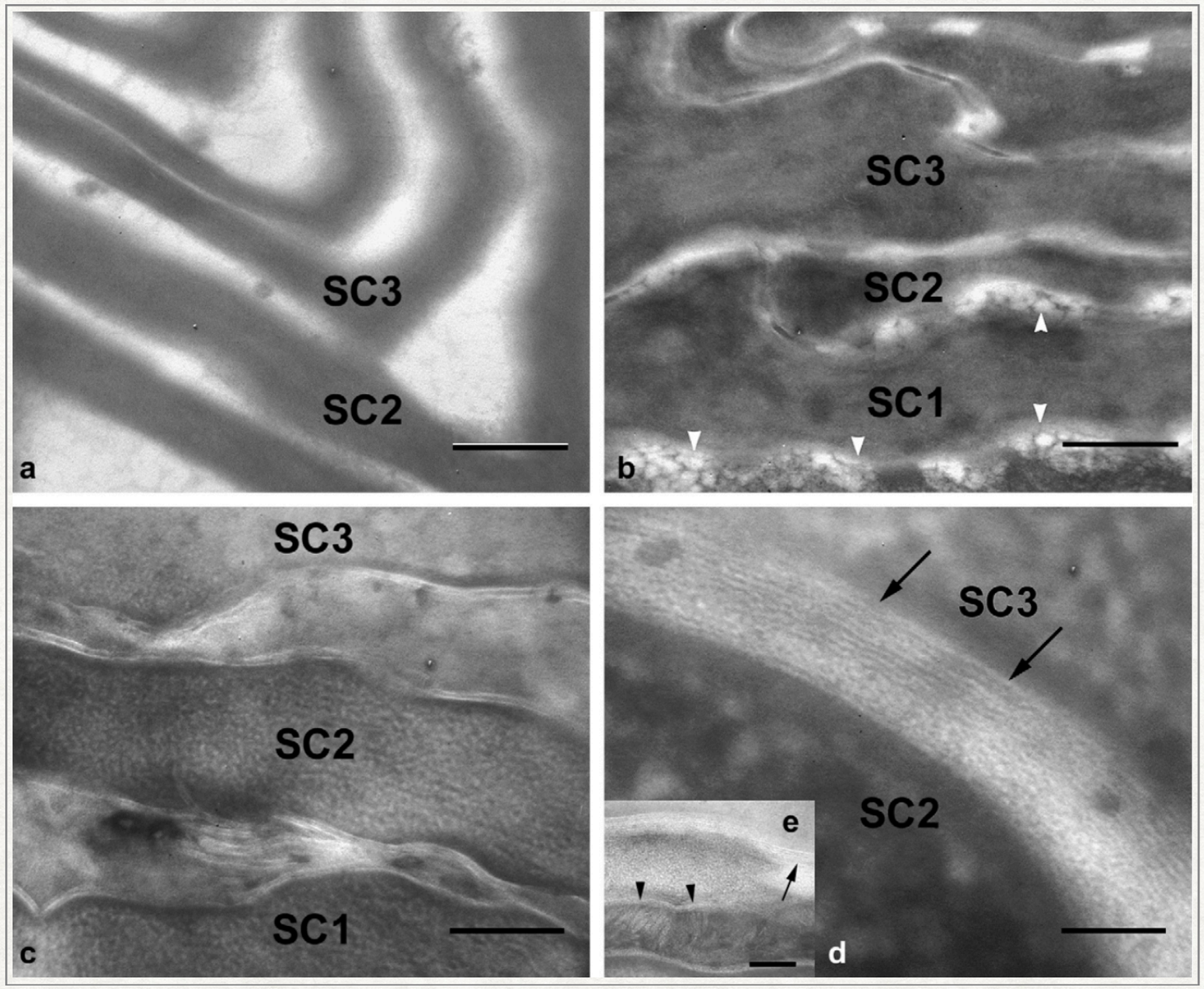

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PERRO SIN TERAPIA

