



Barrera Cutánea y DAC

1ra Parte



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Dermatitis Atópica

→ **Atopia**

- Atopía Concepto Inmunológico (*Condición*)
- Atopía Enfermedad Clínica (*Alergia a Aero-alergenos*)
- Dermatitis Atópica (*Enfermedad Atópica*)
 - ◆ *Dermatitis Atópica en Sentido Estricto (Inducida por Ambientales)*
 - ◆ *Dermatitis Atópica en Sentido Amplio (Inducida por Alimentos y Ambientales / DAIA)*

Dermatitis Atópica

➤ Interpretación Actual

→ Suma de 2 factores



Alteración
Inmunológica

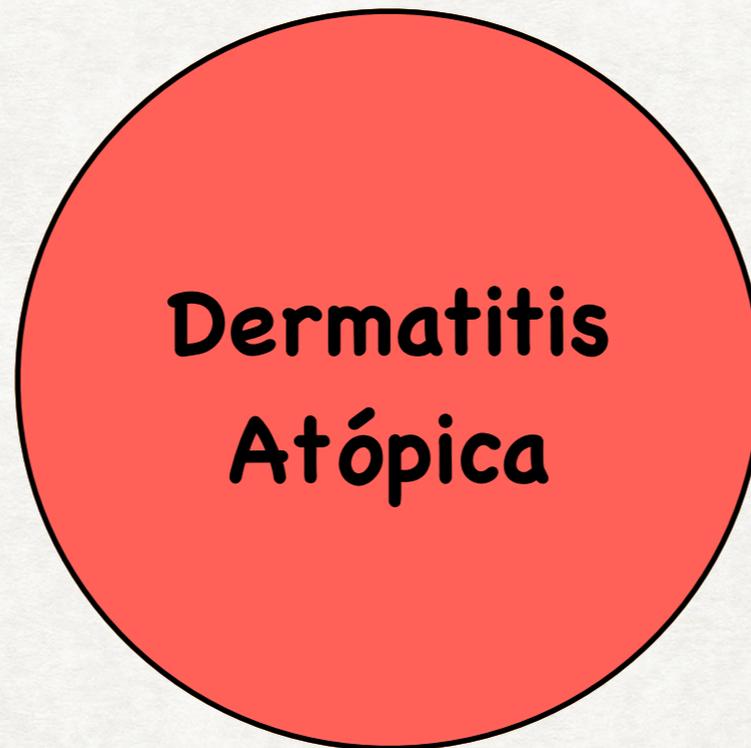


Falla de
Barrera

Dermatitis Atópica

➤ Interpretación Actual

→ Suma de 2 factores



Dermatitis Atópica

➤ Interpretación Actual

→ Suma de 2 factores



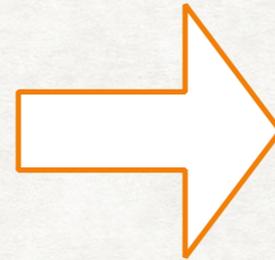
Alteración
Inmunológica



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Dermatitis Atópica

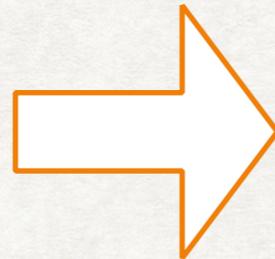
Alteración
Inmunológica



1ria ?

2ria ?

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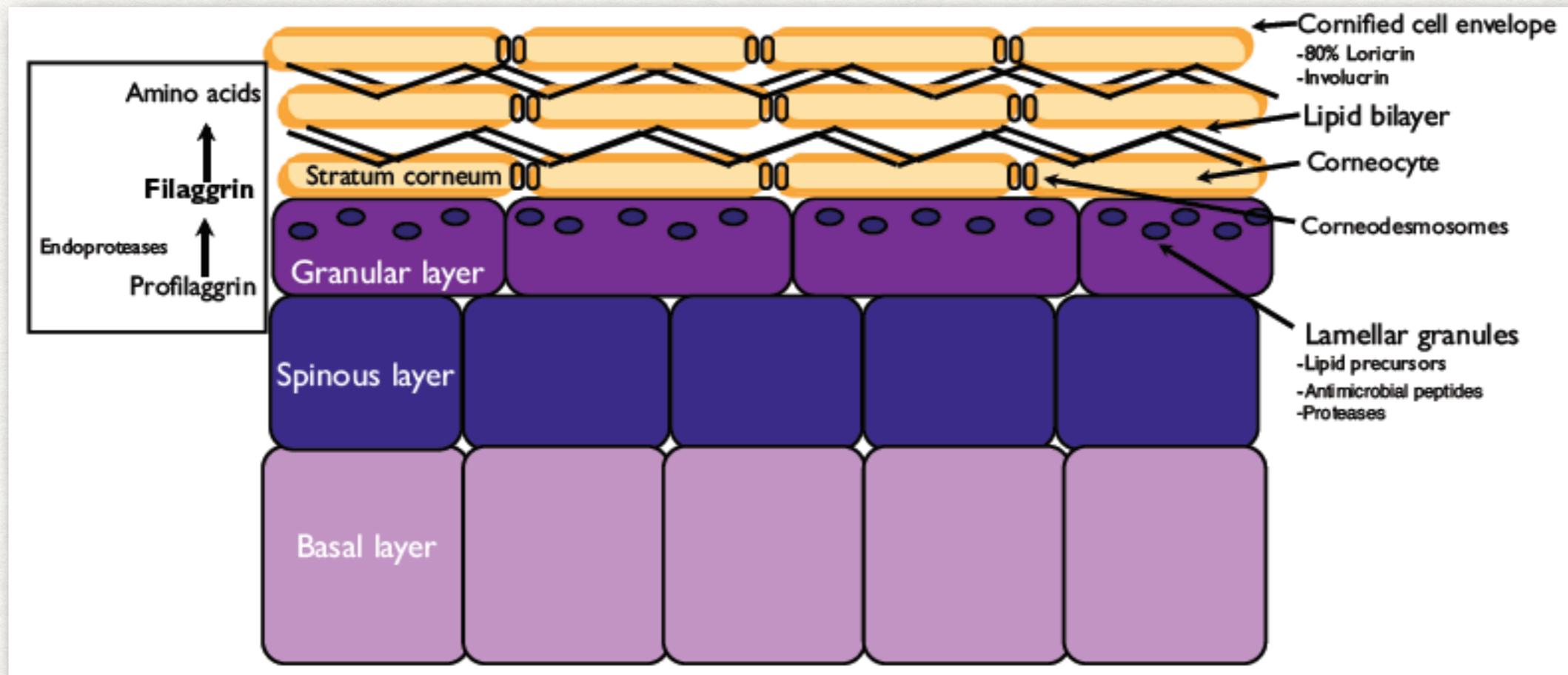


1ria ?

2ria ?

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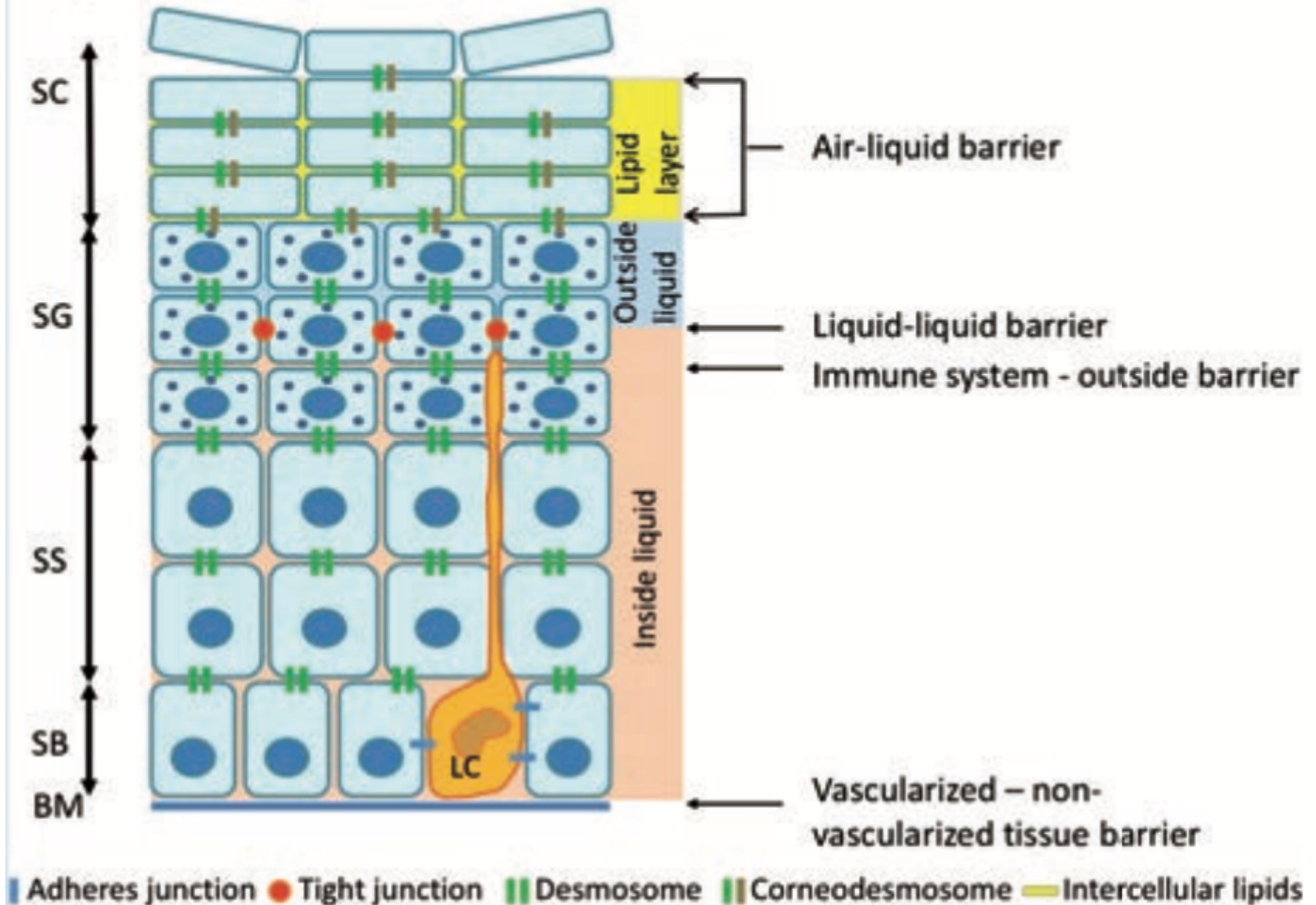
✓ Aspectos Generales



Barrera Cutánea

Hay varios tipos de Barreras

Fig. 1 Epidermal Barriers in Homeostasis (adapted from Kubo et al 2012)



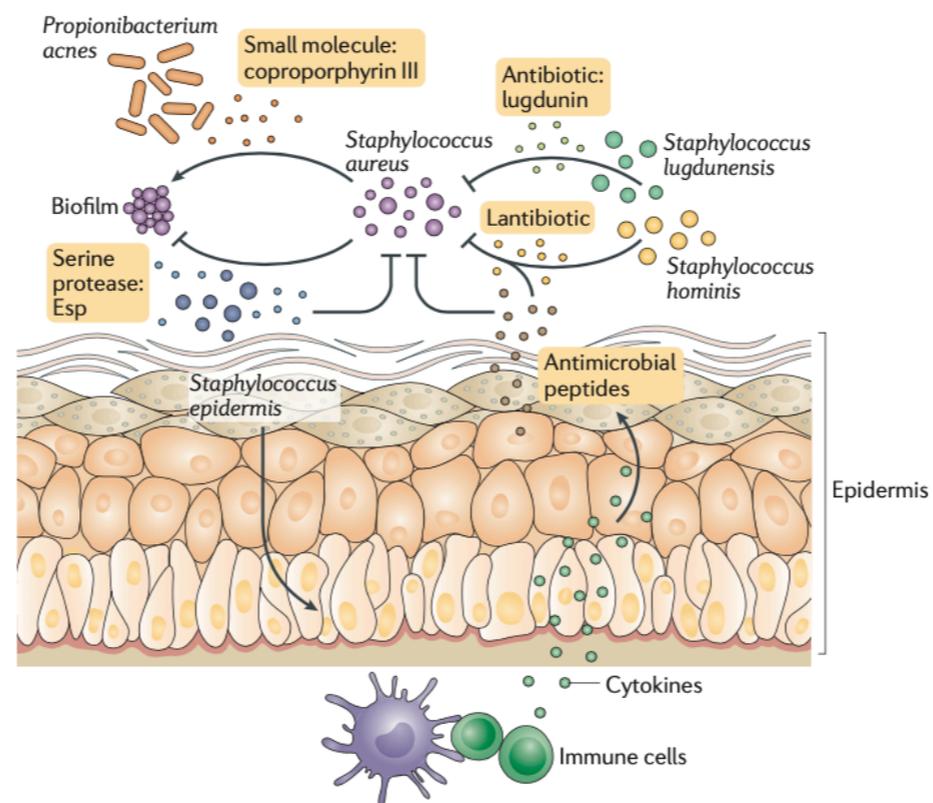


Figure 3 | **Skin commensal interactions with *Staphylococcus aureus*.** Skin microbial communities are shaped by interactions between organisms and with the host. In the skin, many interactions between commensals and *Staphylococcus aureus* have been identified. Antibiotics produced by coagulase-negative *Staphylococcus* and specifically by *Staphylococcus lugdunensis* prohibit colonization of *S. aureus*. Also, *Staphylococcus epidermidis* can inhibit *S. aureus* biofilm formation with production of the serine protease glutamyl endopeptidase (Esp). Moreover, when Esp-expressing *S. epidermidis* induces keratinocytes to produce antimicrobial peptides via immune cell signalling, *S. aureus* is effectively killed. In addition, *Staphylococcus hominis*-produced lantibiotics synergize with human antimicrobial peptide LL-37 to decrease *S. aureus* colonization. In contrast to inhibiting *S. aureus*, *Propionibacterium acnes* produces a small molecule, coproporphyrin III, that promotes *S. aureus* aggregation and biofilm formation.

Byrd, A. L., Belkaid, Y., & Segre, J. A. (2018). The human skin microbiome. *Nature Reviews Microbiology*, 16(3), 143–155. doi:10.1038/nrmicro.2017.157

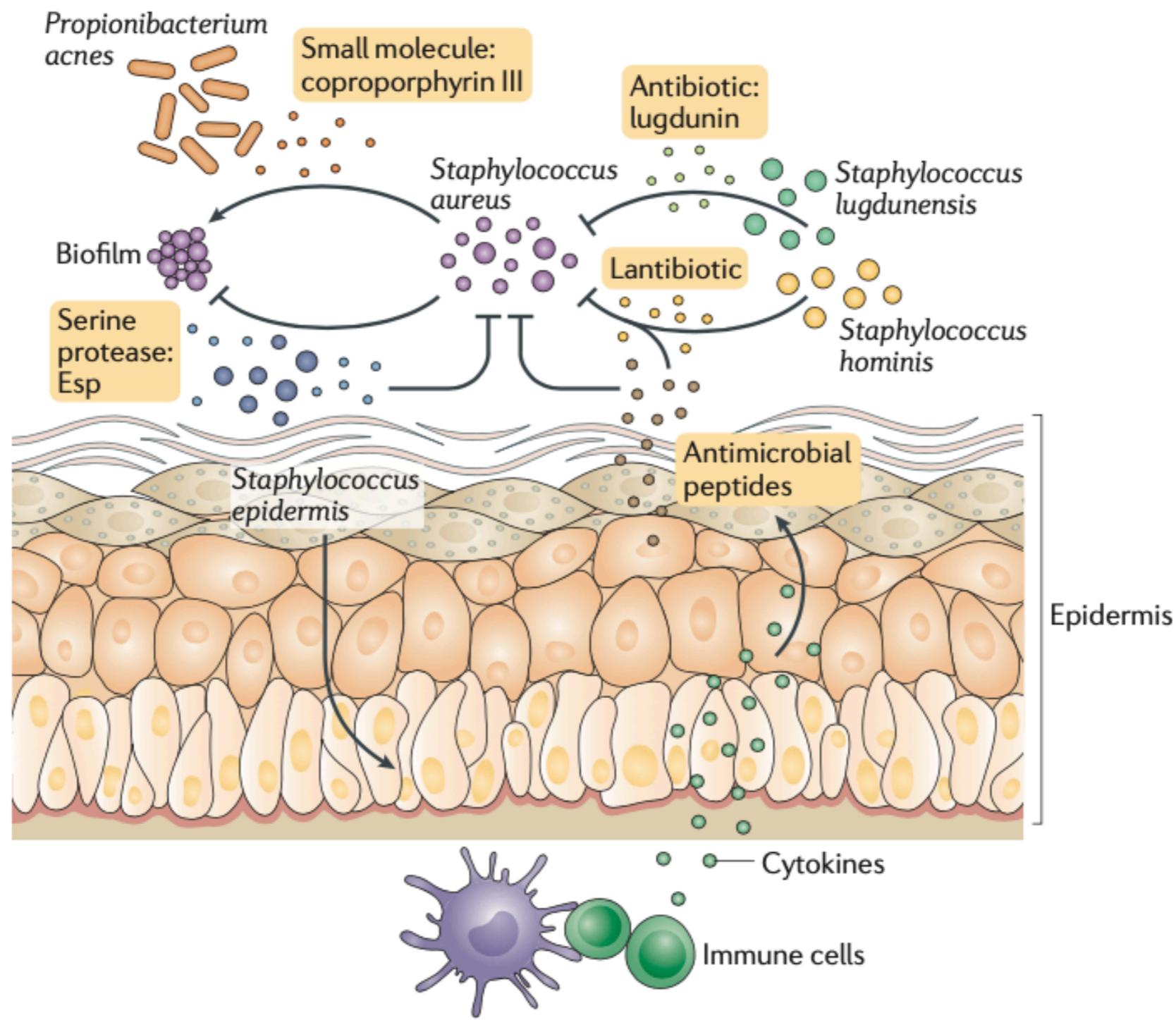


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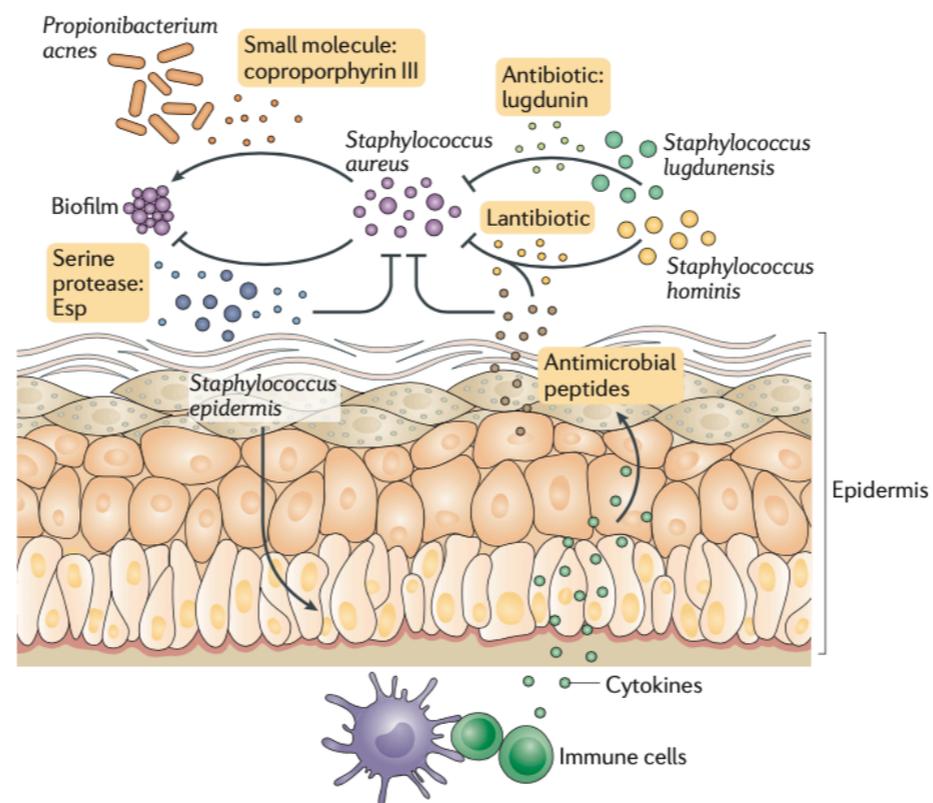


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Barrera Cutánea

● Barrera Aire - Líquido  ***Estrato Corneo***

- ➔ Corneocitos
- ➔ Lípidos Intercelulares
- ➔ Conexiones entre Queratinocitos
- ➔ Conexiones entre Lípidos y Corneocitos
- ➔ Conexiones entre Corneocitos

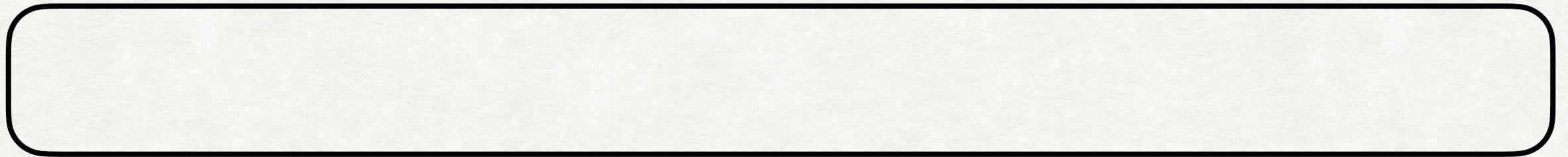
Barrera Cutánea

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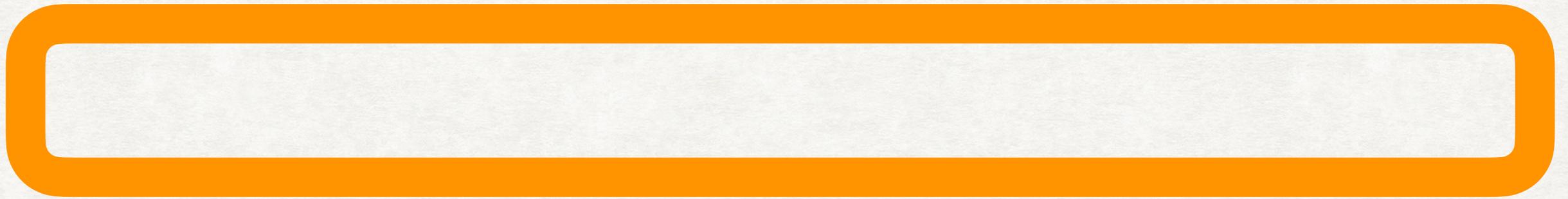
→ Corneocitos

→ Lípidos Intercelulares

Corneocitos

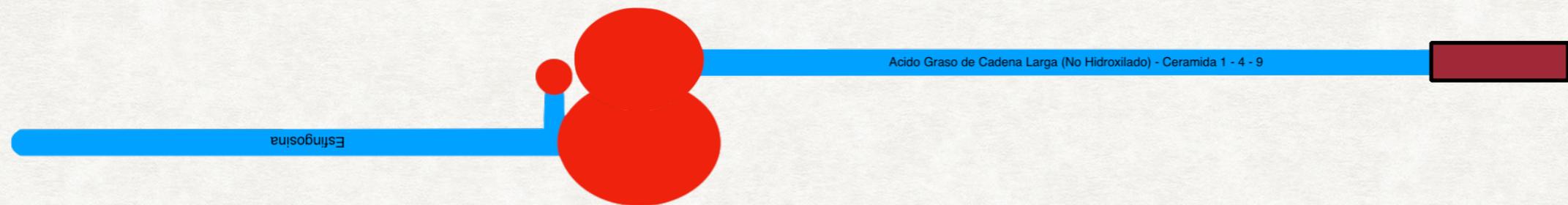


Corneocitos



Envoltura Lipídica
(*Hidroxi-Acil-Ceramidas*)

Envoltura Lipídica (Hidroxi-Acil-Ceramidas)

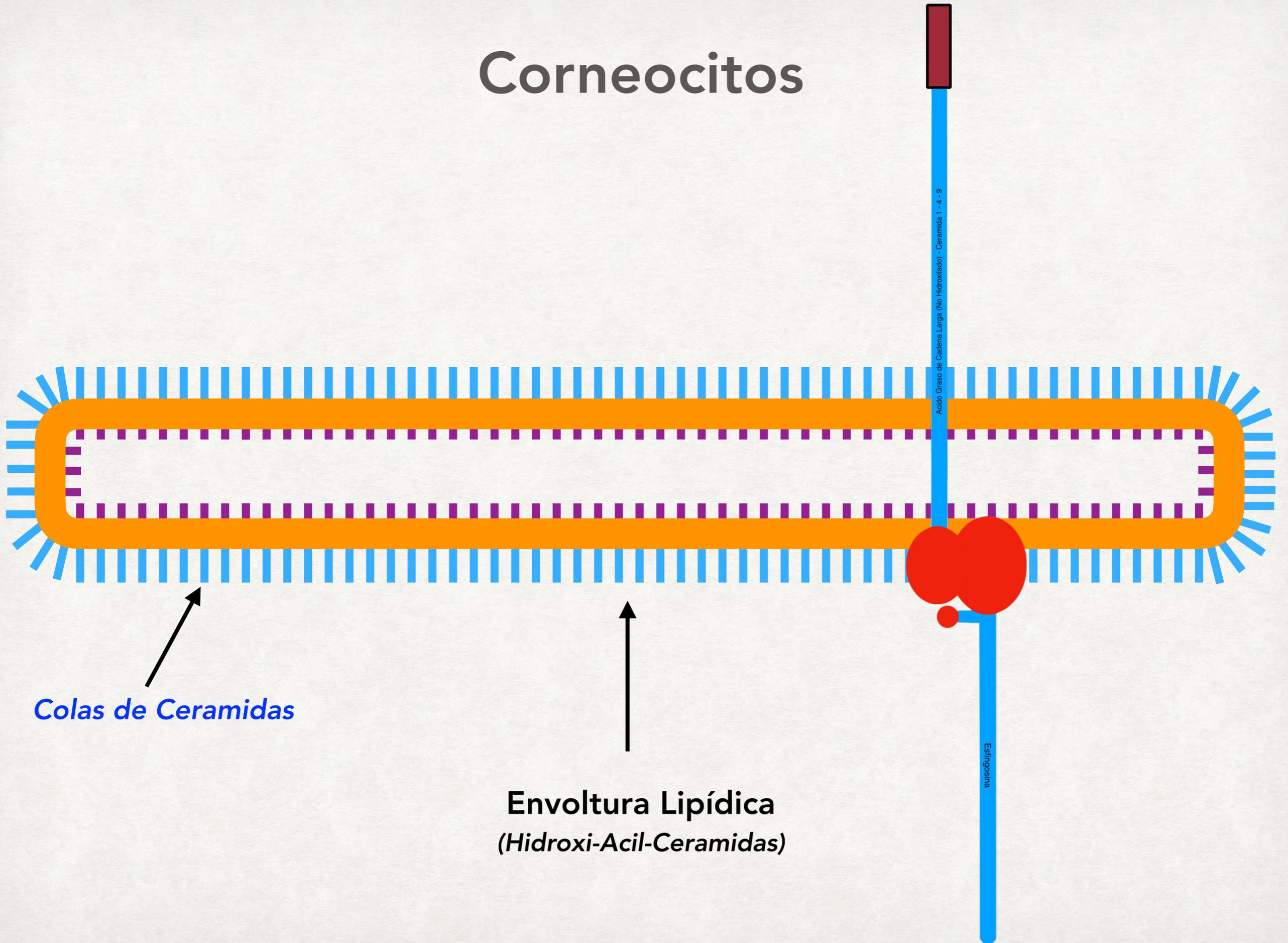


Corneocitos



Envoltura Lipídica
(Hidroxi-Acil-Ceramidas)

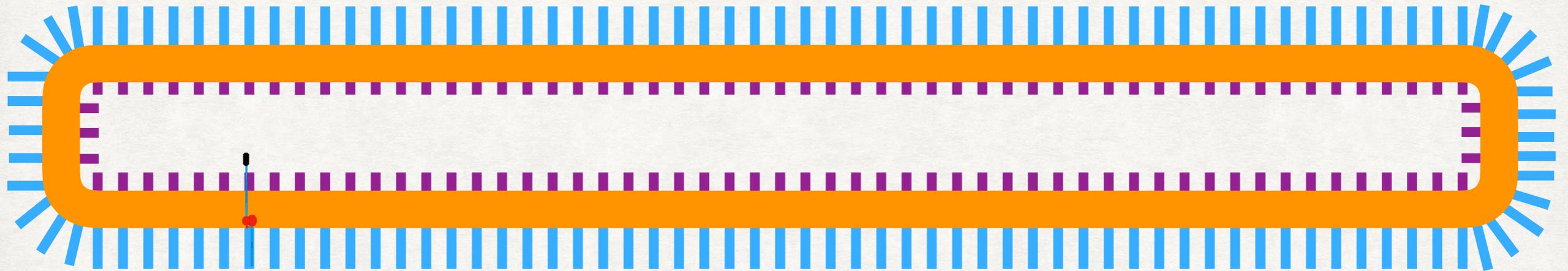
Corneocitos



Corneocitos



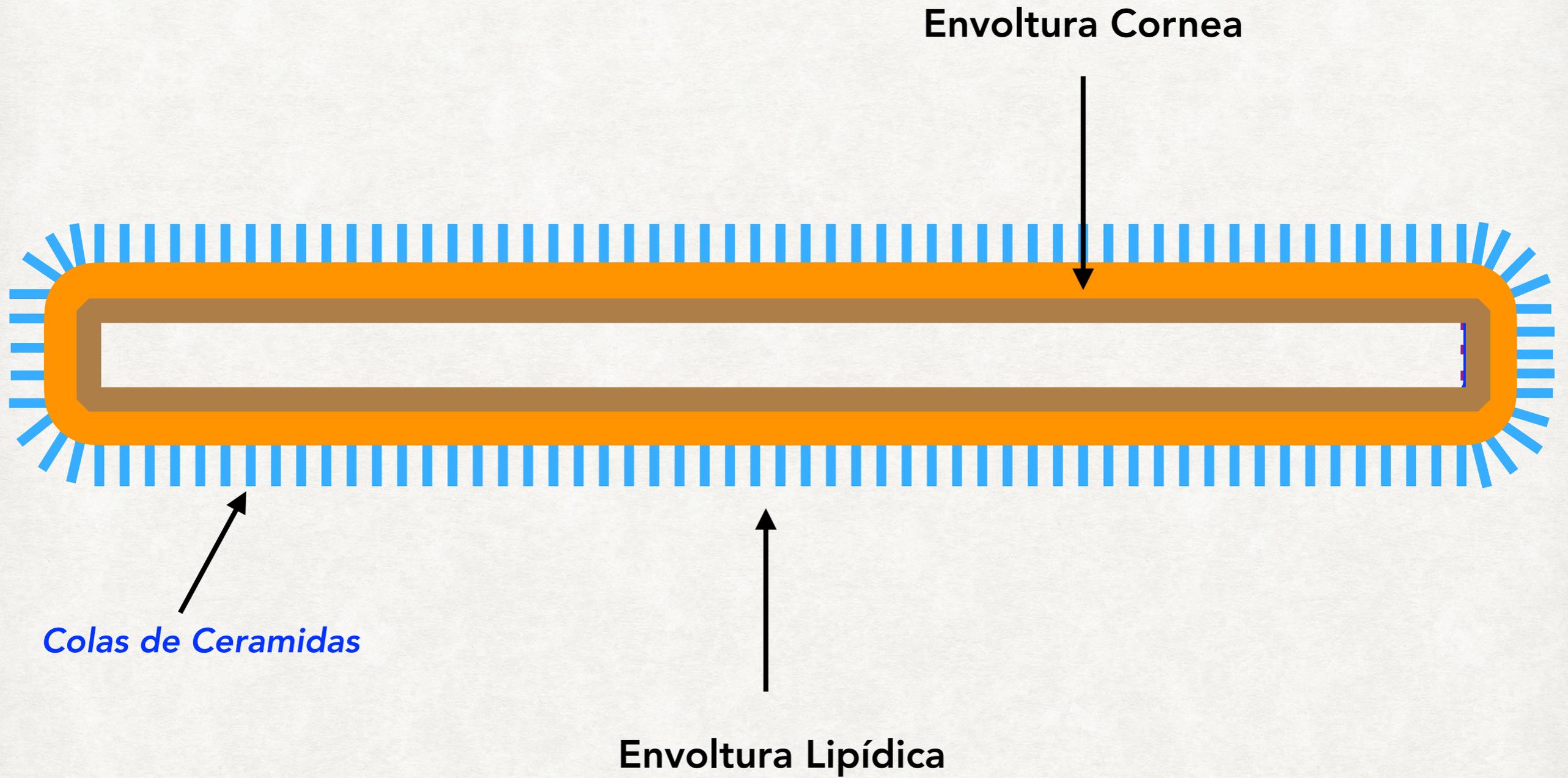
Envoltura Cornea



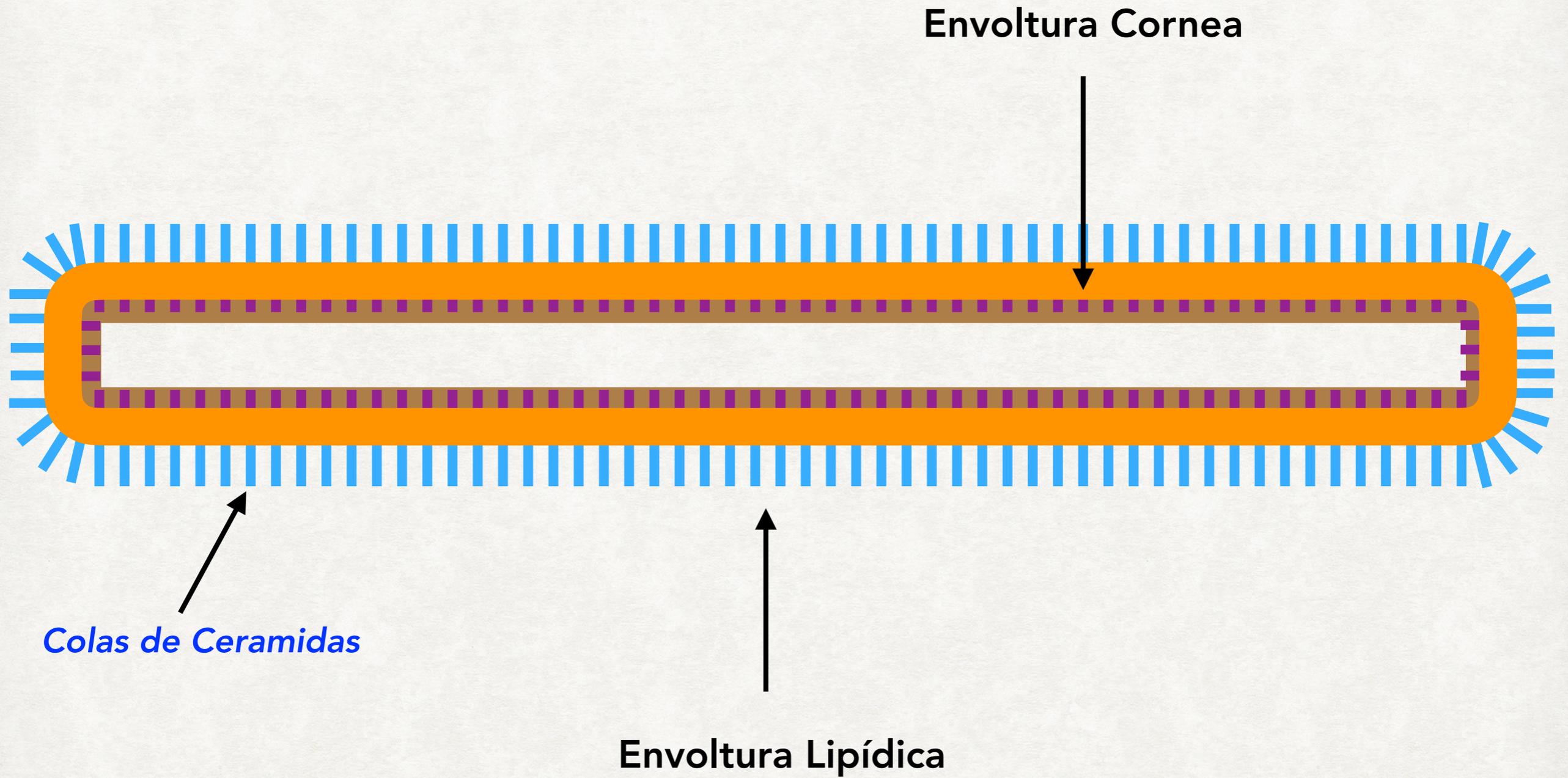
Colas de Ceramidas

Envoltura Lipídica
(Hidroxi-Acil-Ceramidas)

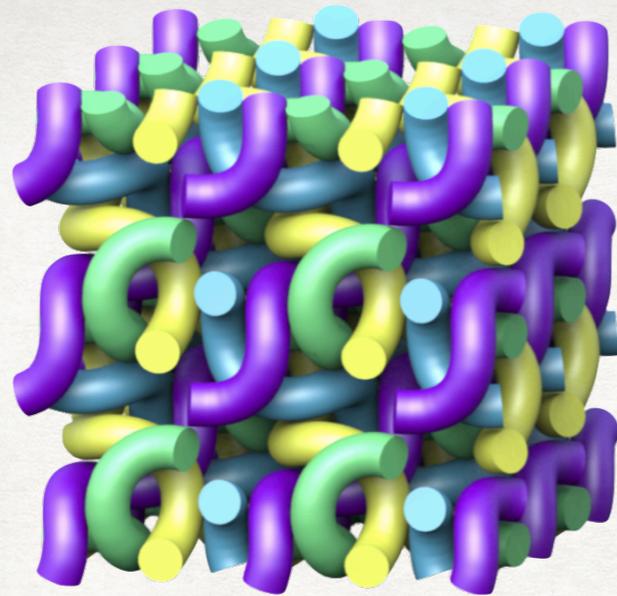
Corneocitos



Corneocitos

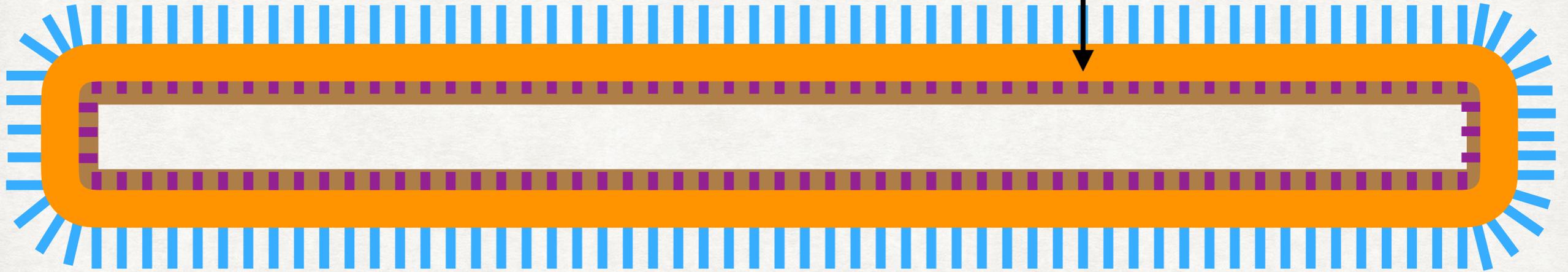


Corneocitos



← Queratina

Envoltura Cornea



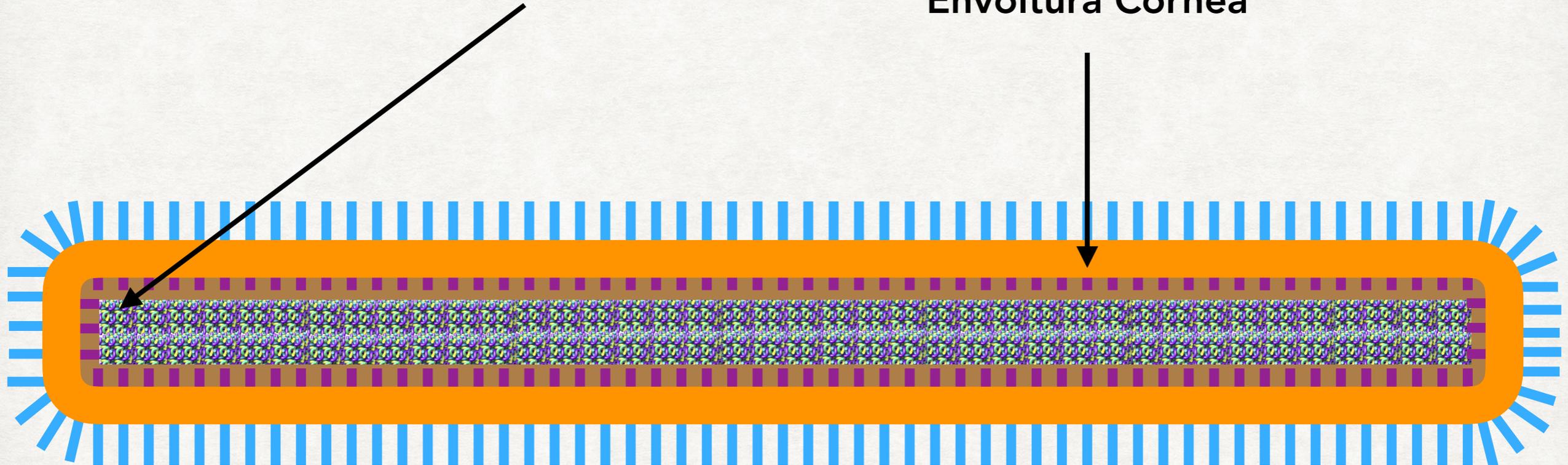
Colas de Ceramidas

Envoltura Lipídica

Corneocitos

Queratina

Envoltura Cornea



Colas de Ceramidas

Envoltura Lipídica

Corneocitos

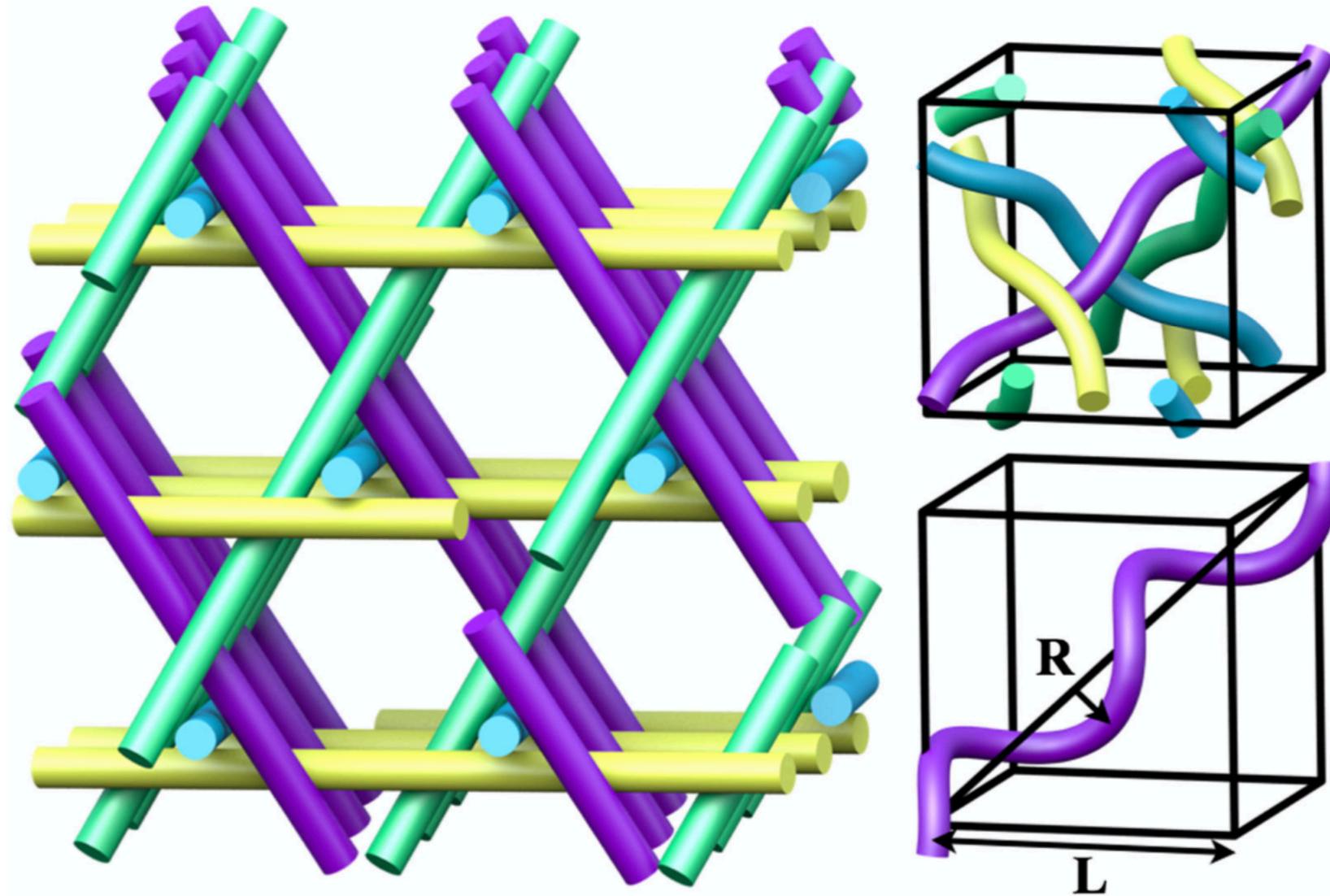


FIG. 1 (color online). (Left) The periodic Σ^+ rod packing composed of straight rods. (Right upper) One unit cell of the structure with slightly helical filaments. (Right lower) A single helix of the structure shown with the variable parameters: L is the unit cell edge length, R the radius of the helix. The tube radial thickness r is 3.7 nm, the radius of keratin IFs.

Evans, M. E., & Roth, R. (2014). Shaping the Skin: The Interplay of Mesoscale Geometry and Corneocyte Swelling. *Physical Review Letters*, 112(3).

Corneocytes

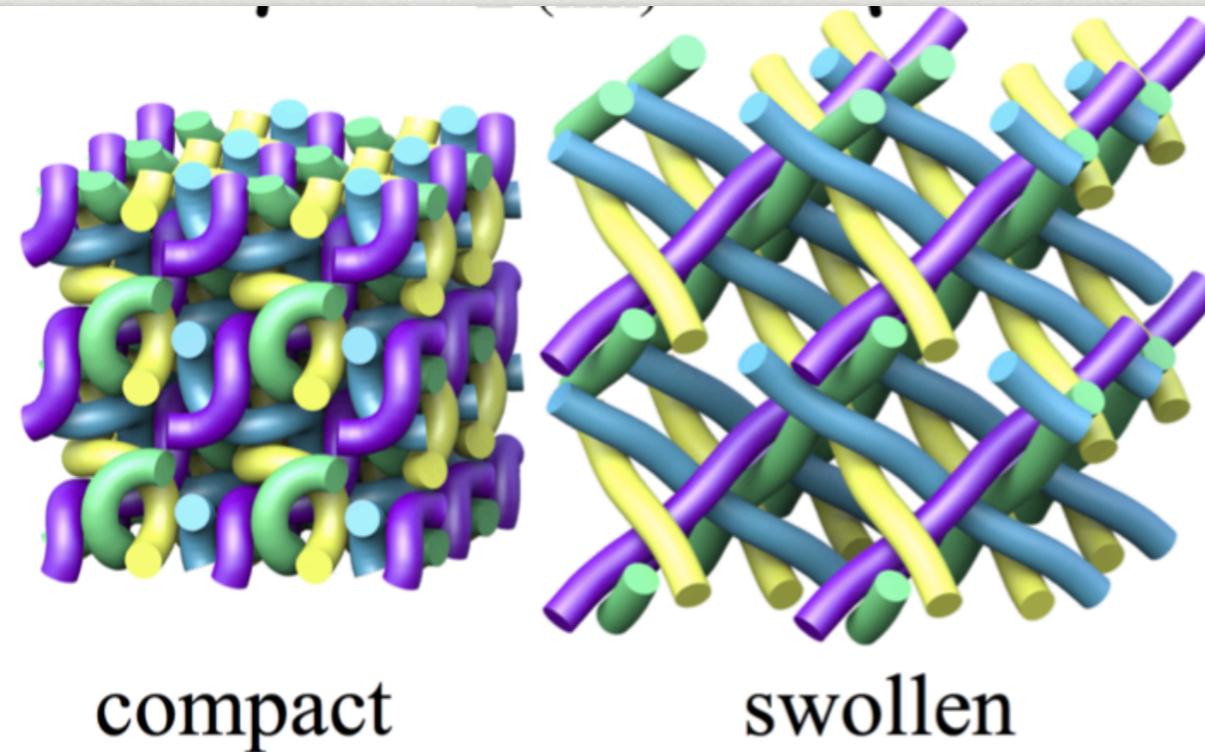
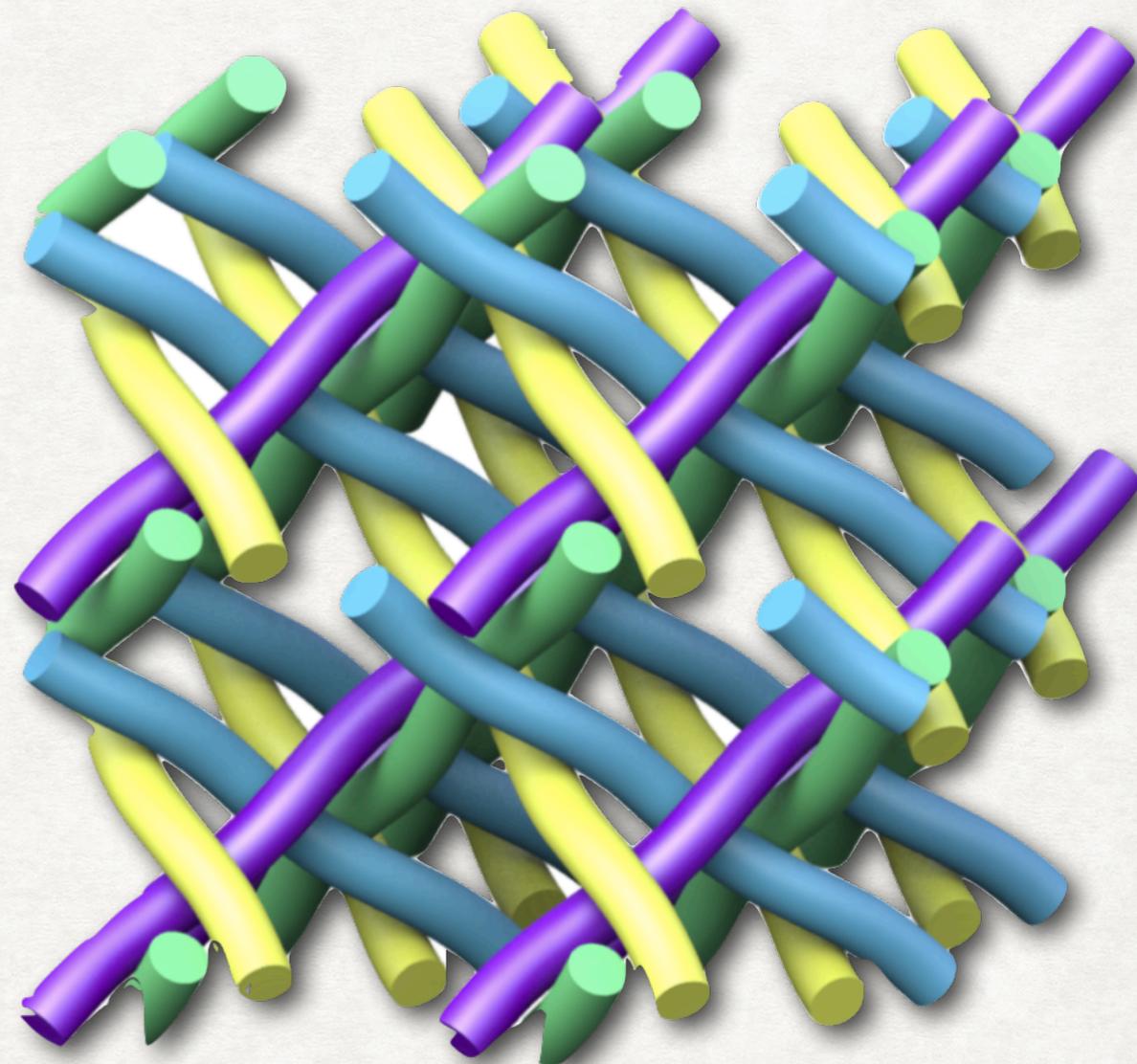
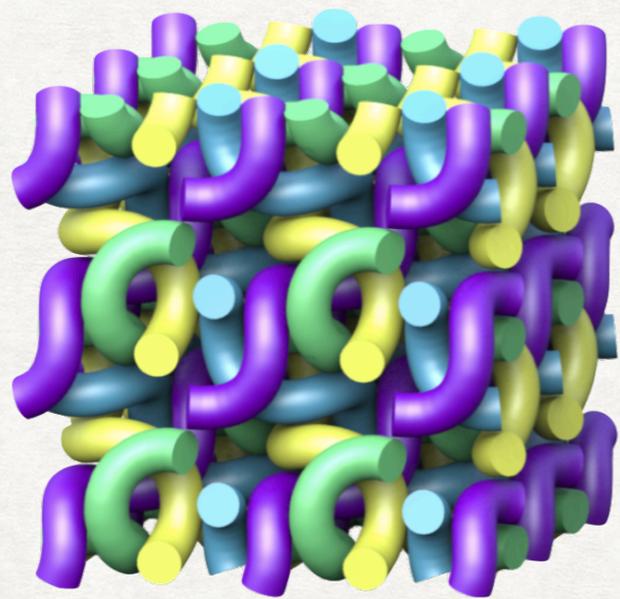
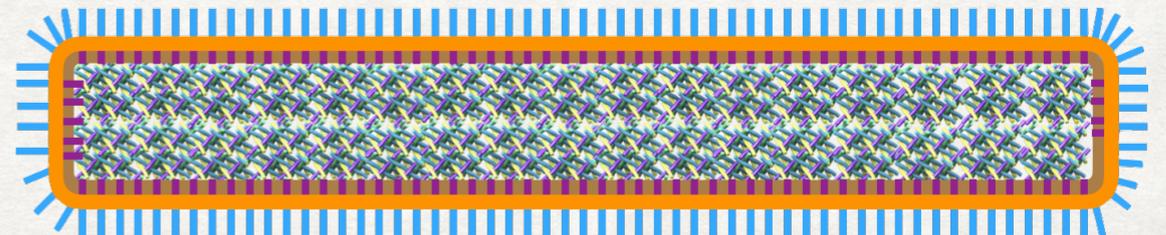
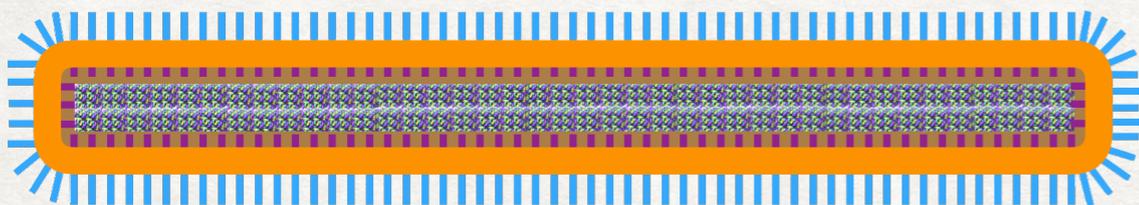
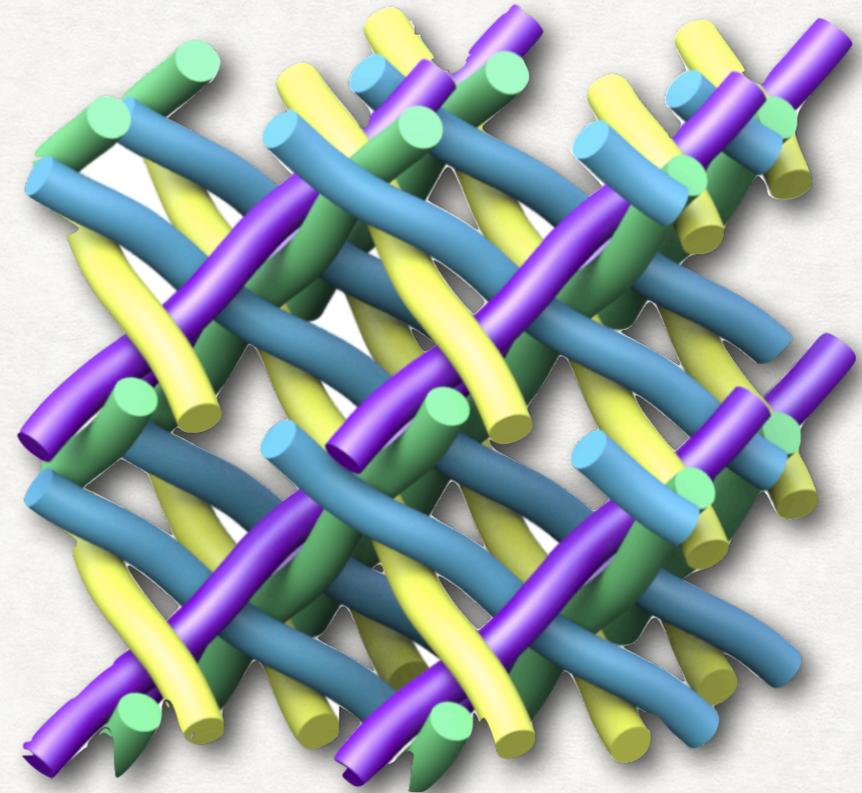
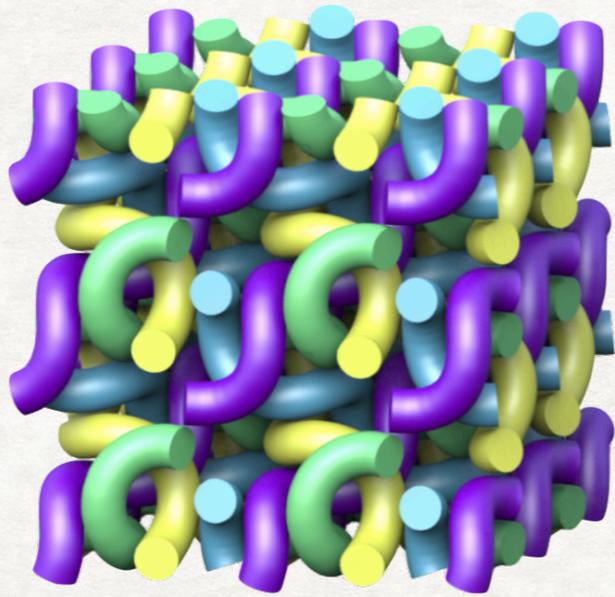


FIG. 3 (color online). Total free energy $\Omega + E$ (per unit cell) of the helical Σ^+ rod packing (Fig. 1), in units of $k_B T \times 10^4$ as a function of unit cell size L and helix radius R . The lower plot shows a smaller region of the upper plot. A valley of low total free energy configurations, whose extremes are indicated on the lower plot, traces a pathway for the swelling of corneocytes and subsequent drying. The packing fractions range from 11% to 38%, comparable to volume fractions (15%–35% [7]) that can be inferred from experimental hydration data [4,5].

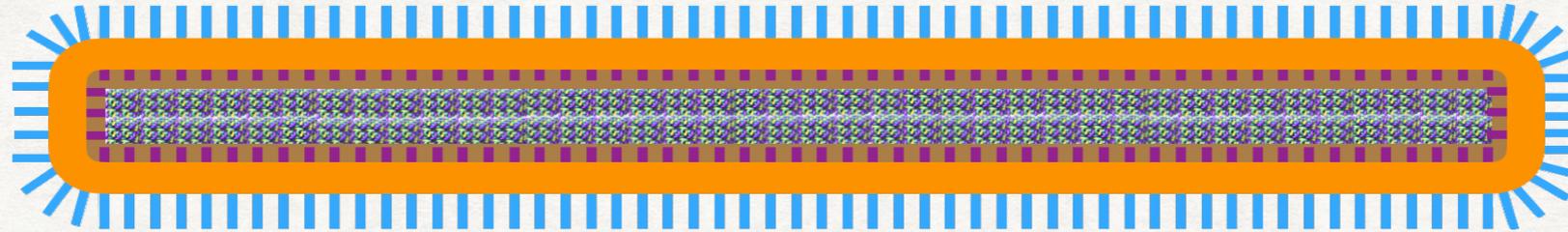
Evans, M. E., & Roth, R. (2014). Shaping the Skin: The Interplay of Mesoscale Geometry and Corneocyte Swelling. *Physical Review Letters*, 112(3).



Corneocitos

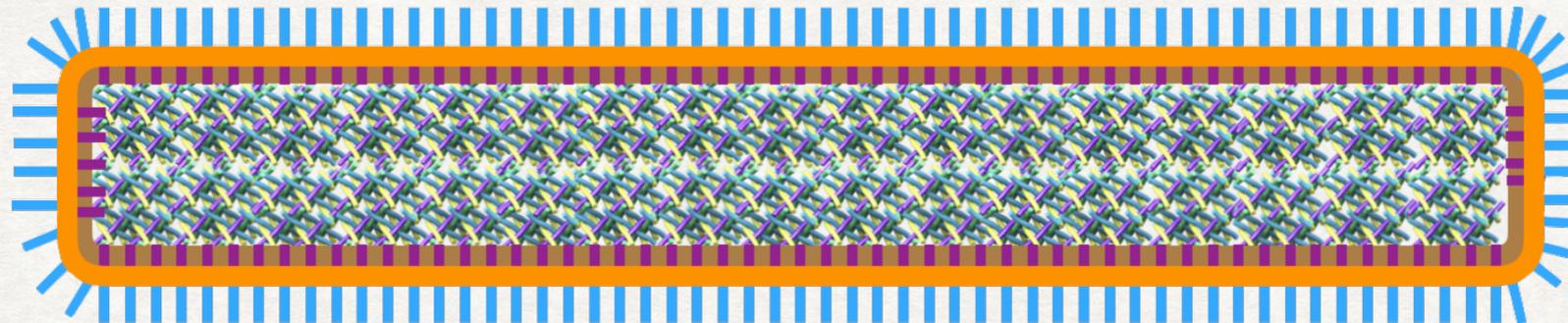


Corneocitos



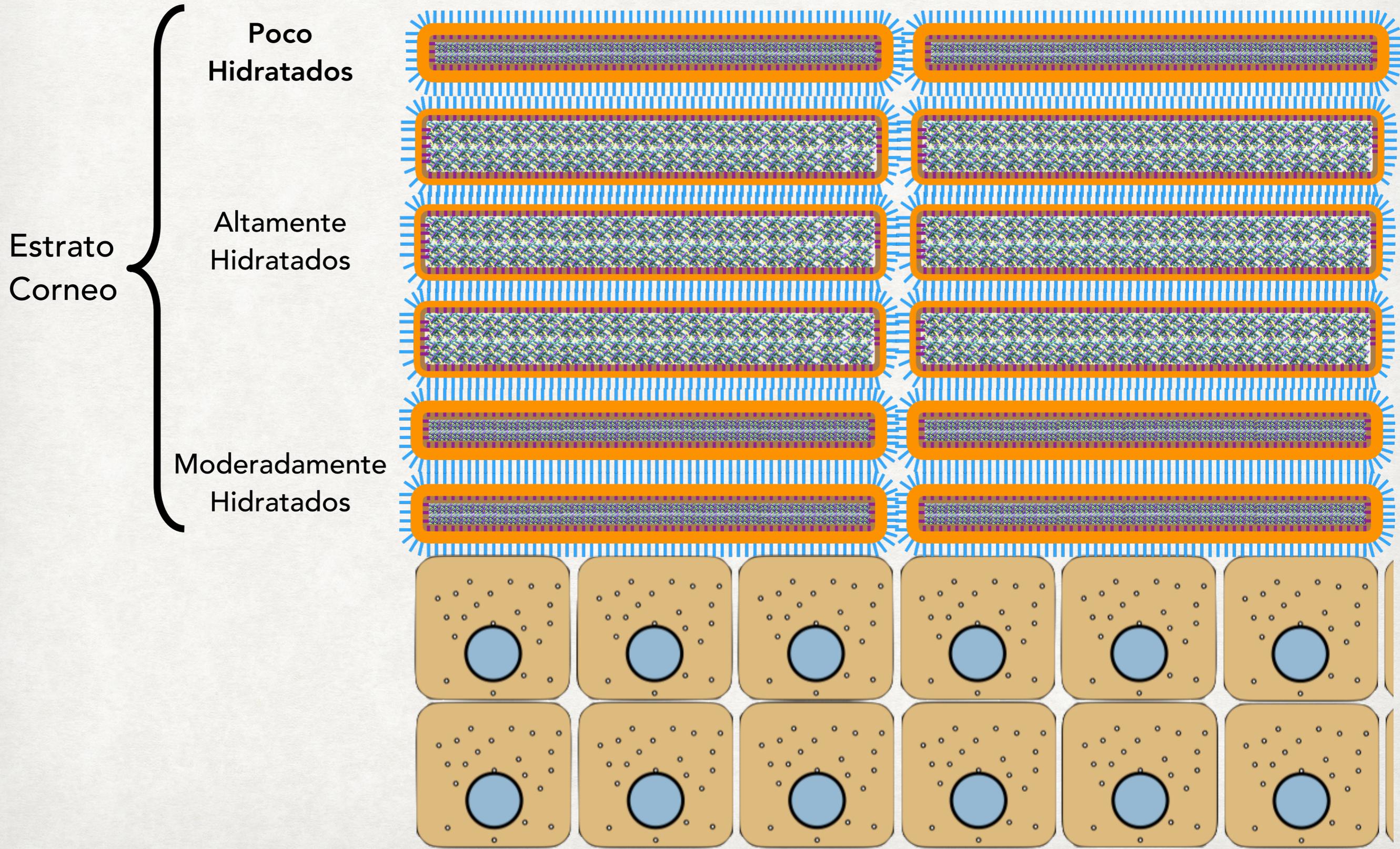
Sin Hidratación

15 al 35 %



Con Hidratación

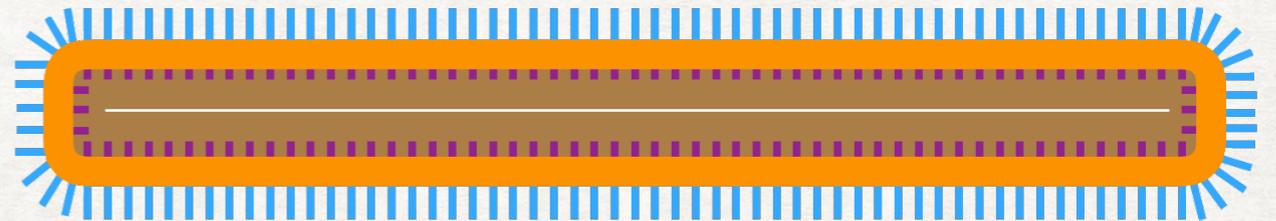
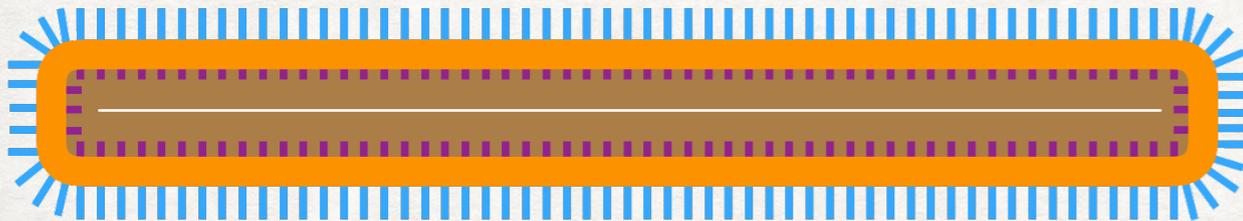
Corneocitos



Corneocitos

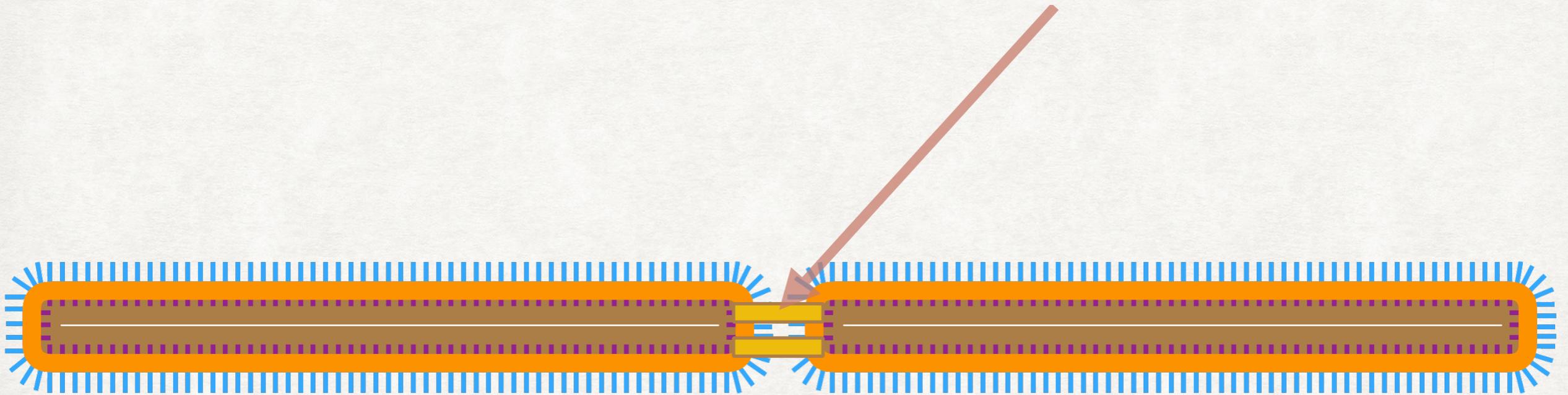


Corneodesmosomas

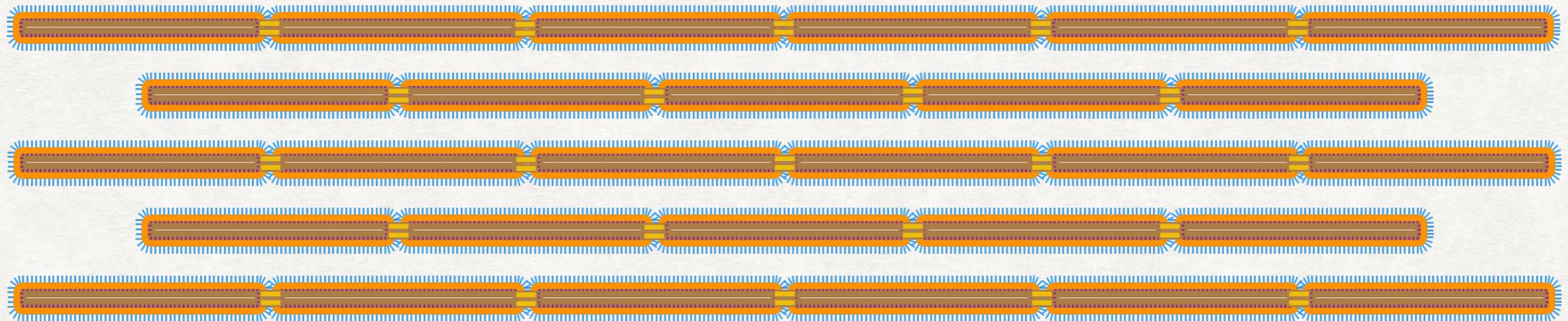


Corneocitos

Corneodesmosomas



Corneocitos



Barrera Cutánea

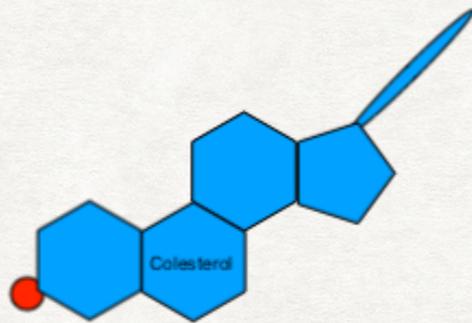
Partes de Estudio

● Barrera Aire - Líquido  ***Estrato Corneo***

- ➔ Corneocitos
- ➔ Lípidos Intercelulares
- ➔ Conexiones entre Queratinocitos
- ➔ Conexiones entre Lípidos y Corneocitos
- ➔ Conexiones entre Corneocitos

Lípidos Intercelulares

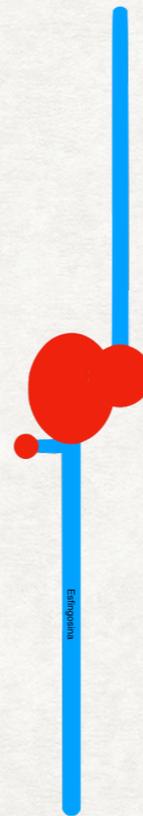
- Colesterol



- Acidos Grasos Libres

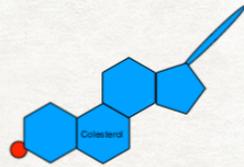


- Ceramidas de Cadena Larga



Lípidos Intercelulares

- Colesterol



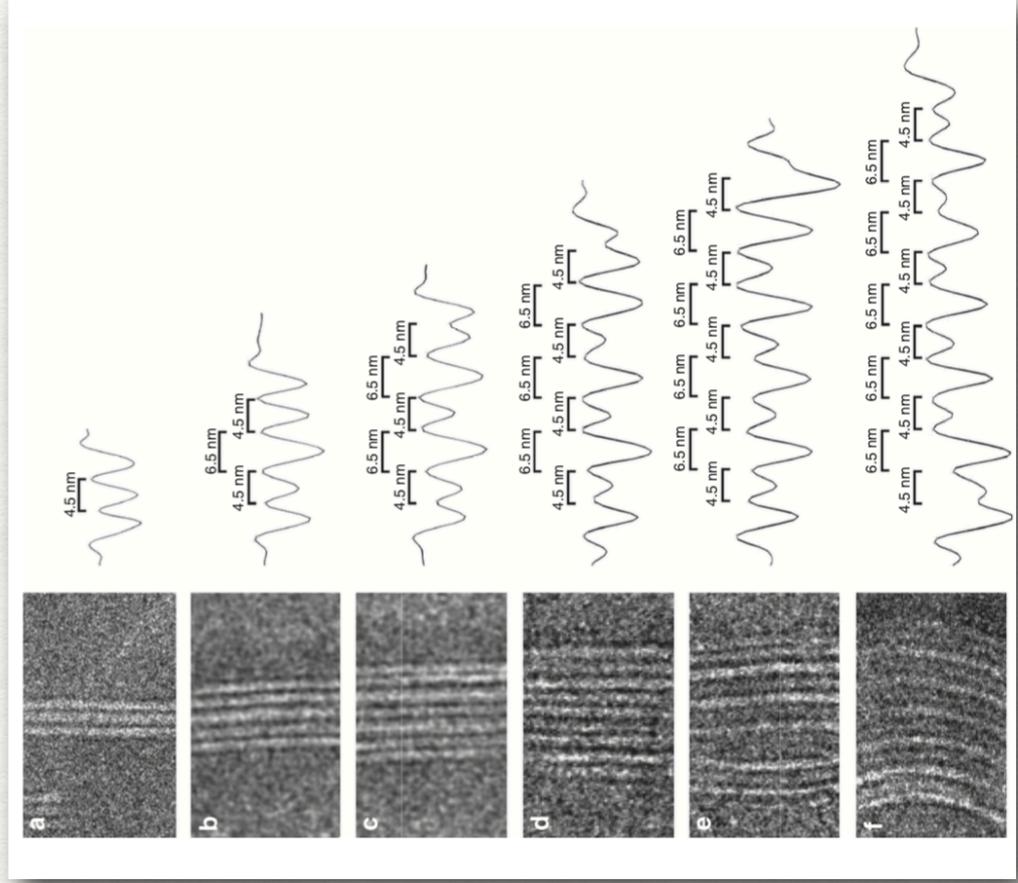
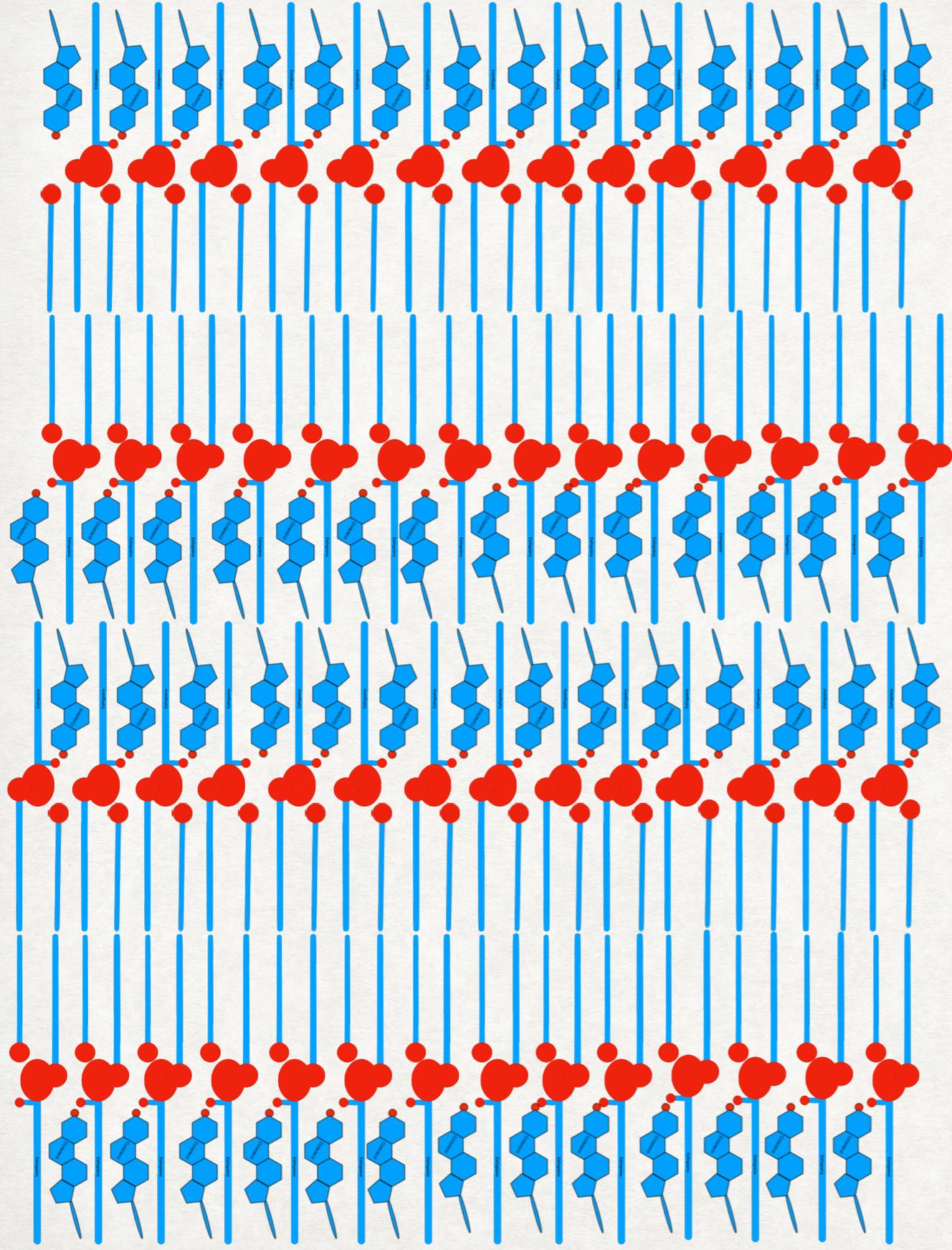
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- Ceramidas de Cadena Larga

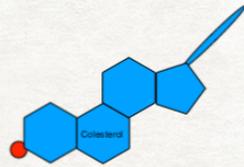


Distribución *LAMELLAR*



Lípidos Intercelulares

- Colesterol



- Acidos Grasos Libres



- Ceramidas de Cadena Larga



Distribución LAMELLAR

Barrera Cutánea

Partes de Estudio

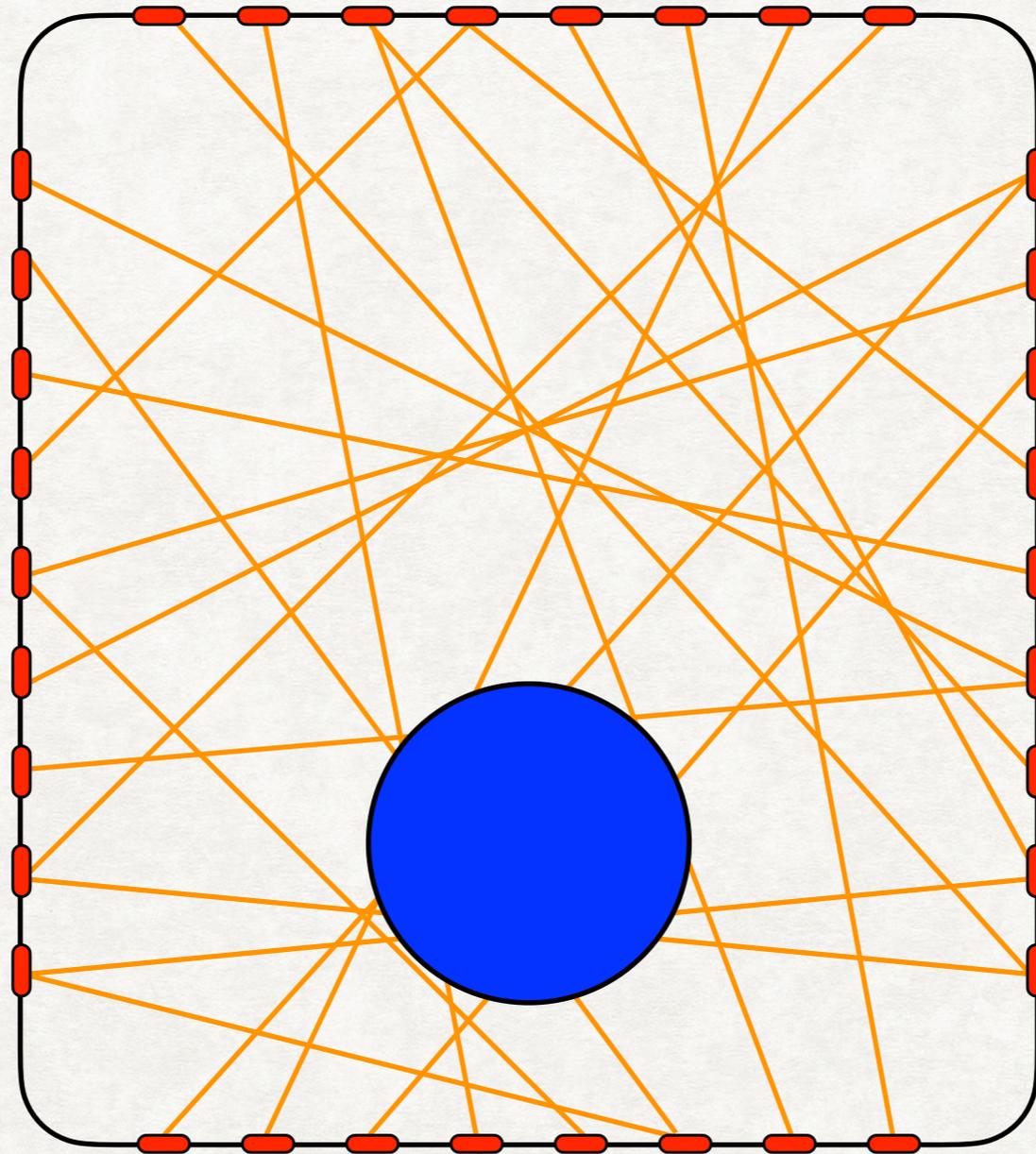
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- ➔ Conexiones entre Corneocitos

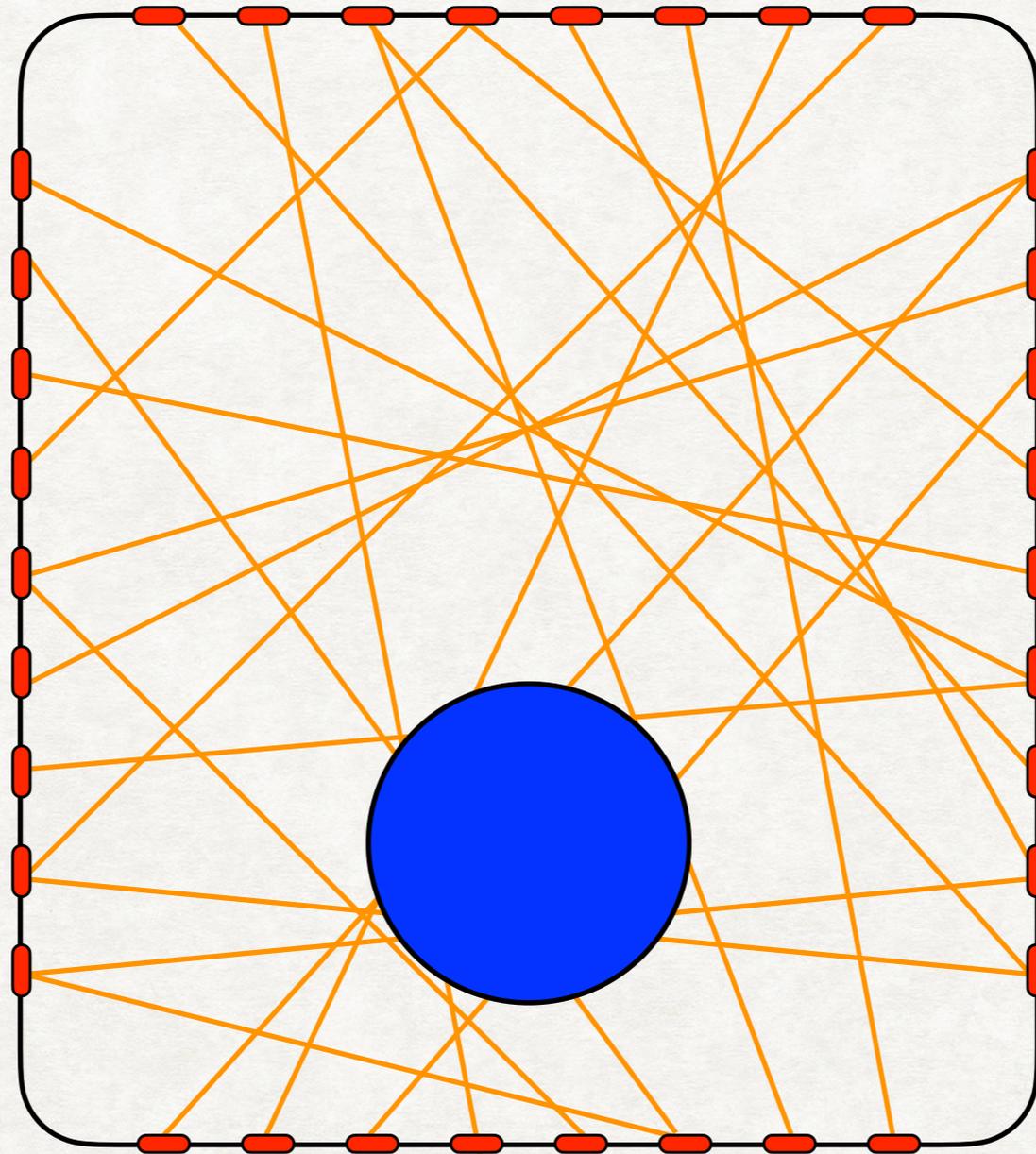
Conexiones entre Queratinocitos

- Queratinas
- Desmosomas
- Uniones Estrechas

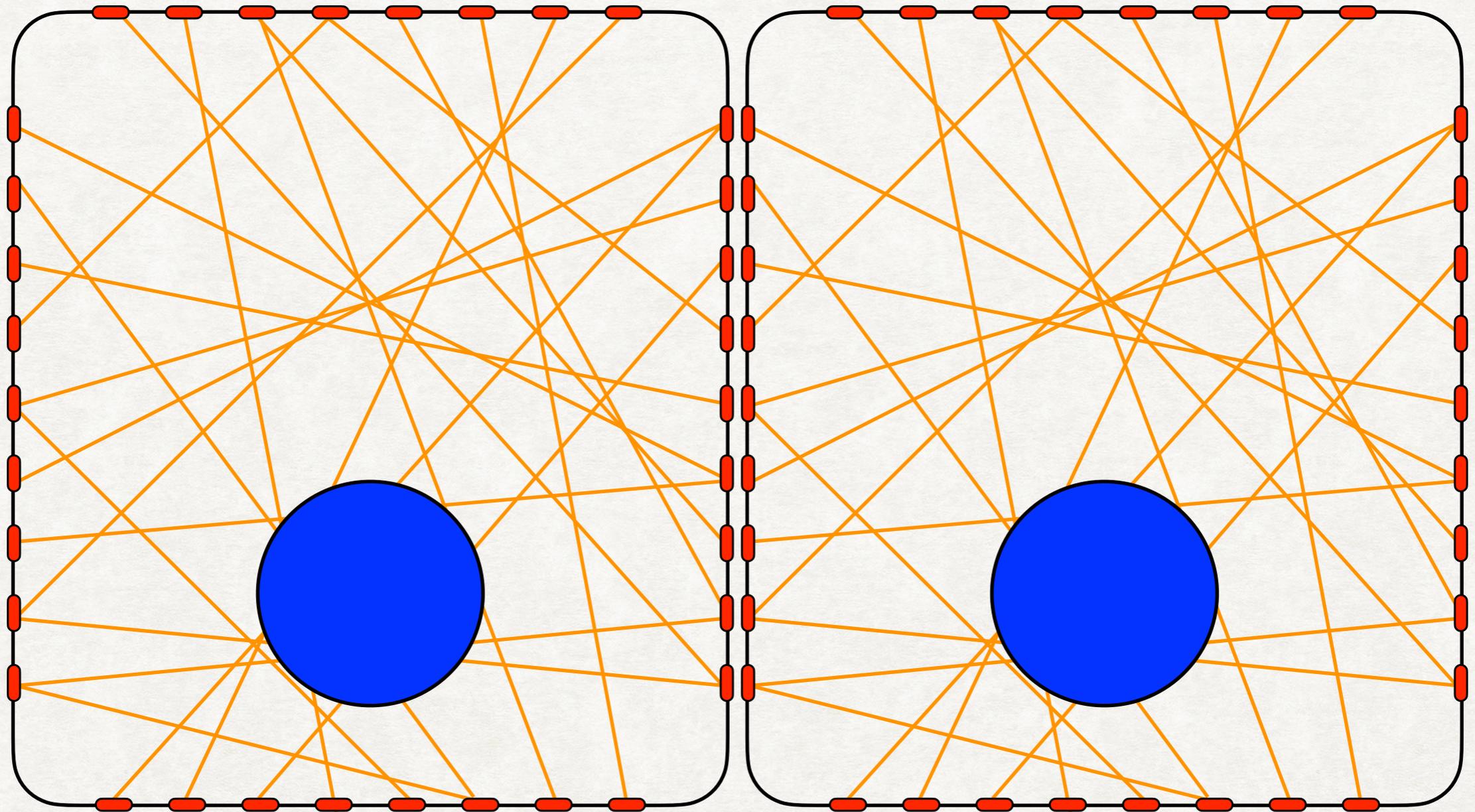
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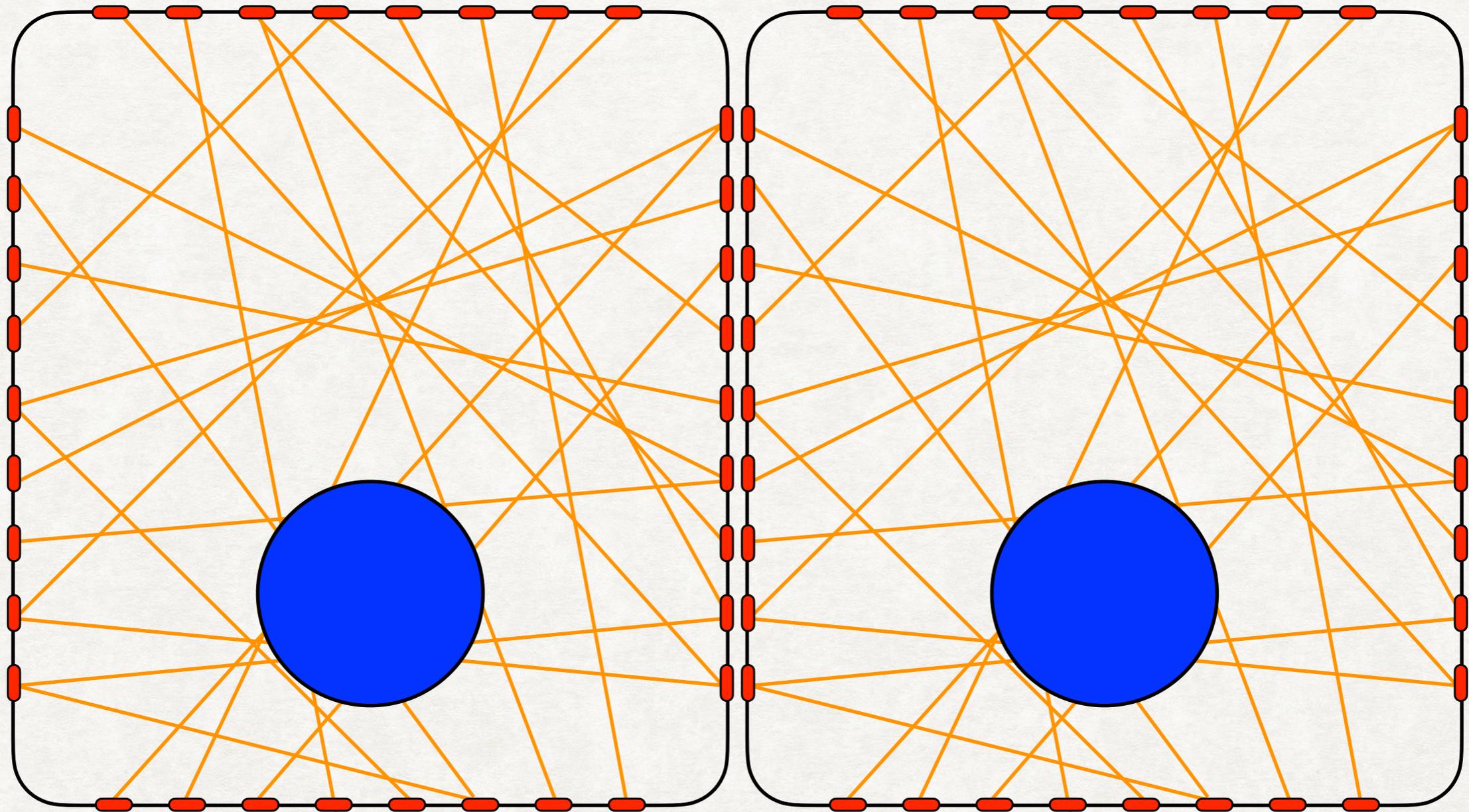
Desmosomas



Desmosomas



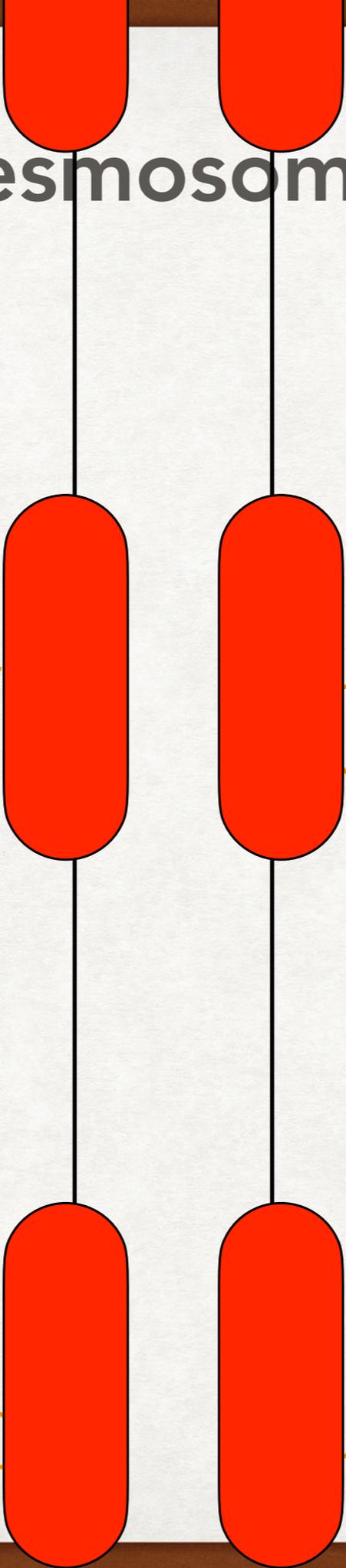
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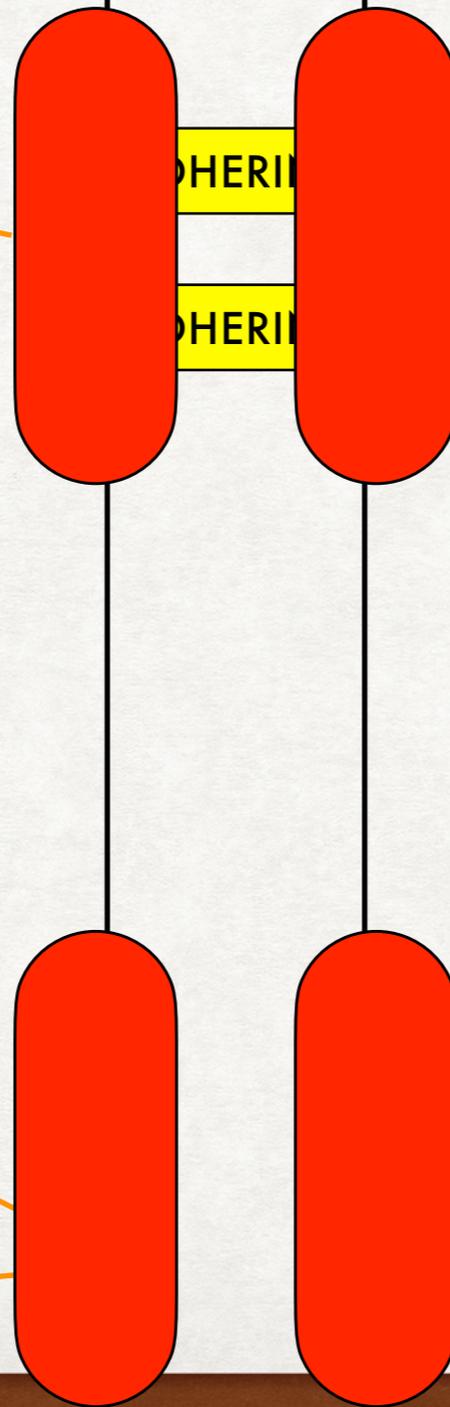
Desmosomas