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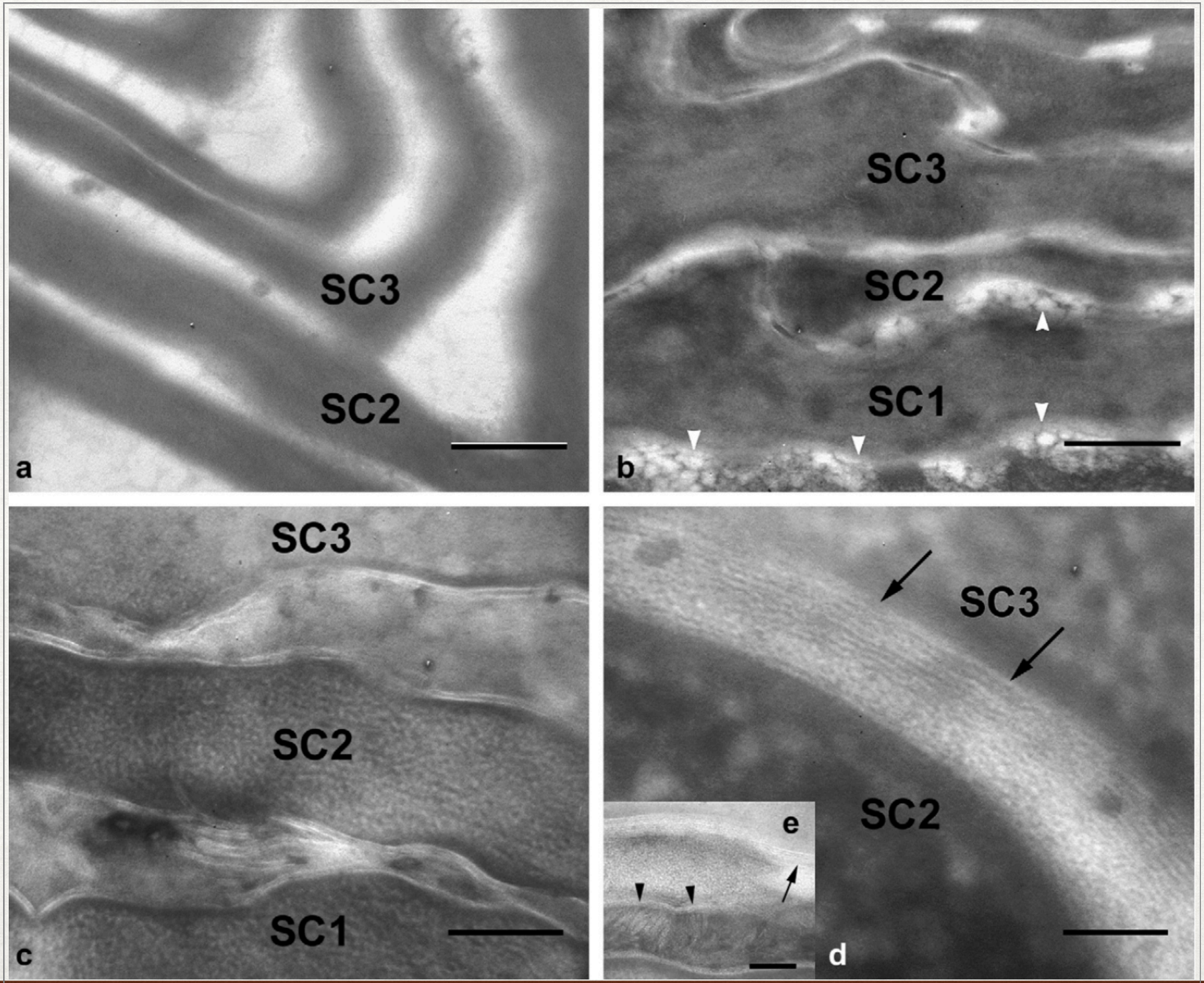