CADHERINAS

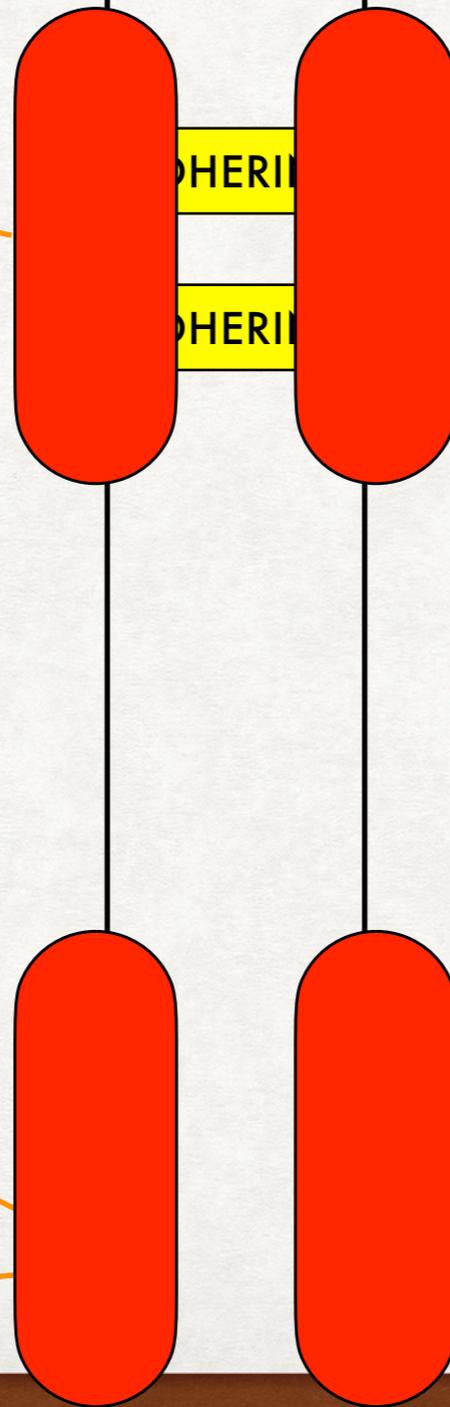
CADHERINAS



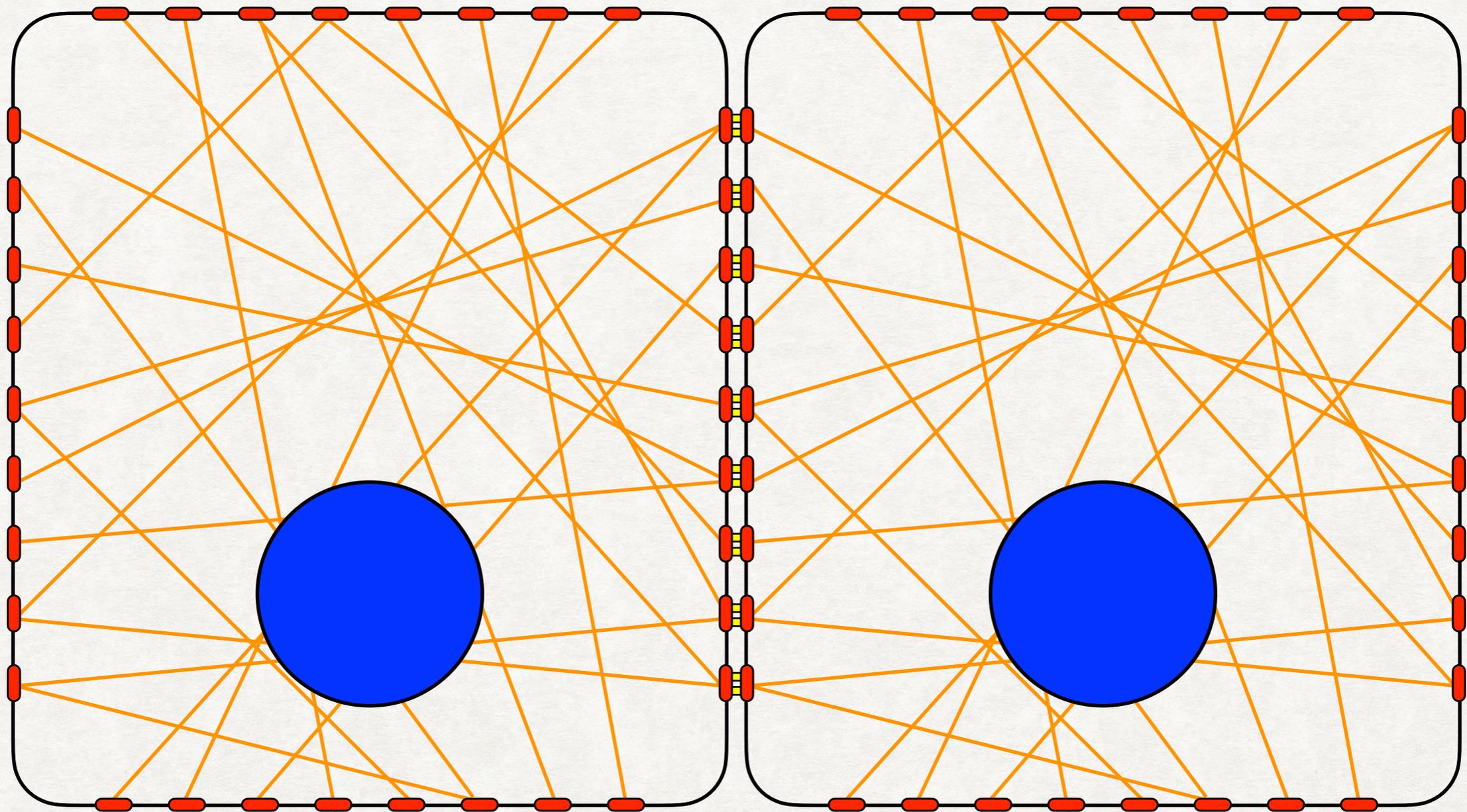
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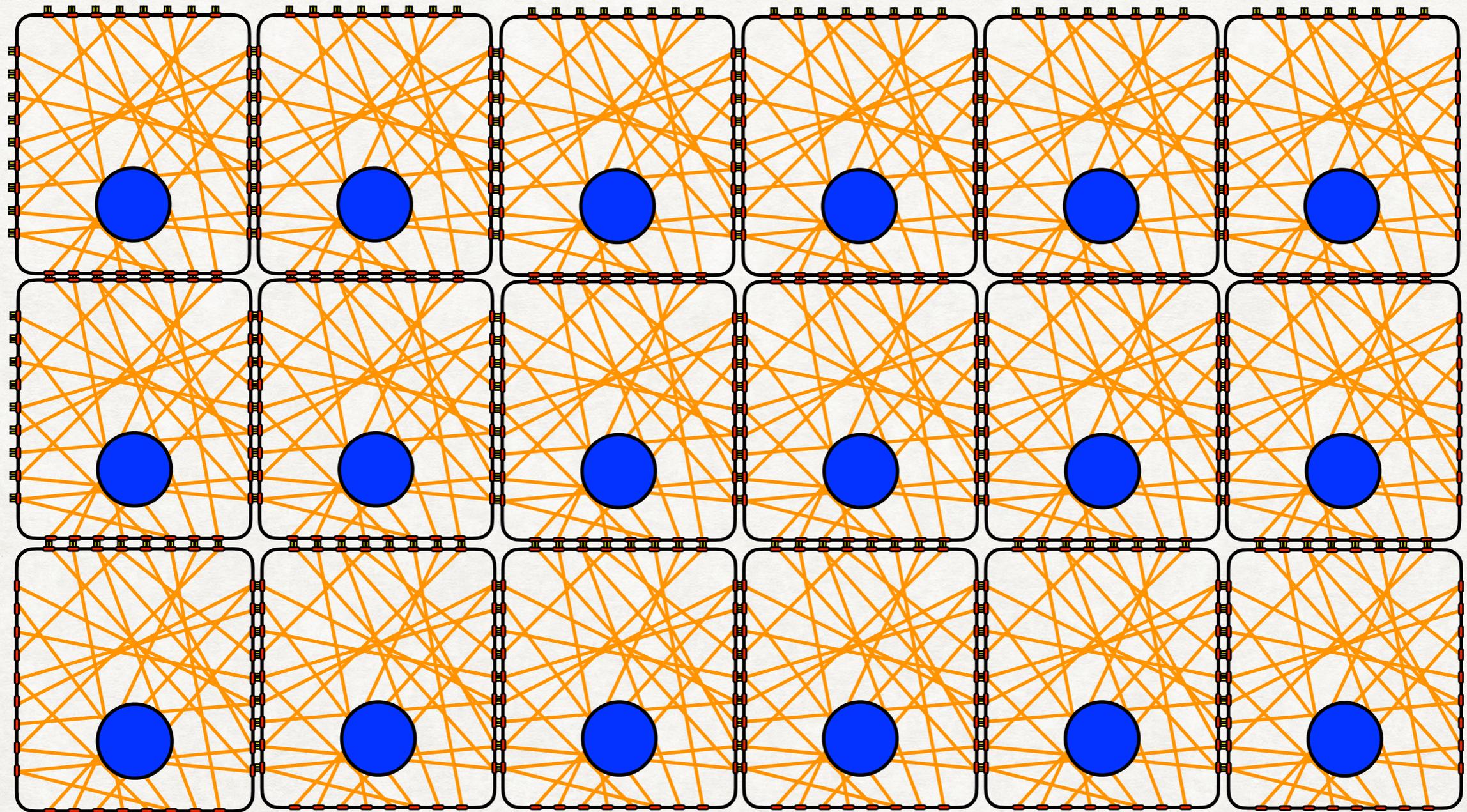
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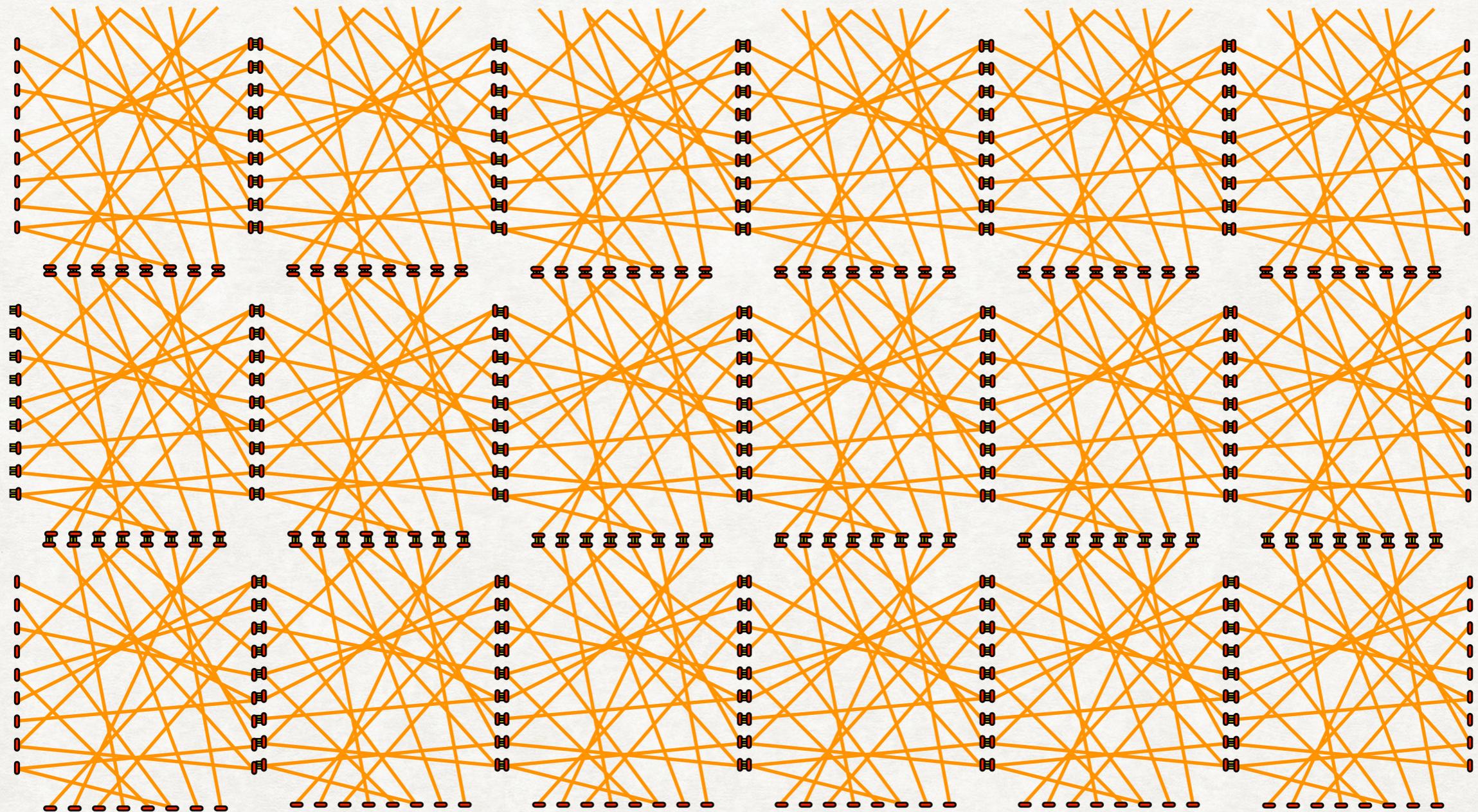
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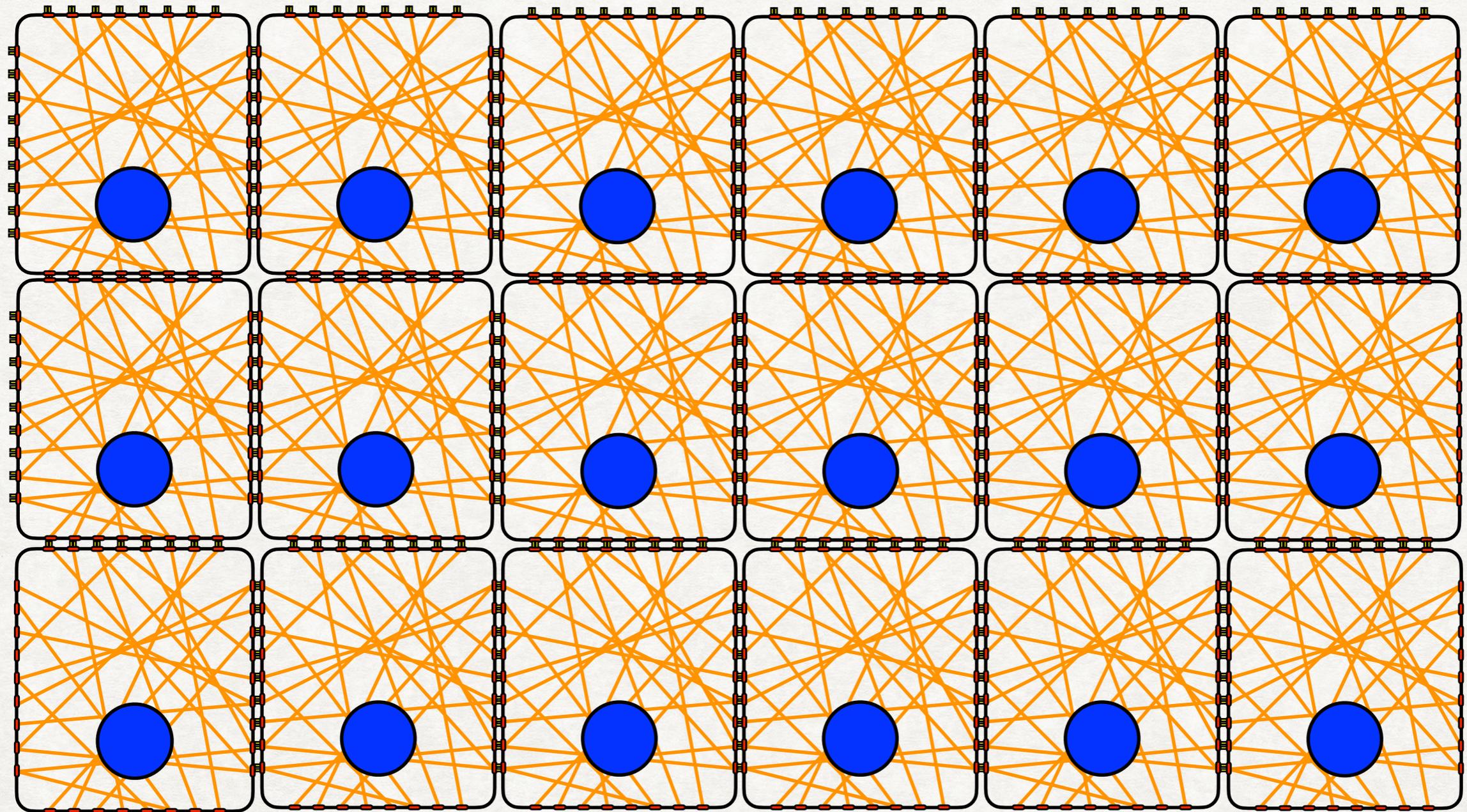
Desmosomas



Desmosomas



Desmosomas



Desmosomas

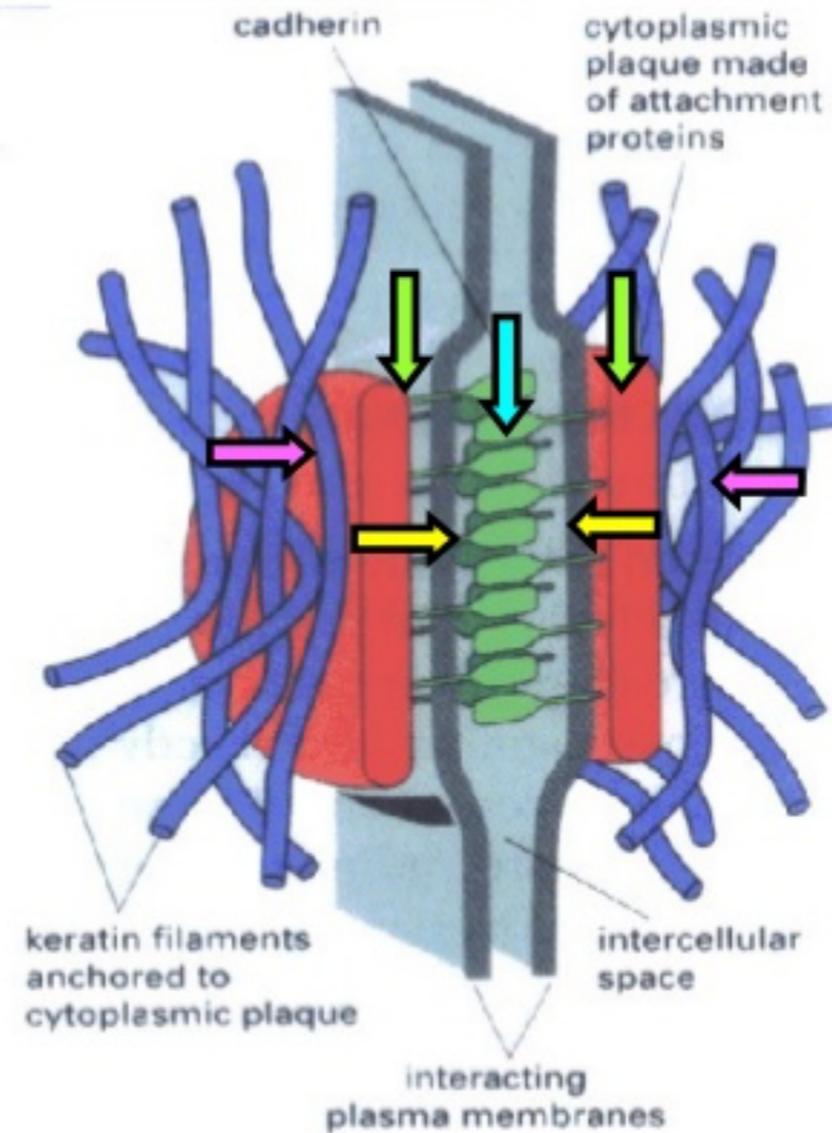
Desmosomes

1. Thickening of adjacent cell membrane

2. A pair of attachment plaque

3. Tonofilaments

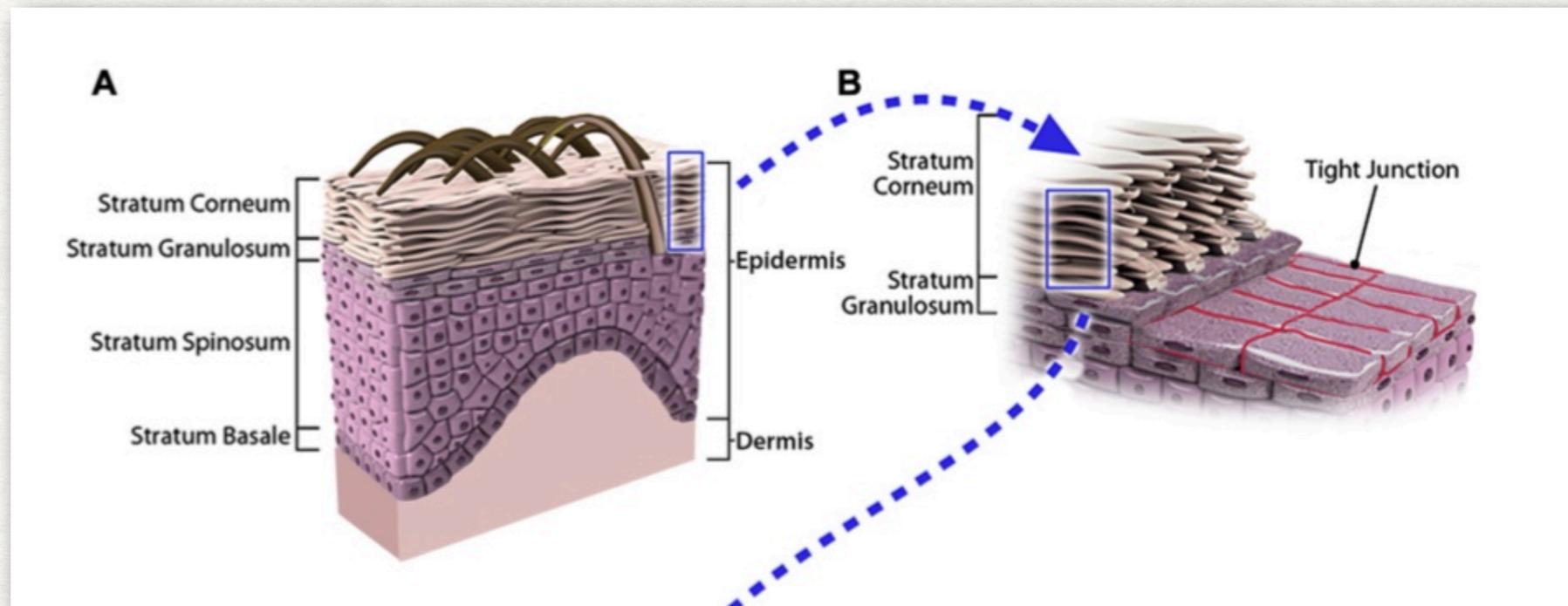
4. Extracellular structure



Conexiones entre Queratinocitos

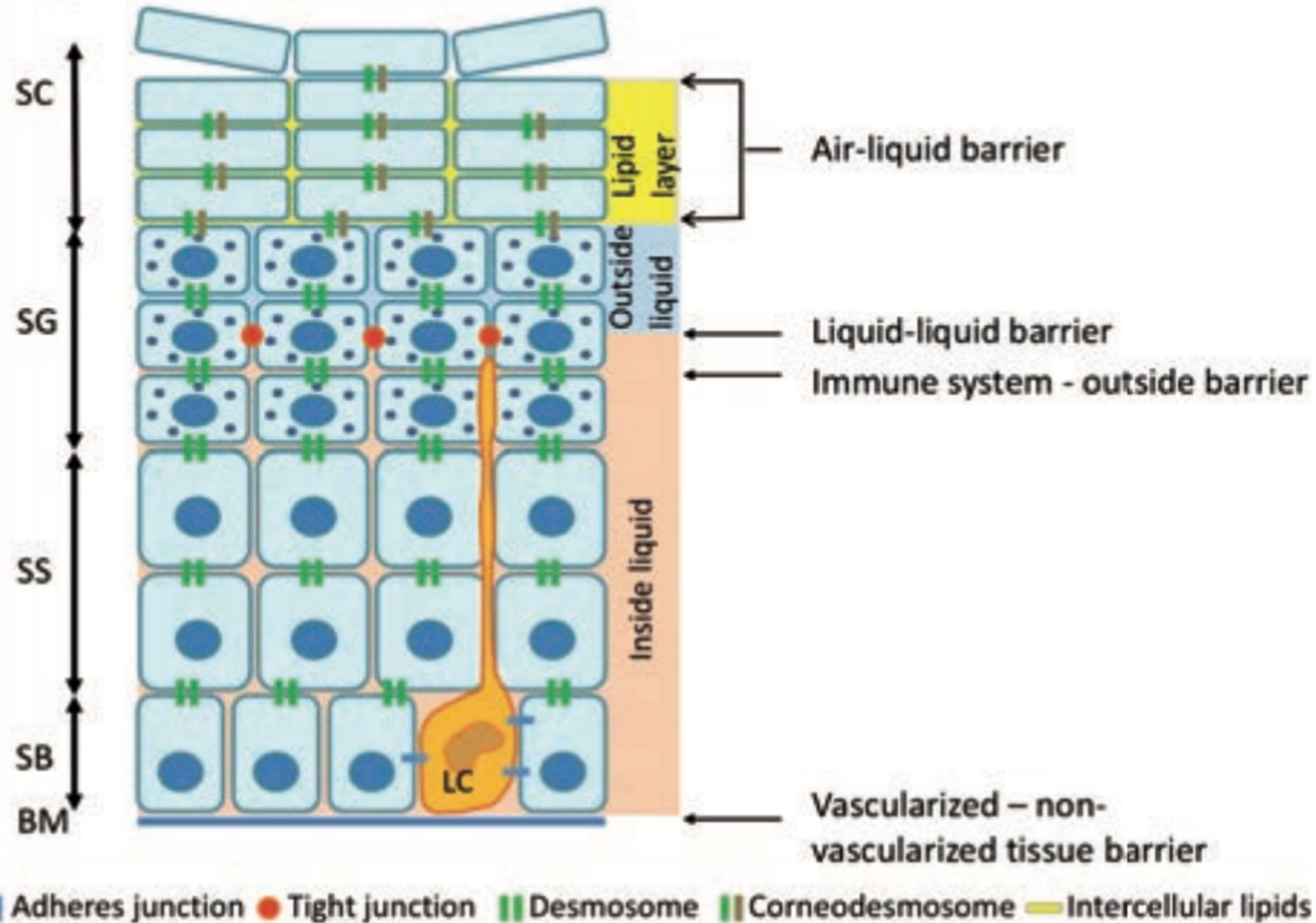
- Queratinas
- Desmosomas
- Uniones Estrechas

Uniones Estrechhas



Uniones Estrechhas

Fig. 1 Epidermal Barriers in Homeostasis (adapted from Kubo et al 2012)



Conexiones entre Queratinocitos

- Queratinas
- Desmosomas
- Uniones Estrechas

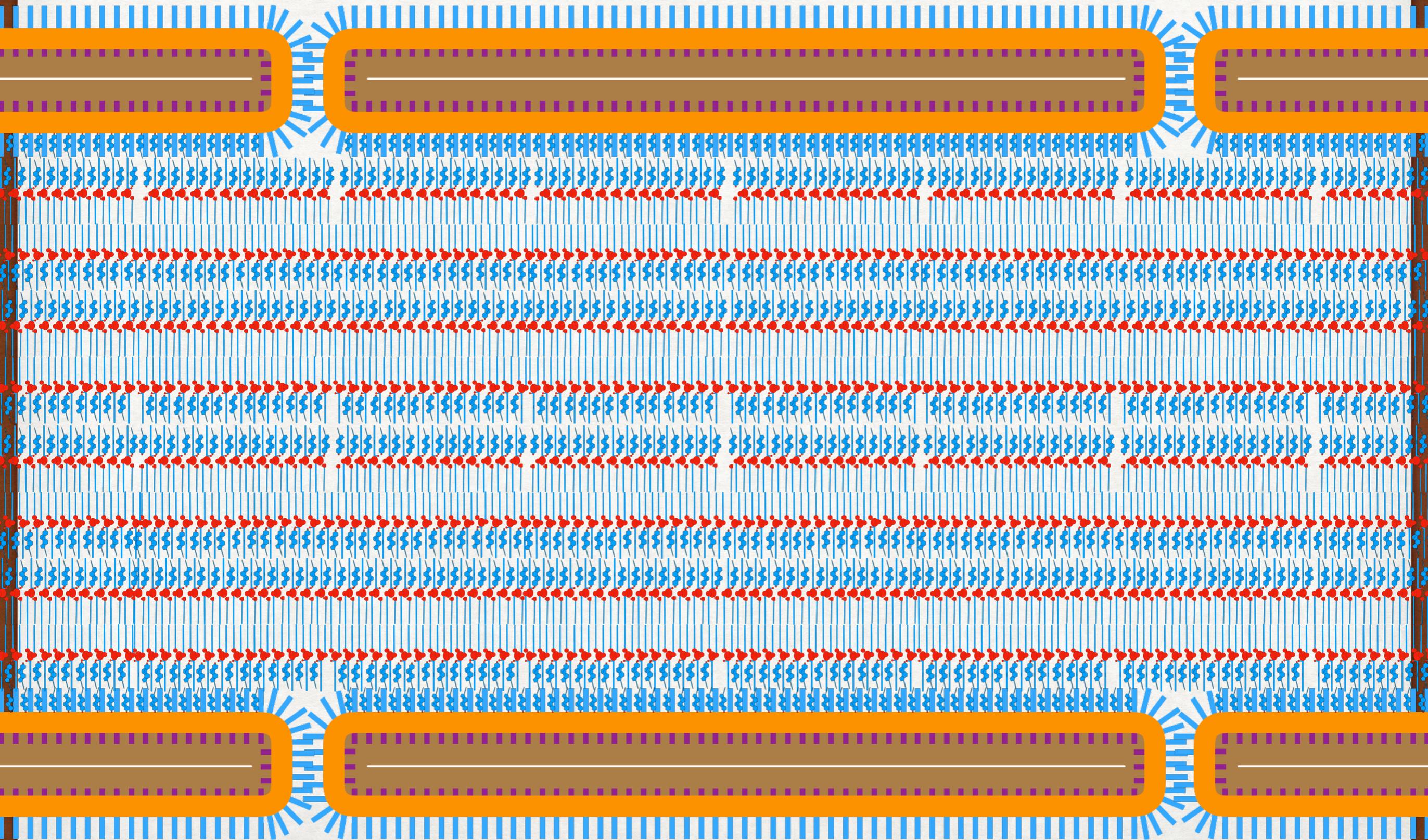
Barrera Cutánea

Partes de Estudio

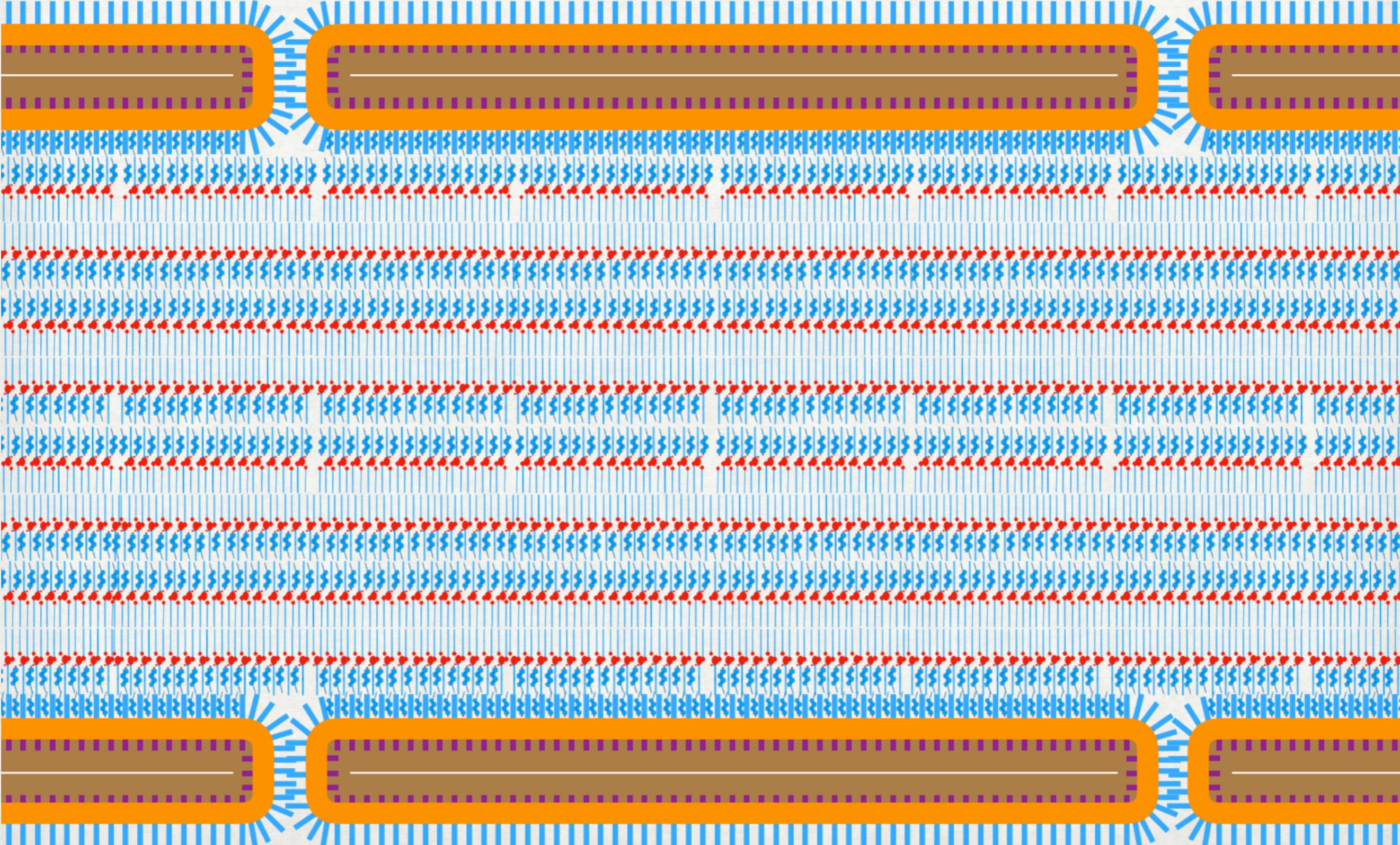
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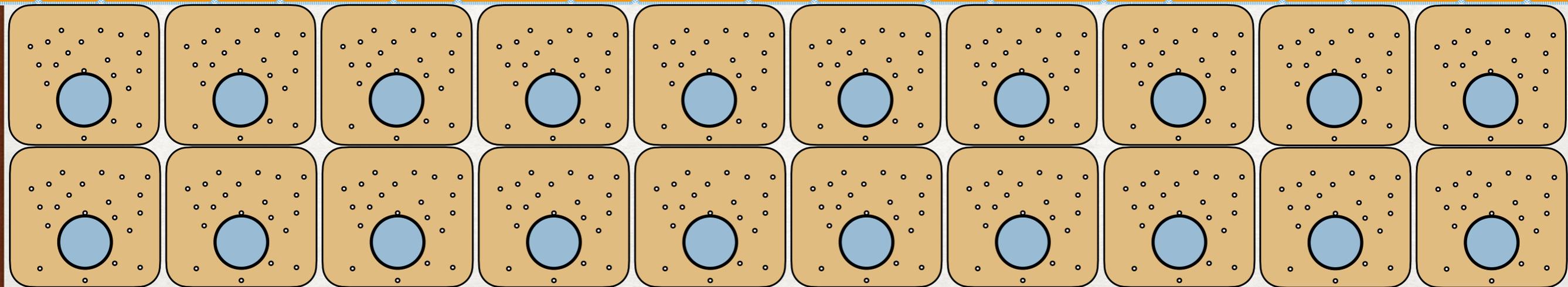
Conexiones entre Lípidos y Corneocitos



Conexiones entre Lípidos y Corneocitos



Conexiones entre Lípidos y Corneocitos



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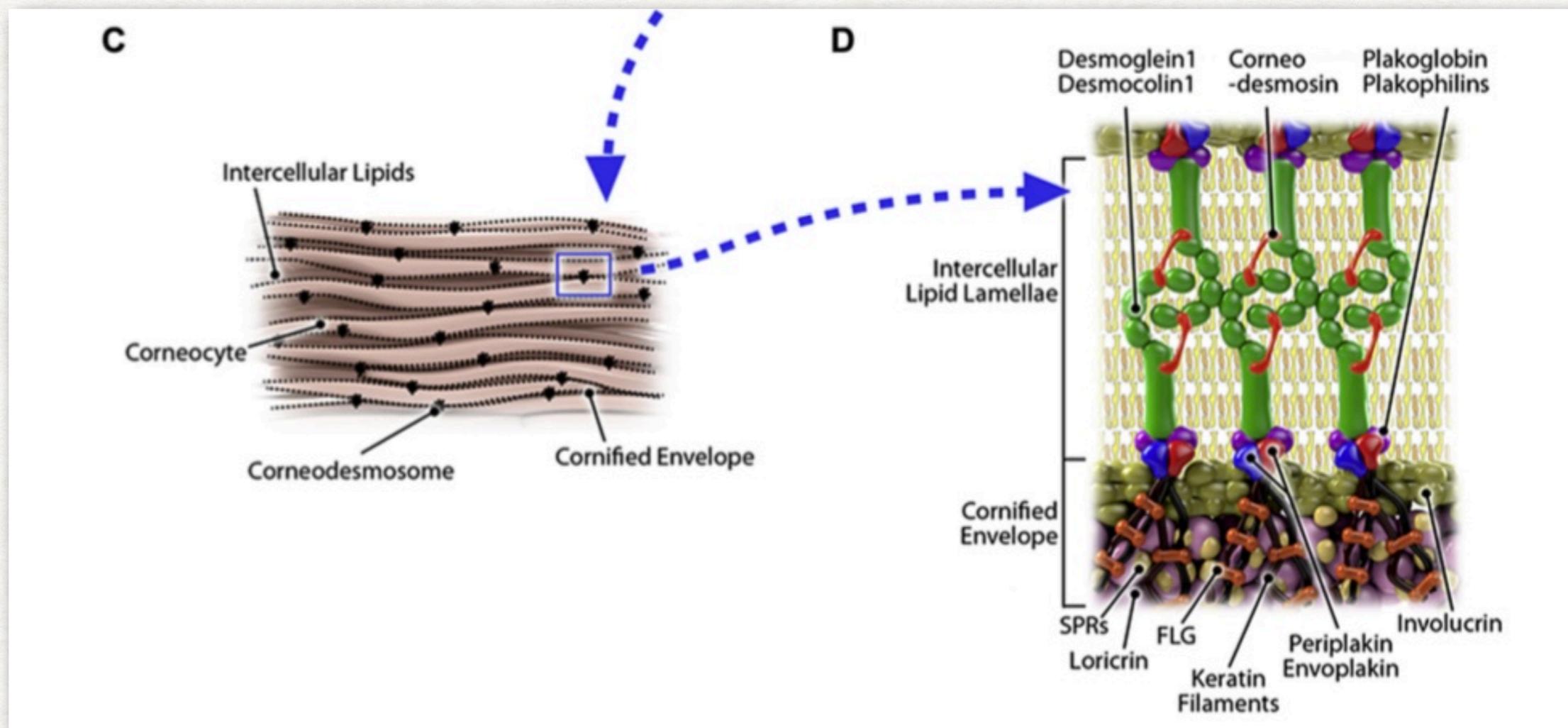
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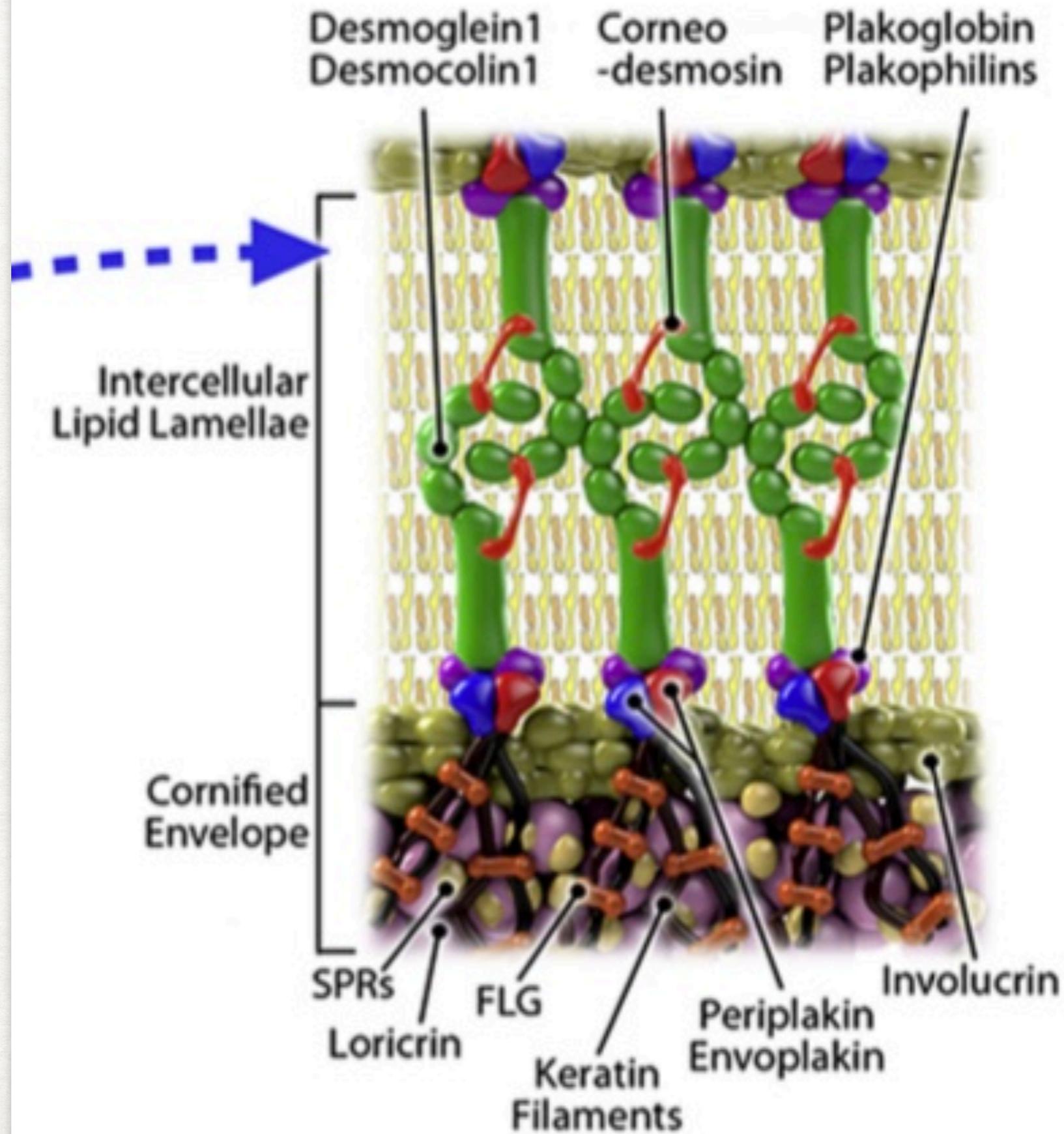
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Conexiones entre Corneocitos

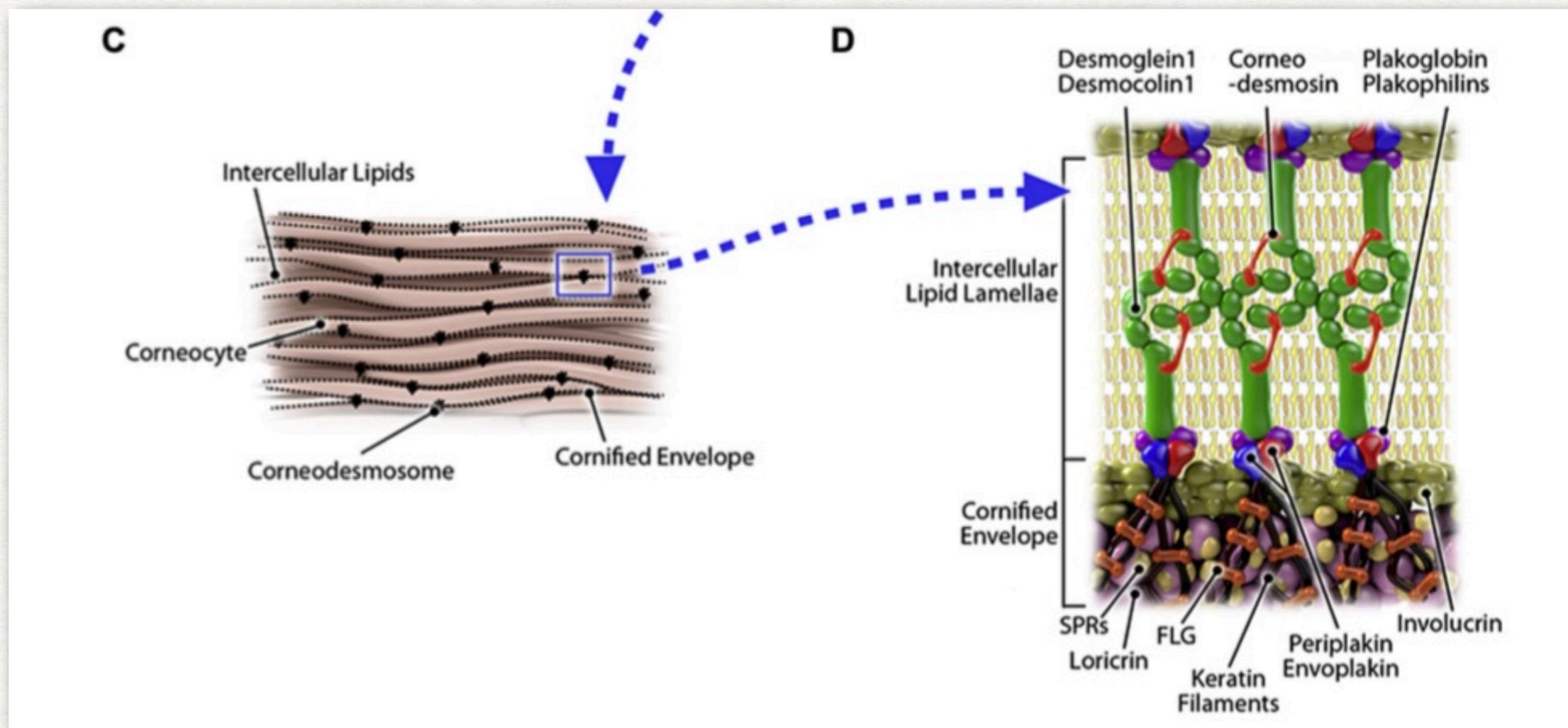
▸ Corneodesmosomas





Conexiones entre Corneocitos

▸ Corneodesmosomas



Barrera Cutánea

Partes de Estudio

● Barrera Aire - Líquido  ***Estrato Corneo***

- ➔ Corneocitos
- ➔ Lípidos Intercelulares
- ➔ Conexiones entre Queratinocitos
- ➔ Conexiones entre Lipidos y Corneocitos
- ➔ Conexiones entre Corneocitos

Barrera Cutánea

Partes de Estudio

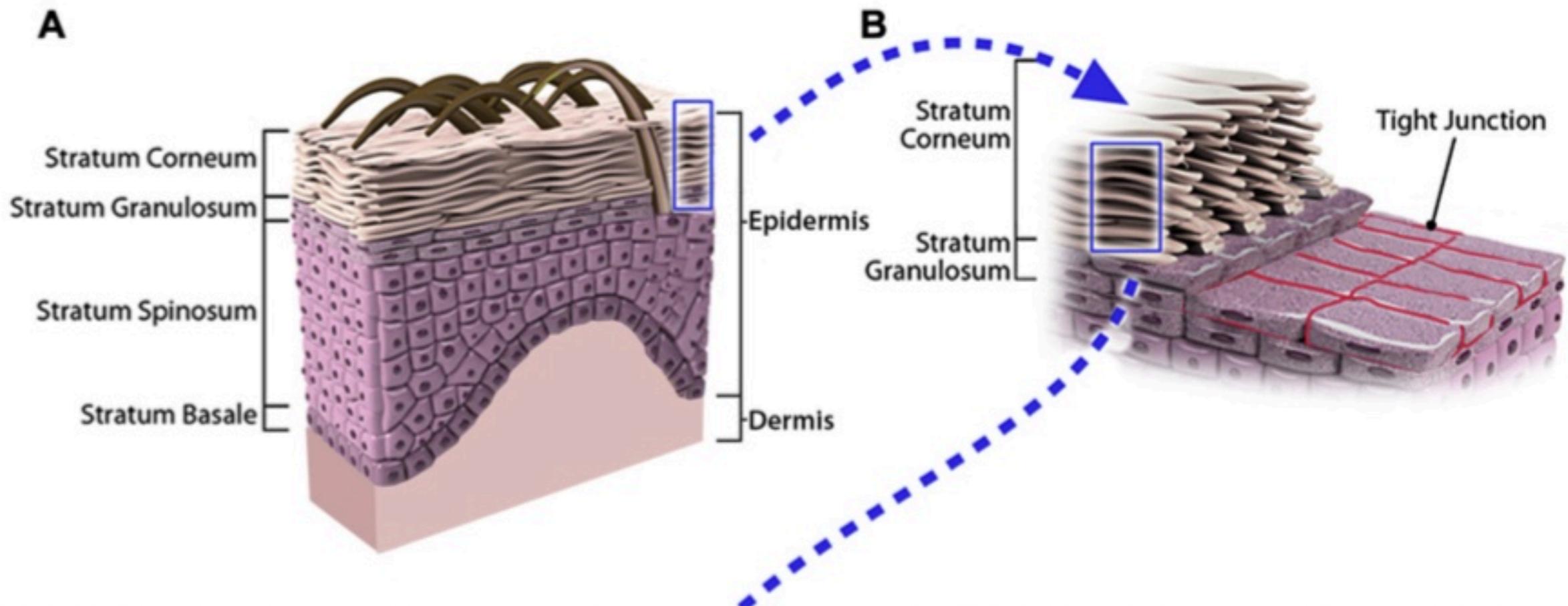
✓ Estructura de la Barrera Cutánea

- Barrera Aire - Líquido
- Líquido - Líquido

Barrera Cutánea

Partes de Estudio

● Líquido - Líquido → *Uniones Estrechas*



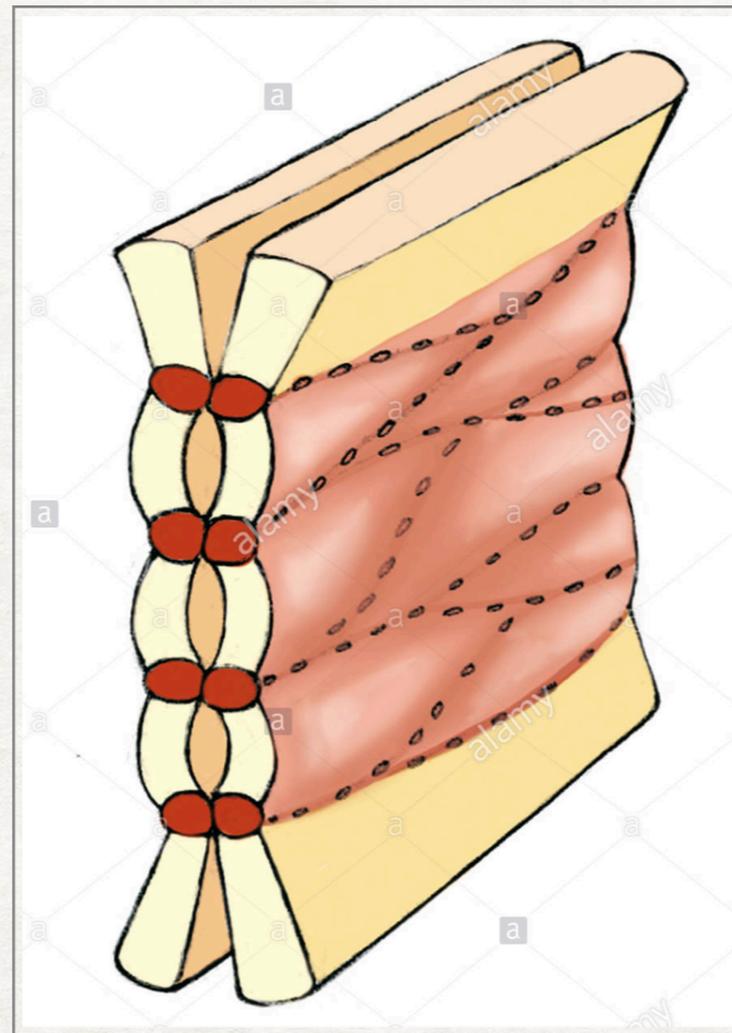
Barrera Cutánea

Partes de Estudio

● Líquido - Líquido



Uniones Estrechadas



Barrera Cutánea

Partes de Estudio

● Líquido - Líquido → *Uniones Estrechas*

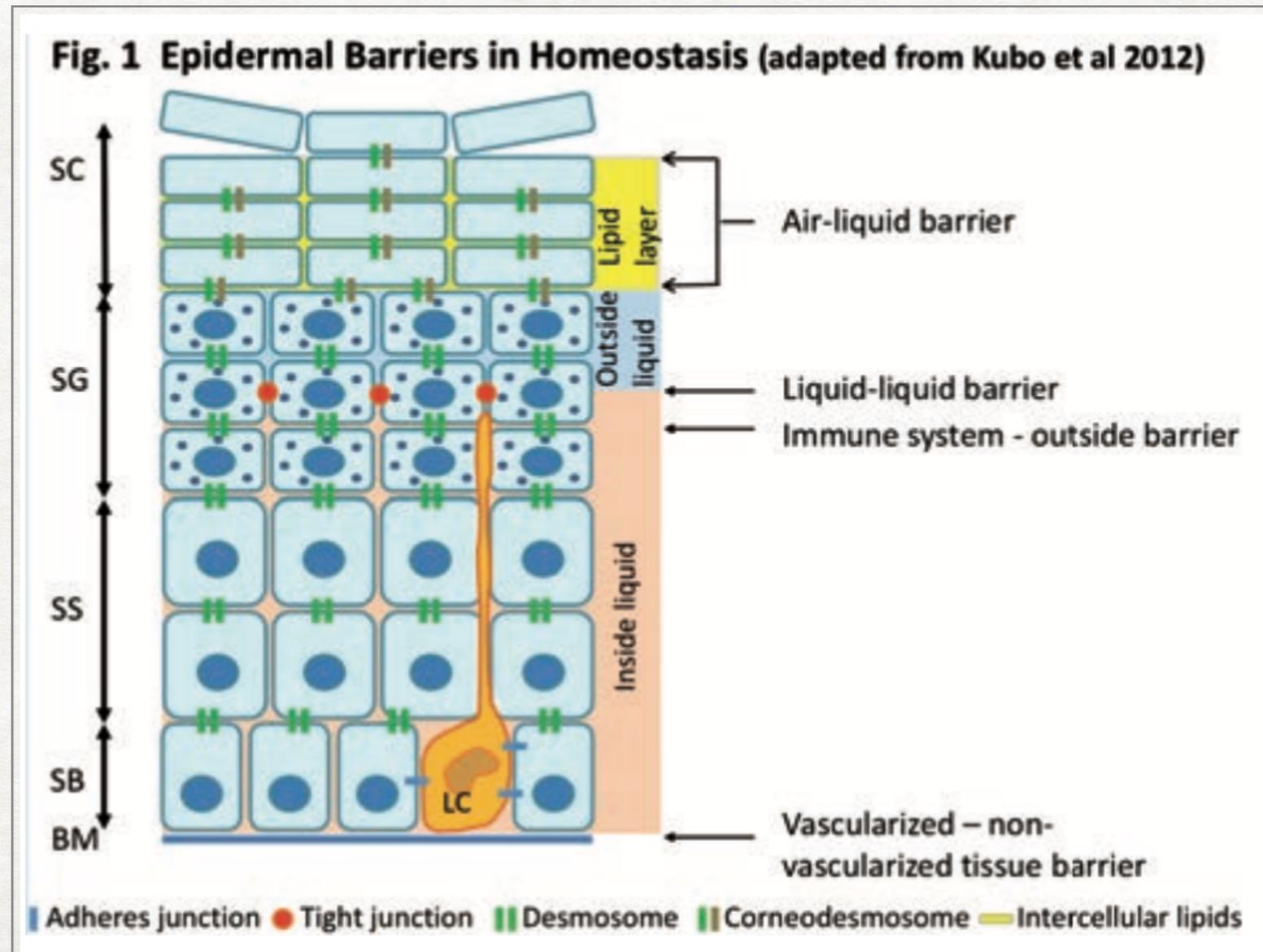
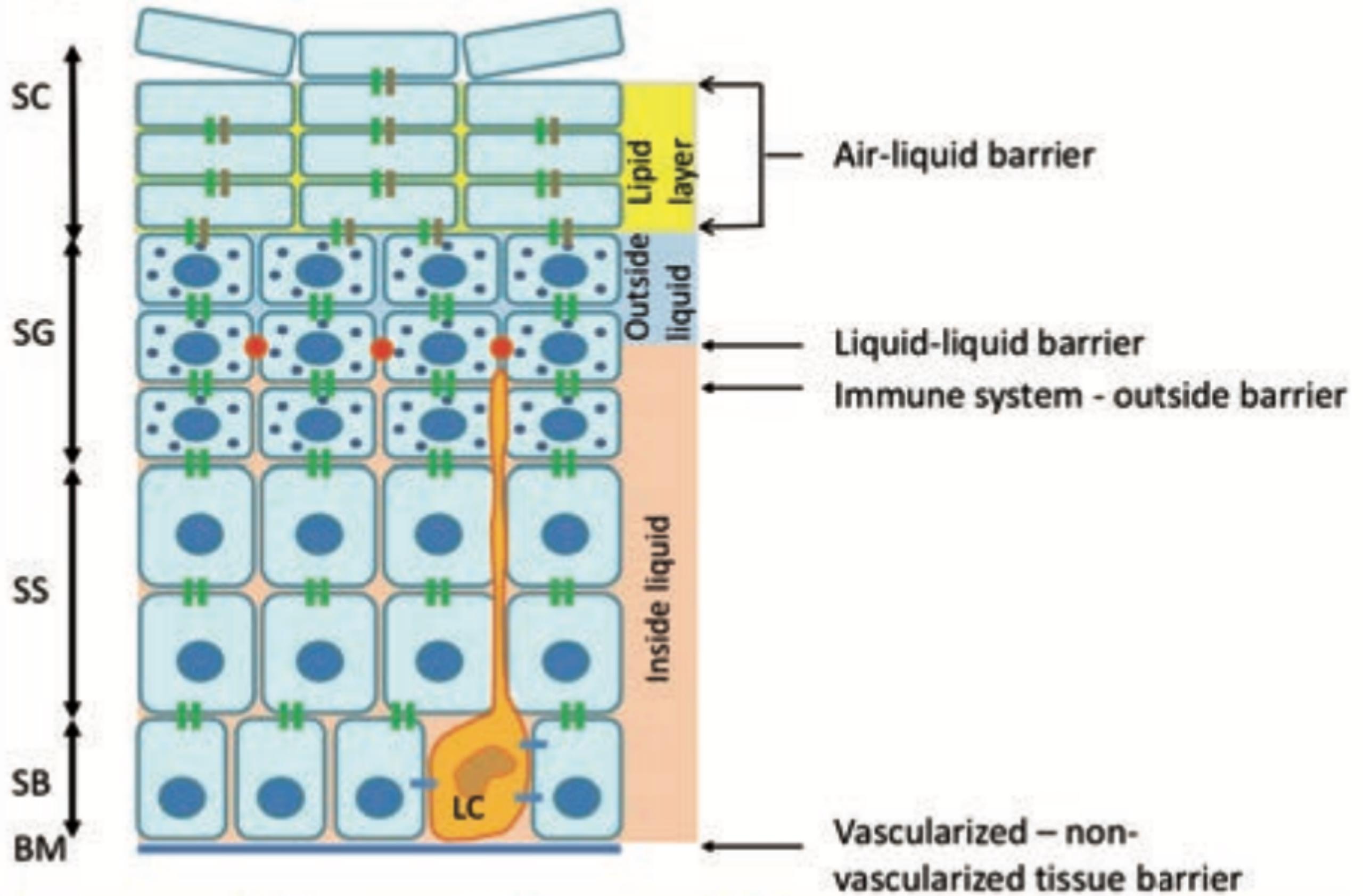


Fig. 1 Epidermal Barriers in Homeostasis (adapted from Kubo et al 2012)

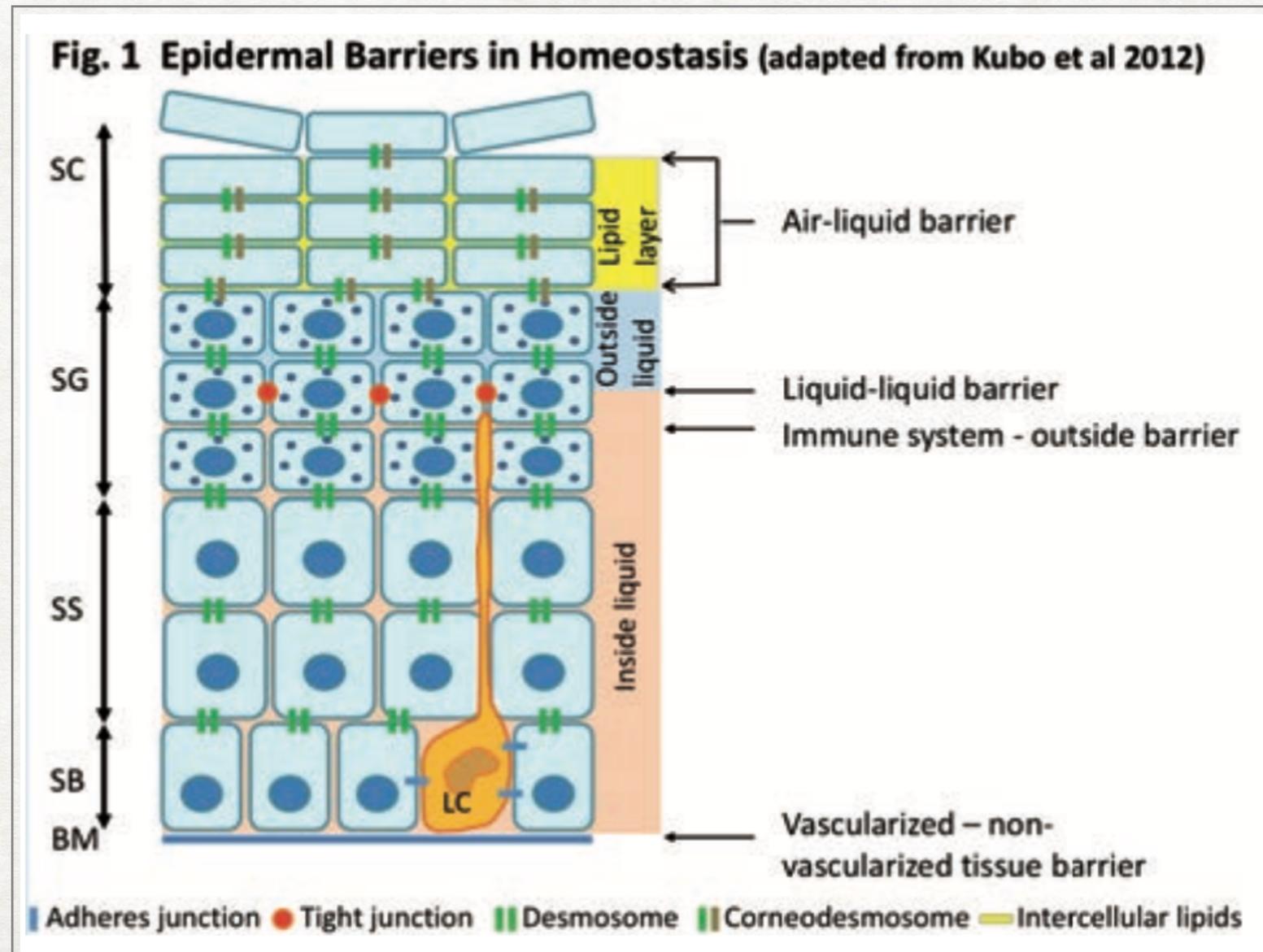


■ Adherens junction ● Tight junction ■■ Desmosome ■■ Corneodesmosome — Intercellular lipids

Barrera Cutánea

Partes de Estudio

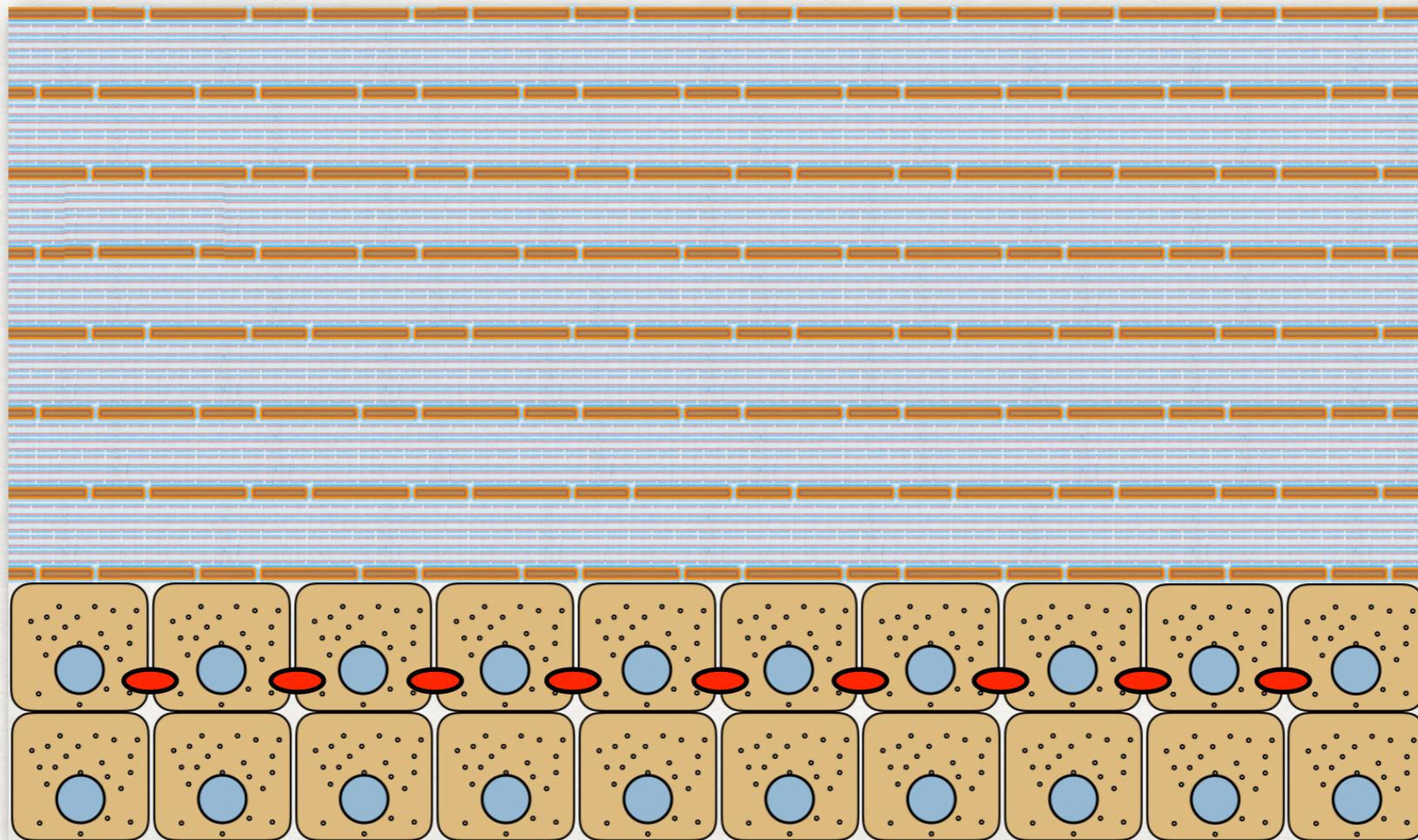
● Líquido - Líquido → *Uniones Estrechas*



Barrera Cutánea

Partes de Estudio

● Líquido - Líquido  ***Uniones Estrechadas***



Barrera Cutánea

Partes de Estudio

✓ Estructura de la Barrera Cutánea

- Barrera Aire - Líquido
- Líquido - Líquido

Barrera Cutánea

Partes de Estudio

- ✓ Estructura de la Barrera Cutánea
- ✓ Fisiología y Formación de la Barrera Cutánea
- ✓ Barrera Cutánea y Diferentes Enfermedades

Barrera Cutánea

Partes de Estudio

✓ Fisiología y Formación de la Barrera Cutánea

- Formación de la Envoltura Cornea
- Síntesis y Liberación de Ceramidas
- Degradación de la Membrana Celular
- Colapso Controlado del Citoesqueleto
- Síntesis y Secreción de Cuerpos Laminares
- Maduración y Descamación del Estrato Corneo

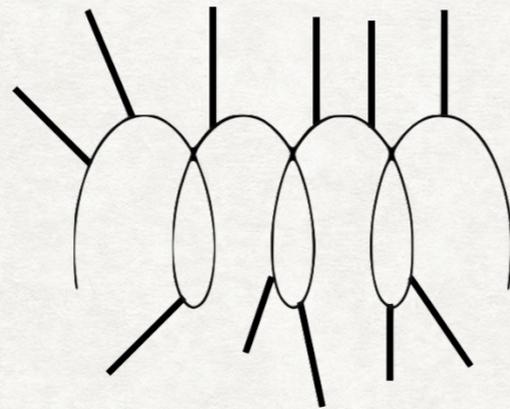
Barrera Cutánea

Partes de Estudio

● Formación de la Envoltura Cornea

→ Involucrina

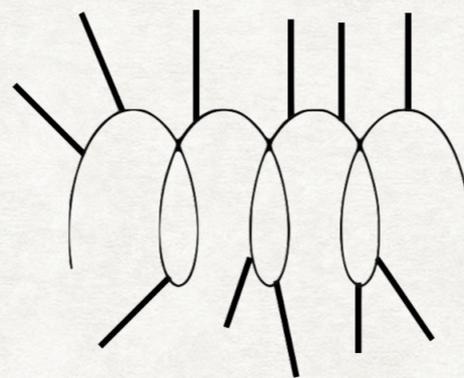
- Union a Ceramidas
- Union a Proteinas de la Envoltura Cornea



Barrera Cutánea

Partes de Estudio

Union a Ceramidas



Union a Proteinas de la Envoltura Cornea

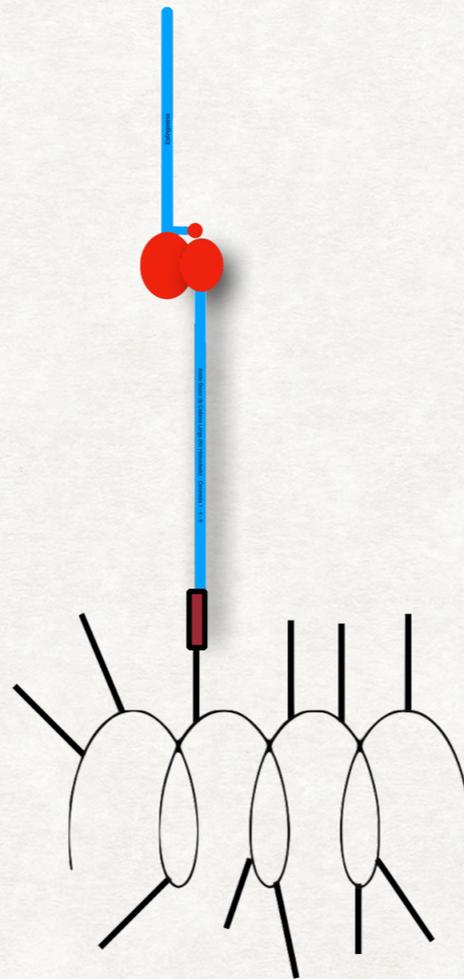


Acil Ceramida

Barrera Cutánea

Partes de Estudio

Union a Ceramidas

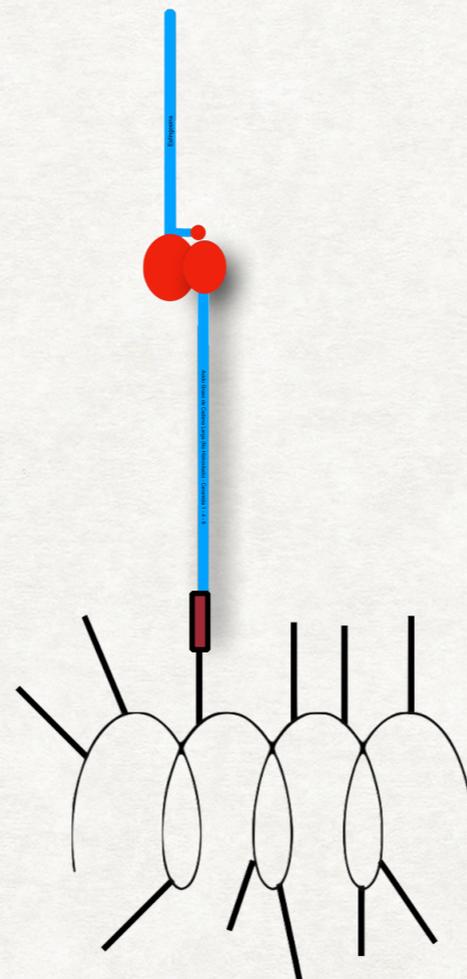


Union a Proteinas de la Envoltura Cornea

Barrera Cutánea

Partes de Estudio

Union a Ceramidas



Envoplaquina



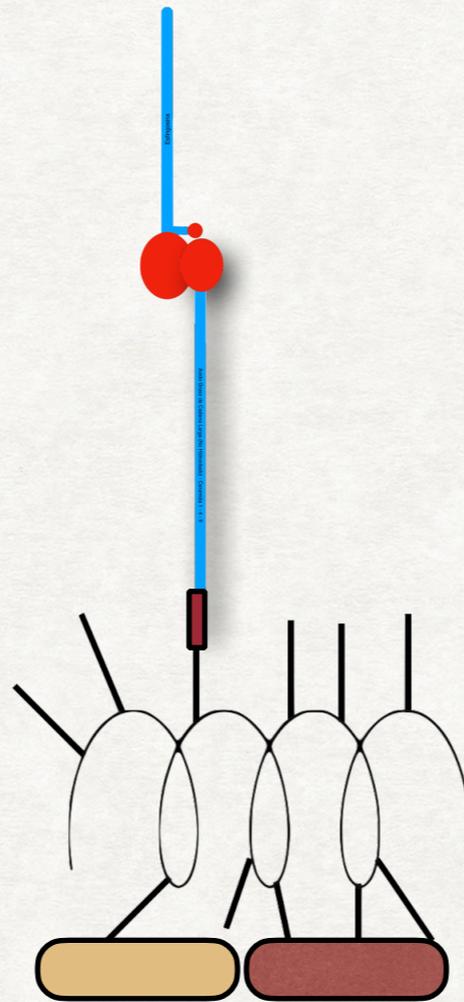
Periplaquina

Union a Proteinas de la Envoltura Cornea

Barrera Cutánea

Partes de Estudio

Union a Ceramidas



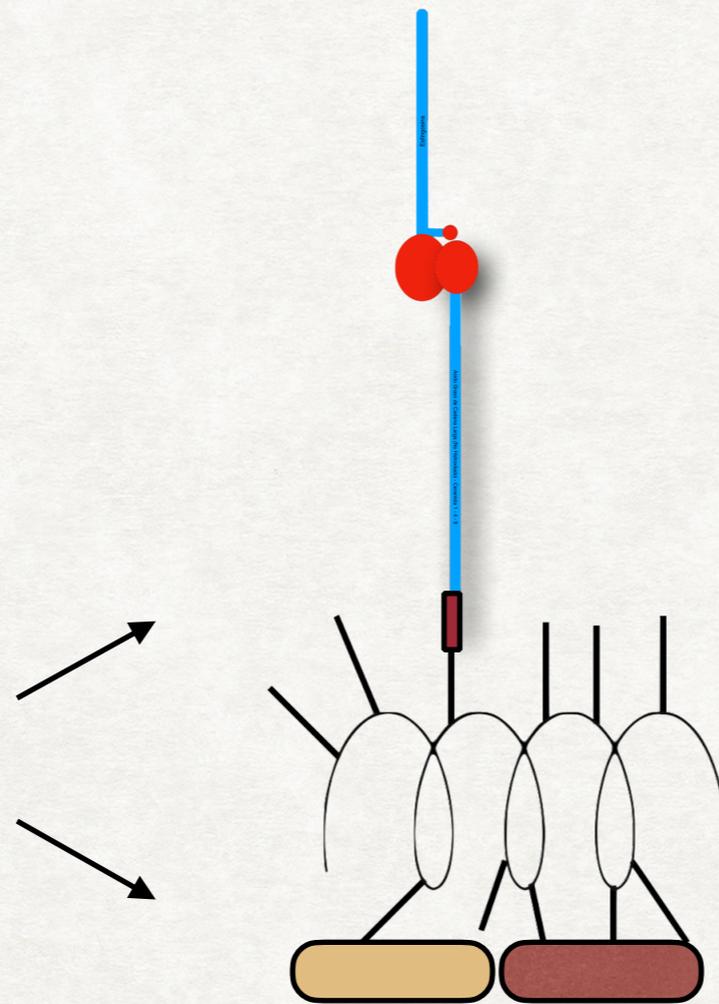
Union a Proteinas de la Envoltura Cornea

Barrera Cutánea

Partes de Estudio

Union a Ceramidas

Transglutaminasa 1



Union a Proteinas de la Envoltura Cornea

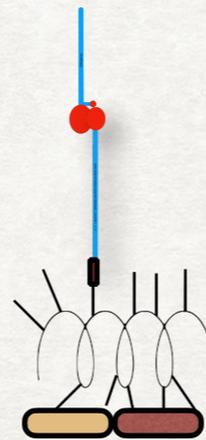
Barrera Cutánea

Partes de Estudio

● Formación de la Envoltura Cornea

→ Involucrina

- Union a Ceramidas
- Union a Proteinas de la Envoltura Cornea

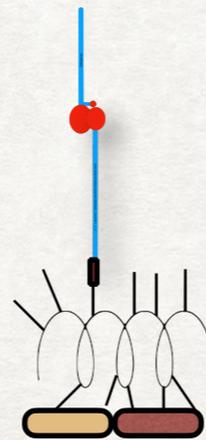


Barrera Cutánea

Partes de Estudio

● Formación de la Envoltura Cornea

- Involucrina
- Envoplakina y Periplakina
- Loricrina

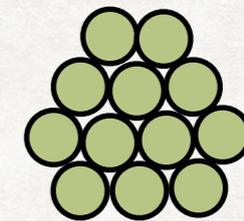
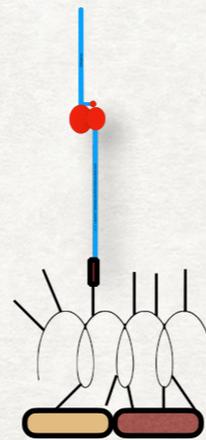


Barrera Cutánea

Partes de Estudio

● Formación de la Envoltura Cornea

- Involucrina
- Envoplakina y Periplakina
- Loricrina



Cuerpos de Loricrina



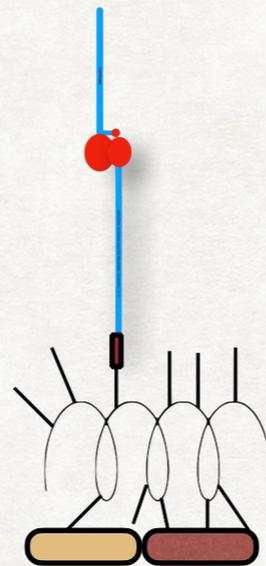
SPRPs

(Proteínas Pequeñas Ricas en Prolina)

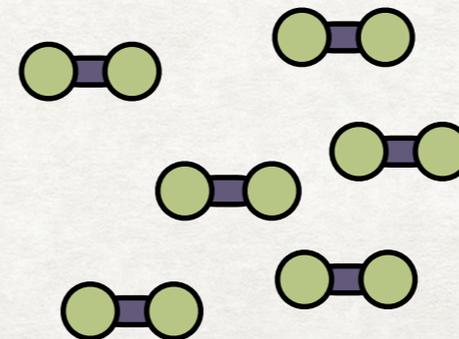
Barrera Cutánea

Partes de Estudio

- Formación de la Envoltura Cornea



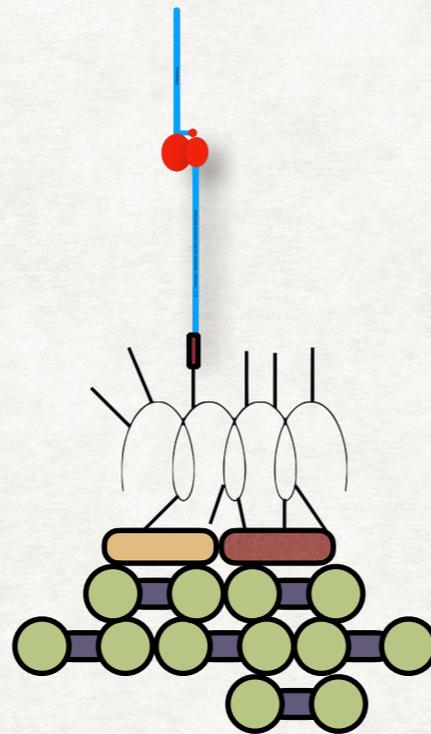
Transglutaminasa 3 →



Barrera Cutánea

Partes de Estudio

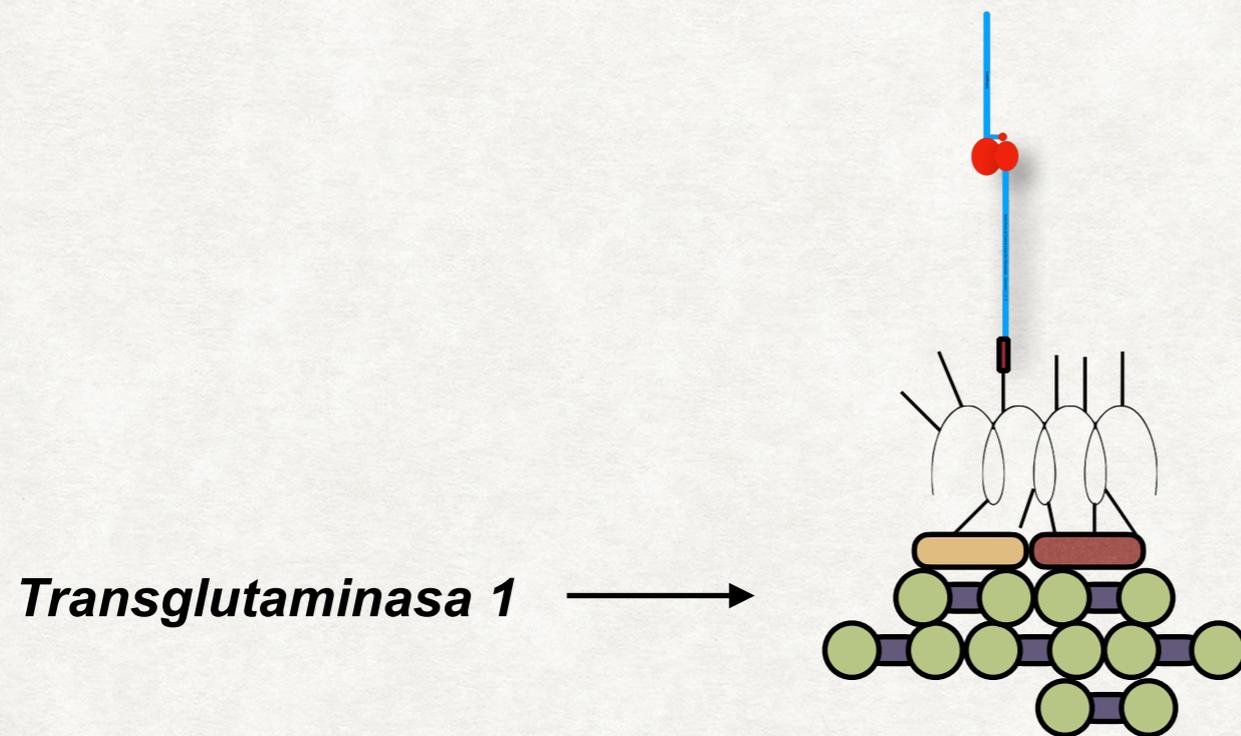
- Formación de la Envoltura Cornea



Barrera Cutánea

Partes de Estudio

- Formación de la Envoltura Cornea

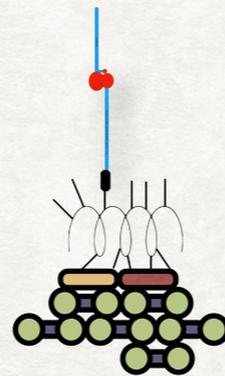


Barrera Cutánea

Partes de Estudio

● Formación de la Envoltura Cornea

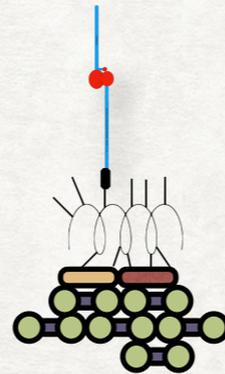
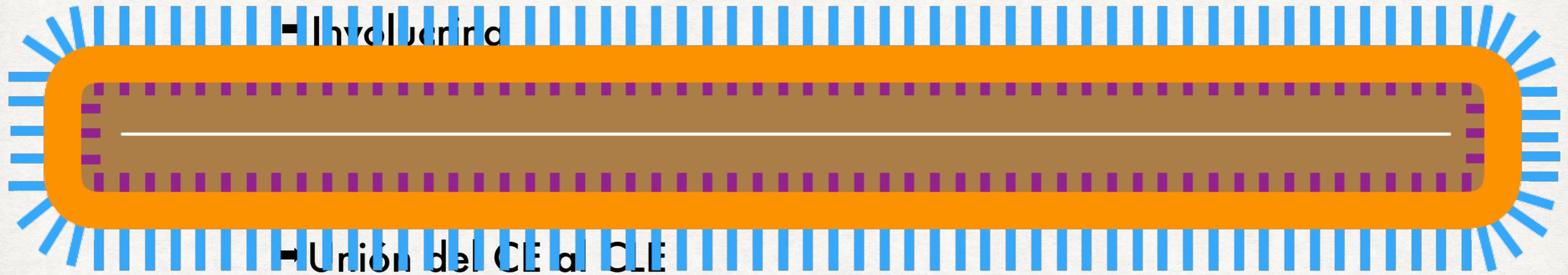
- Involucrina
- Envoplakina y Periplakina
- Loricrina
- Unión del CE al CLE



Barrera Cutánea

Partes de Estudio

- Formación de la Envoltura Cornea

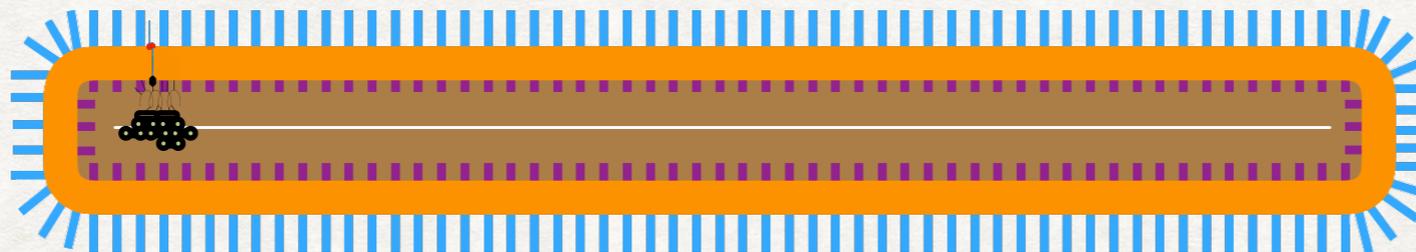


Barrera Cutánea

Partes de Estudio

- Formación de la Envoltura Cornea

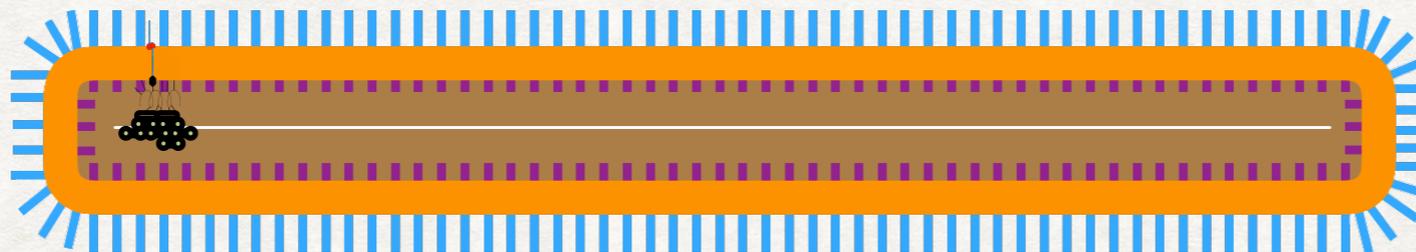
- Involucrina
- Envoplakina y Periplakina
- Loricrina
- Unión del CE al CLE



Barrera Cutánea

Partes de Estudio

- Formación de la Envoltura Cornea
 - Involucrina
 - Envoplakina y Periplakina
 - Loricrina
 - Unión del CE al CLE

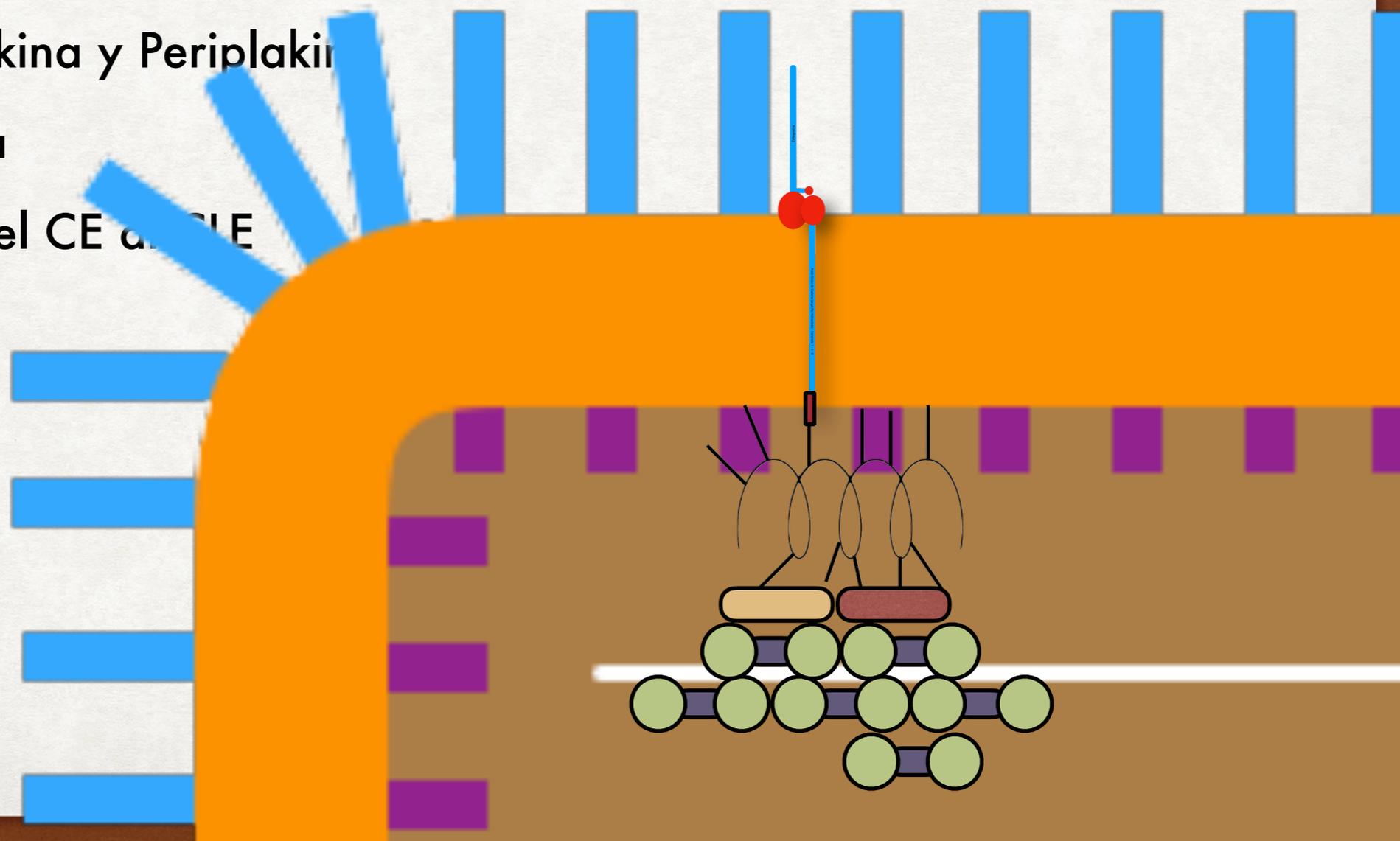


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Partes de Estudio

● Formación de la Envoltura Cornea

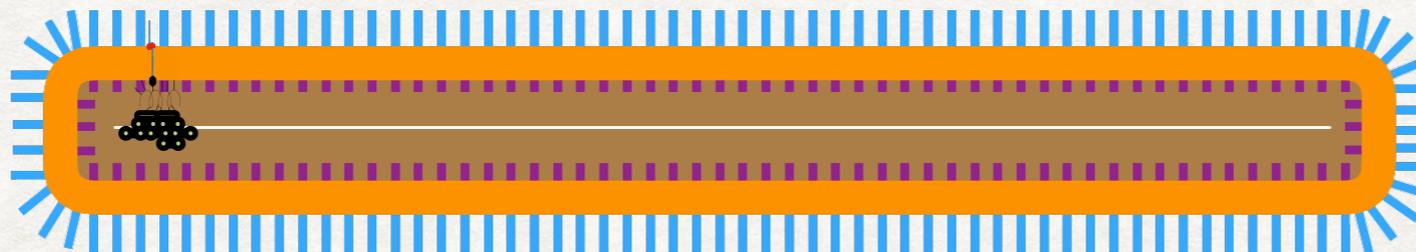
- Involucrina
- Envoplakina y Periplakin
- Loricrina
- Unión del CE al SLE



Barrera Cutánea

Partes de Estudio

- Formación de la Envoltura Cornea
 - Involucrina
 - Envoplakina y Periplakina
 - Loricrina
 - Unión del CE al CLE

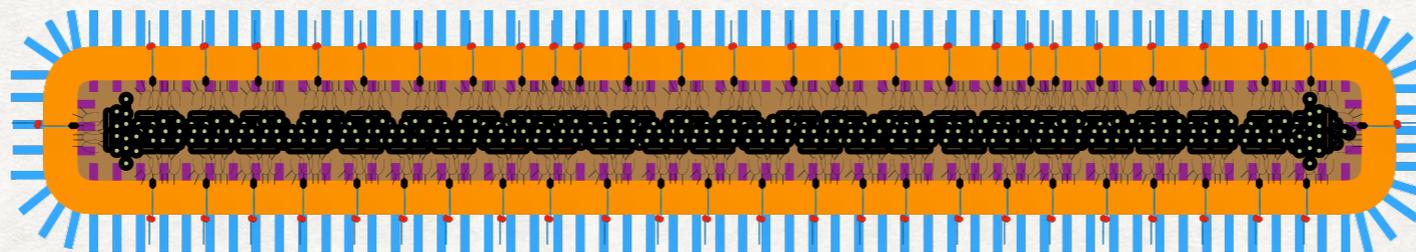


Barrera Cutánea

Partes de Estudio

- Formación de la Envoltura Cornea

- Involucrina
- Envoplakina y Periplakina
- Loricrina
- Unión del CE al CLE



Barrera Cutánea

Partes de Estudio

● Formación de la Envoltura Cornea

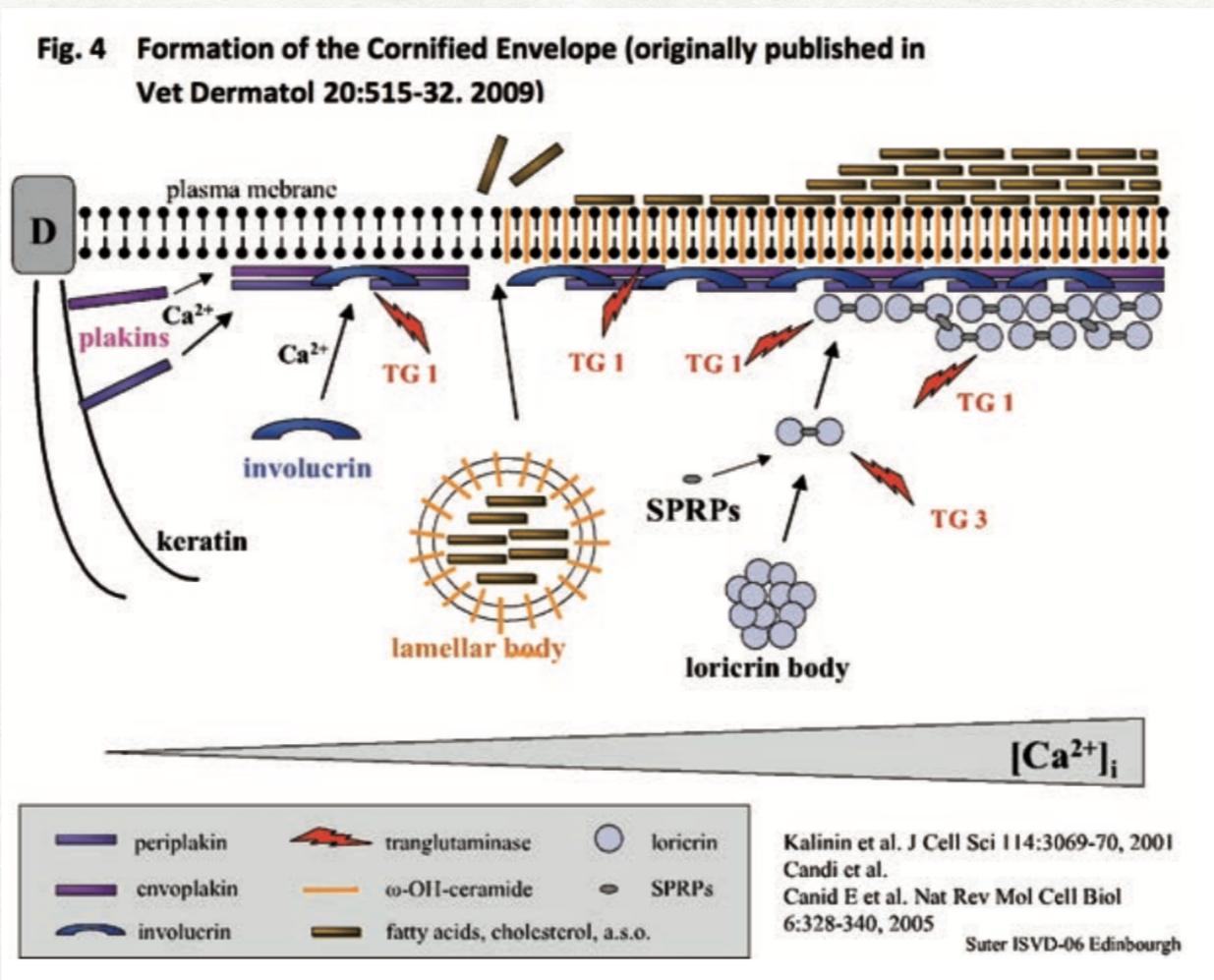
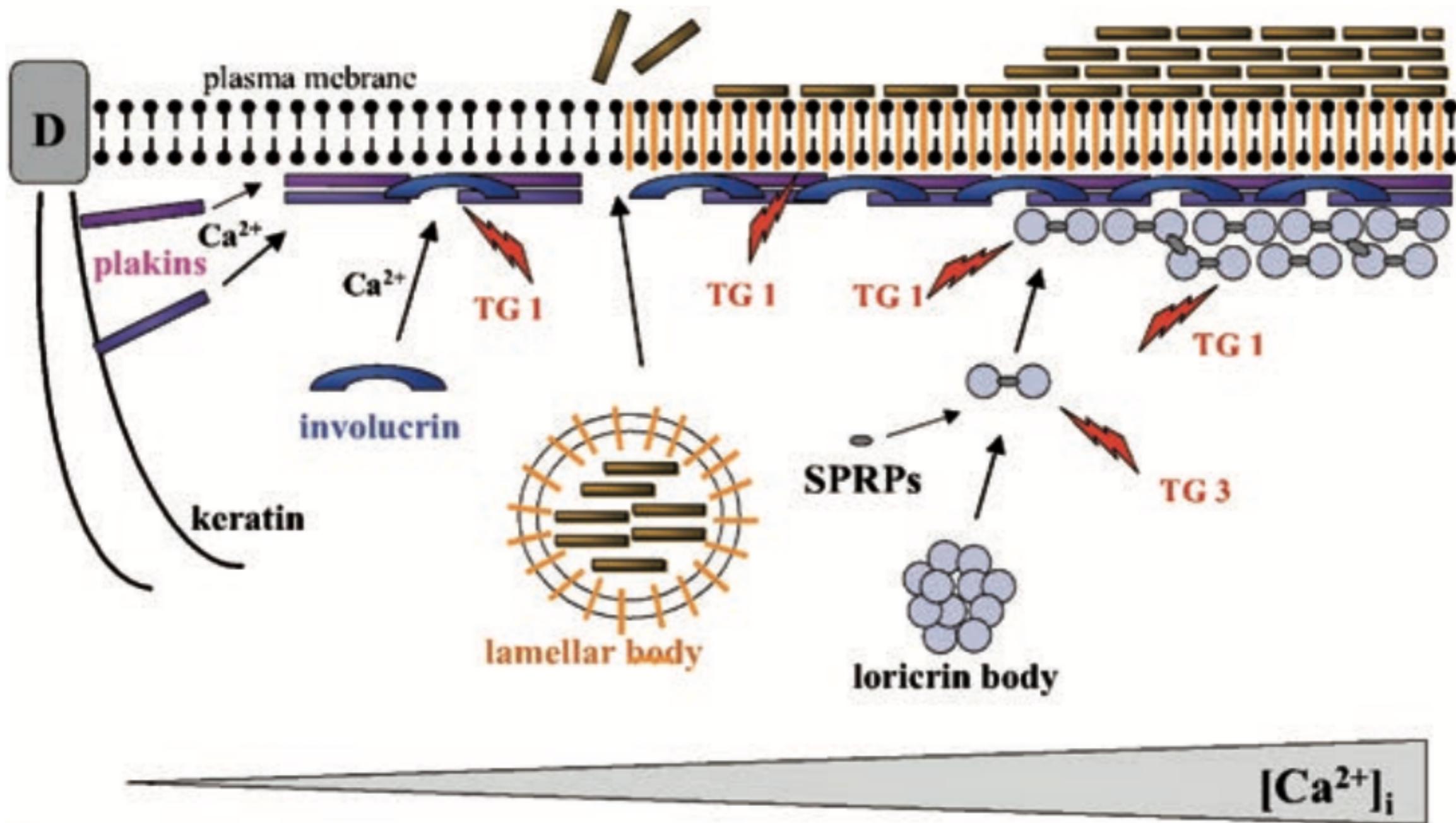
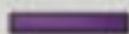


Fig. 4 Formation of the Cornified Envelope (originally published in Vet Dermatol 20:515-32. 2009)



 periplakin	 transglutaminase	 loricrin
 envoplakin	 ω -OH-ceramide	 SPRPs
 involucrin	 fatty acids, cholesterol, a.s.o.	

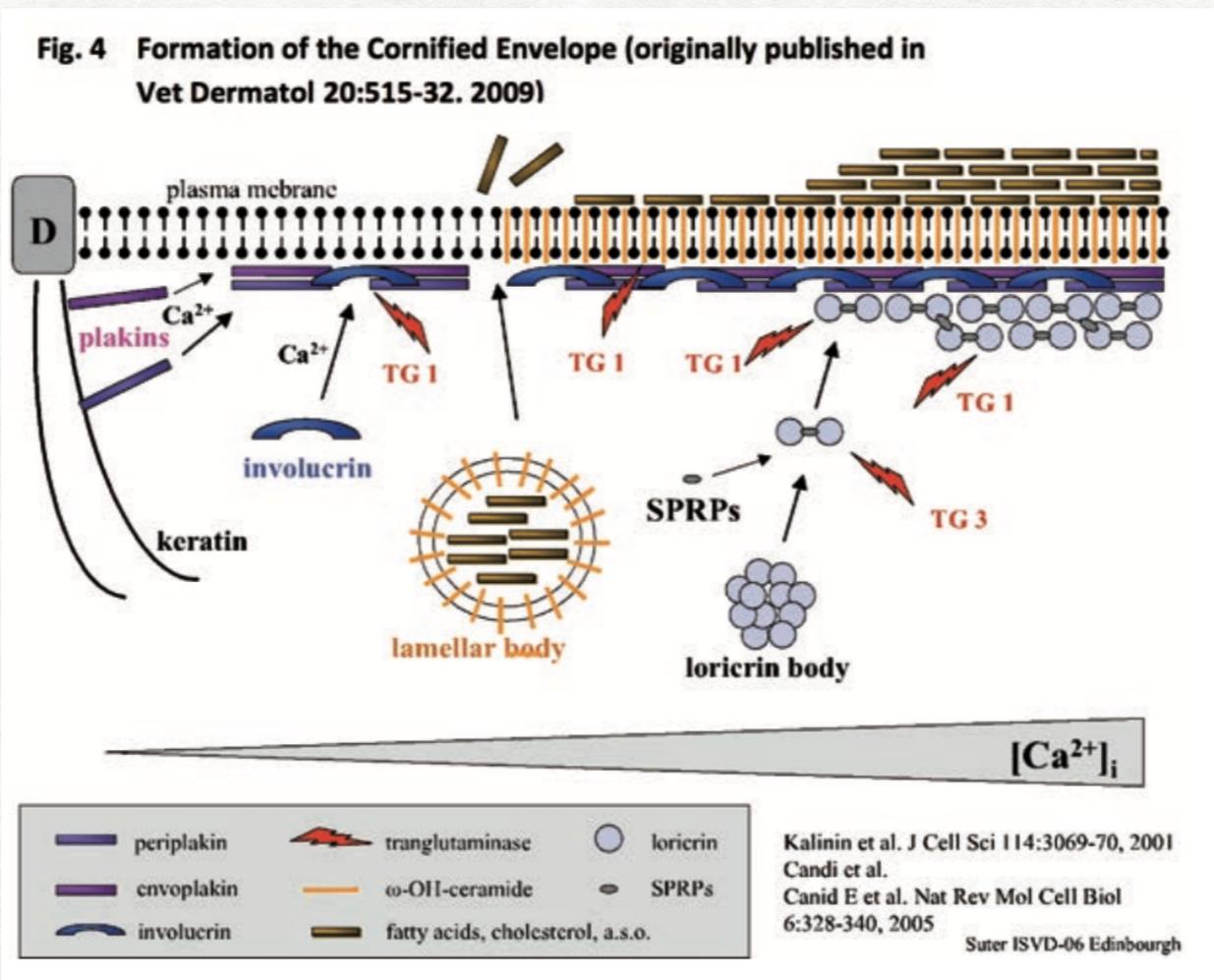
Kalinin et al. J Cell Sci 114:3069-70, 2001
 Candi et al.
 Canid E et al. Nat Rev Mol Cell Biol
 6:328-340, 2005

Suter ISVD-06 Edinburgh

Barrera Cutánea

Partes de Estudio

● Formación de la Envoltura Cornea



Barrera Cutánea

Partes de Estudio

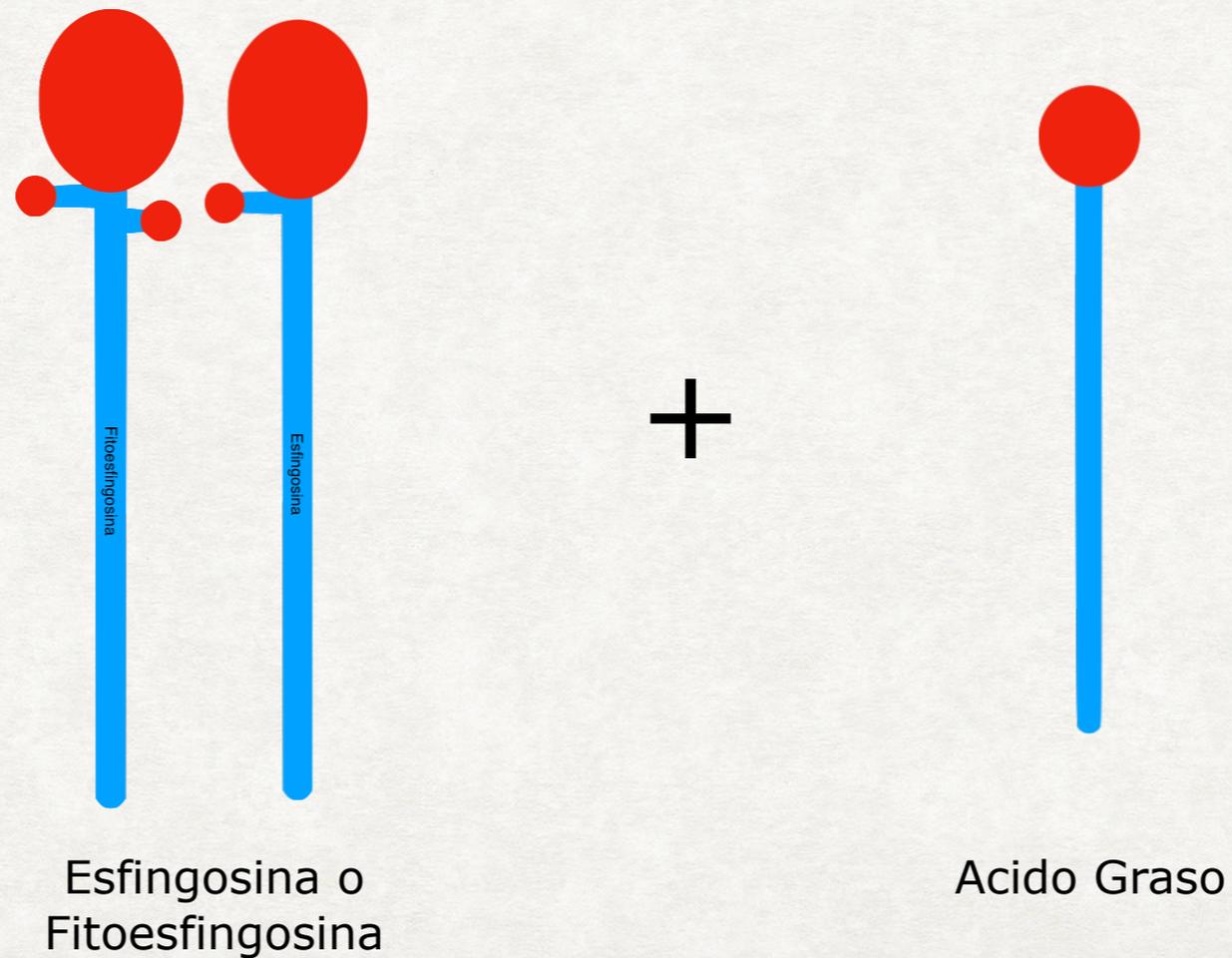
✓ Fisiología y Formación de la Barrera Cutánea

- Formación de la Envoltura Cornea
- Síntesis y Liberación de Ceramidas
- Degradación de la Membrana Celular
- Colapso Controlado del Citoesqueleto
- Síntesis y Secreción de Cuerpos Laminares
- Maduración y Descamación del Estrato Corneo

Barrera Cutánea

Partes de Estudio

- Síntesis y Liberación de Ceramidas

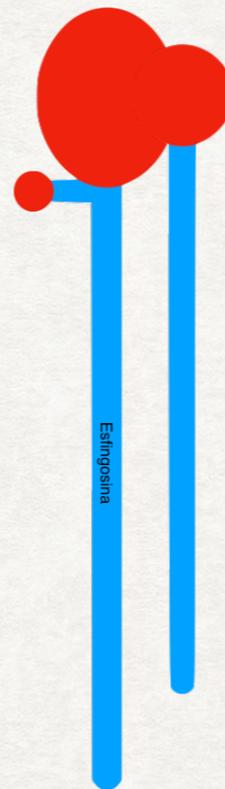


Barrera Cutánea

Partes de Estudio

- Síntesis y Liberación de Ceramidas

Ceramida

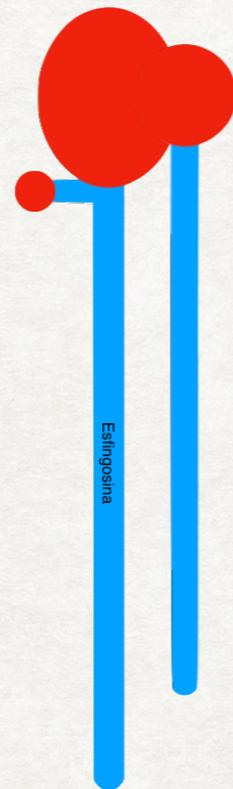


Barrera Cutánea

Partes de Estudio

- Síntesis y Liberación de Ceramidas

Ceramida



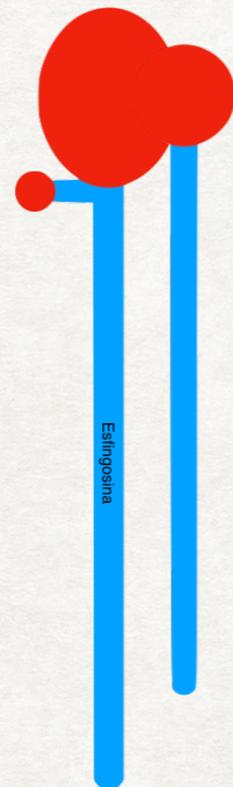
Forma Compacta

Barrera Cutánea

Partes de Estudio

- Síntesis y Liberación de Ceramidas

Ceramida



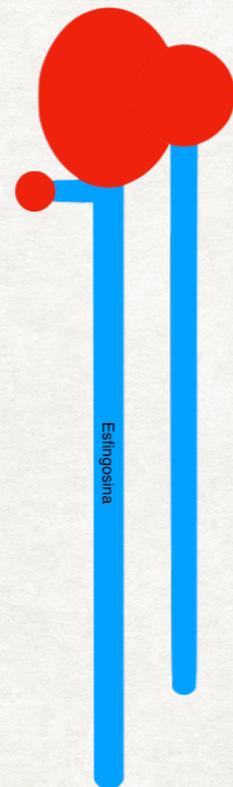
Forma Compacta

Barrera Cutánea

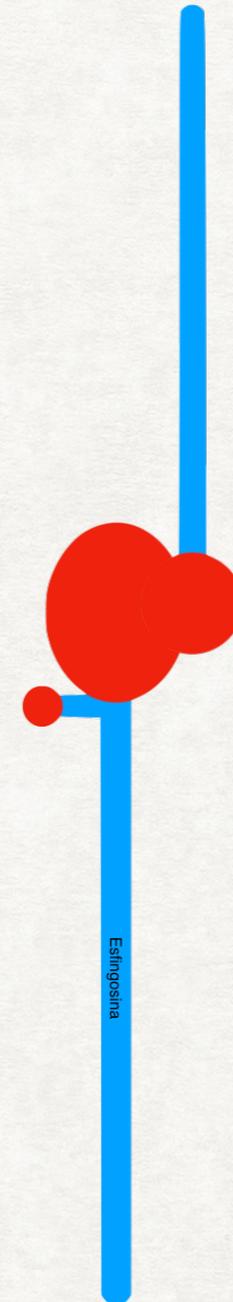
Partes de Estudio

- Síntesis y Liberación de Ceramidas

Ceramida



Forma Compacta

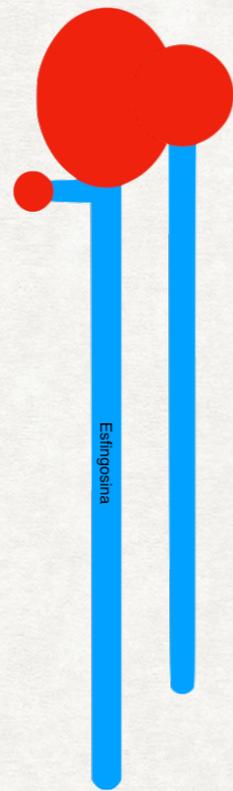


Forma Extendida

Barrera Cutánea

Partes de Estudio

- Síntesis y Liberación de Ceramidas



Ceramida



Glucosa

Barrera Cutánea

Partes de Estudio

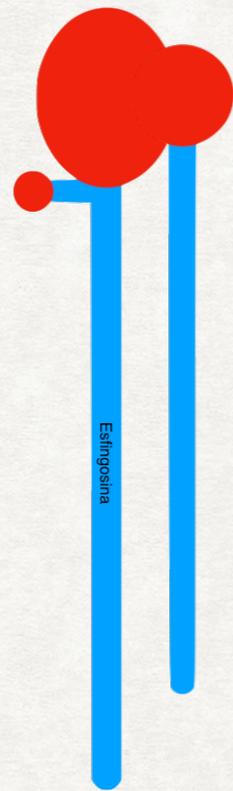
- Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