PERRO SIN TERAPIA

SC3

SC2

PERRO CON TERAPIA

SC2

SC1

b

Corneocito 3

Espacio vacío

Corneocito 2

Corneocito 1

Espacio con Lamelas

Corneocito 3

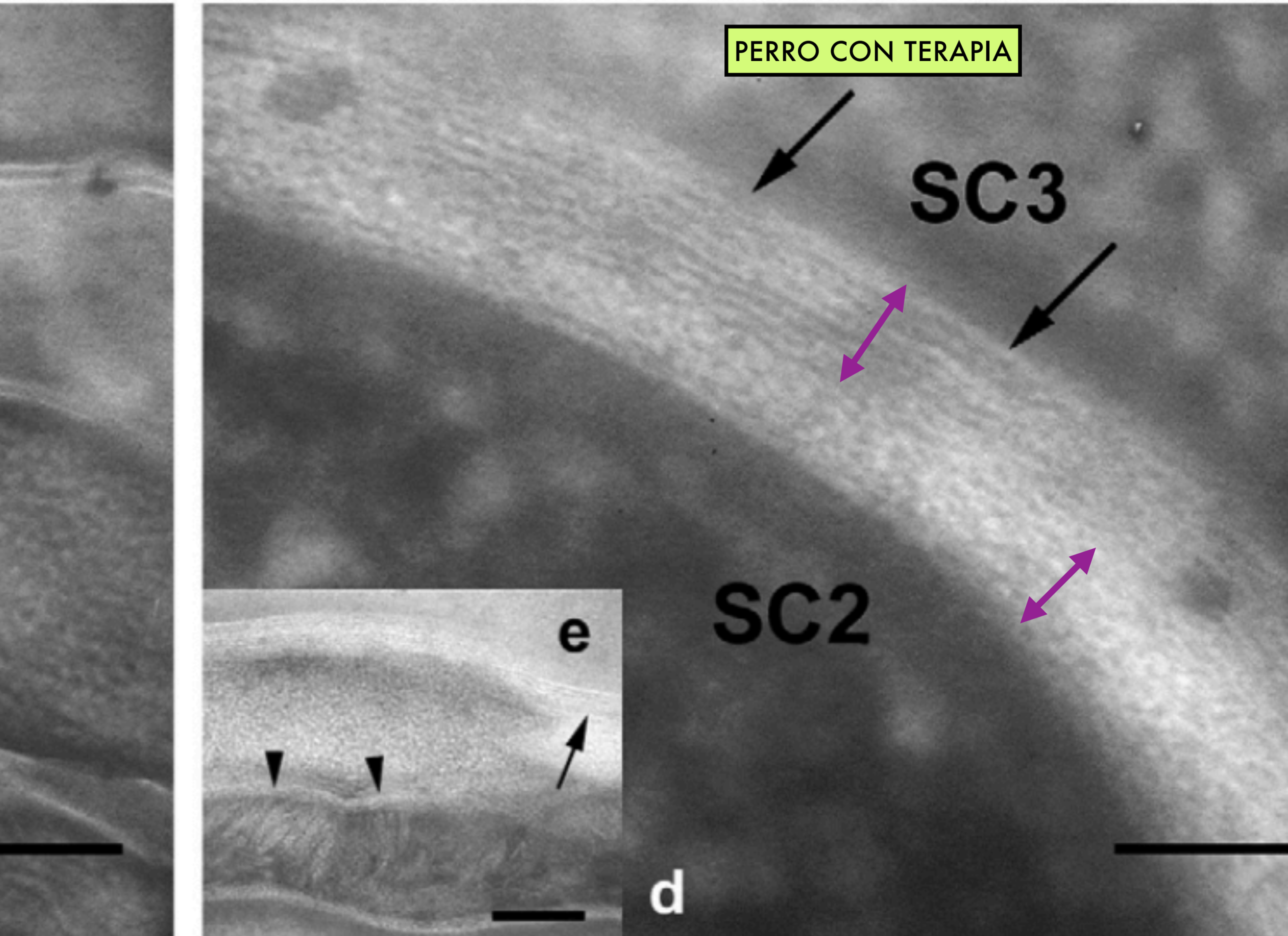
SC3

Corneocito 2

SC2

e

d


PERRO CON TERAPIA
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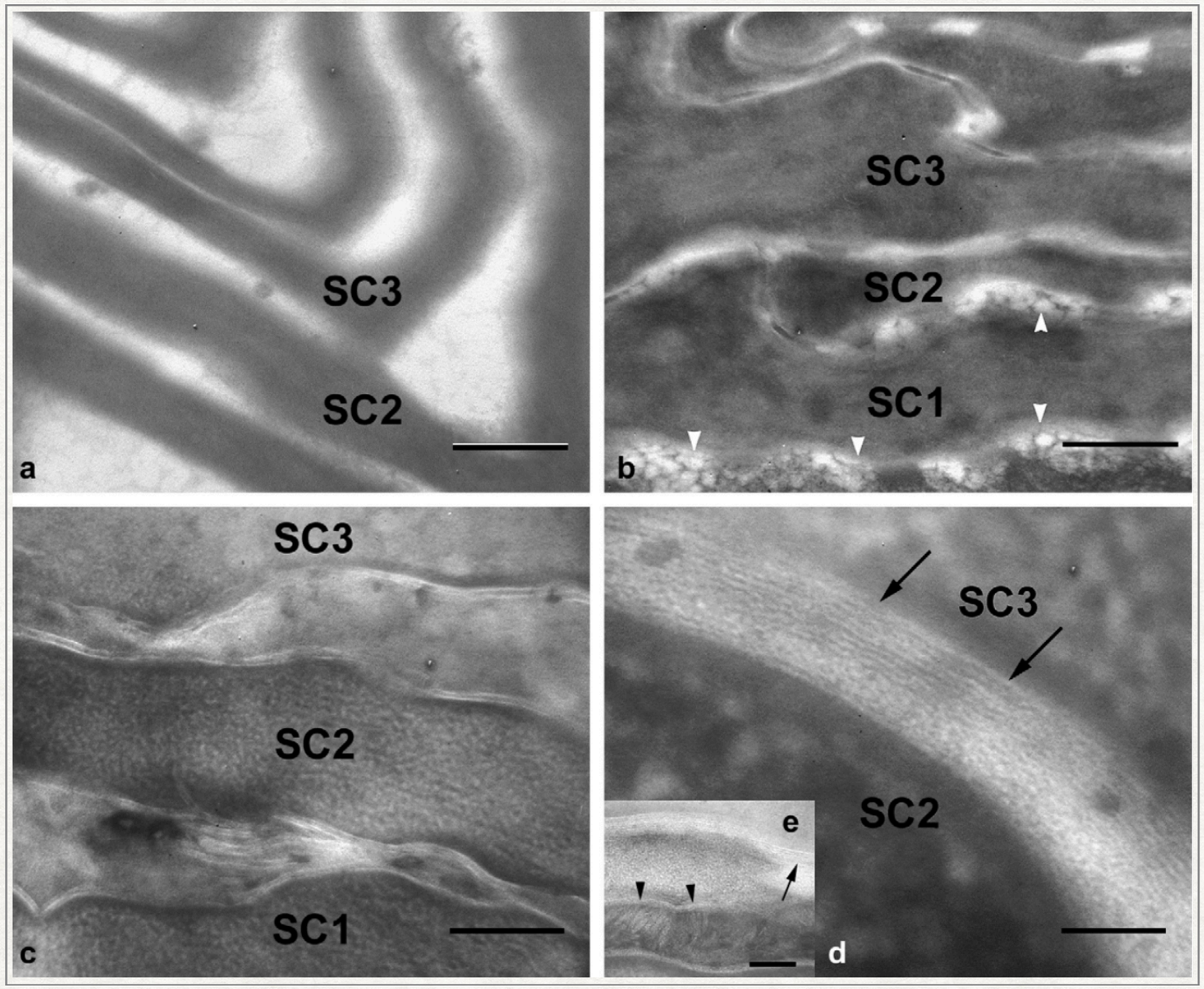

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SAGE-Hindawi Access to Research
Veterinary Medicine International
Volume 2011, Article ID 281846, 5 pages
doi:10.4061/2011/281846

Research Article

Spot-On Skin Lipid Complex as an Adjunct Therapy in Dogs with Atopic Dermatitis: An Open Pilot Study

Masato Fujimura,[1] Yoshinobu Nakatsuji,[2] Subaru Fujiwara,[2,3] Christophe Rème,[4] and Hugues Gatto[4]

[1] *Fujimura Animal Allergy Hospital, Aomatanihigashi 5-10-26, Minou-shi, Osaka 562-0022, Japan*
[2] *Virbac Japan, New Awajimachi Building 6F, 1-3-14 Awaji-machi, Chuo-ku, Osaka 541-0047, Japan*
[3] *Virbac Japan, Kanto Office, Sumisei Shinyokohama 2nd Building 7F, 3-18-14 Shinyokohama, Kohoku-ku, Yokohama-shi, Kanagawa 222-0033, Japan*
[4] *Virbac SA, BP27, 06511 Carros Cedex, France*

Navarro C[2]

La aplicación de ceramidas es beneficiosa en pacientes con Dermatitis Atópica

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

1- Mucho componente es SECUNDARIO INFLAMATORIO

2- Desinflamar la piel no mejora la TEWL

3- ¿ Si se Colocan Ceramidas es suficiente ?