- Síntesis y Liberación de Ceramidas



Ceramida



Colina

Barrera Cutánea

Partes de Estudio

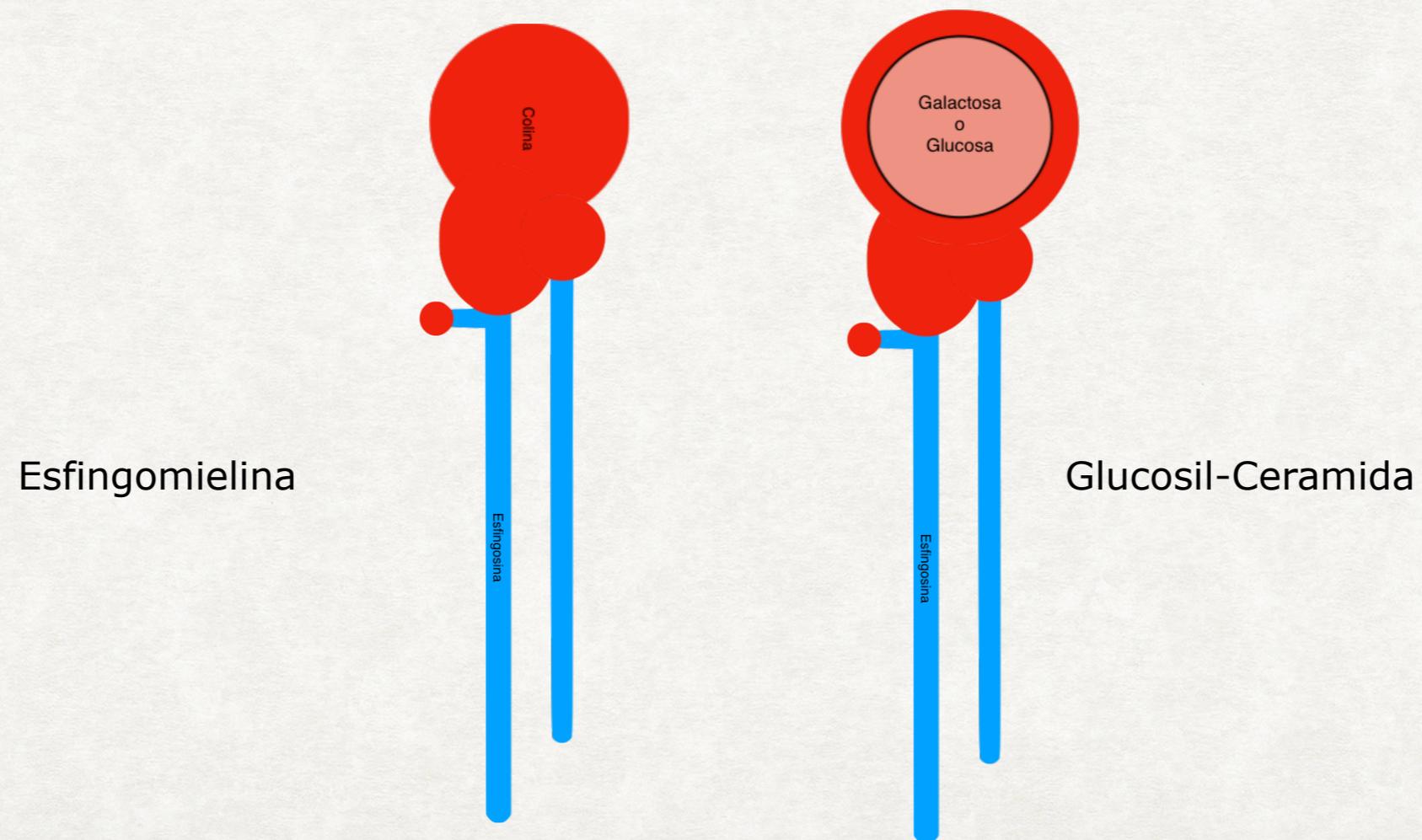
- Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

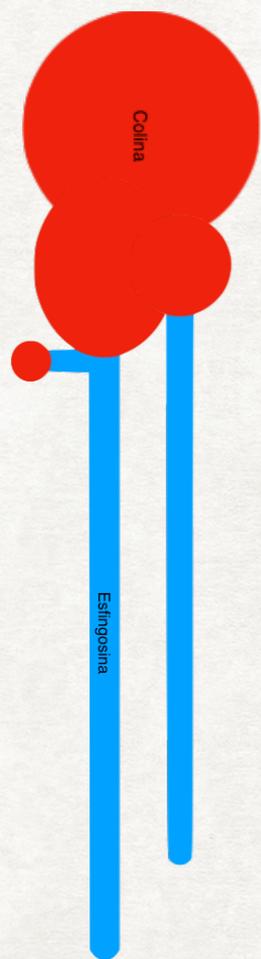
- Síntesis y Liberación de Ceramidas



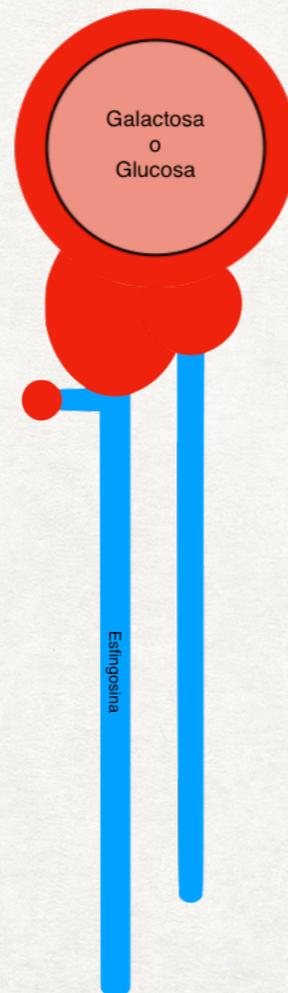
Barrera Cutánea

Partes de Estudio

● Síntesis y Liberación de Ceramidas



Esfingomielina



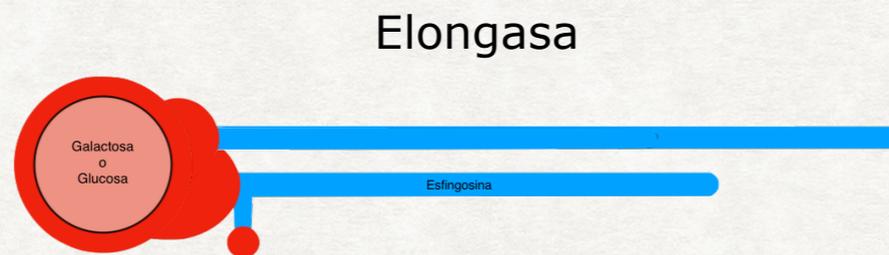
Glucosil-Ceramida

Formas *Inactivas*
(Compactas)

Barrera Cutánea

Partes de Estudio

- Síntesis y Liberación de Ceramidas

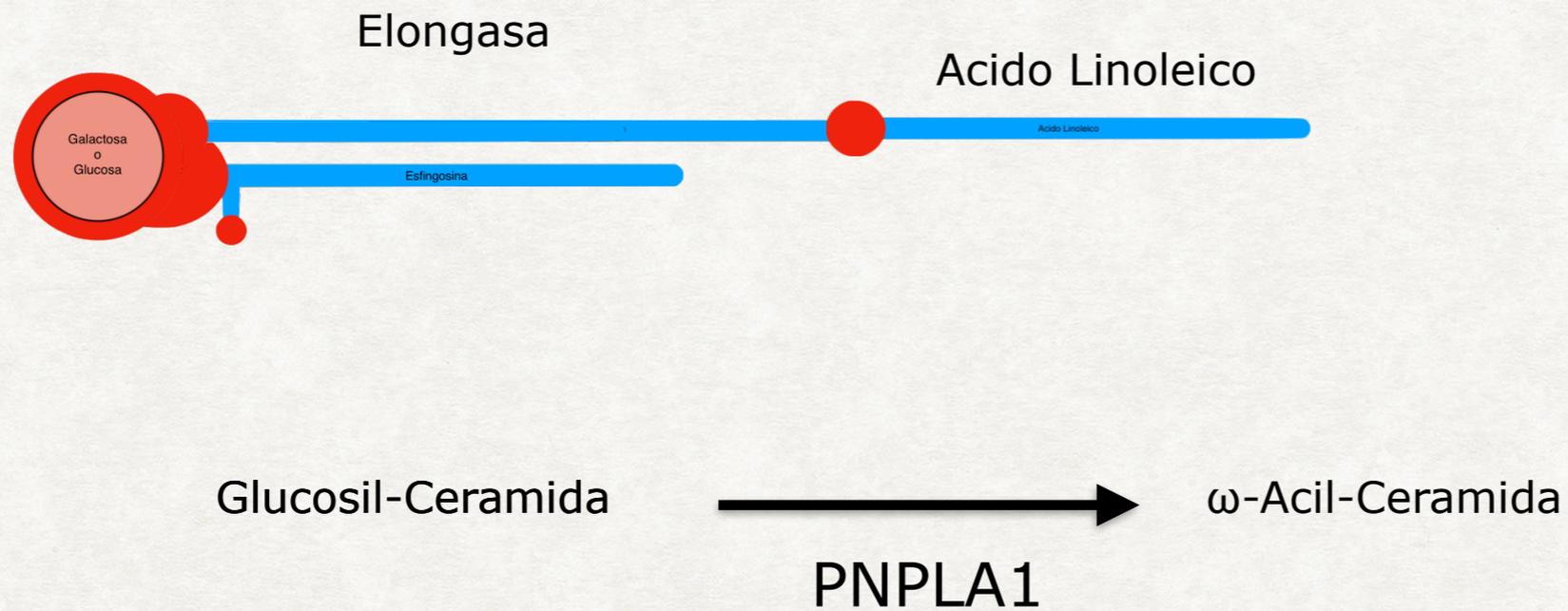


Glucosil-Ceramida

Barrera Cutánea

Partes de Estudio

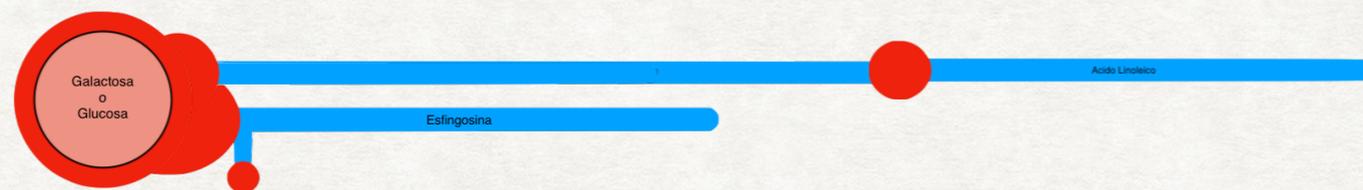
- Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

- Síntesis y Liberación de Ceramidas



ω -Acil-Ceramida

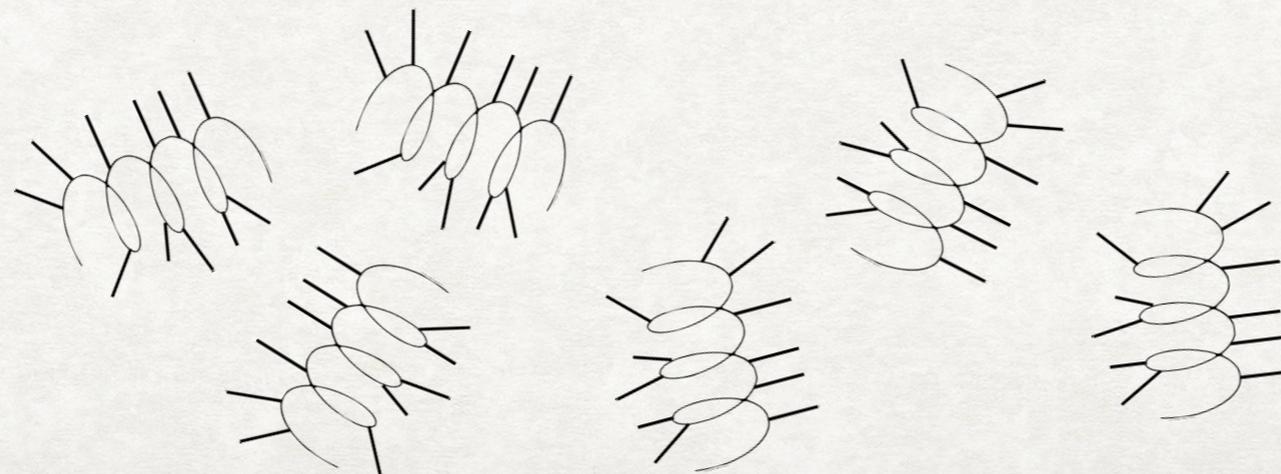
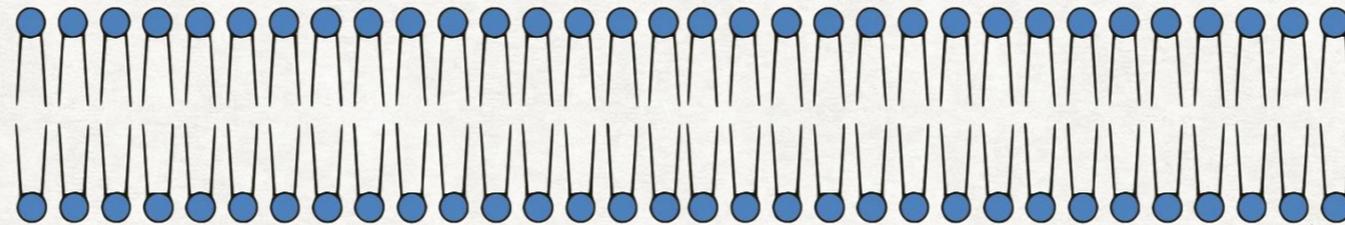


Envoltura Corneo Lipídica (CLE)

Barrera Cutánea

Partes de Estudio

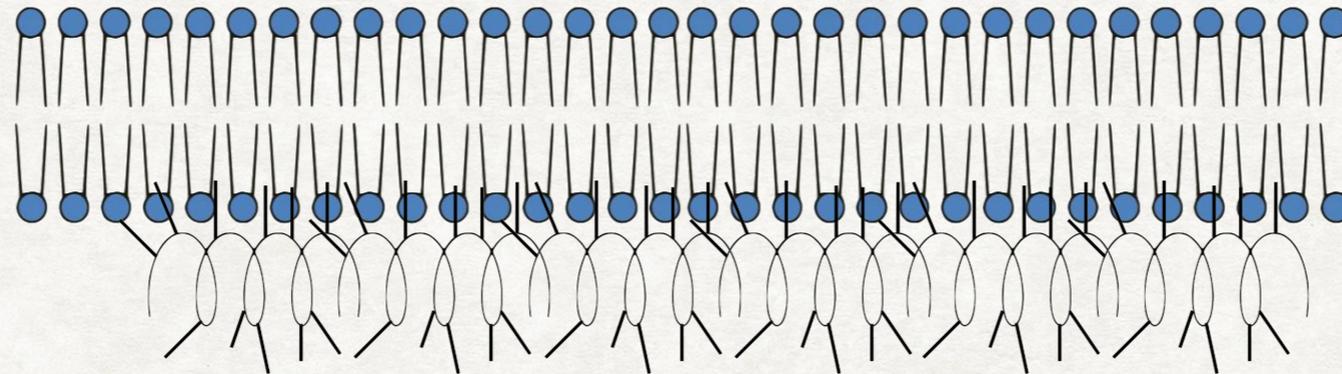
- Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

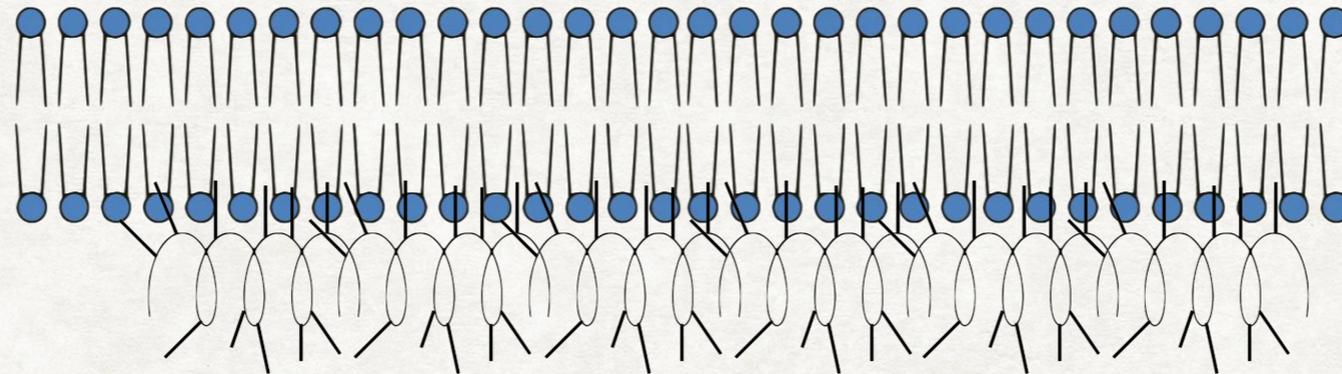
- Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

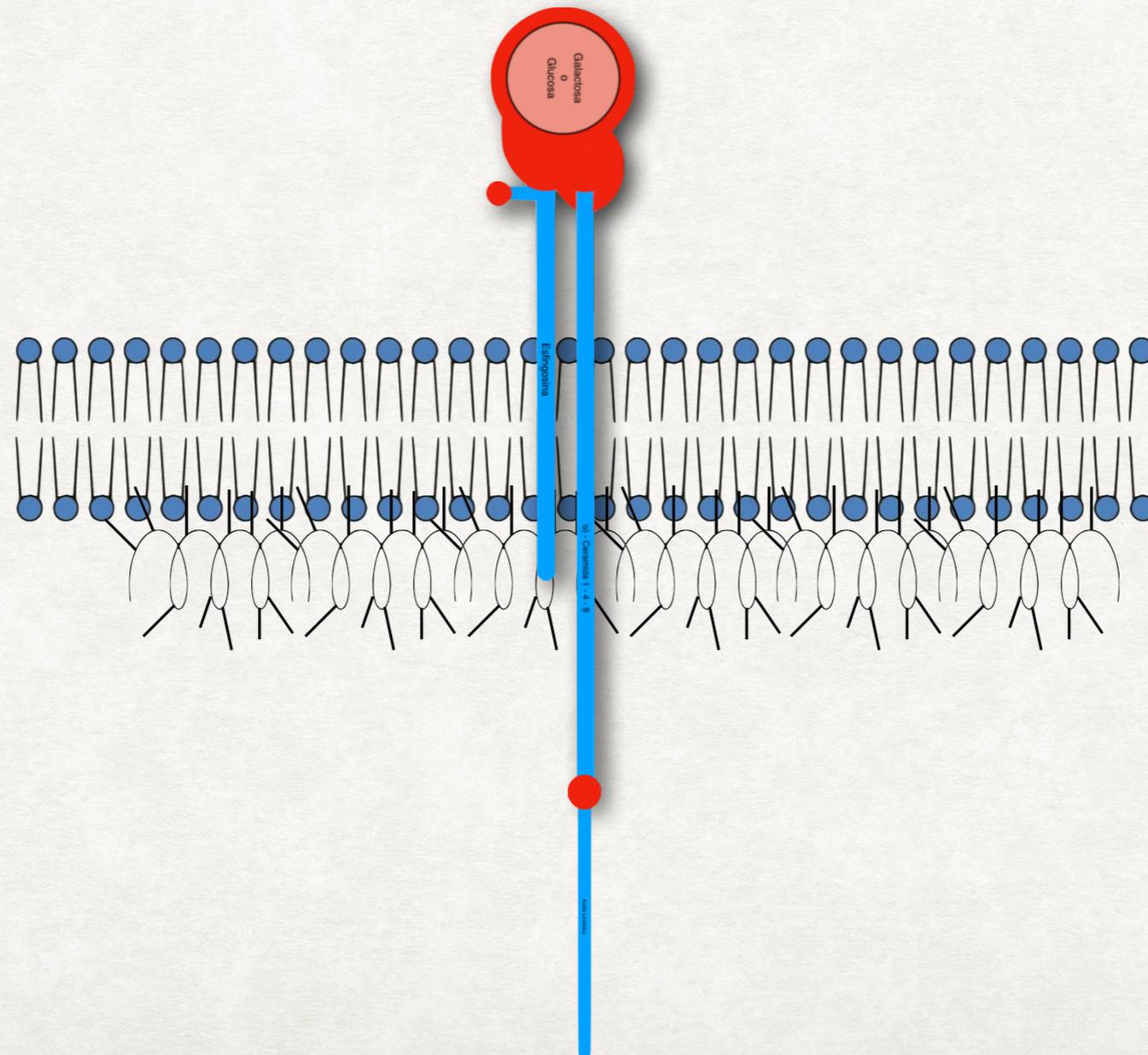
- Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

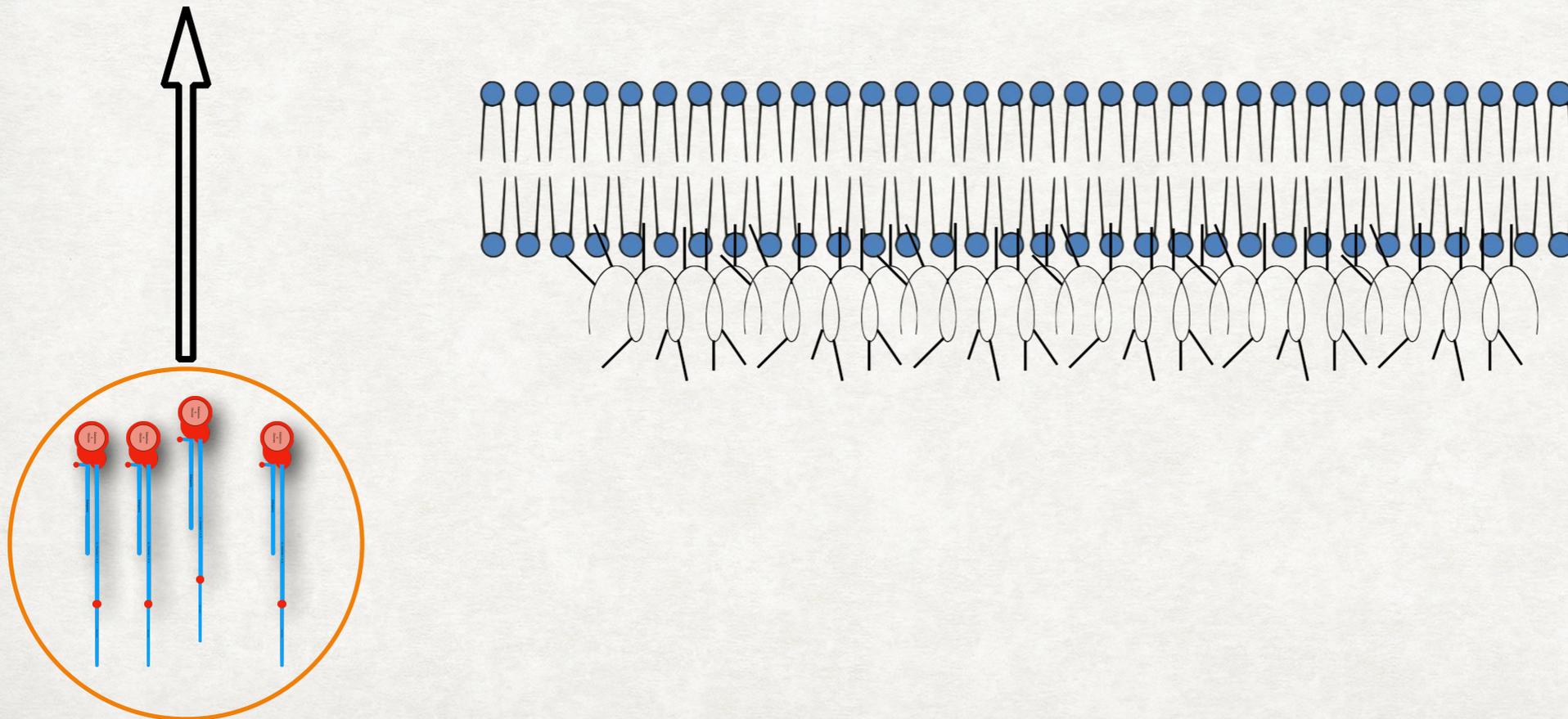
- Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

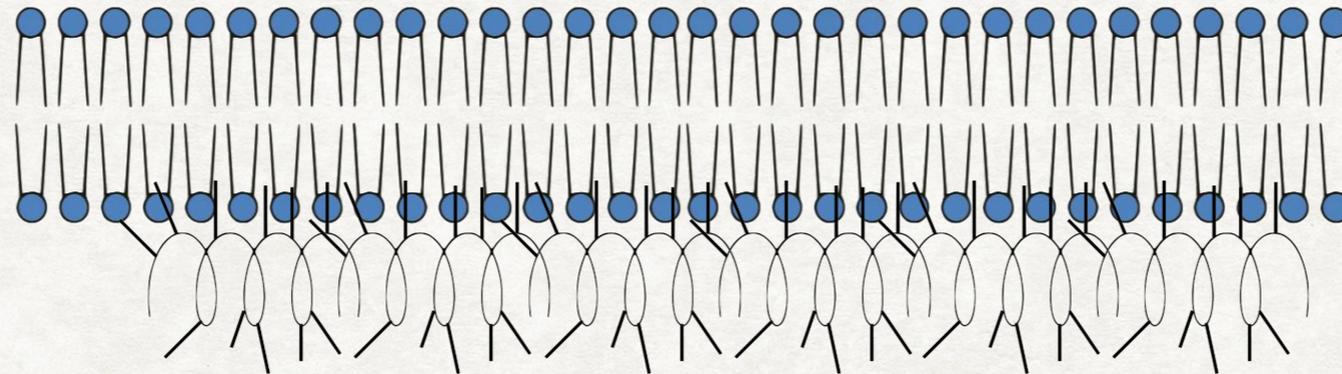
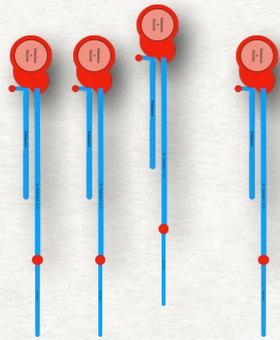
- Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

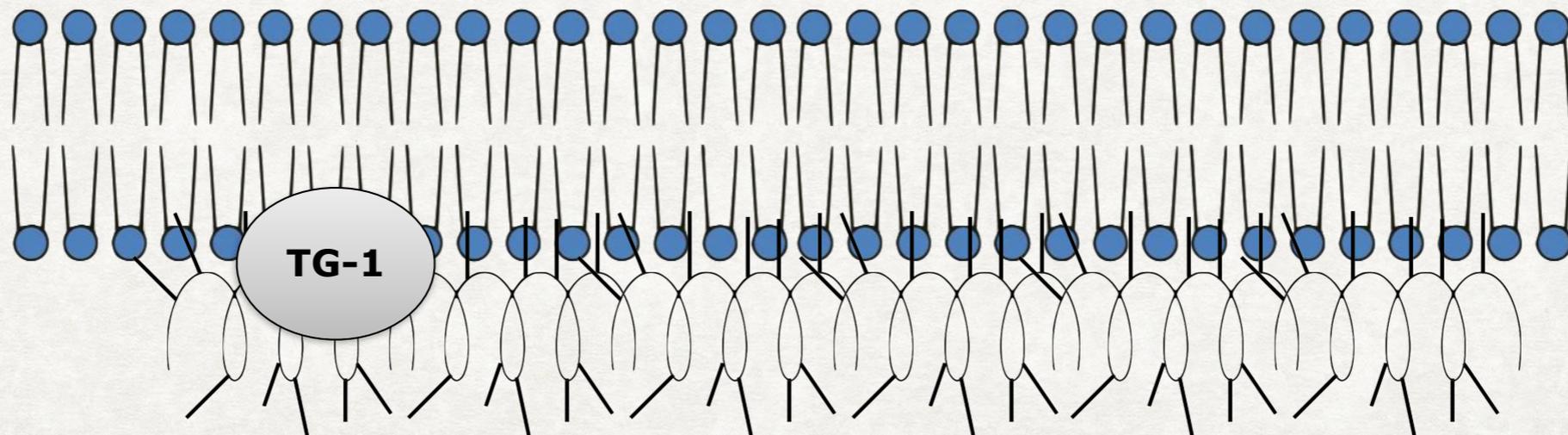
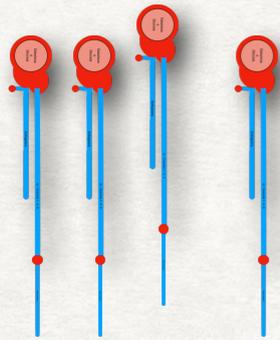
● Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

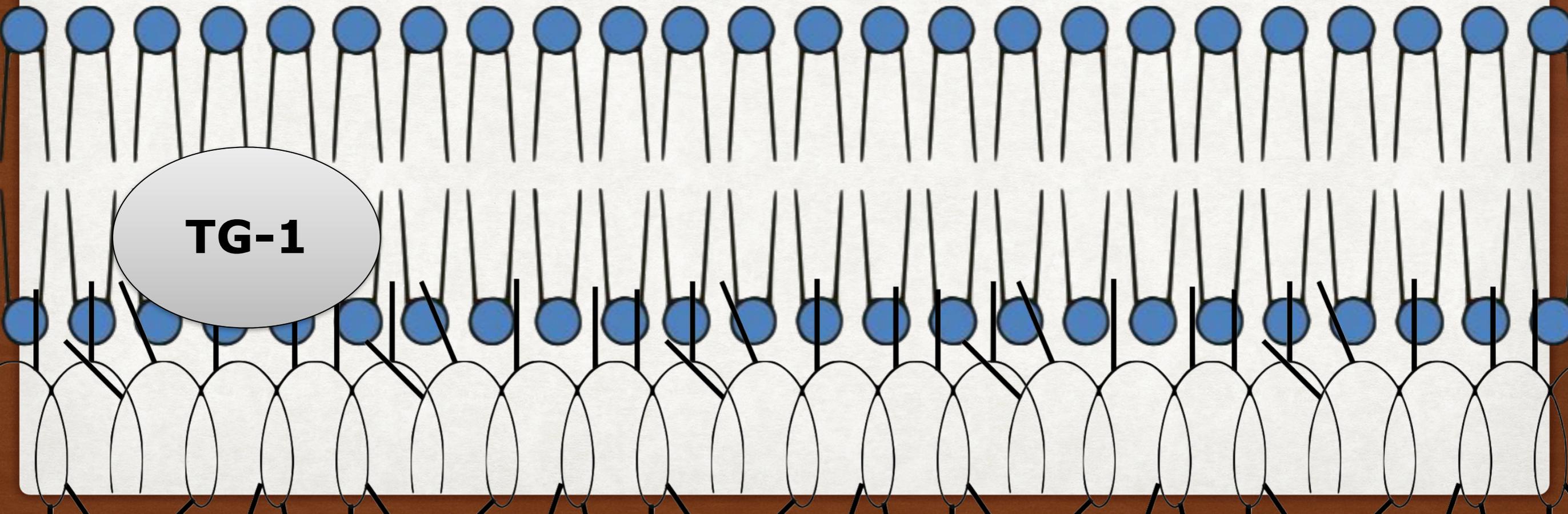
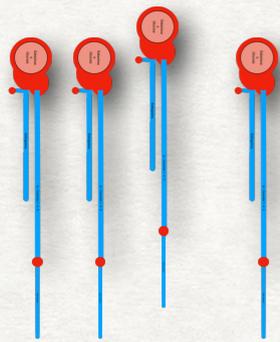
● Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

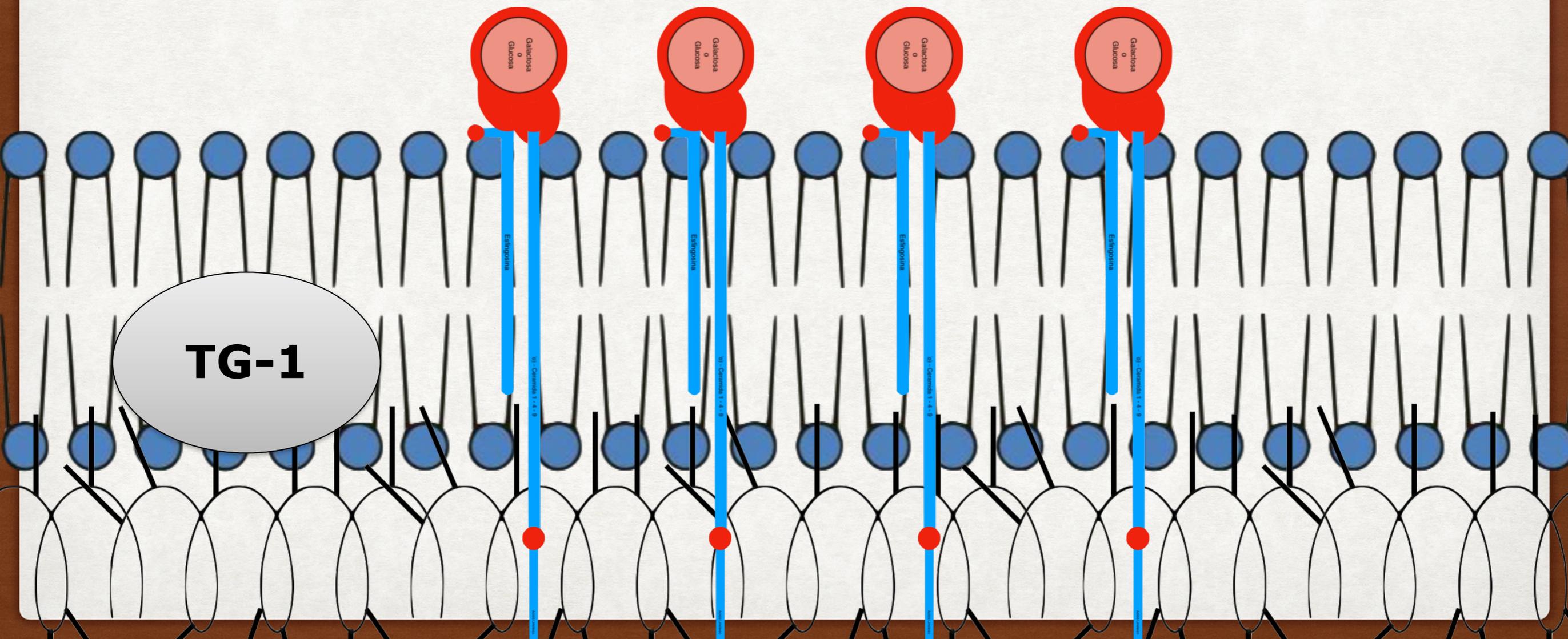
● Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

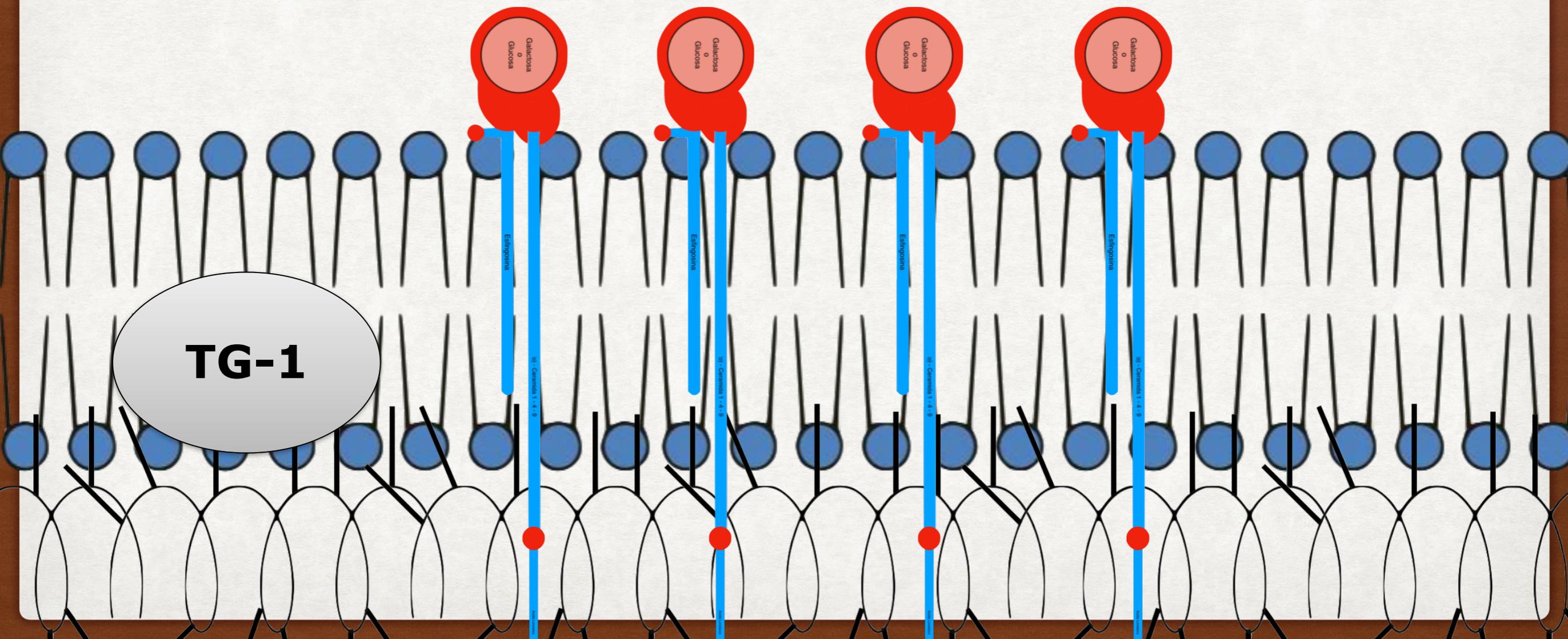
● Síntesis y Liberación de Ceramidas



Barrera Cutánea

Partes de Estudio

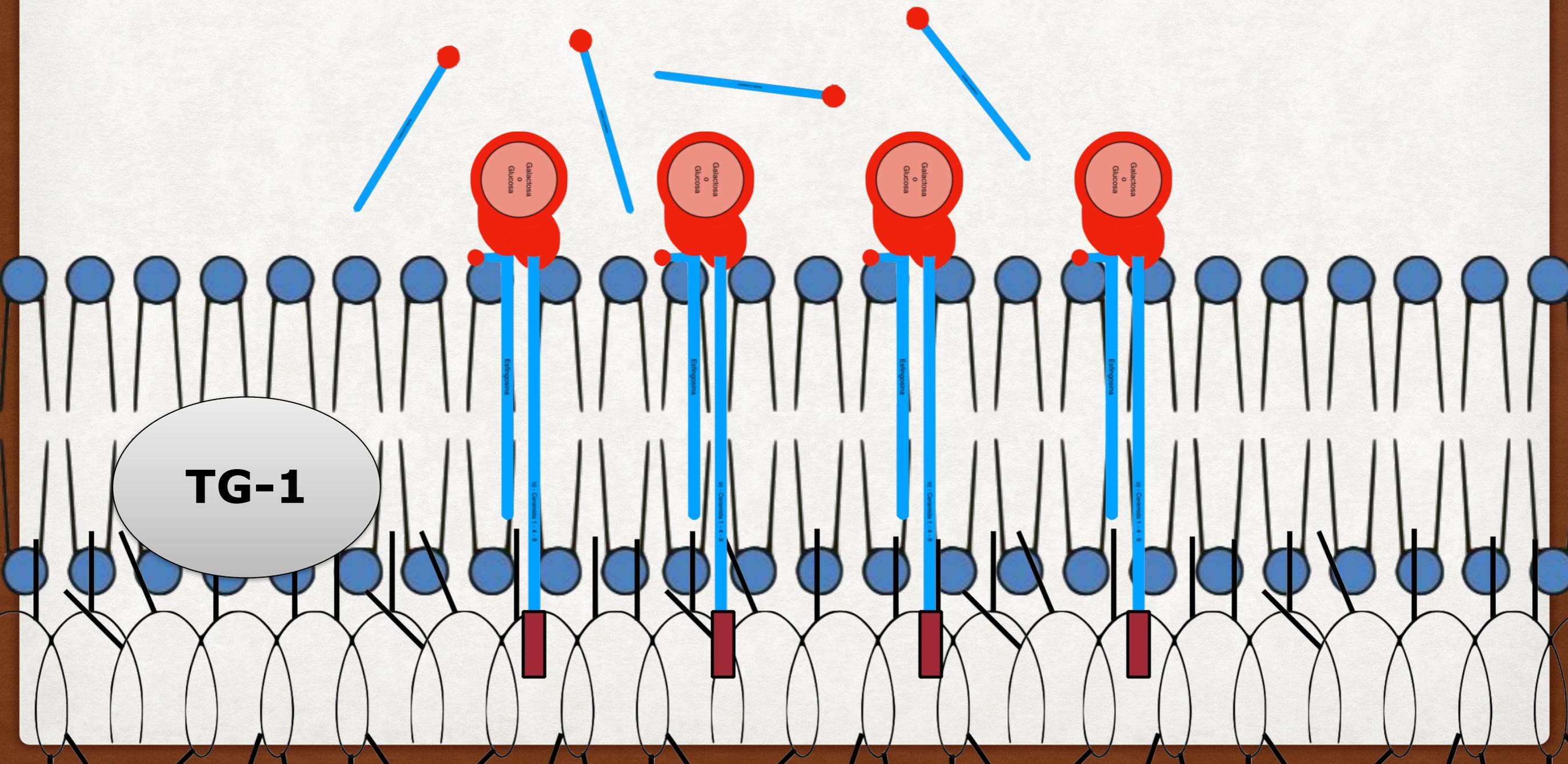
● Síntesis y Liberación de Ceramidas



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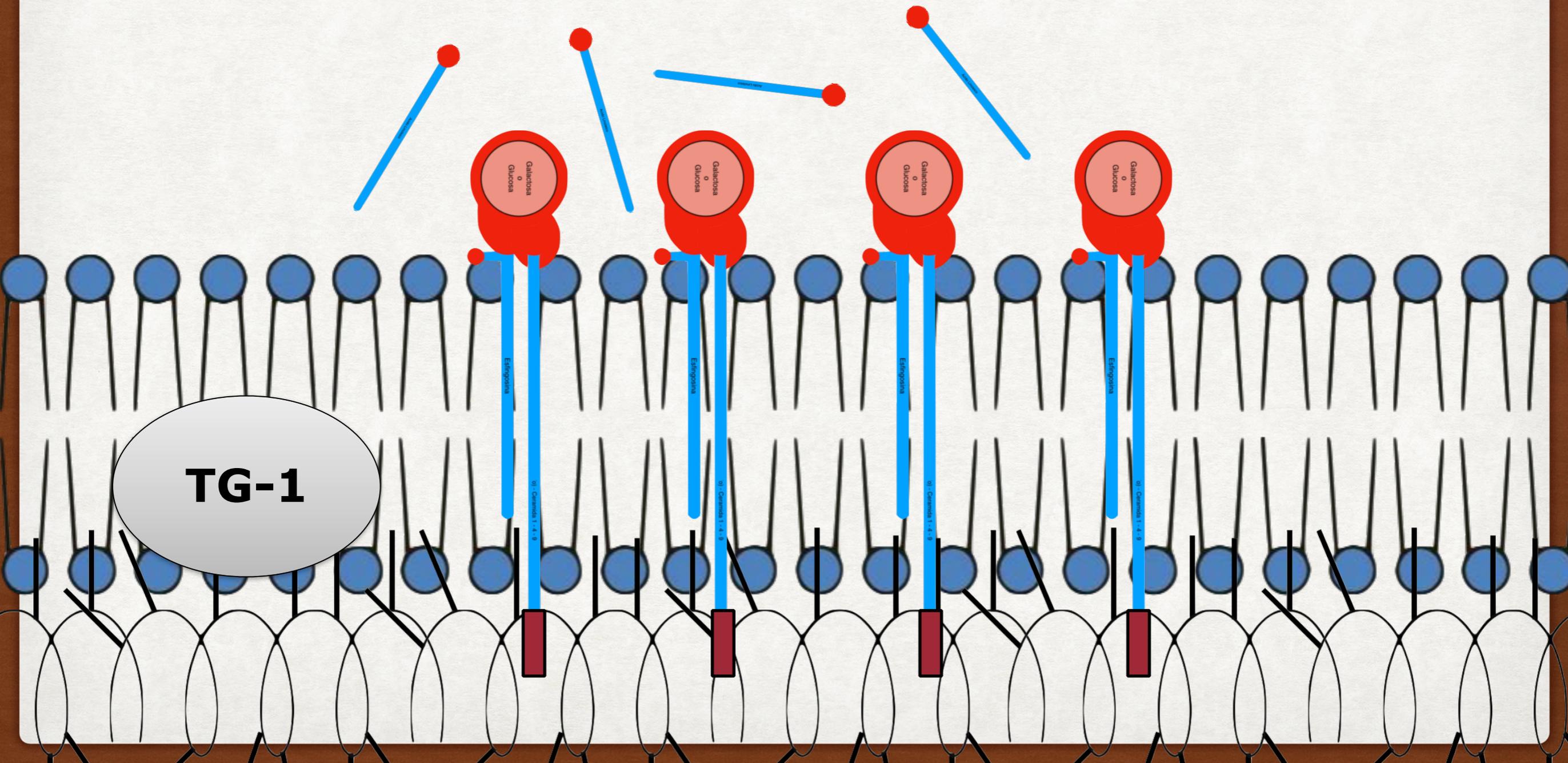
● Síntesis y Liberación de Ceramidas



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Partes de Estudio

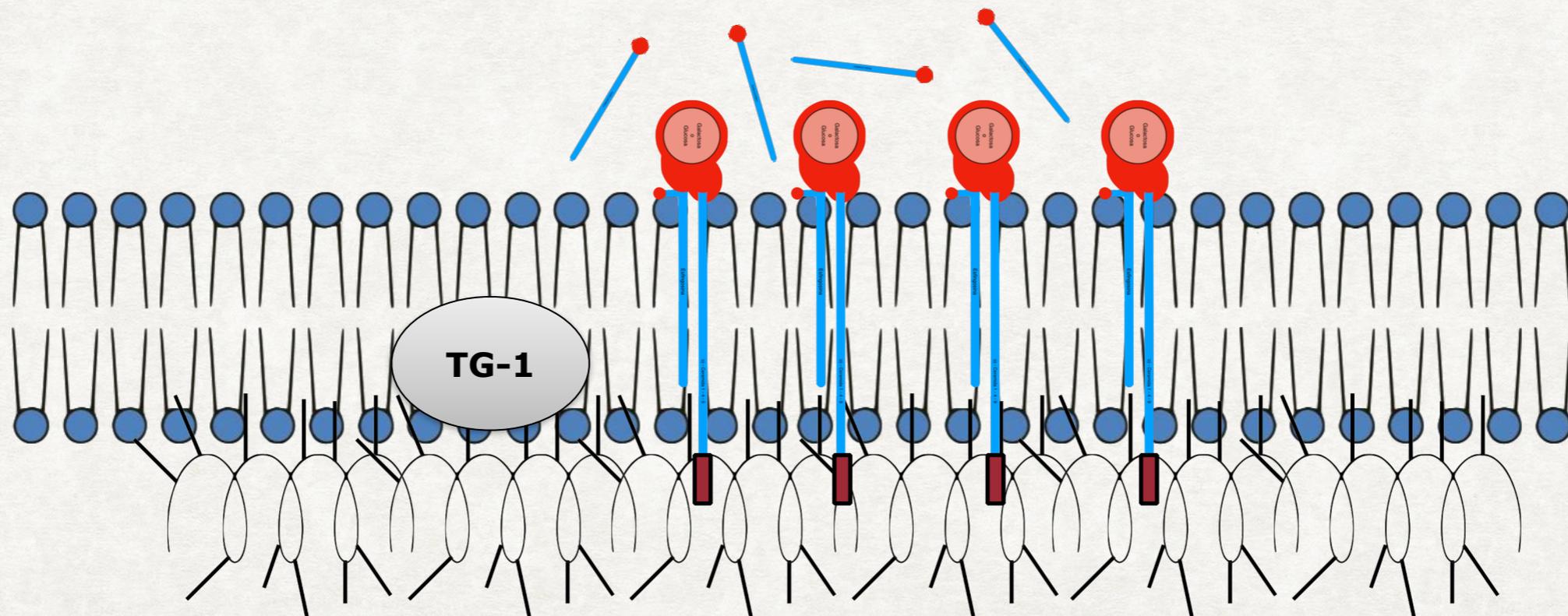
● Síntesis y Liberación de Ceramidas



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Partes de Estudio

- Síntesis y Liberación de Ceramidas

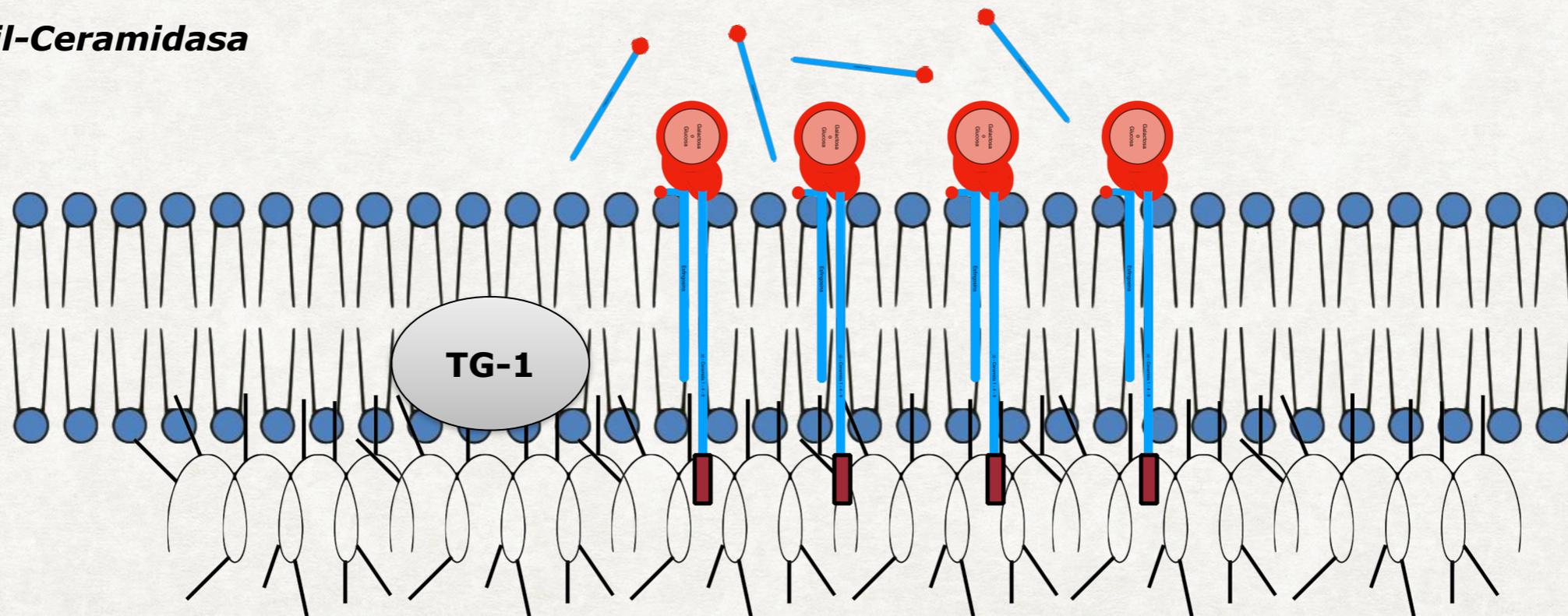


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- Síntesis y Liberación de Ceramidas

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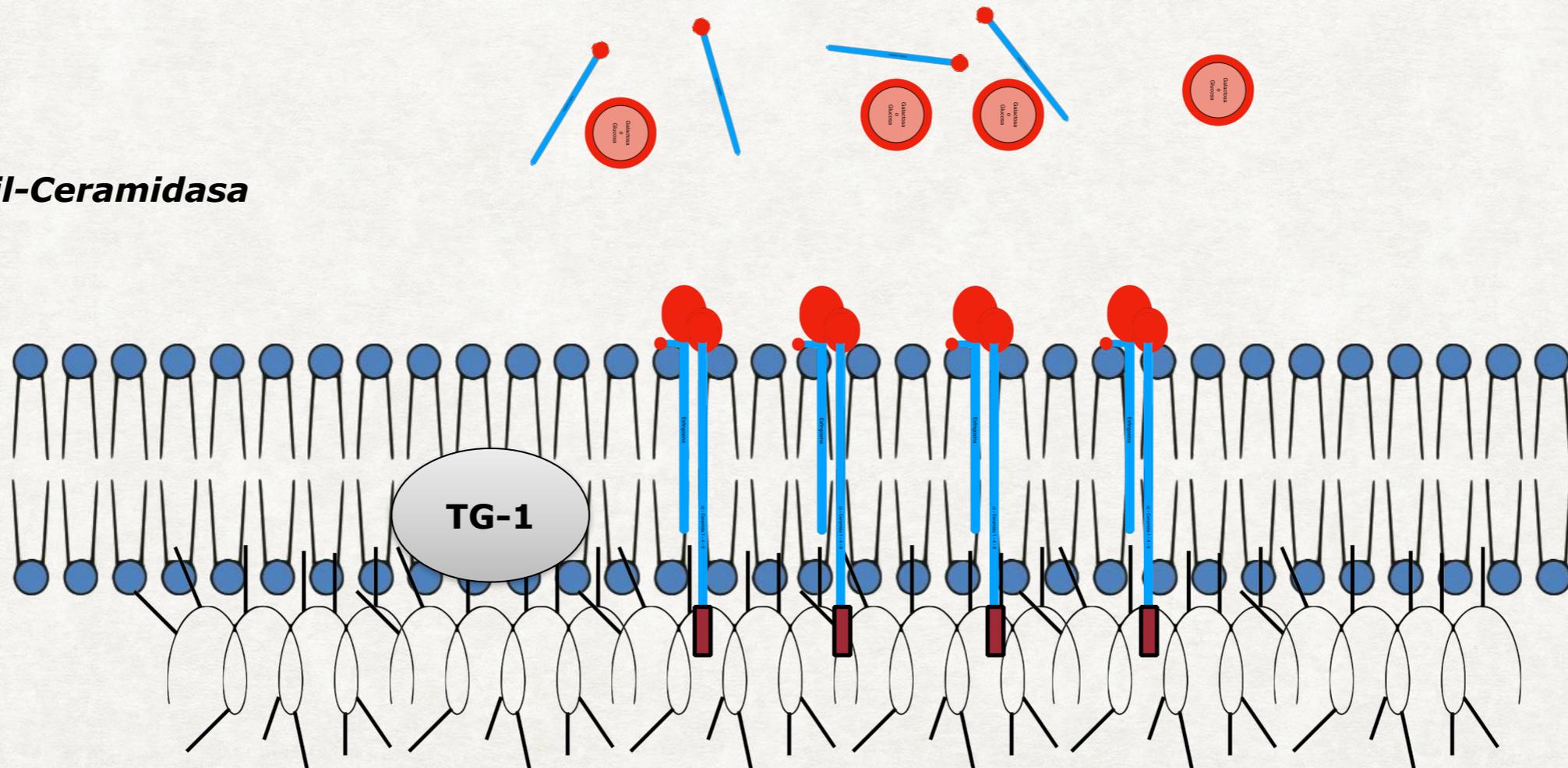


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Partes de Estudio

- Síntesis y Liberación de Ceramidas

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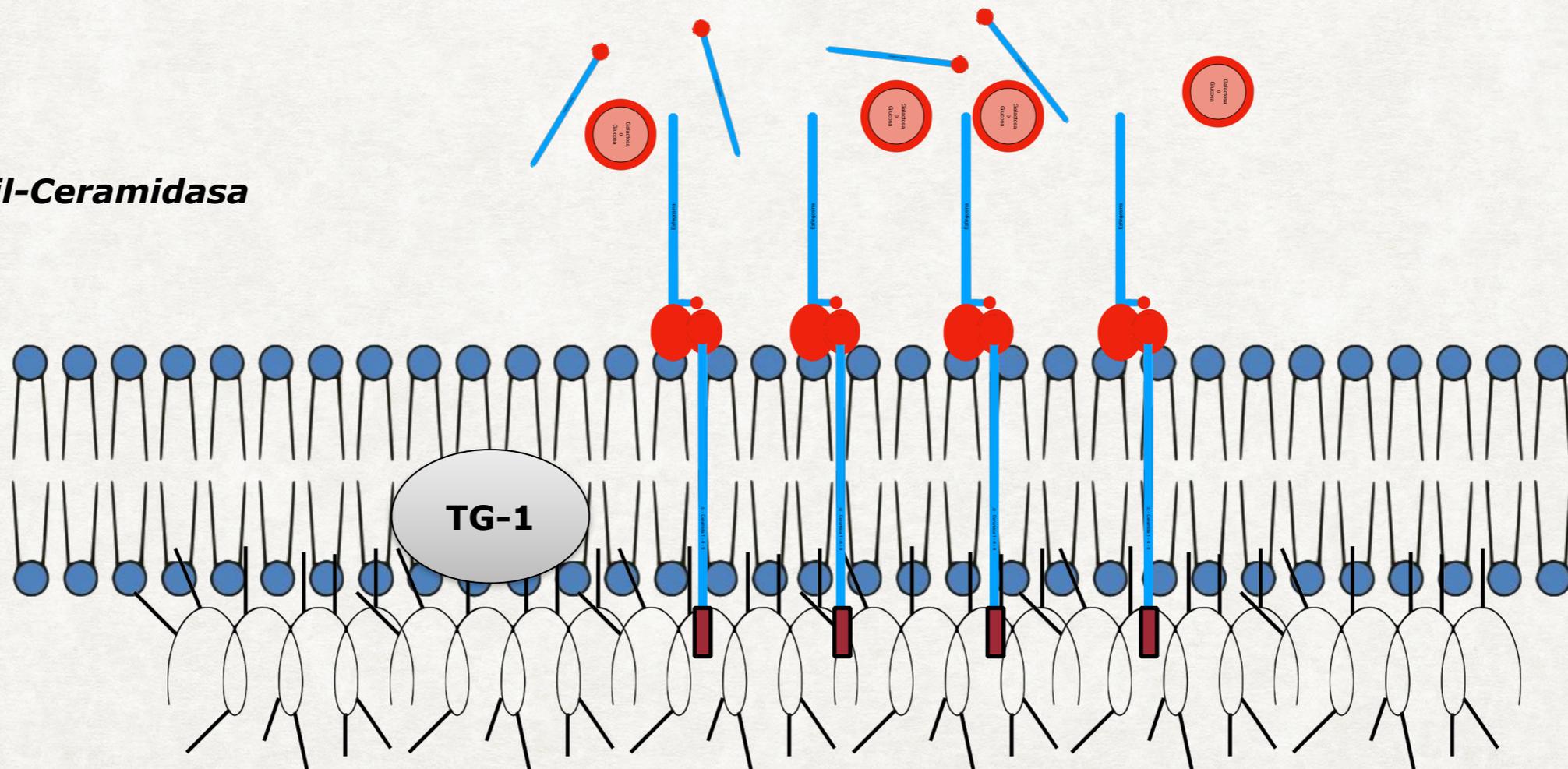


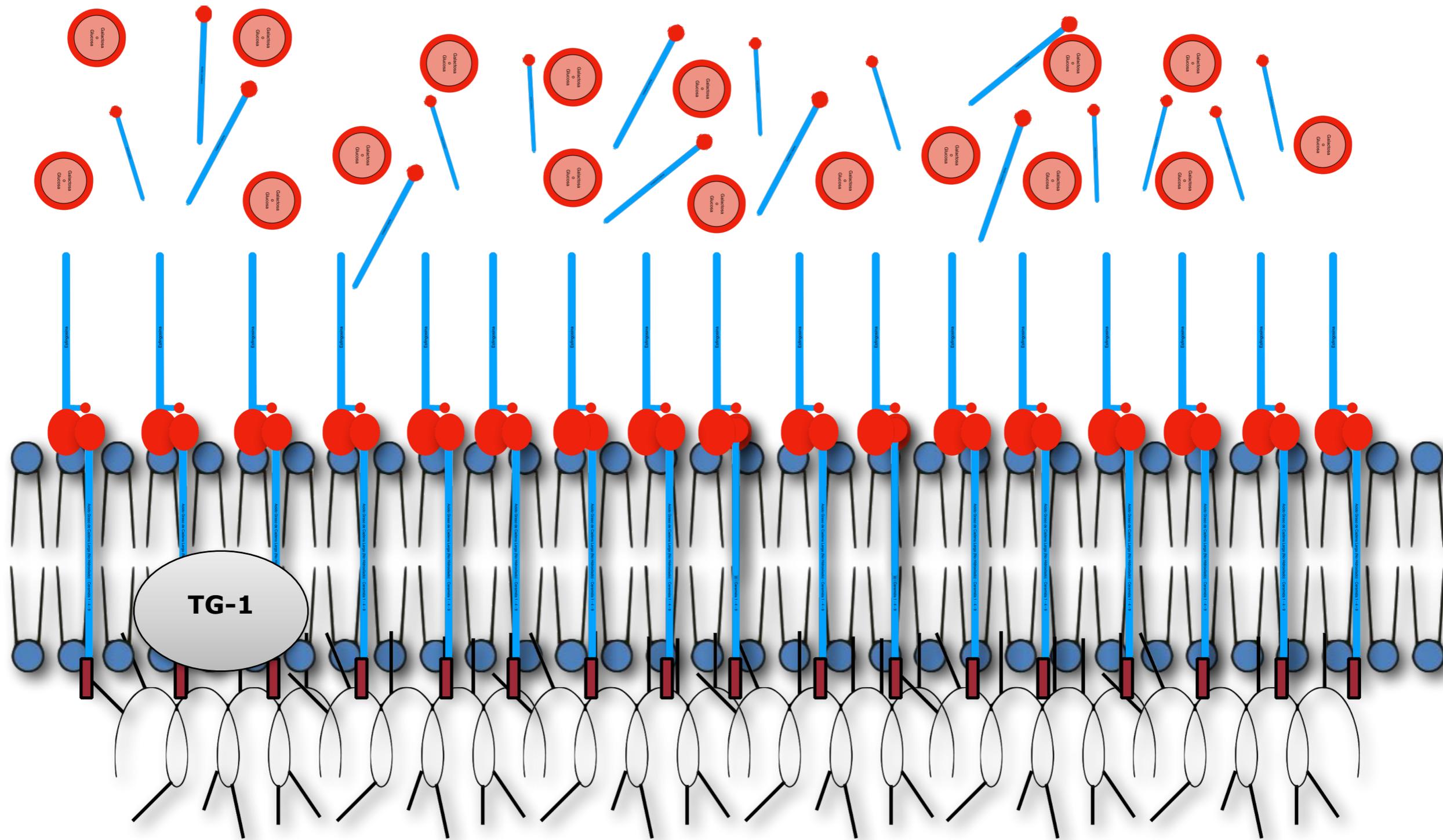
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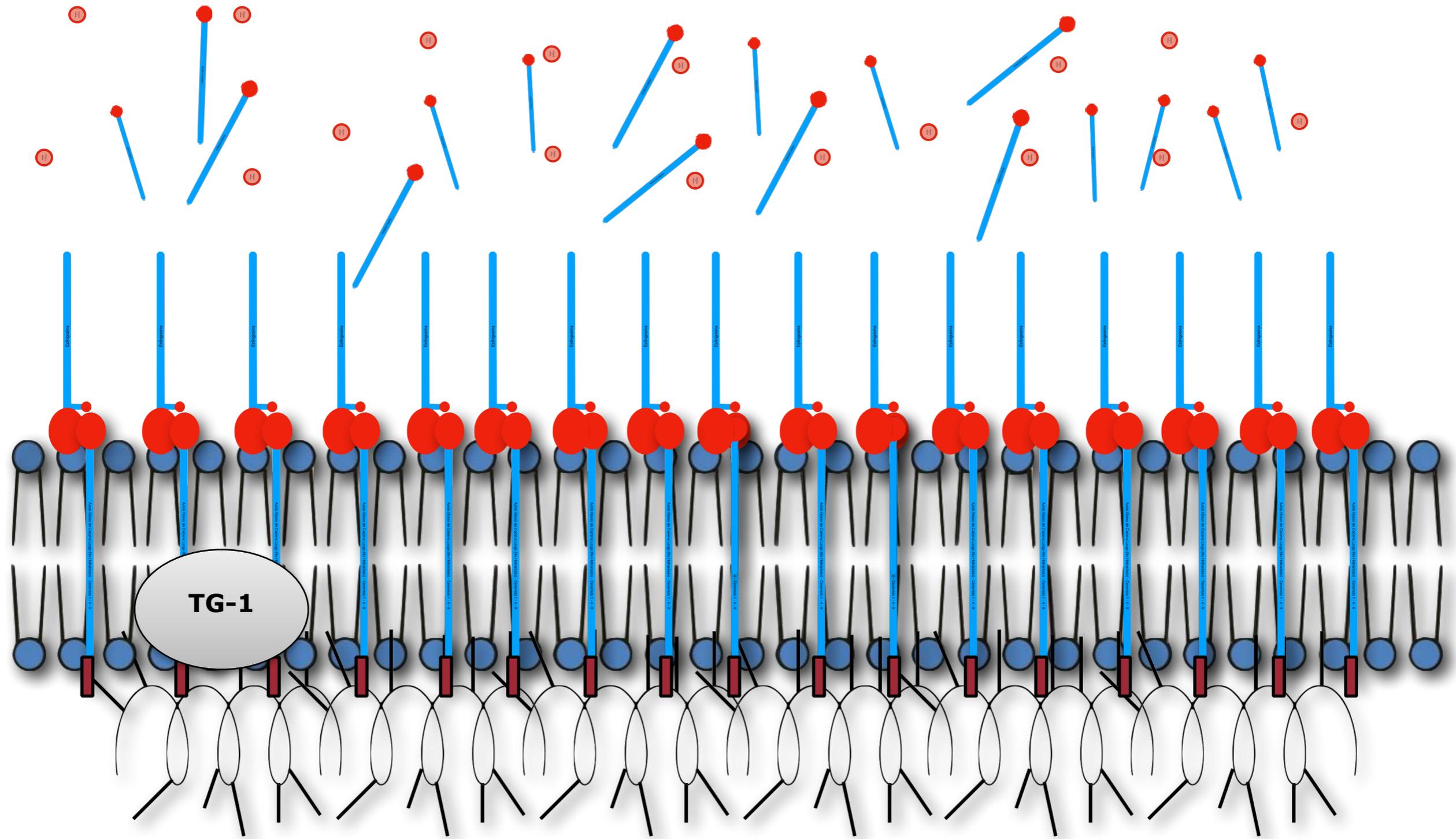
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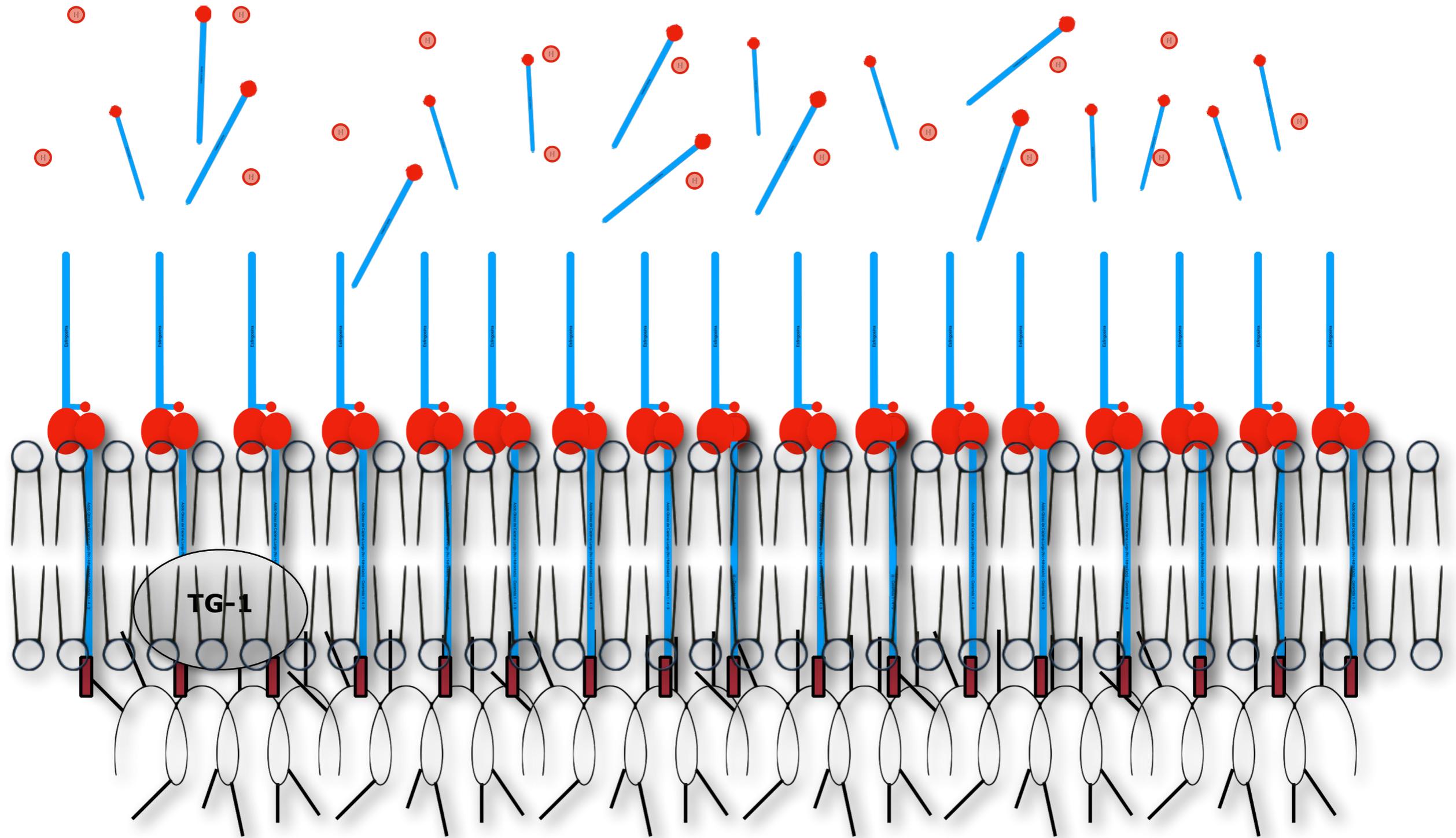
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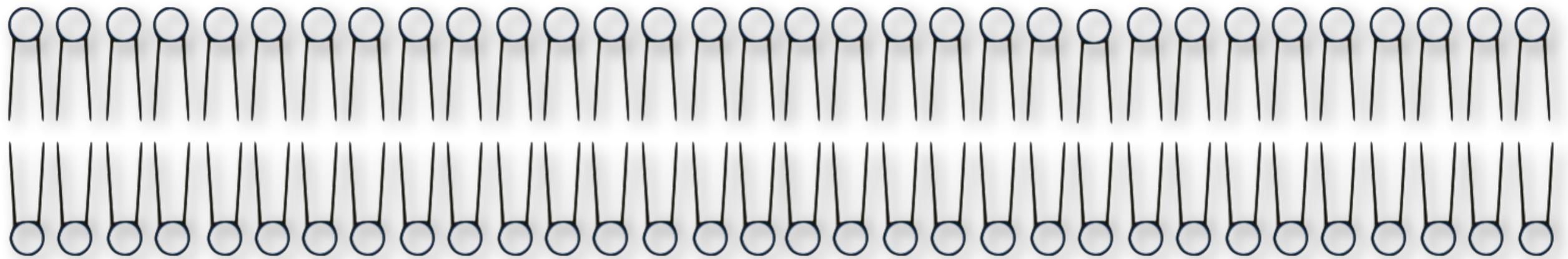
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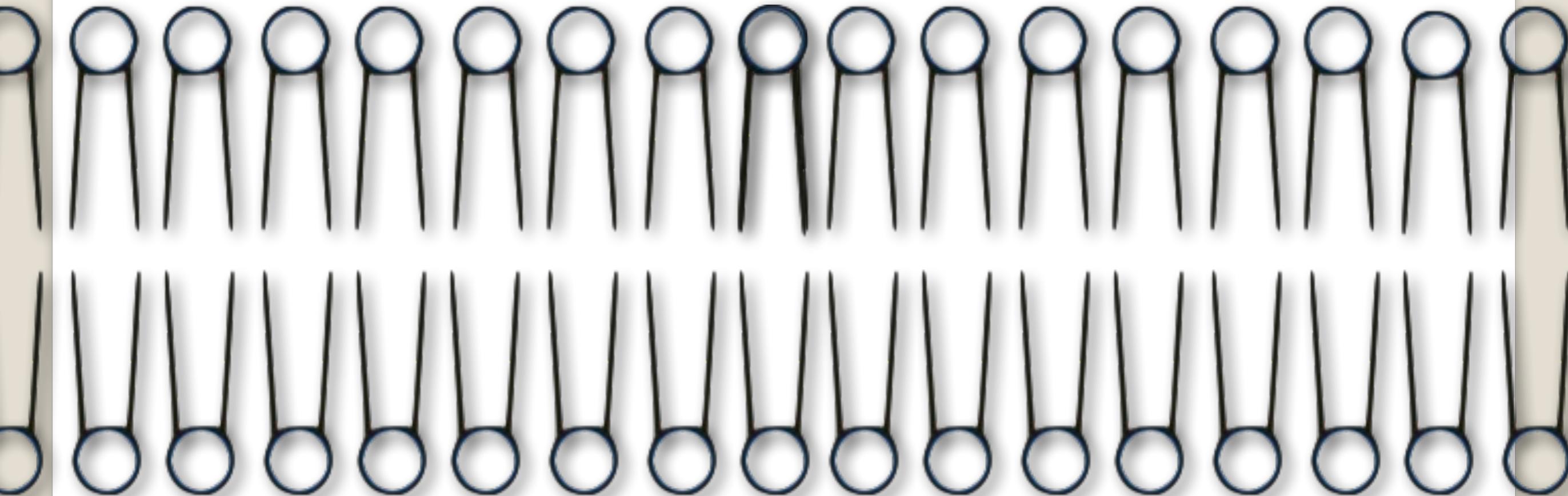




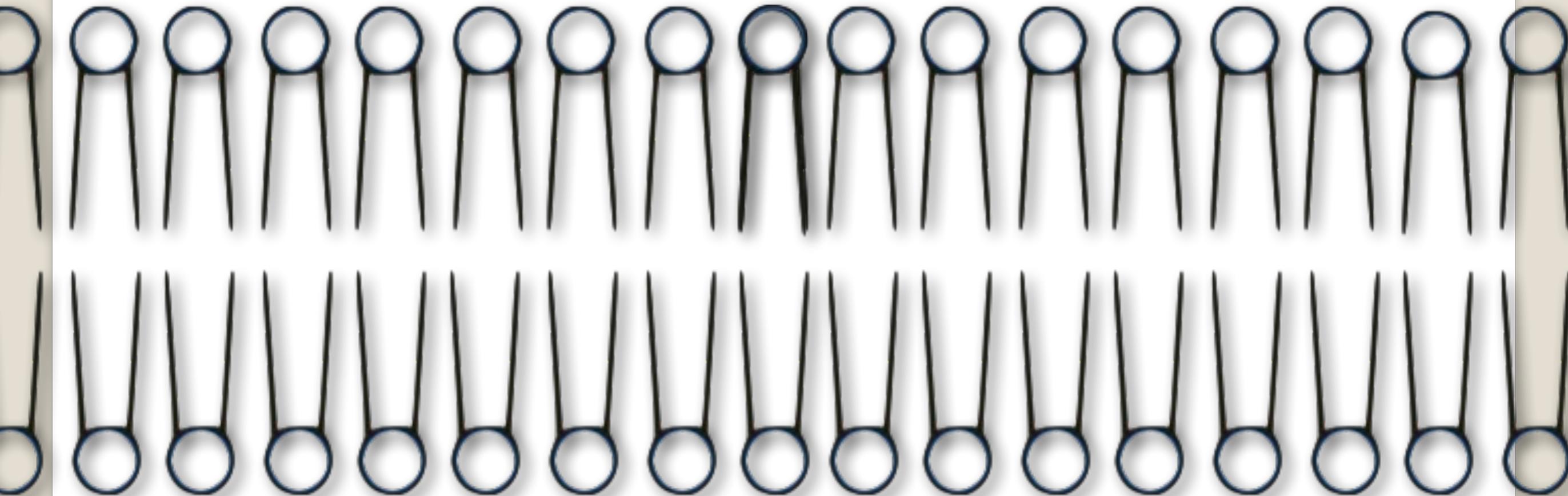






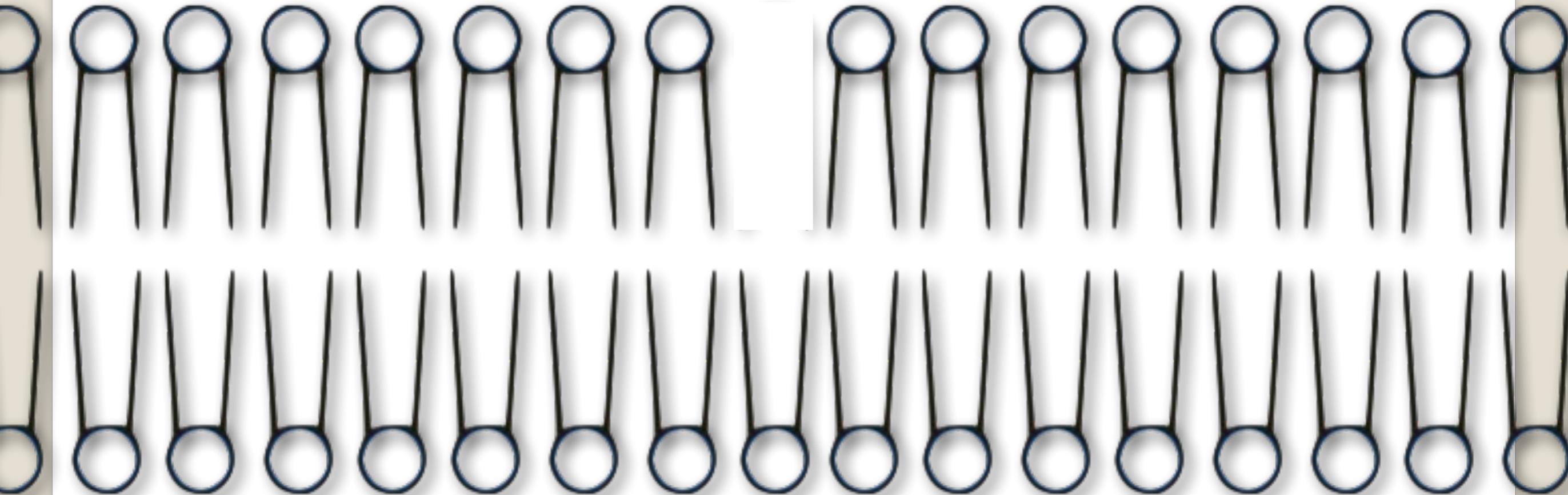


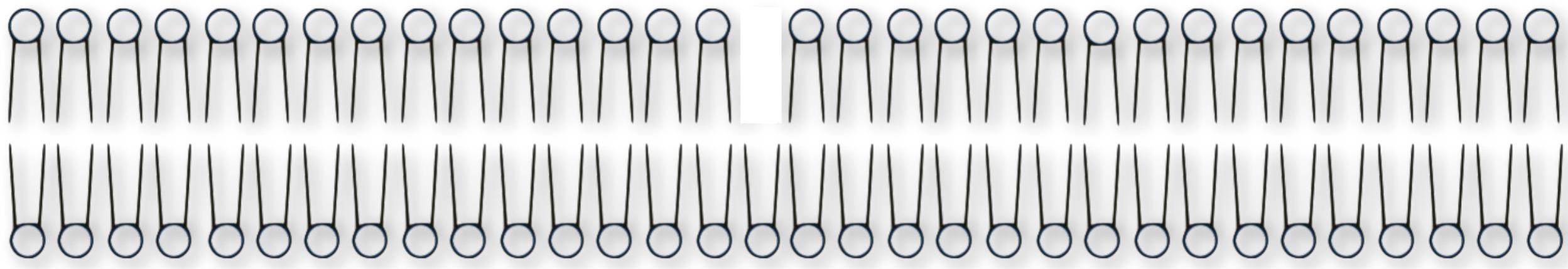
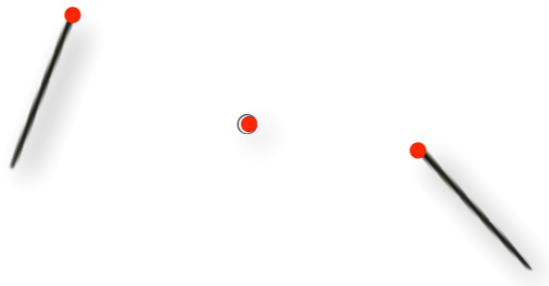
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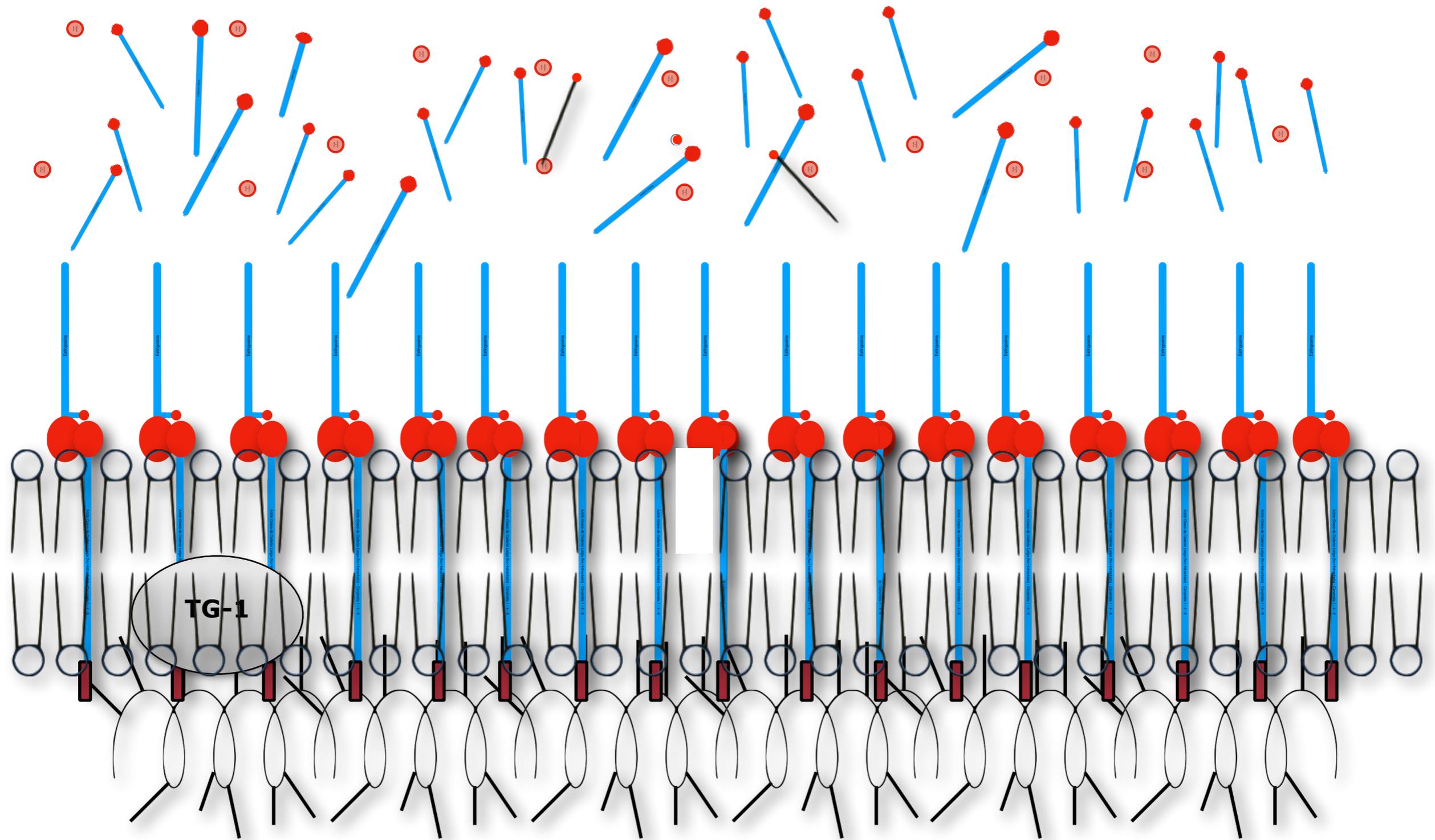


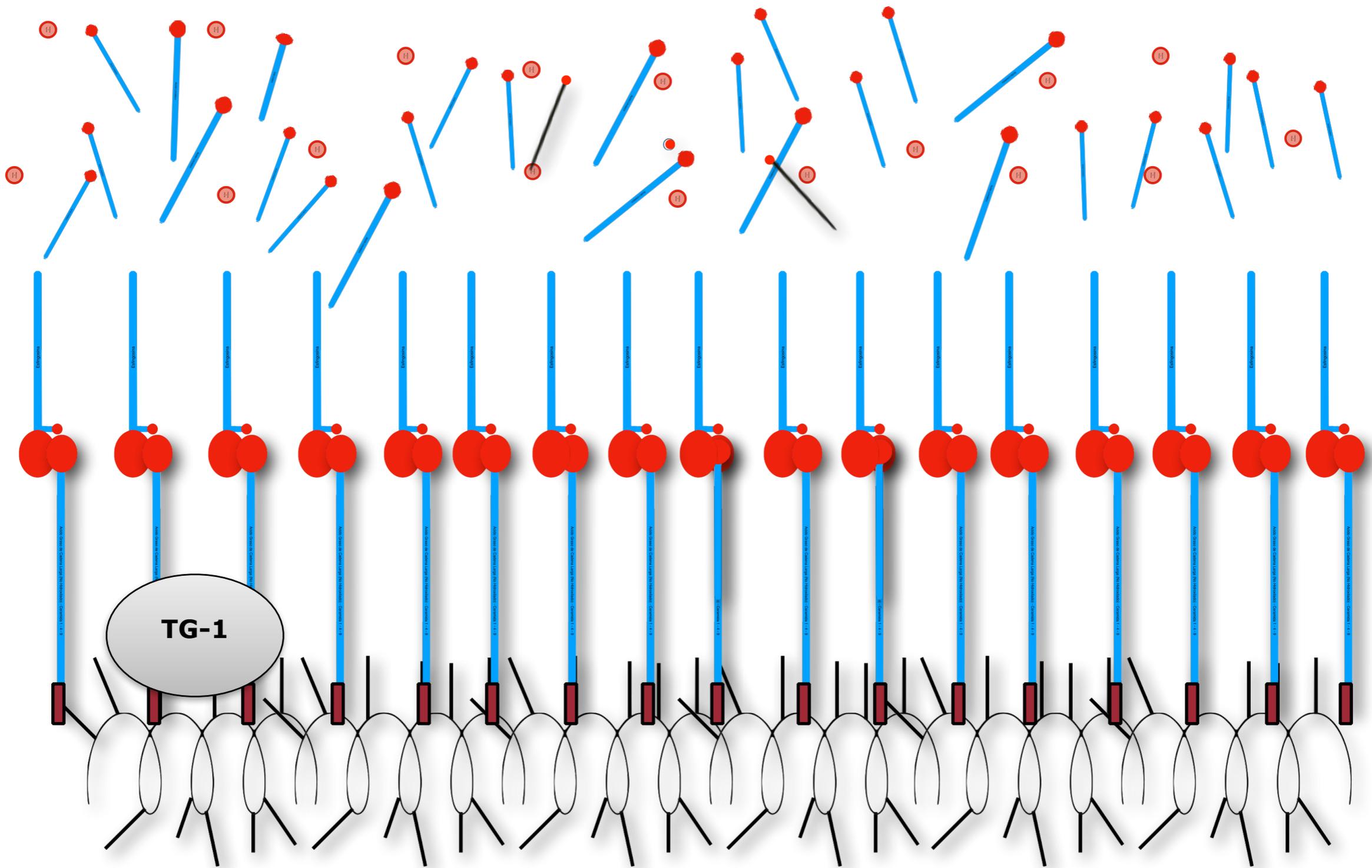


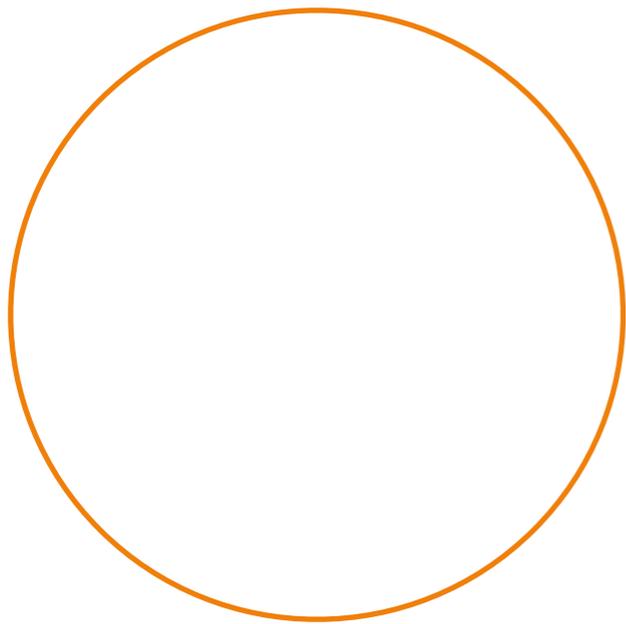
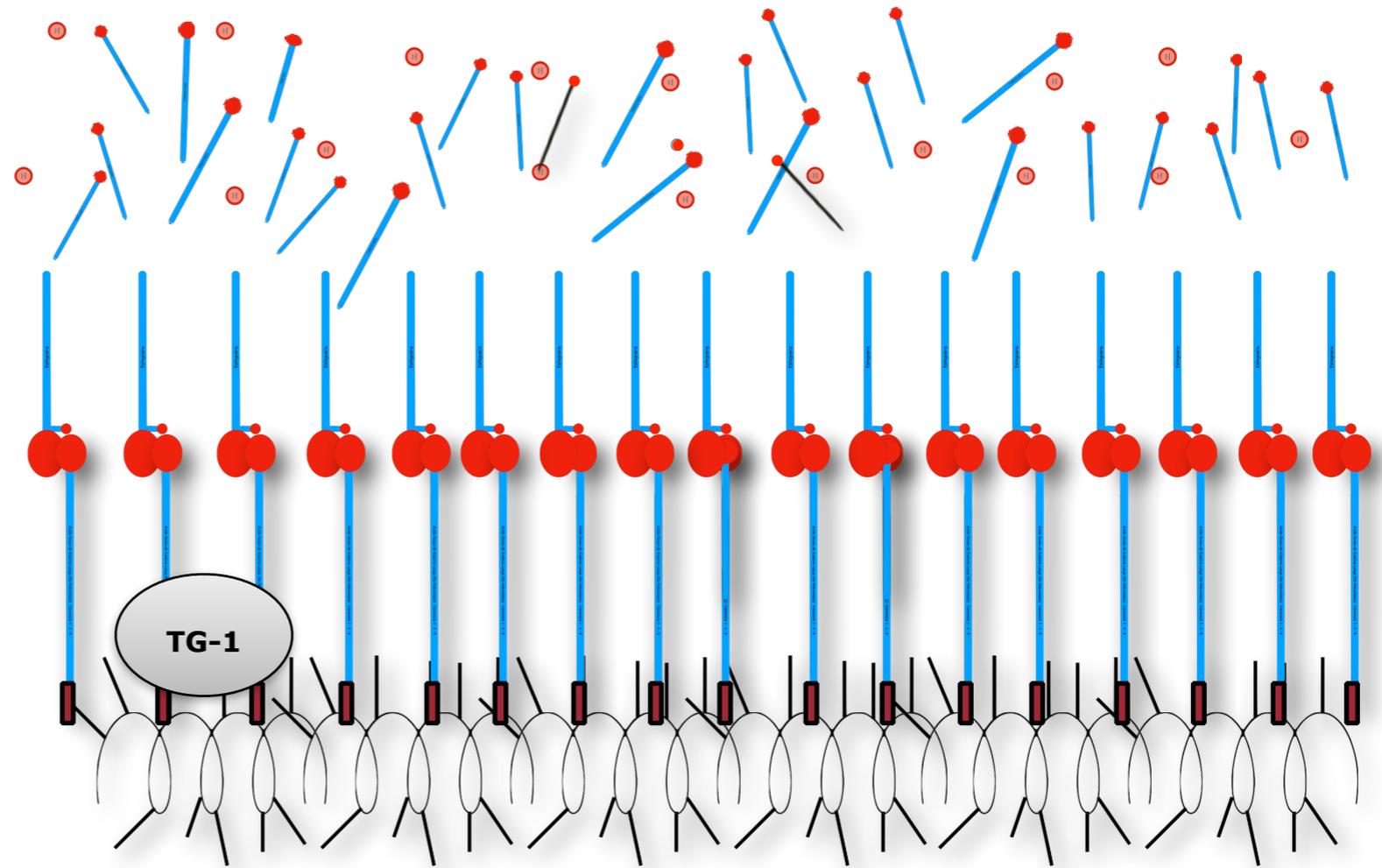
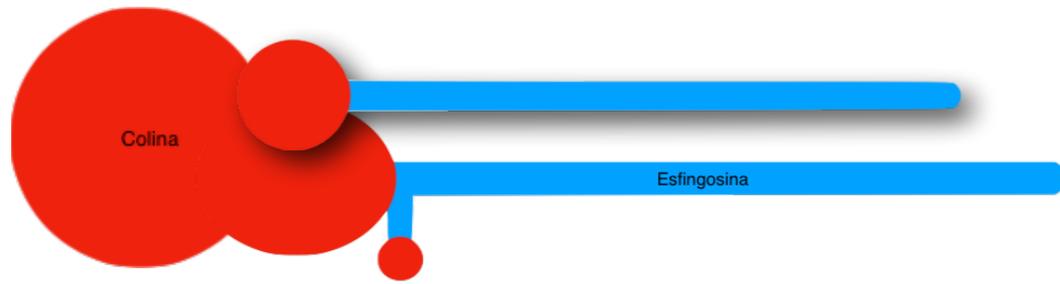
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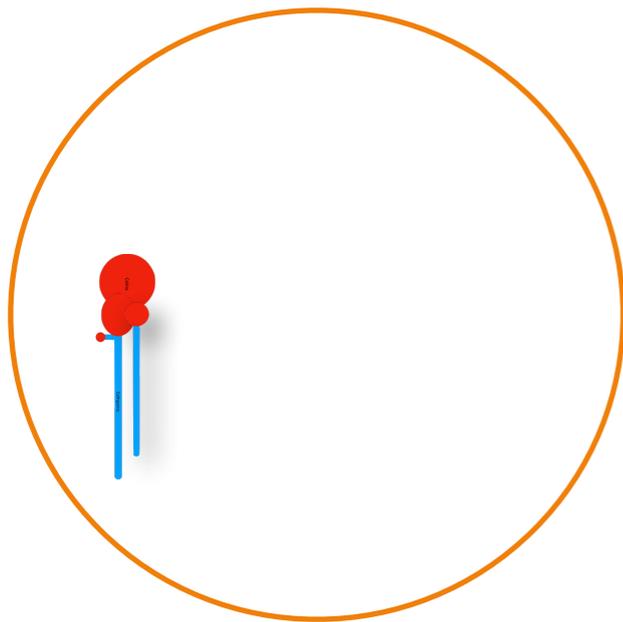
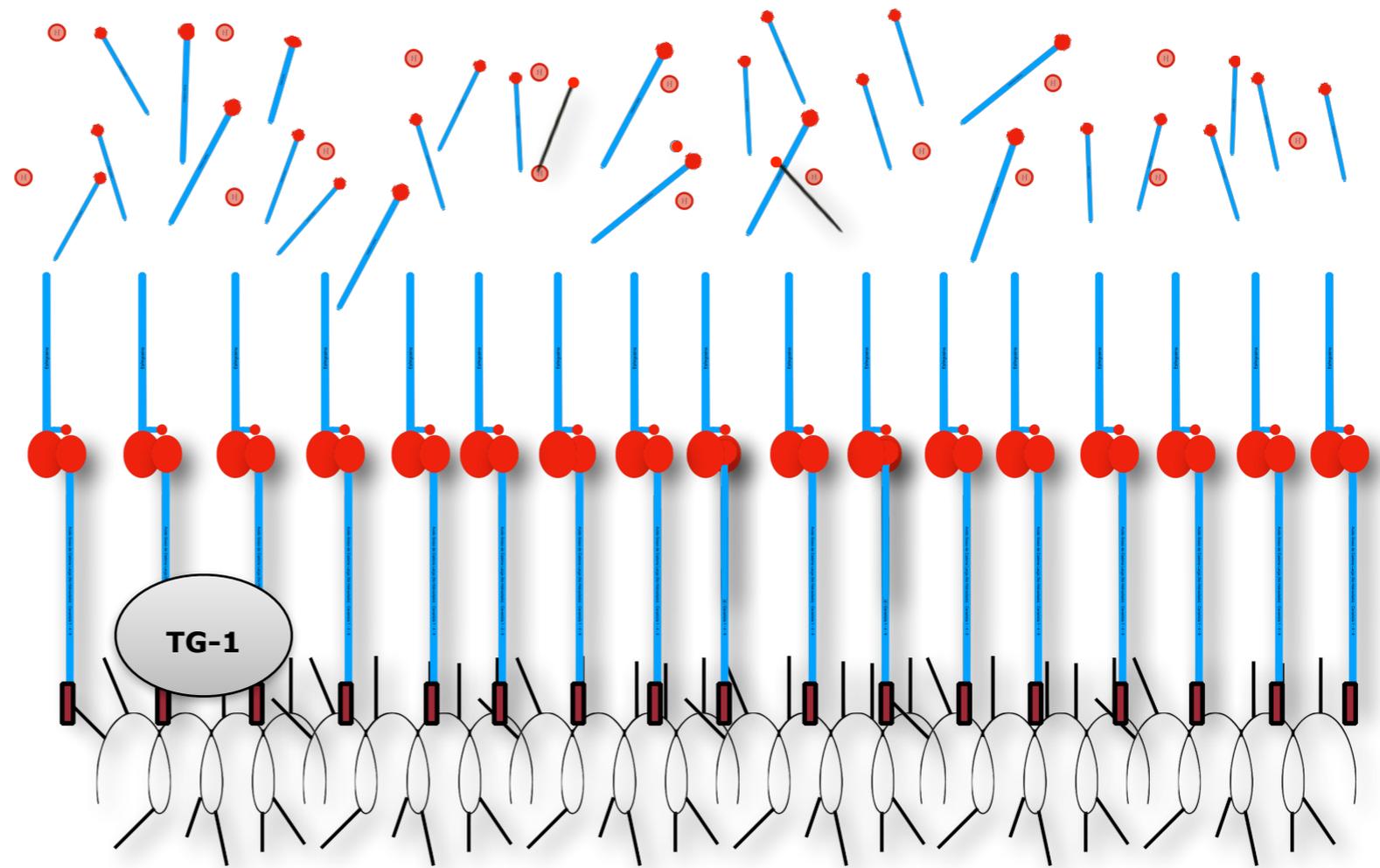
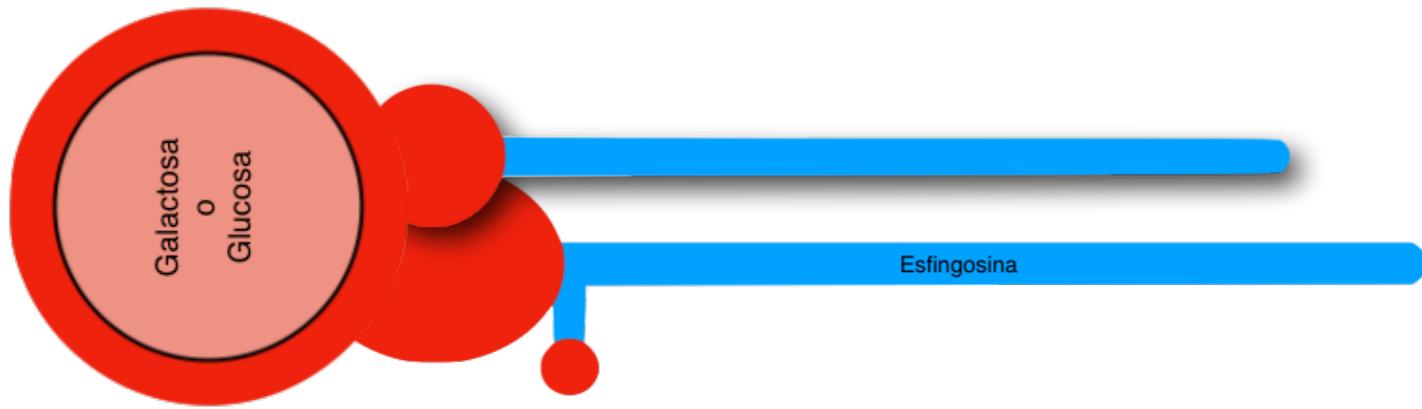


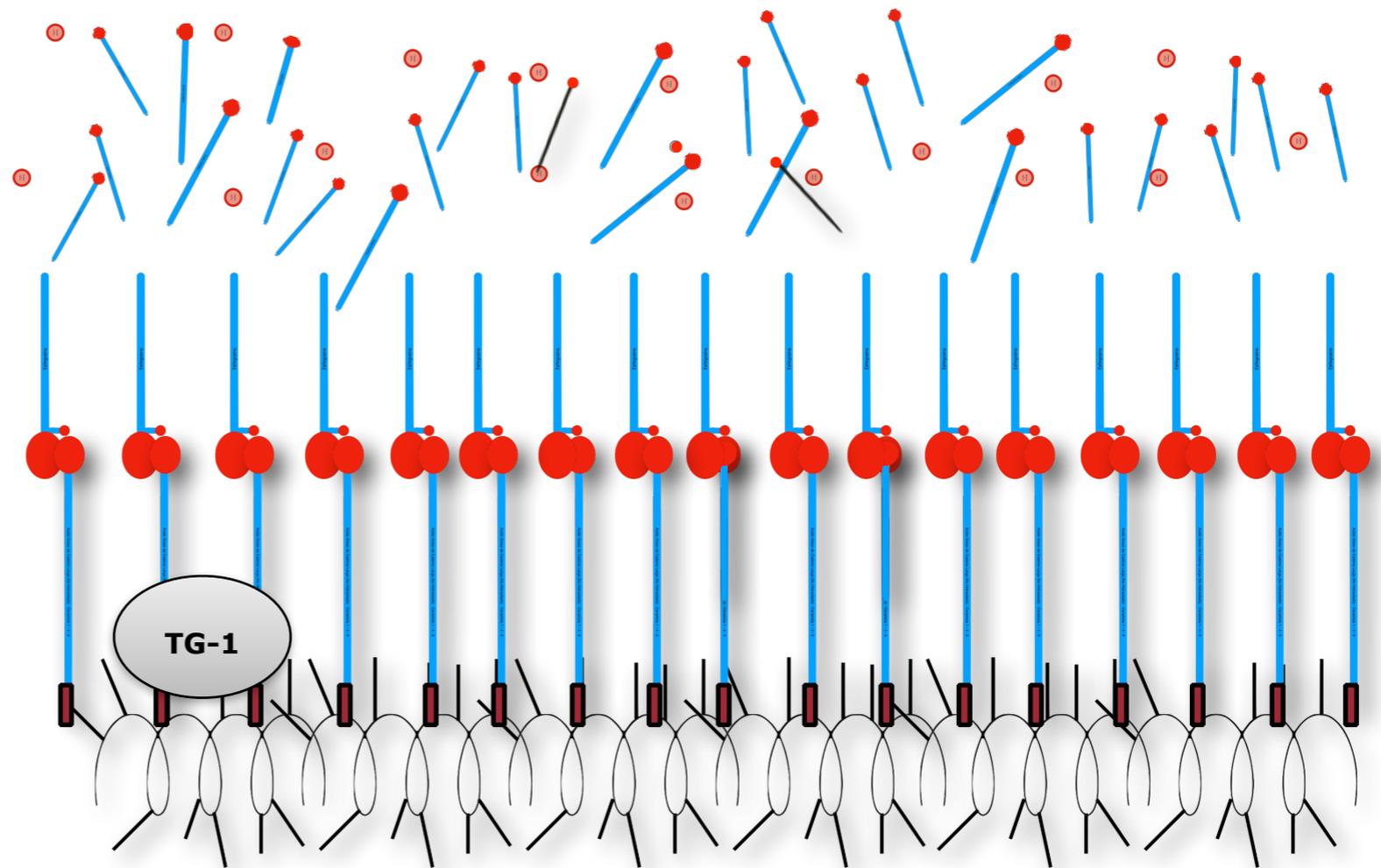
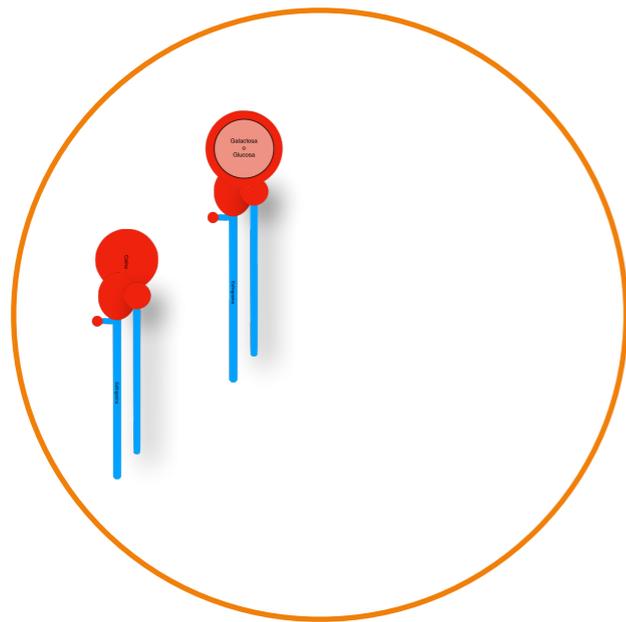