4- ¿ Y otros Humectantes ?

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

4- ¿ Y otros Humectantes ?

- Petrolatum (Vaselina)
  - Incrementa los Péptidos Antibacterianos
  - Disminuye TEWL

Petrolatum: Barrier repair and antimicrobial responses underlying this "inert" moisturizer

Tali Czarnowicki, MD,[a]* Dana Malajian, BA,[a,b]* Saakshi Khattri, MD,[a,c]* Joel Correa da Rosa, PhD,[a,d] Riana Dutt, ScB,[a,c] Robert Finney, MD,[e] Nikhil Dhingra, MD,[c] Peng Xiangyu, MSc,[a,c] Hui Xu, MSc,[a,c] Yeriel D. Estrada, BS,[c] Xiuzhong Zheng, MSc,[a] Patricia Gilleaudeau, NP,[a] Mary Sullivan-Whalen, NP,[a] Mayte Suaréz-Fariñas, PhD,[a,c,g,h,i] Avner Shemer, MD,[f] James G. Krueger, MD, PhD,[a] and Emma Guttman-Yassky, MD, PhD[a,c] *New York, NY, Philadelphia, Pa, and Tel Aviv, Israel*

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

4- ¿ Y otros Humectantes ?

- Petrolatum (Vaselina)
- Parafina y Aceites Vegetales
    - Acción en estratos superficiales
    - Disminuye TEWL
    - Pueden afectar la expresión de Involucrina, TGA-1 y Kalikreina
      (Puede ser Bueno o Malo según el producto)

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

4- ¿ Y otros Humectantes ?

- Petrolatum (Vaselina)
- Parafina y Aceites Vegetales
- Urea
    - Hidratante
    - Efecto Antibacteriano
    - Incrementa Producción de Péptidos Antibacterianos

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

1- Mucho componente es SECUNDARIO INFLAMATORIO

2- Desinflamar la piel no mejora la TEWL

3- ¿ Si se Colocan Ceramidas es suficiente ?

4- ¿ Y otros Humectantes ?

5- ¿ Y antiinflamatorios tópicos ?

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

5- ¿ Y antiinflamatorios tópicos ?

- Glucocorticoides Tópicos (Betametasona)
  - Mejoran TEWL
  - No mejora la producción de Lamelas (atrofia ?)

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

5- ¿ Y antiinflamatorios tópicos ?

- Glucocorticoides Tópicos (Betametasona)
- Tacrolimus
    - Disminuye calidad de Barrera
    - Disminuye Péptidos Antimicrobianos

Kim M, Jung M, Hong SP et al. Topical calcineurin inhibitors compromise stratum corneum integrity, epidermal permeability and antimicrobial barrier function. Exp Dermatol 2010; 19: 501– 510

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

5- ¿ Y antiinflamatorios tópicos ?

- Glucocorticoides Tópicos (Betametasona)
- Tacrolimus
- Pimecrolimus
    - Mejora calidad de Barrera
    - Incrementa Péptidos Antimicrobianos

Grzanka A, Zebracka-Gala J, Rachowska R et al. The effect of pimecrolimus on expression of genes associated with skin bar- rier dysfunction in atopic dermatitis skin lesions. Exp Dermatol 2012; 21: 184–188.

Barrera Cutánea

Partes de Estudio

¿ Se puede corregir el Déficit de Barrera ?

1- Mucho componente es SECUNDARIO INFLAMATORIO

2- Desinflamar la piel no mejora la TEWL

3- ¿ Si se Colocan Ceramidas es suficiente ?

4- ¿ Y otros Humectantes ?

5- ¿ Y antiinflamatorios tópicos ?

Final

2da Parte

LATIN AMERICAN COLLEGE OF VETERINARY DERMATOLOGY