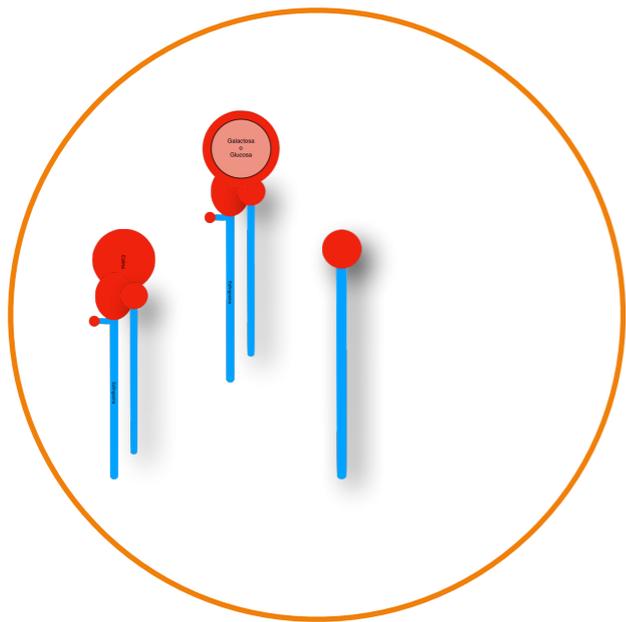
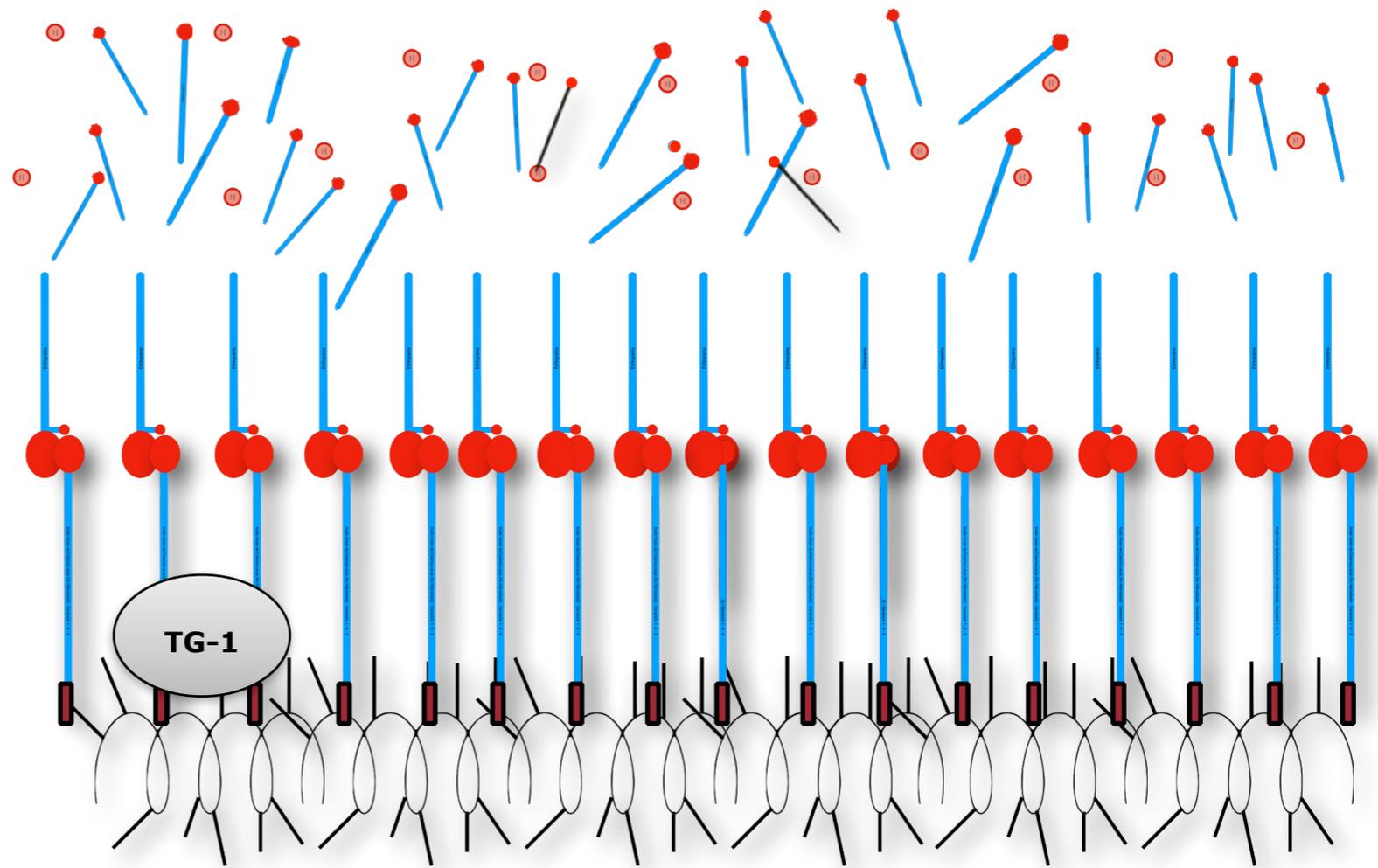
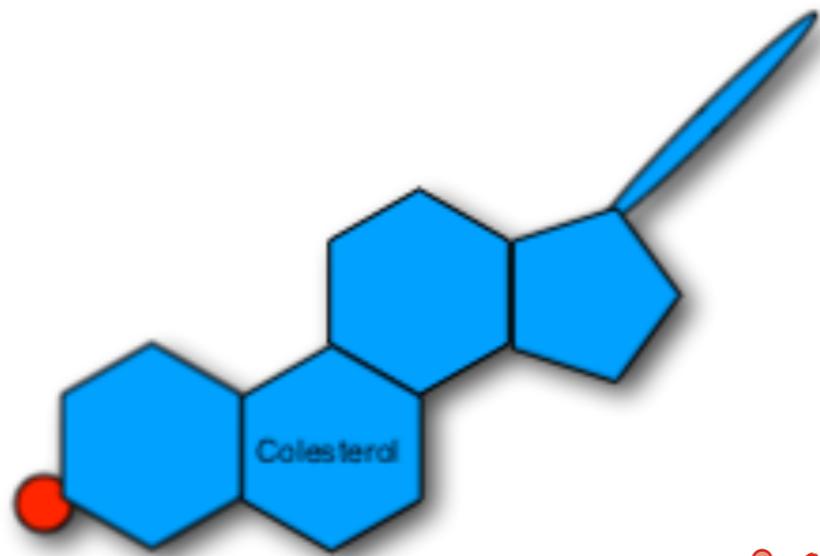


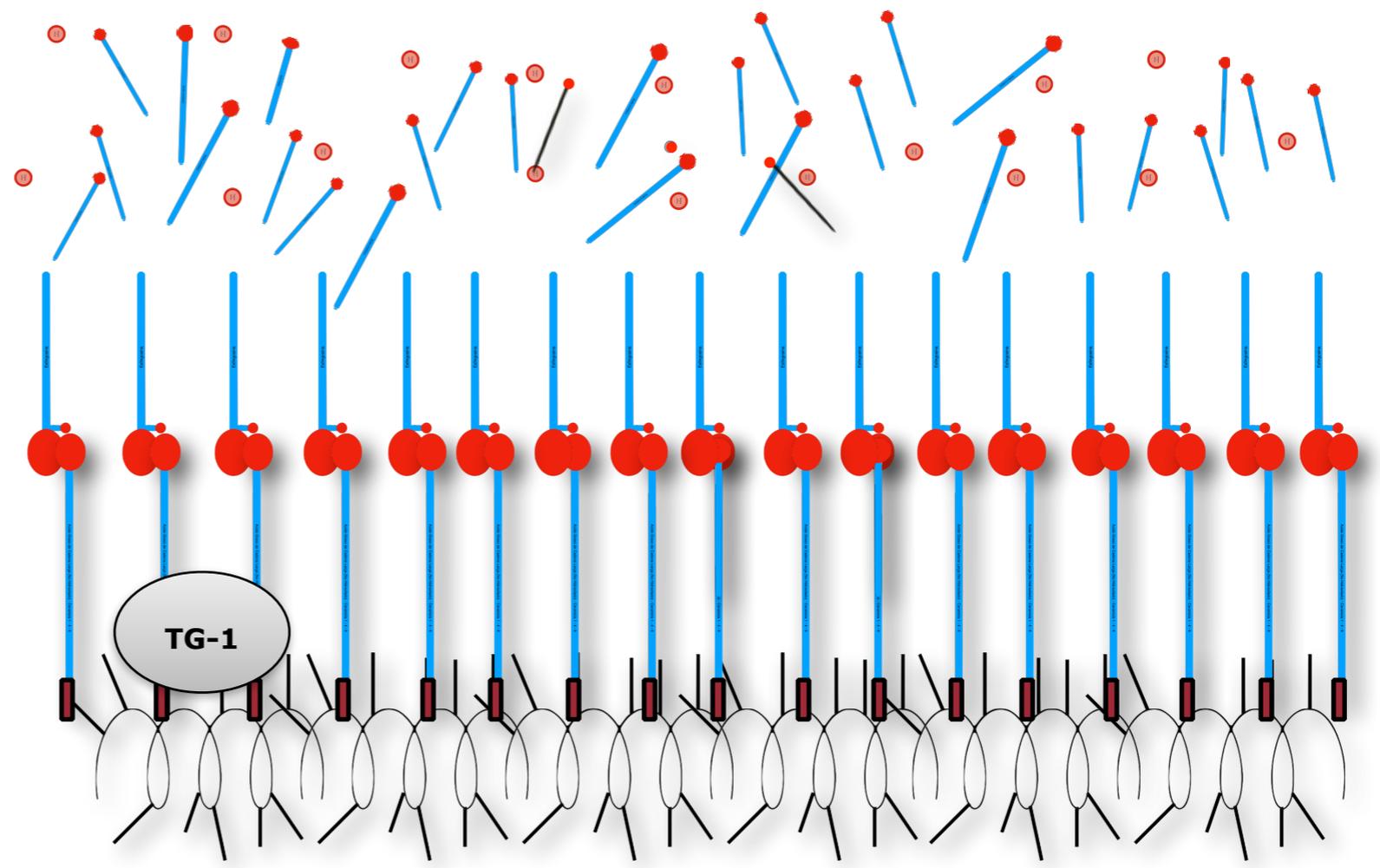
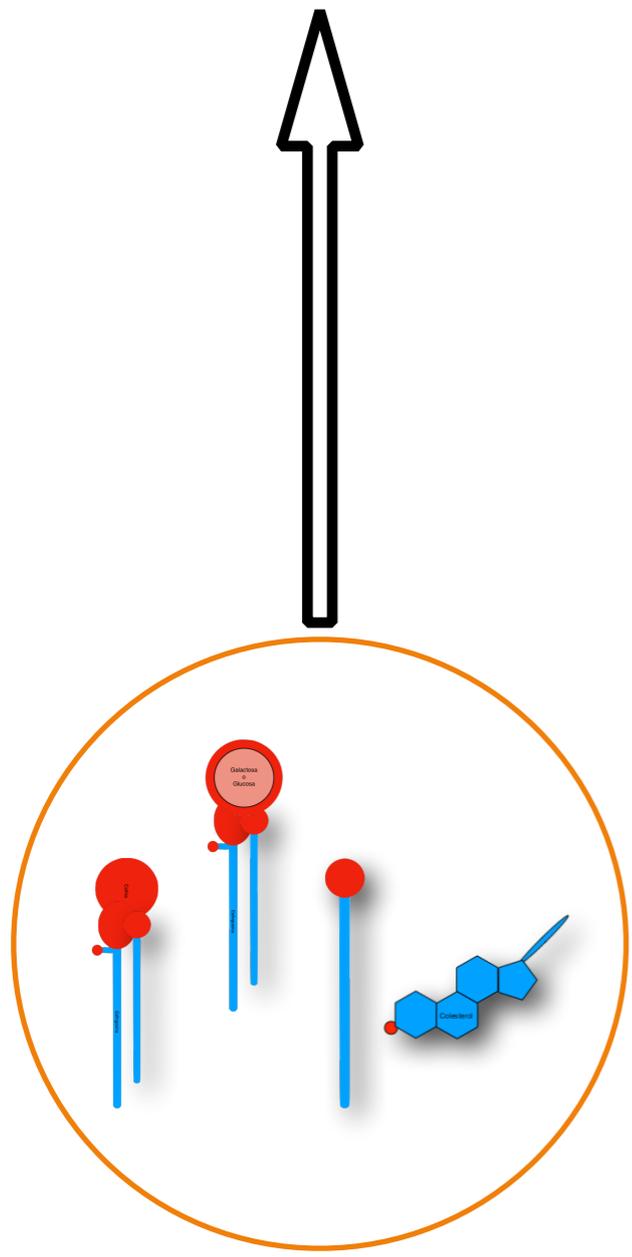


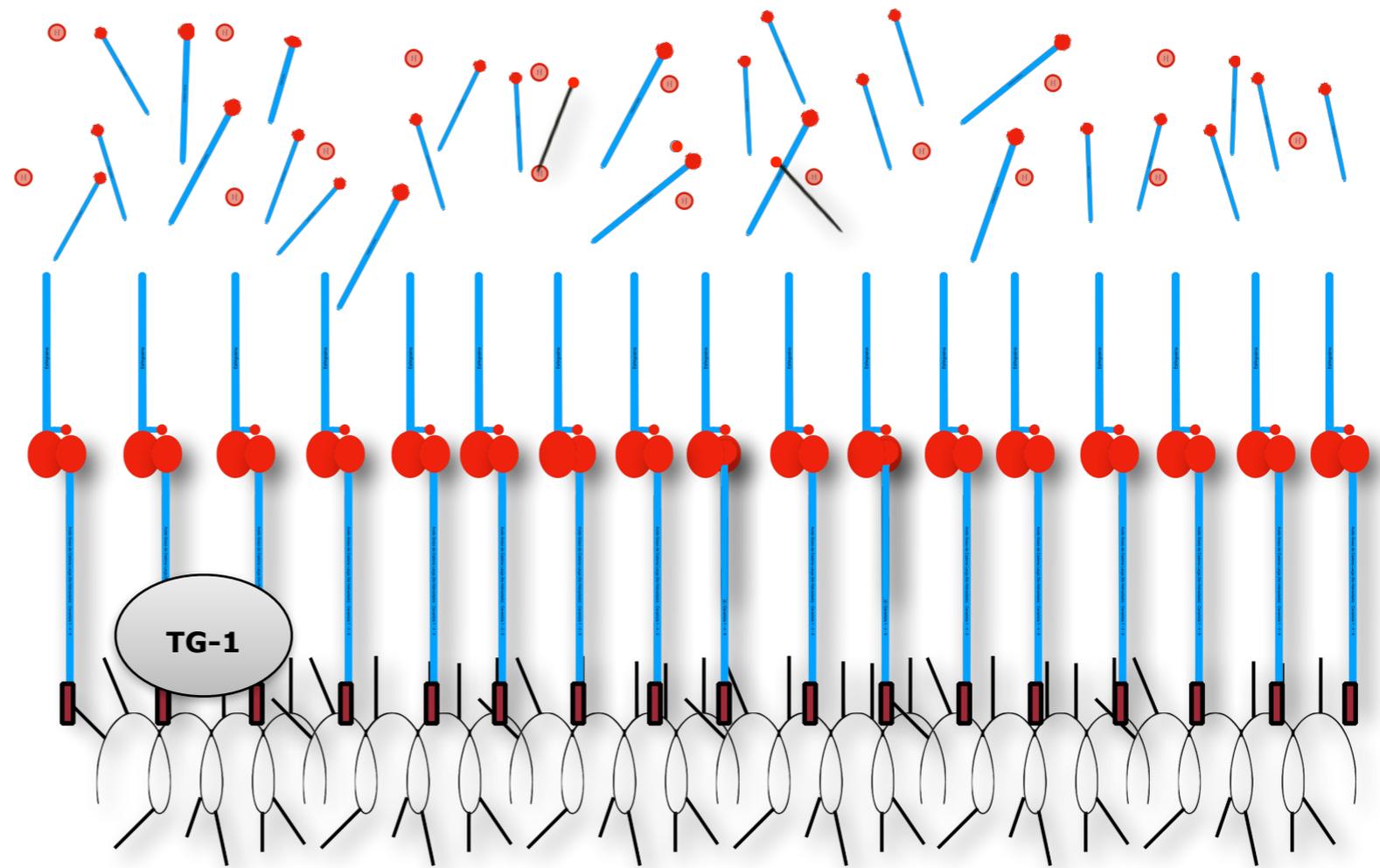
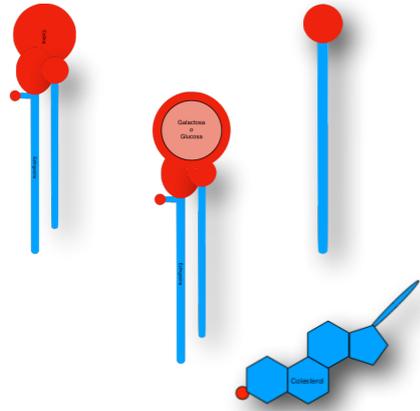


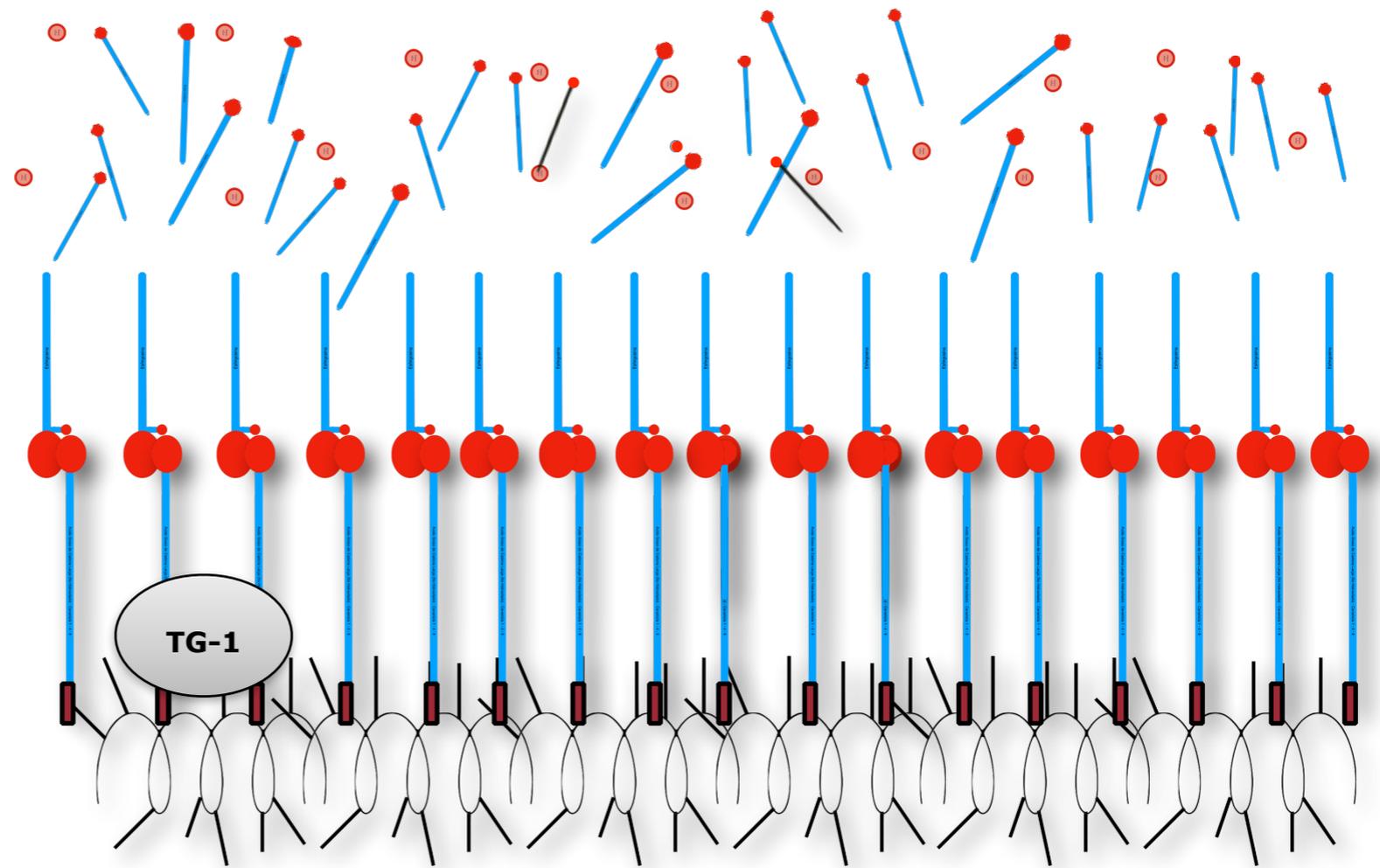
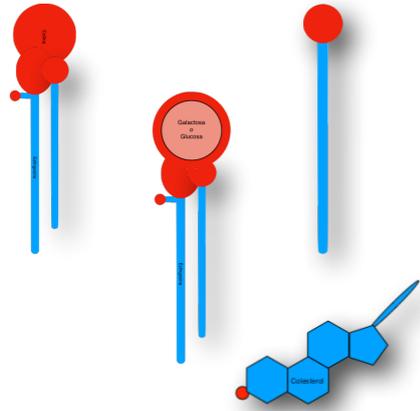




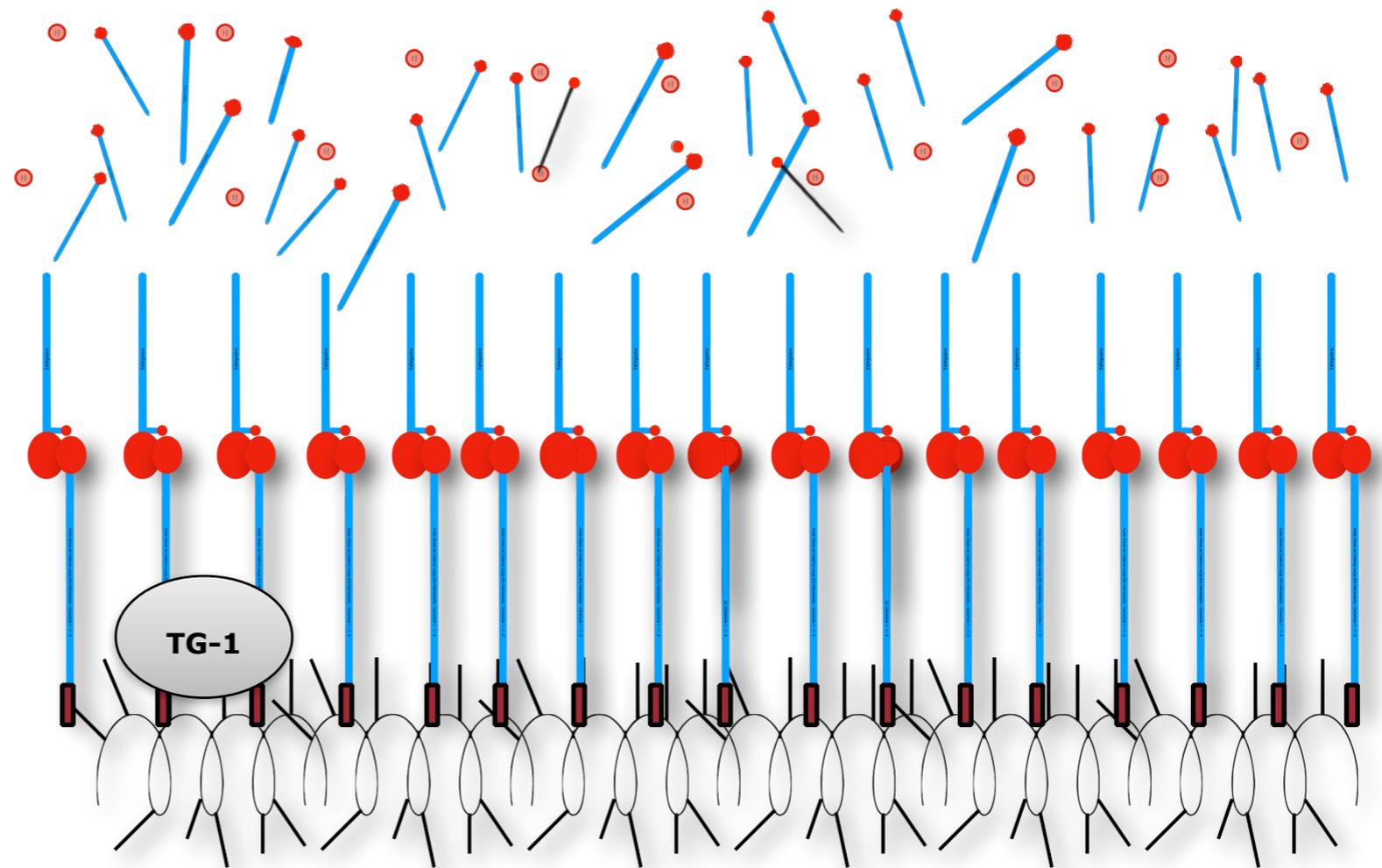
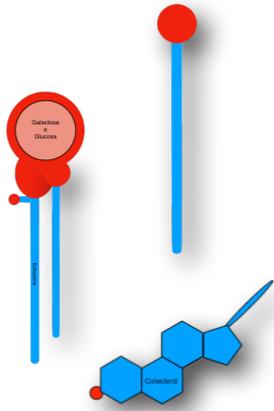


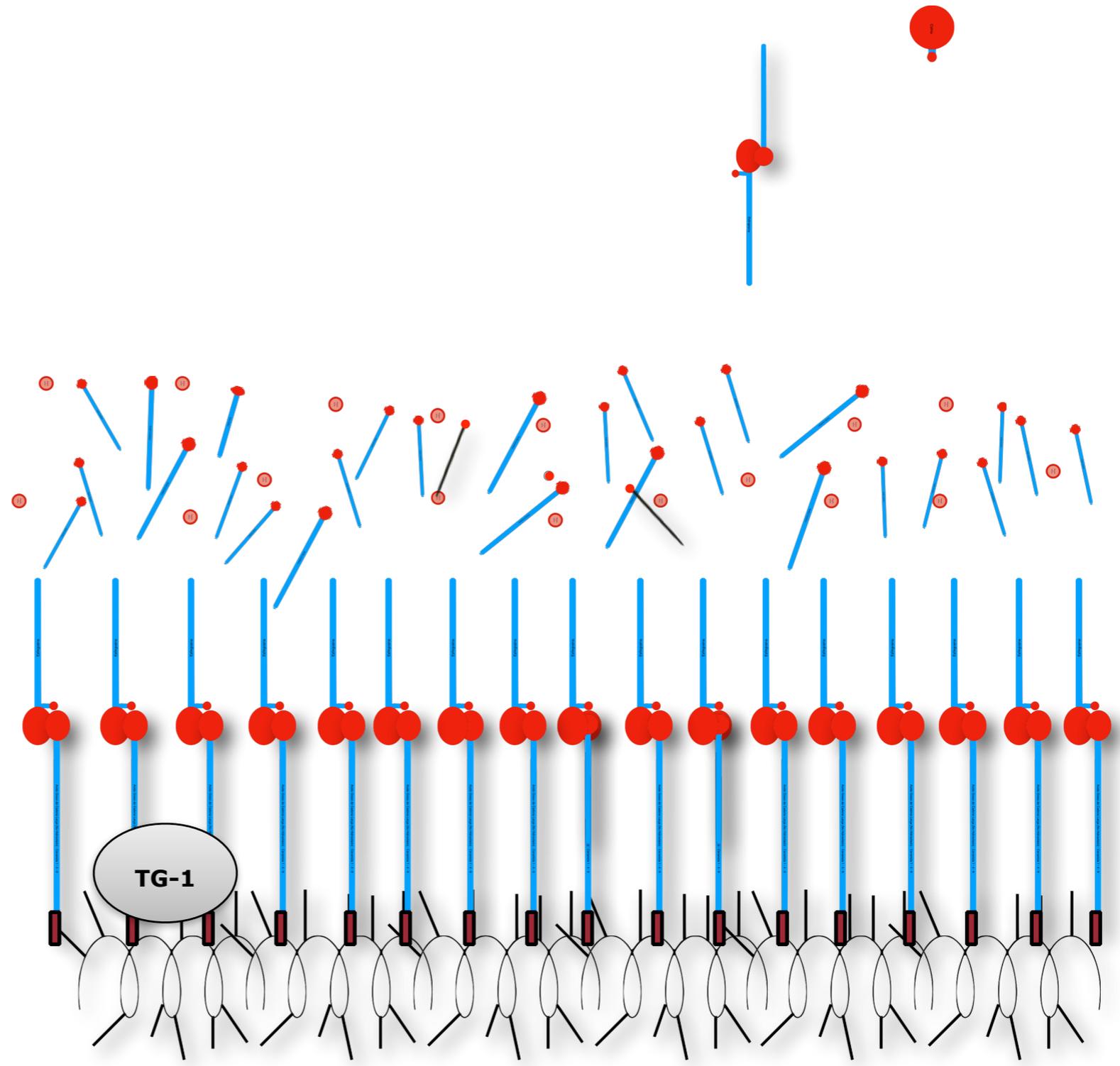
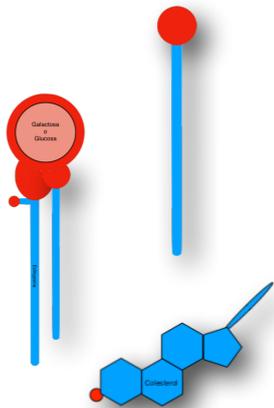




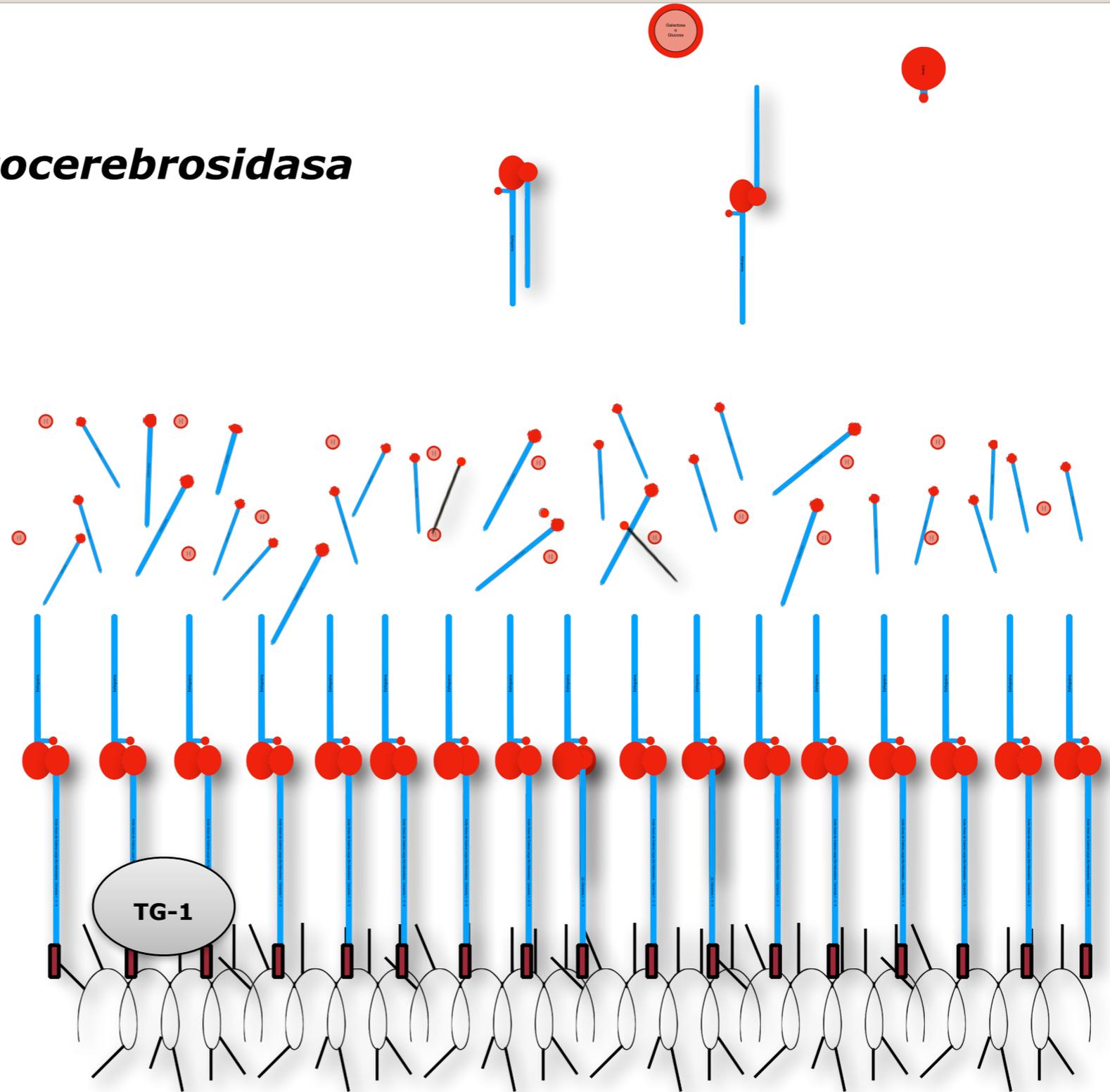
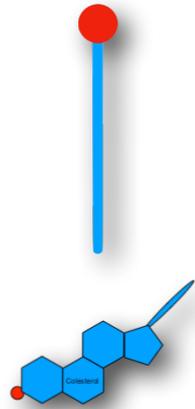


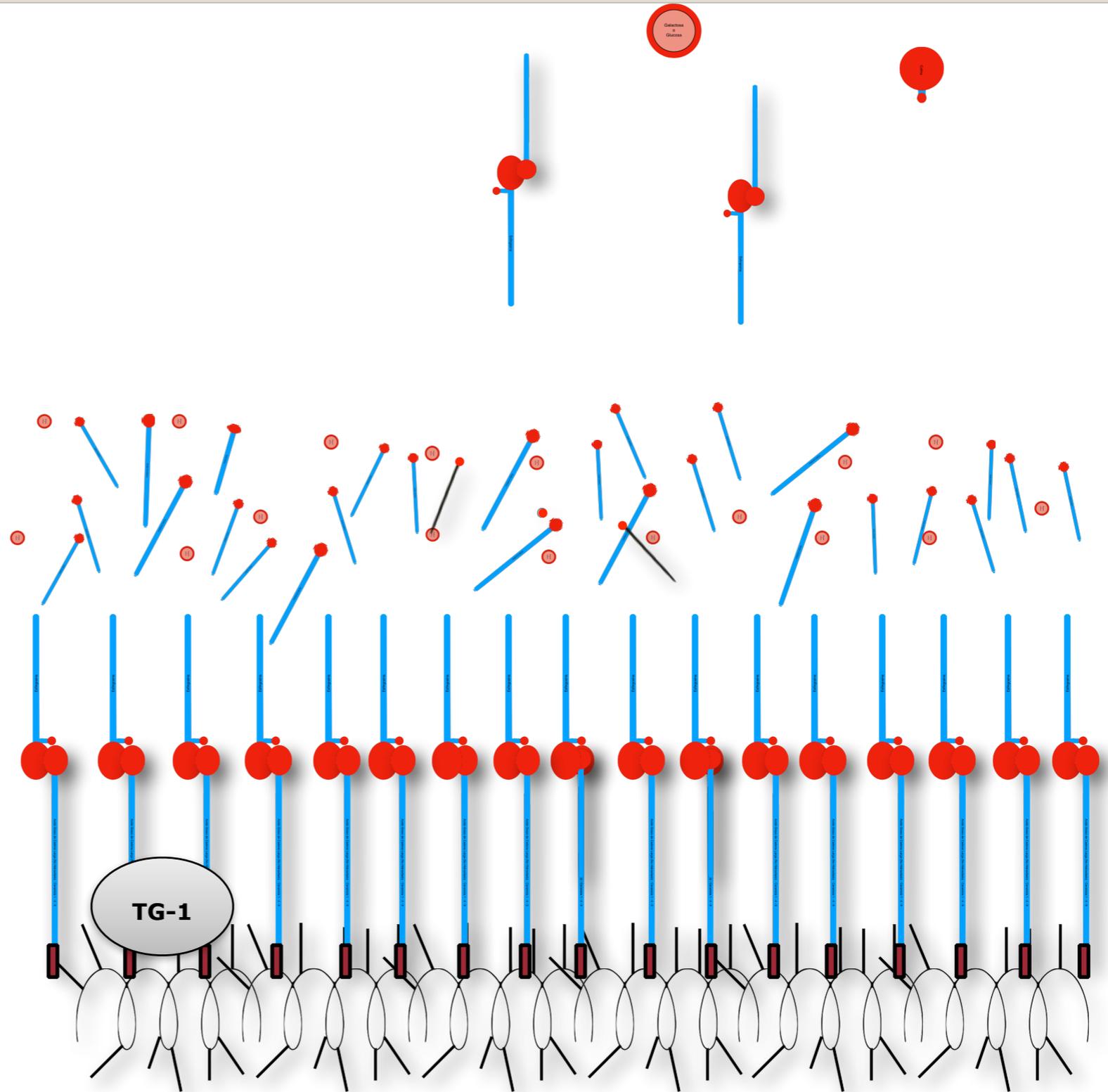
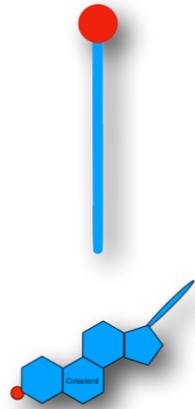
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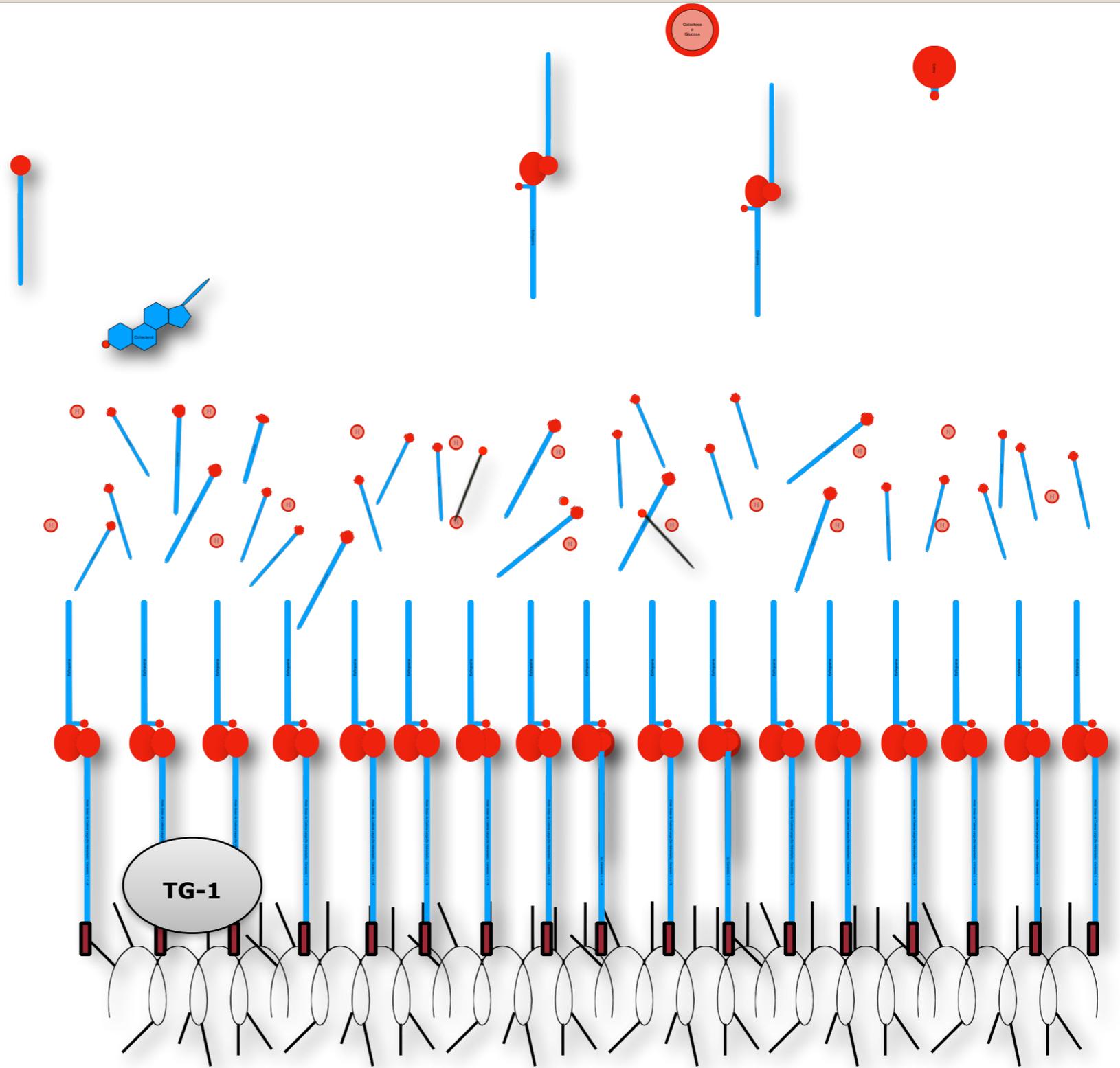


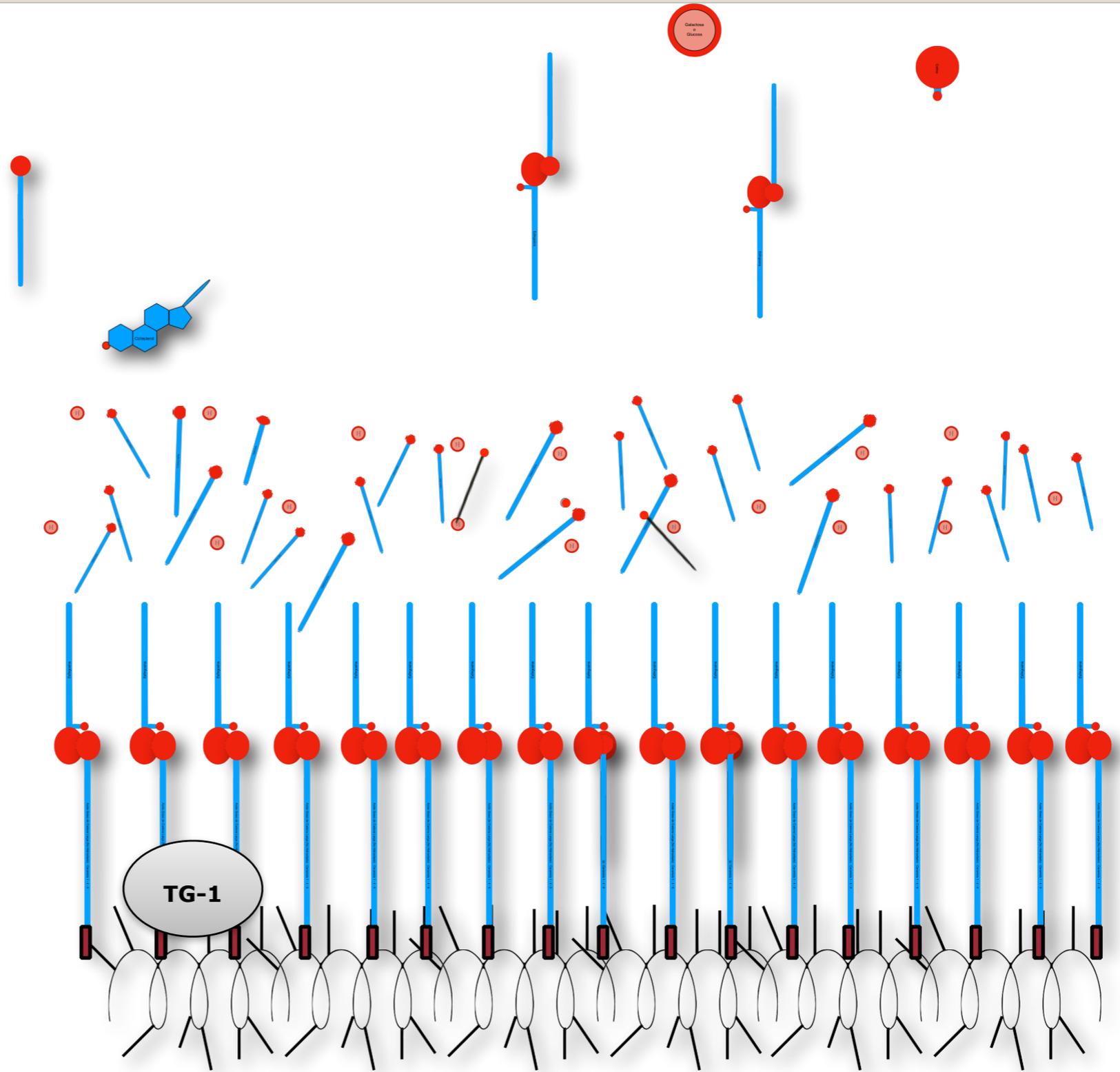


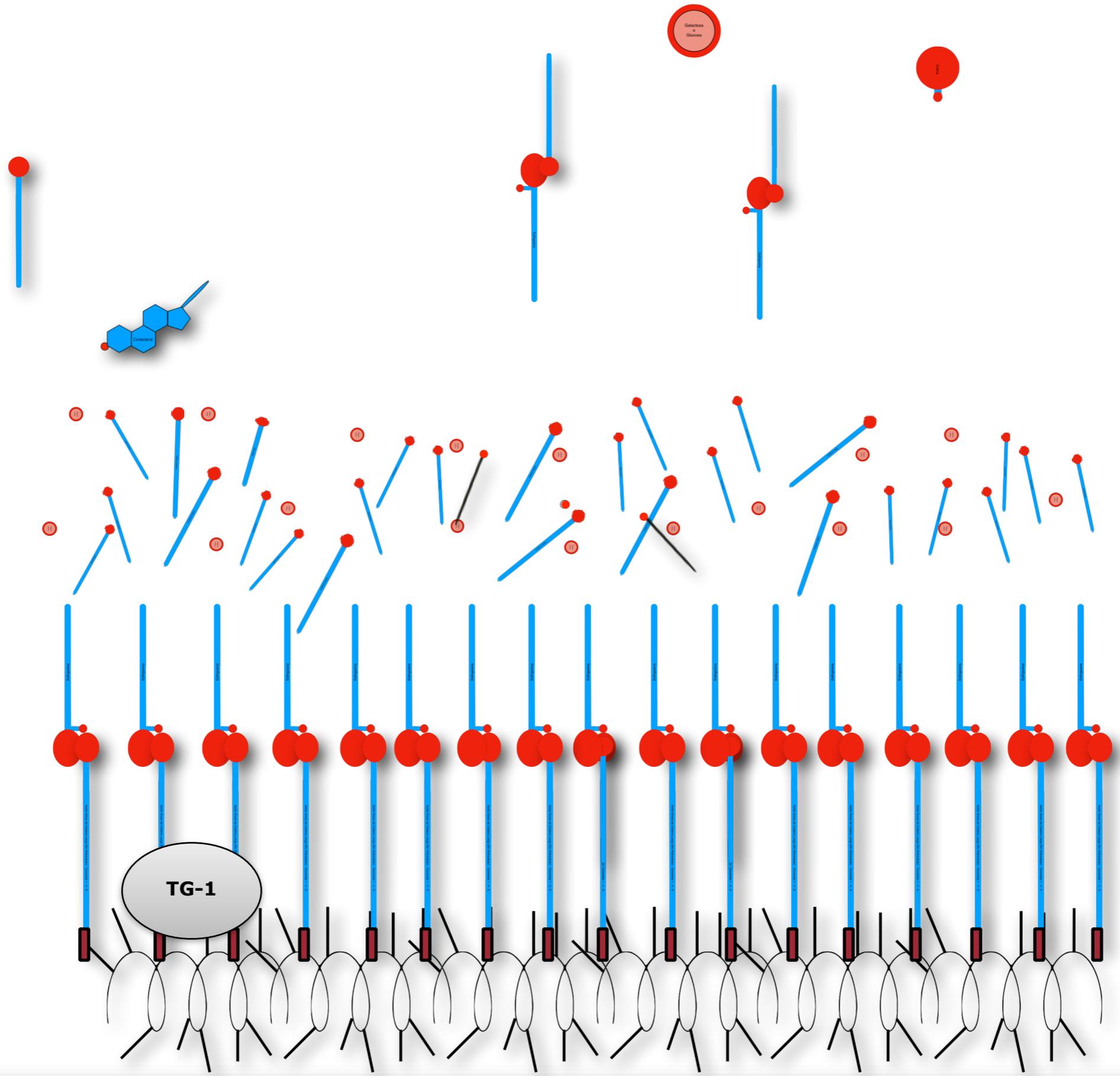
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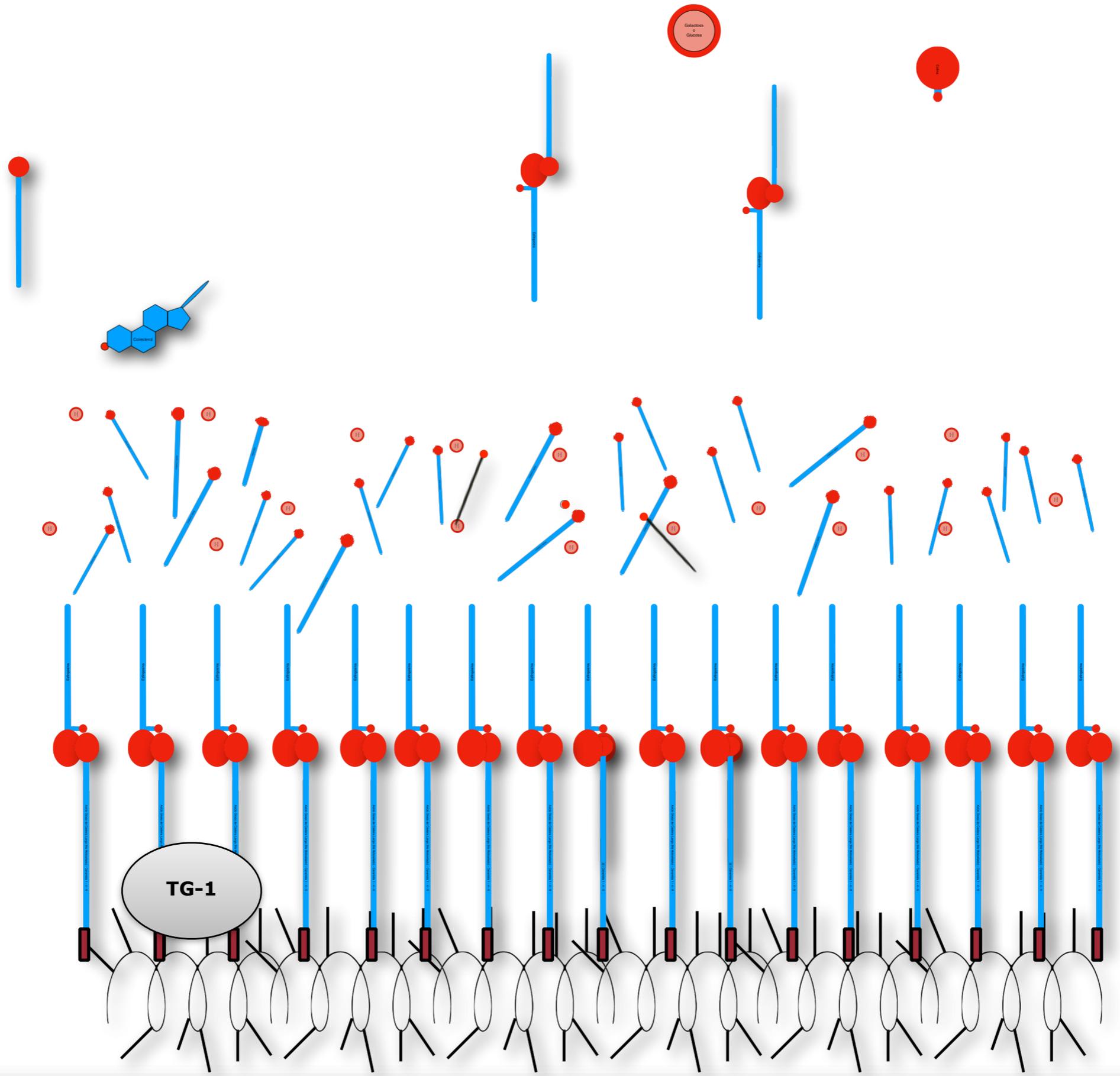


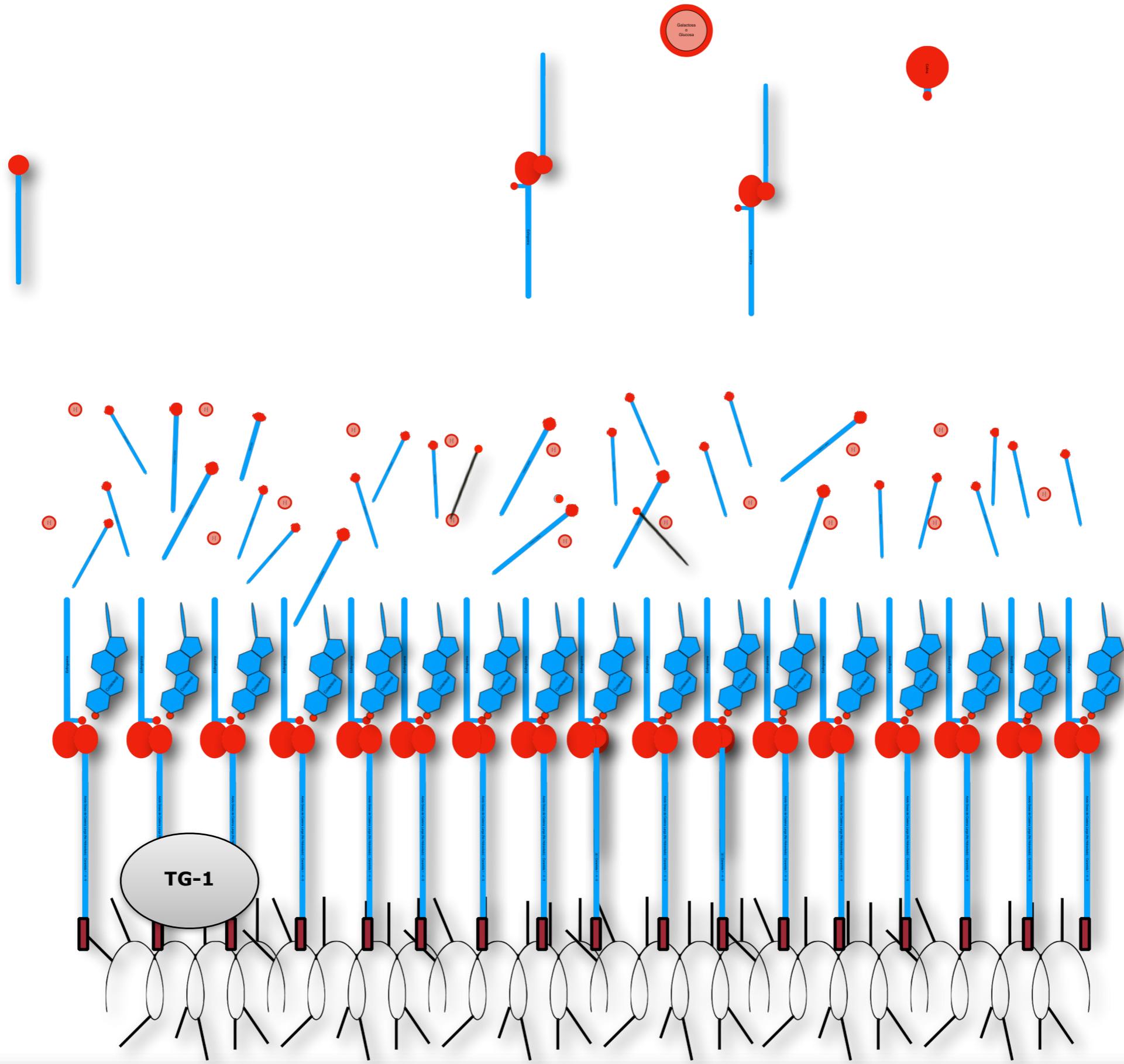


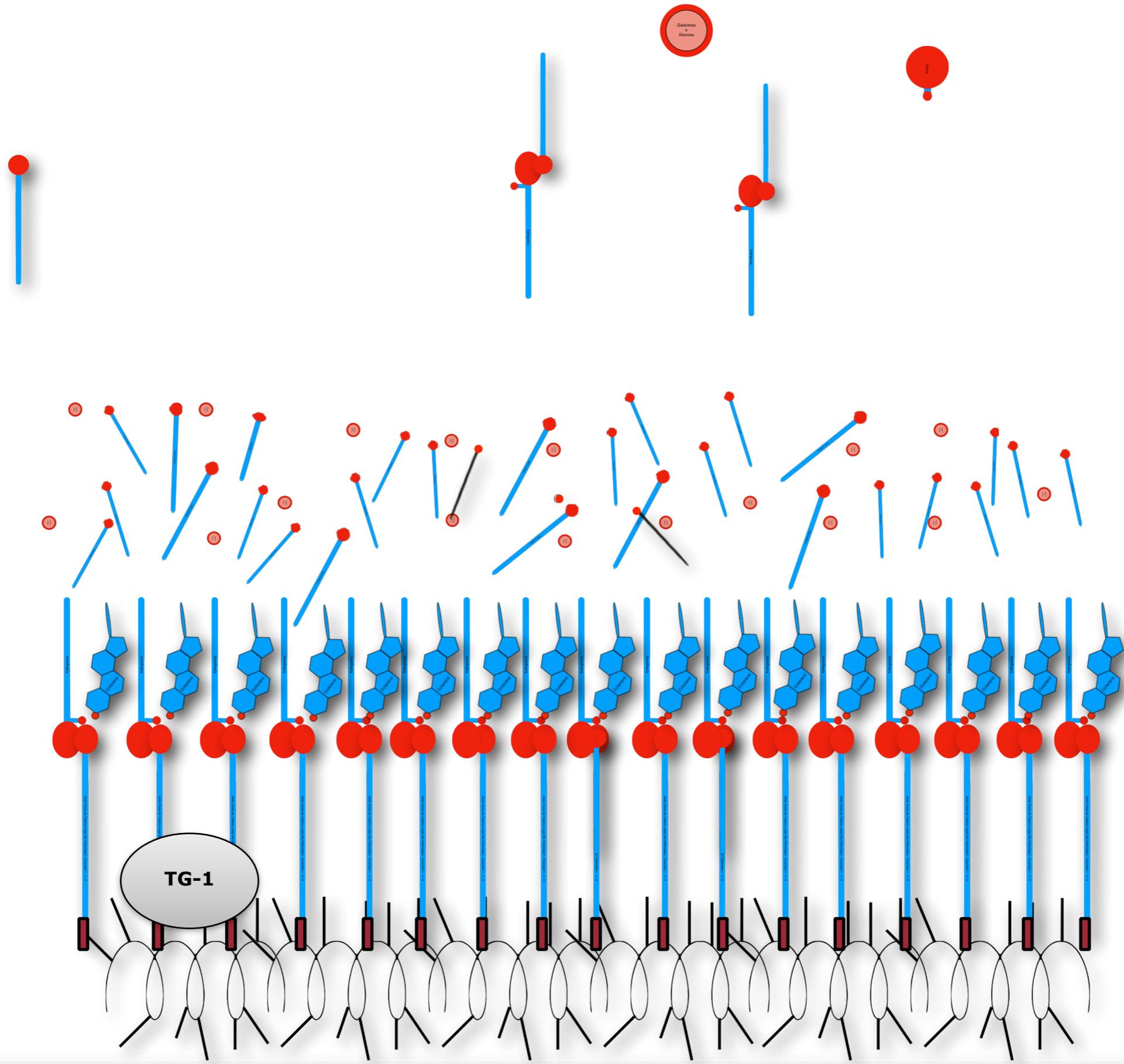


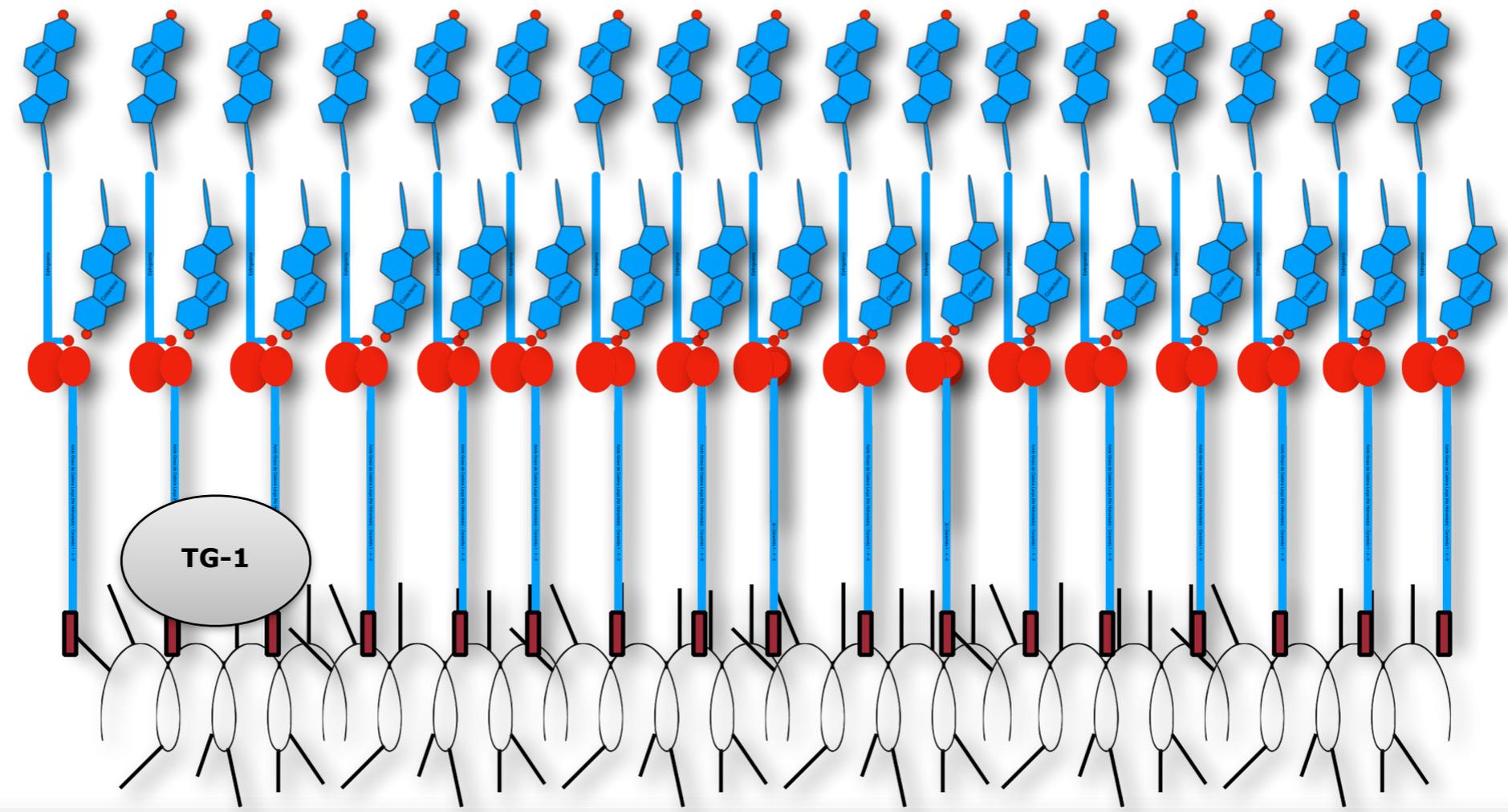
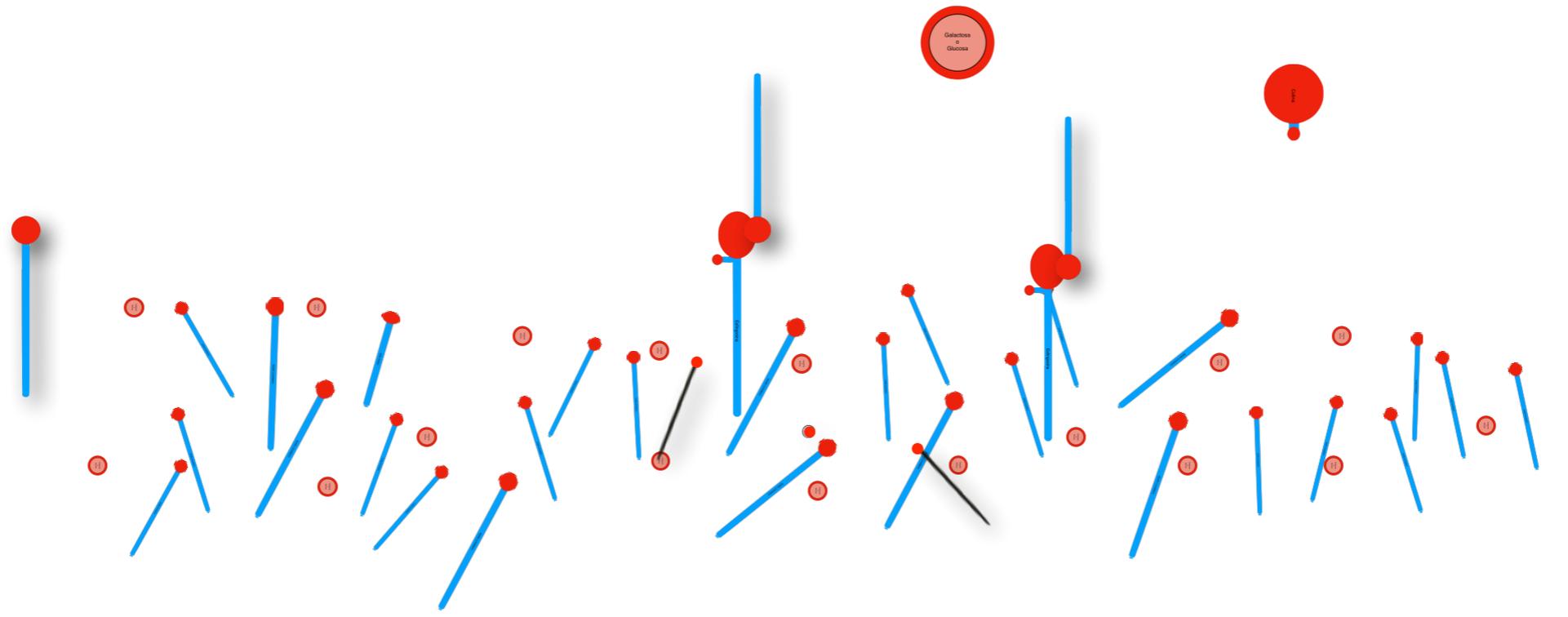


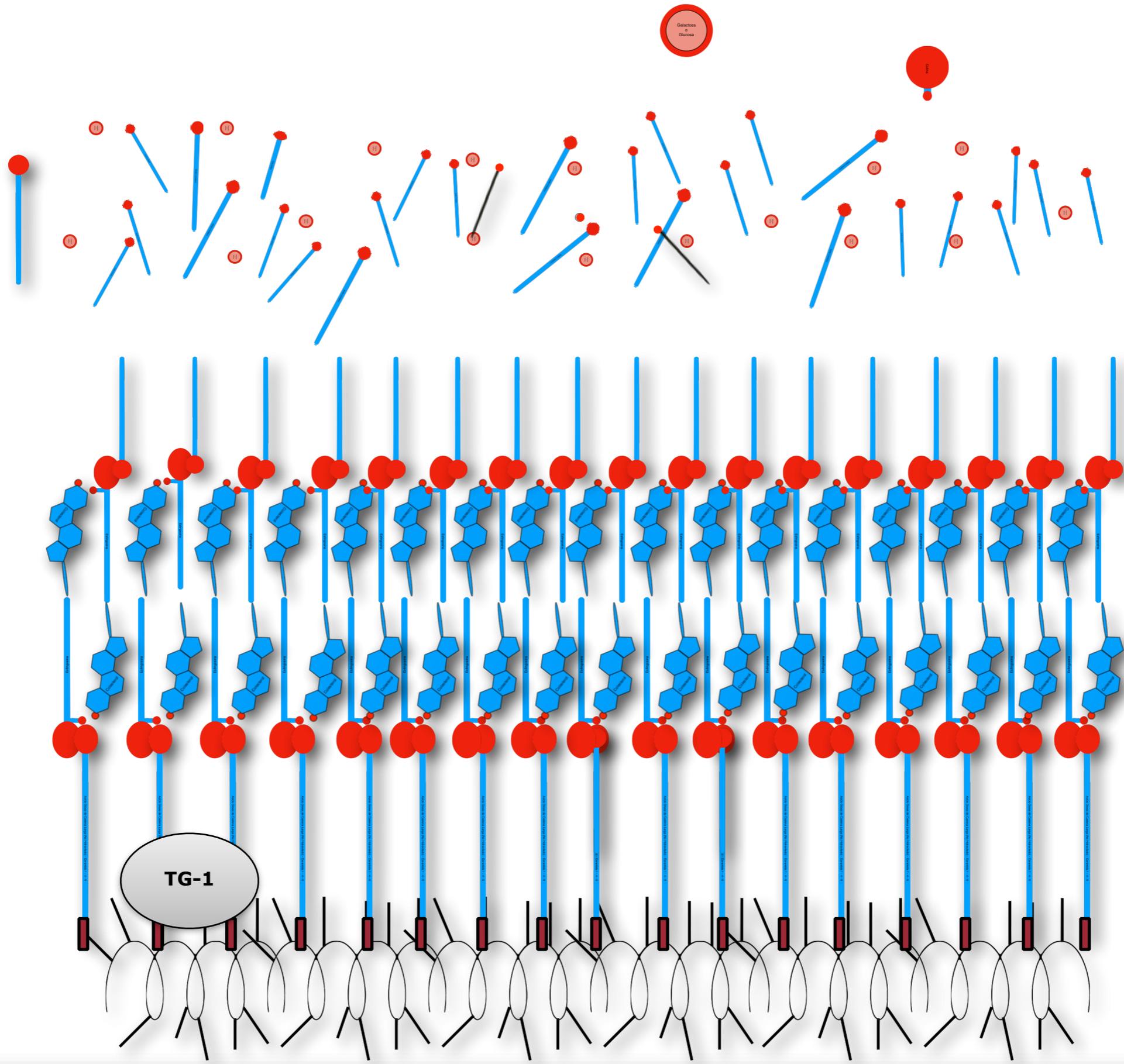


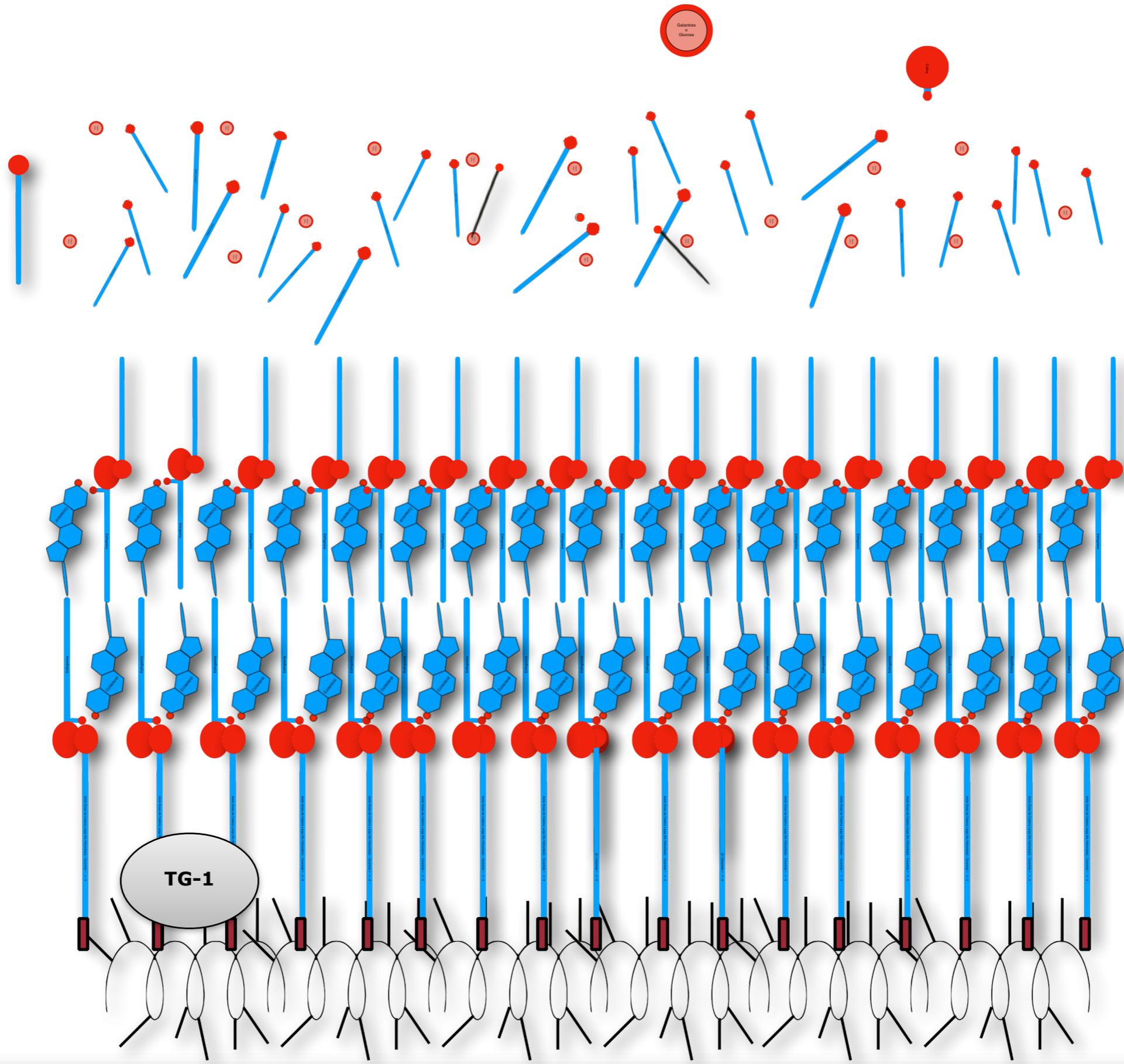


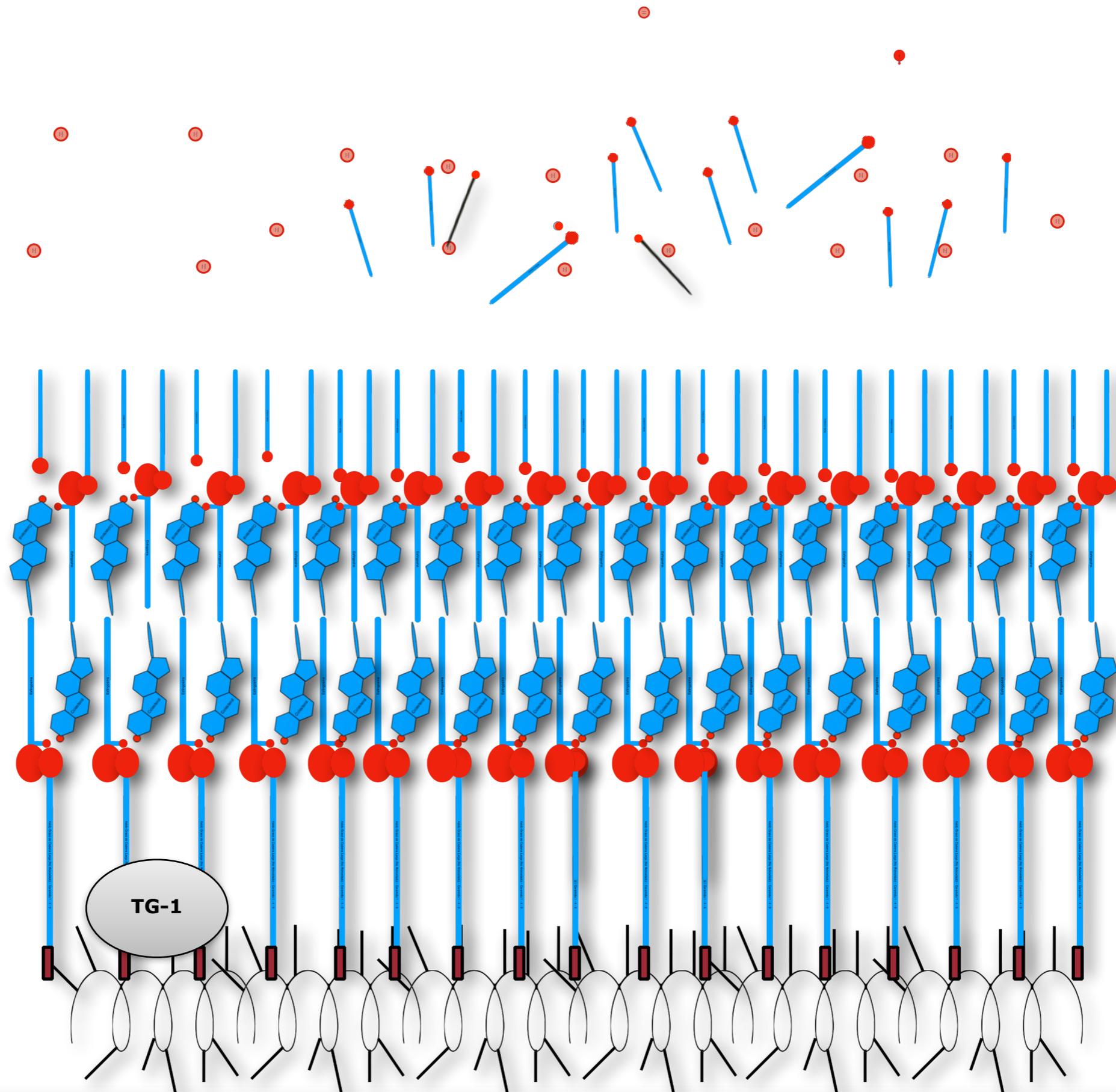


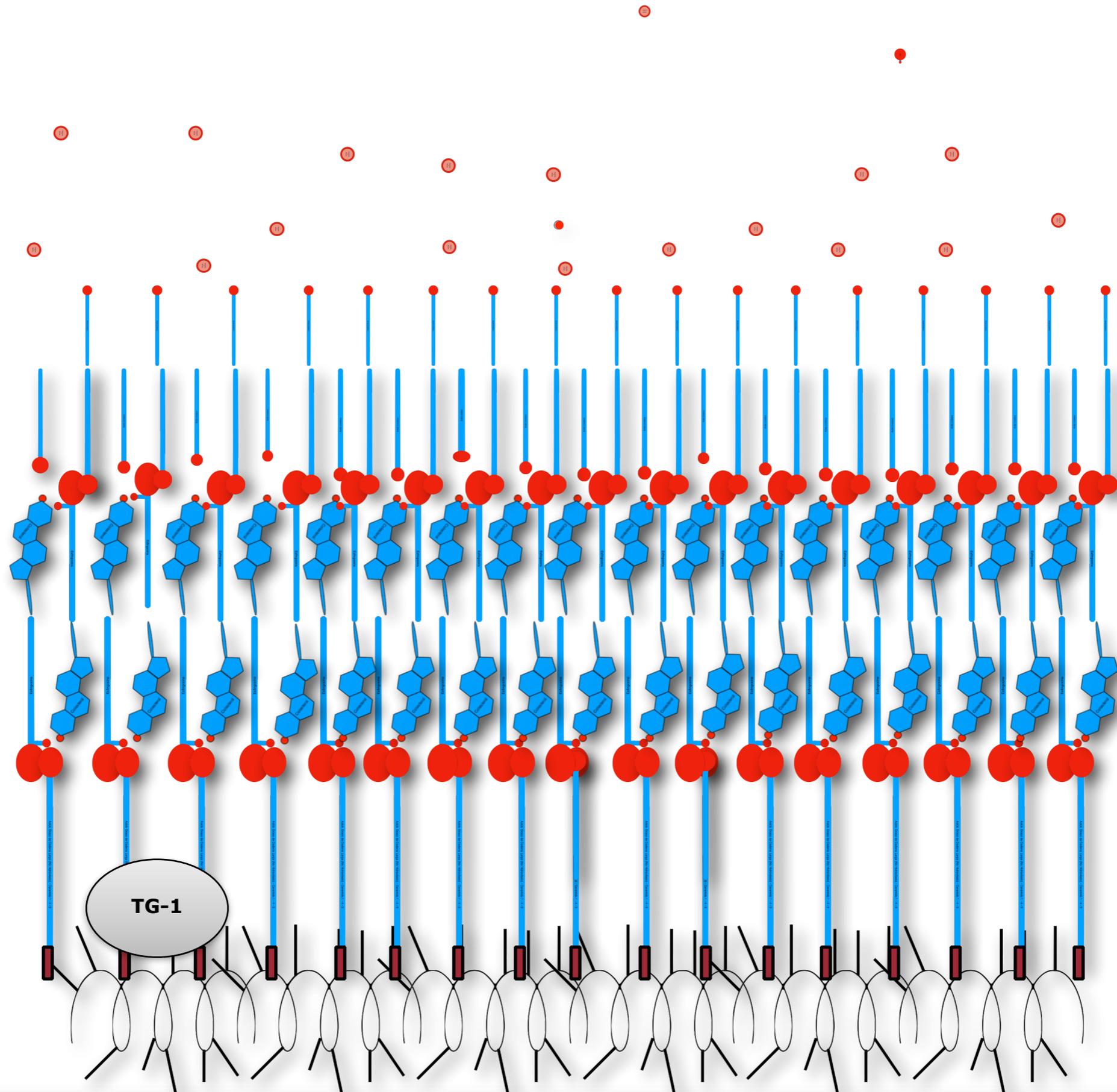


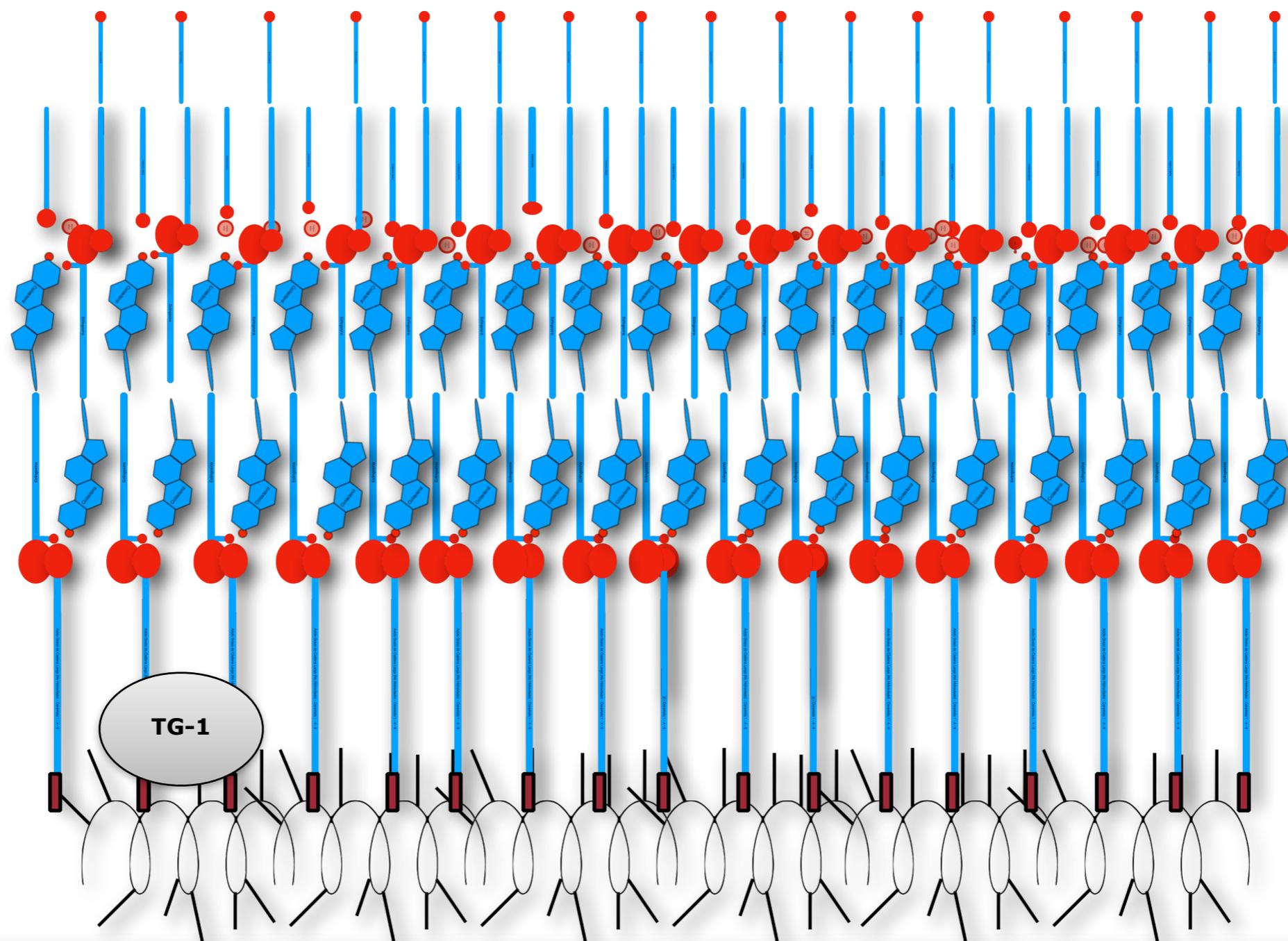


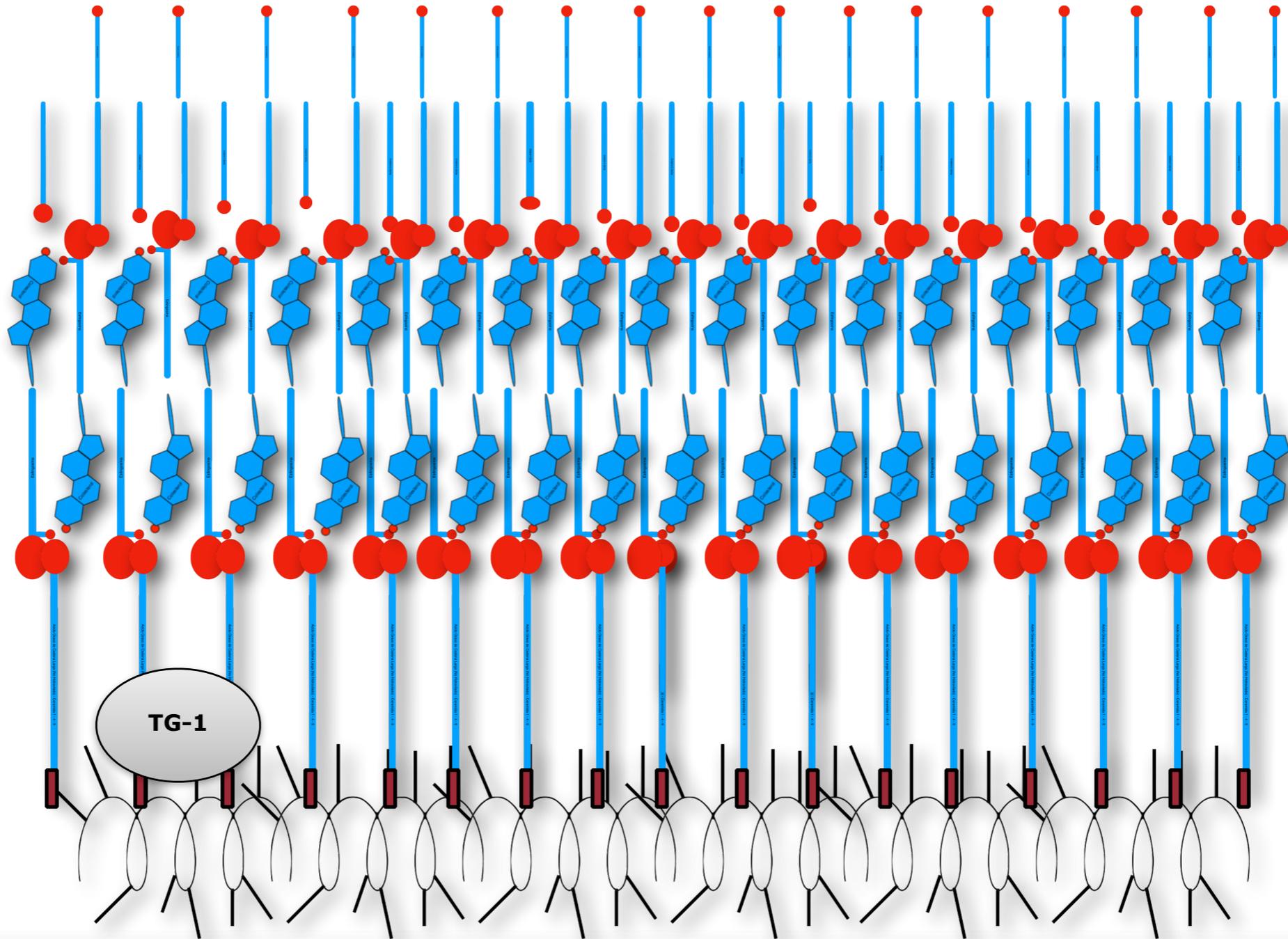
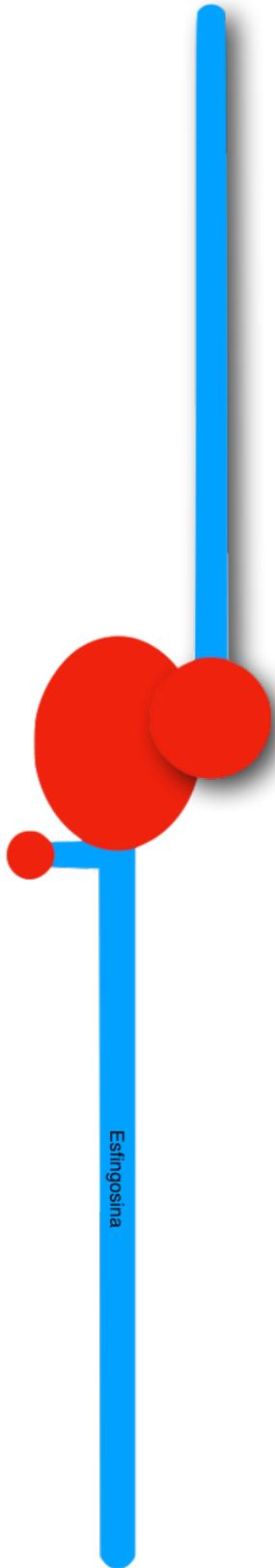




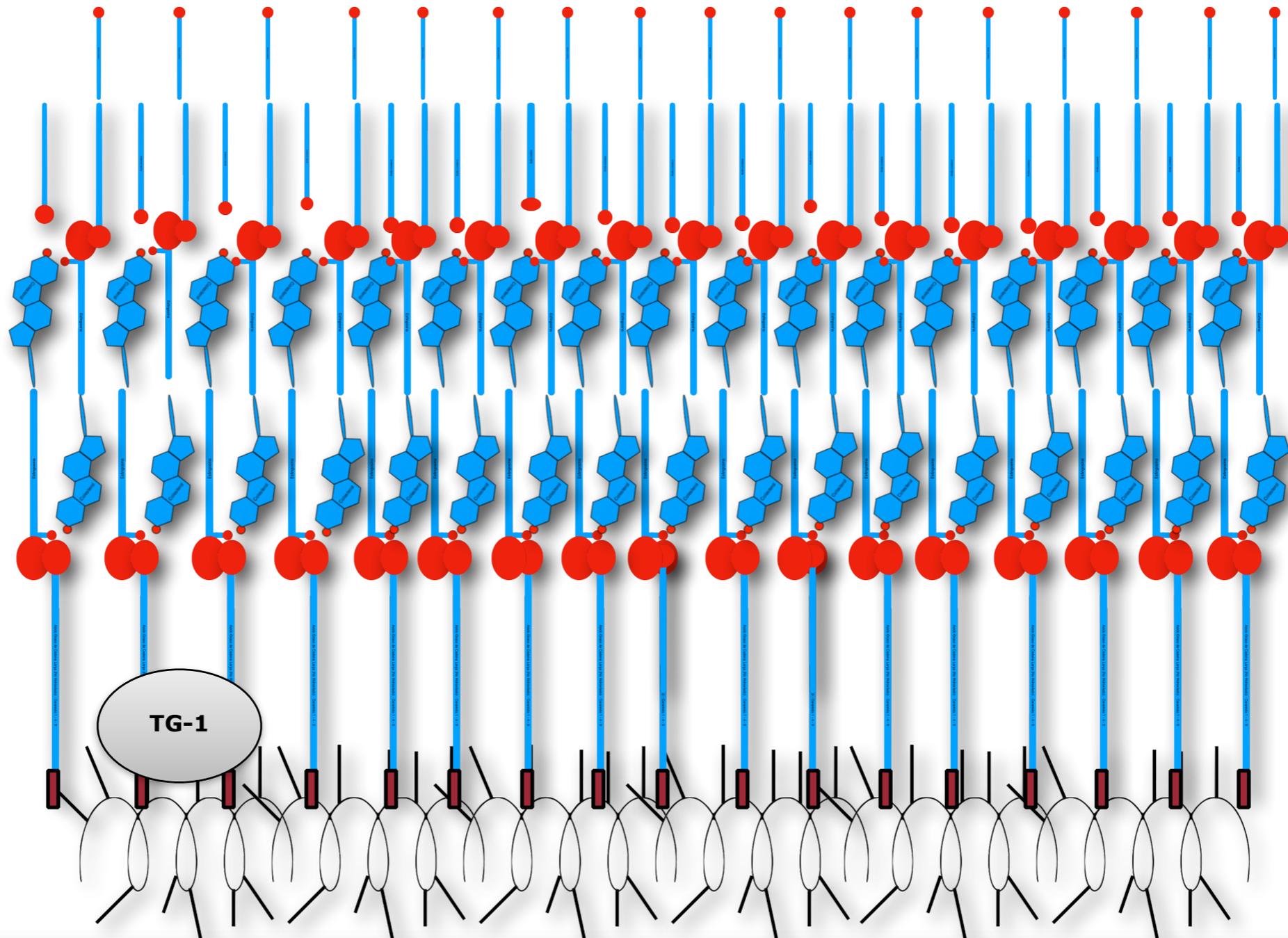
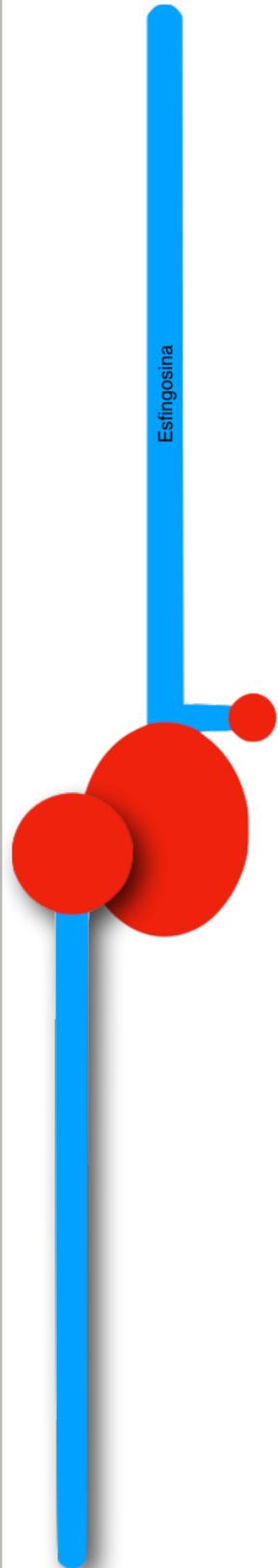


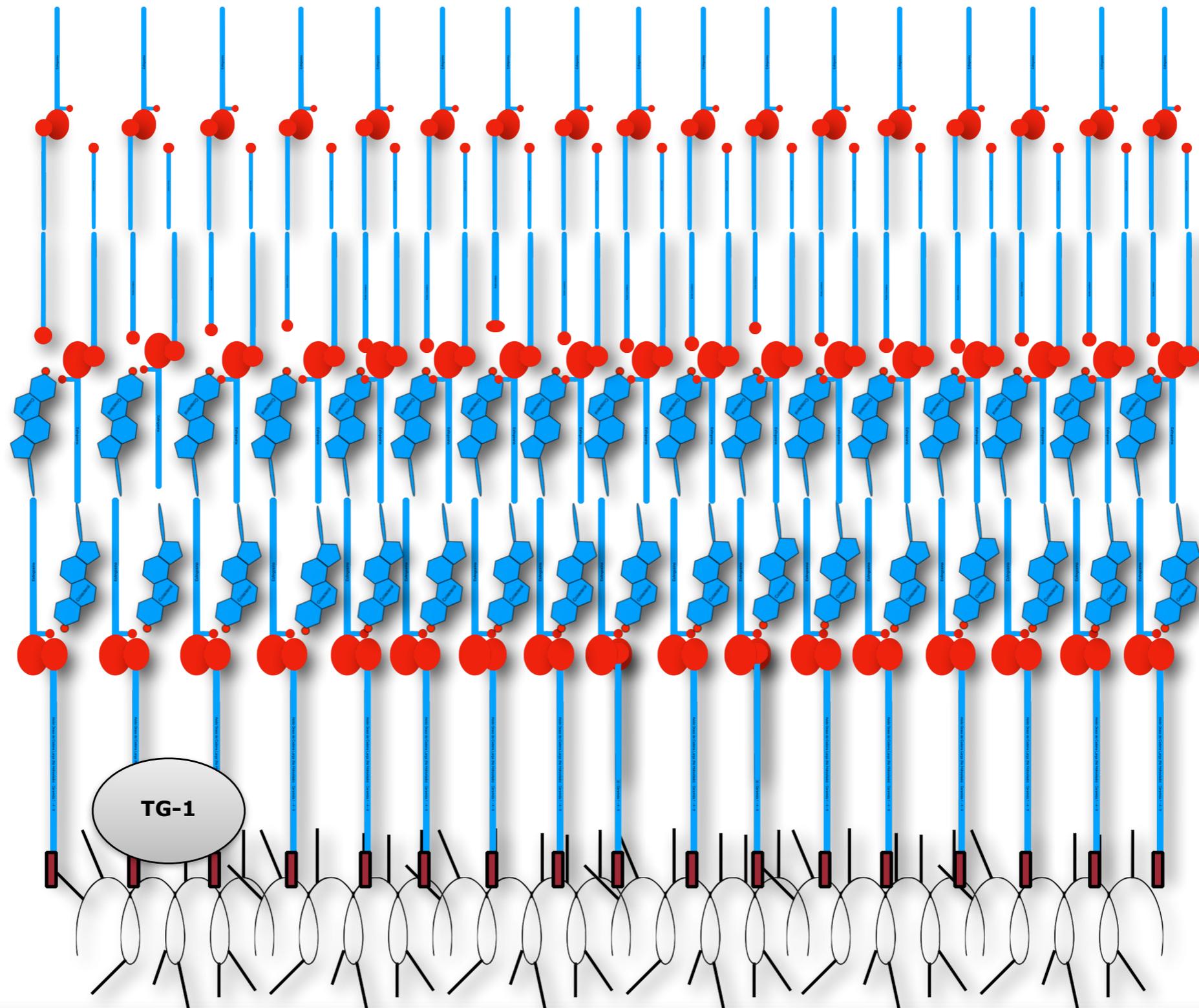


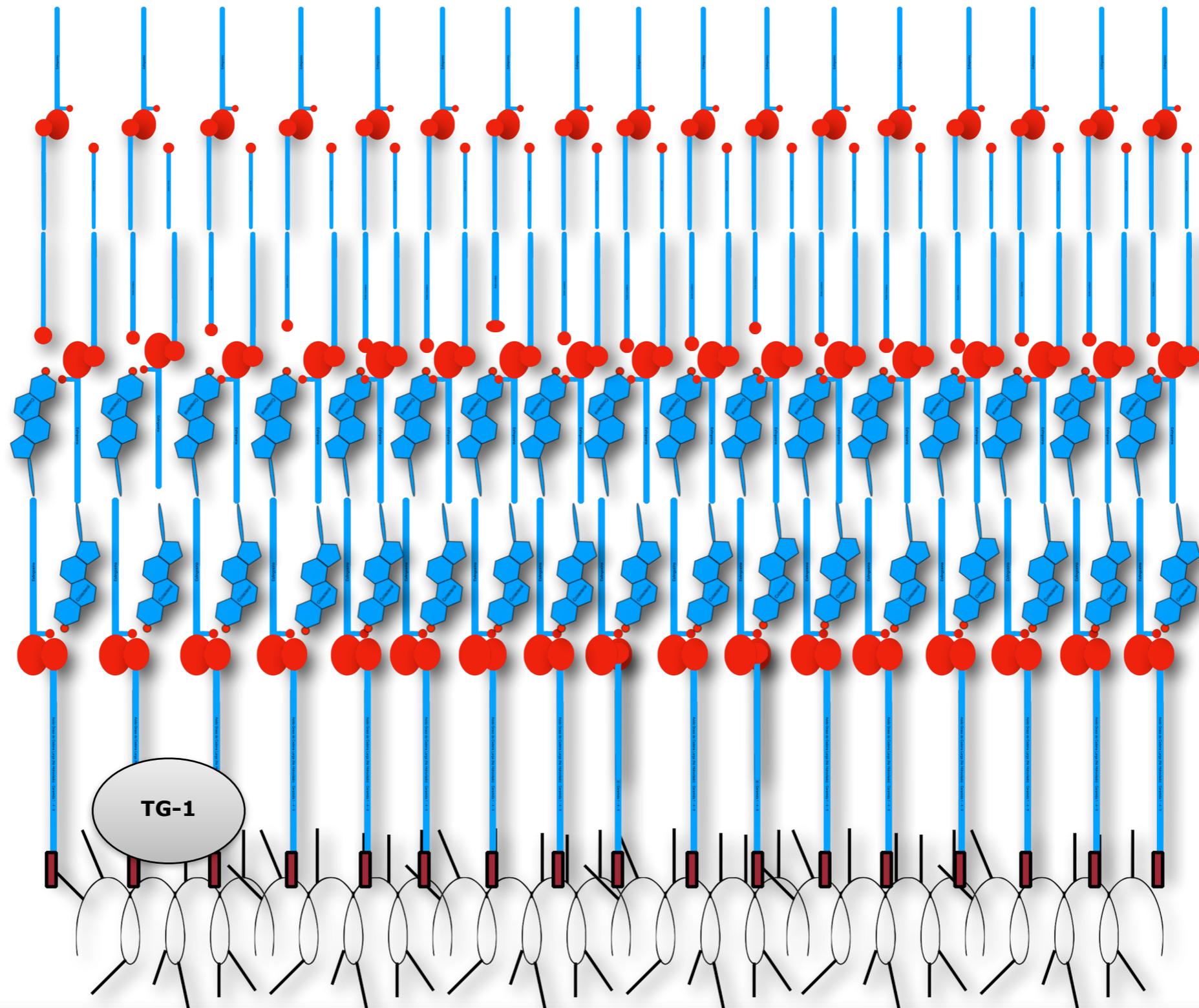


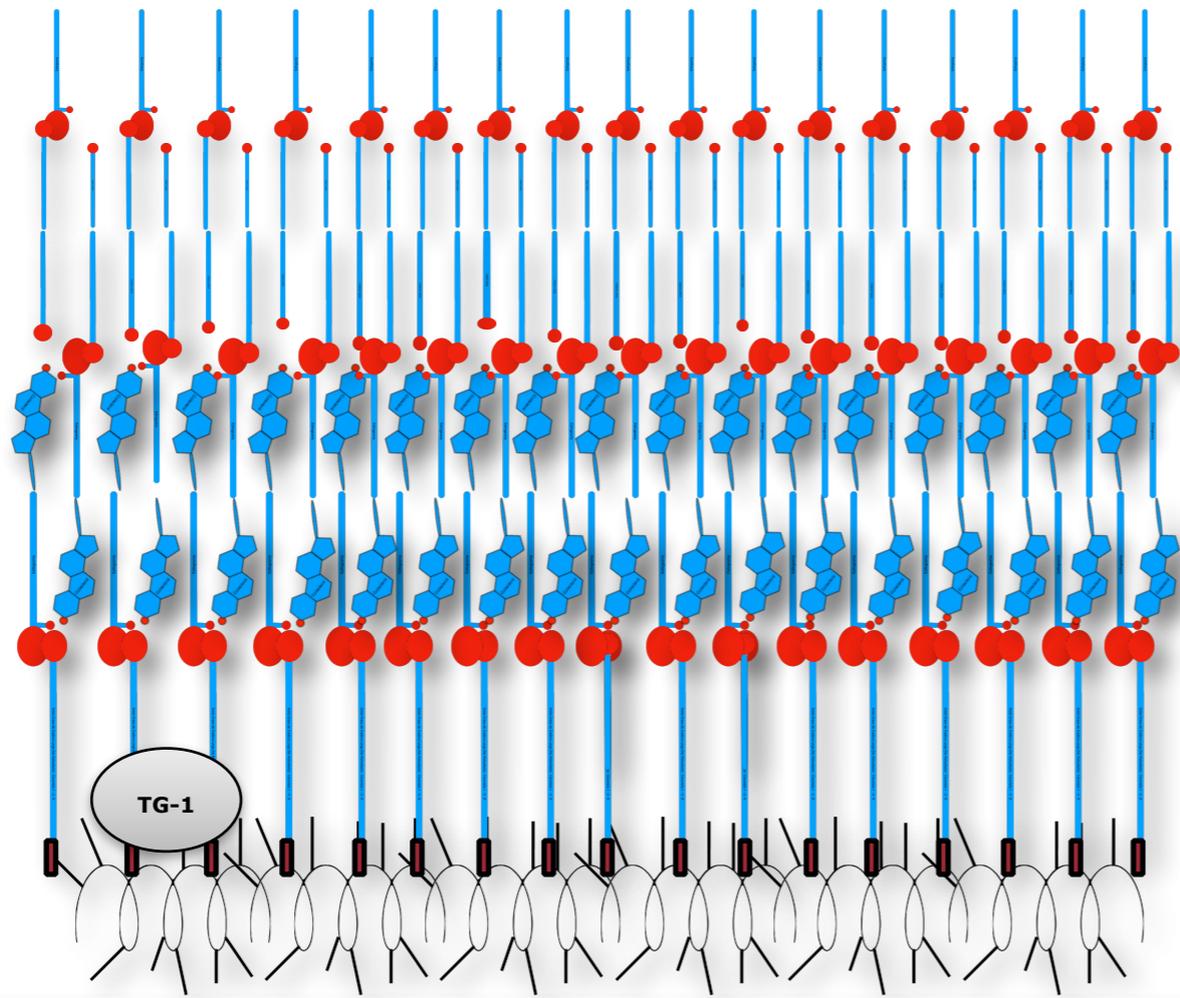
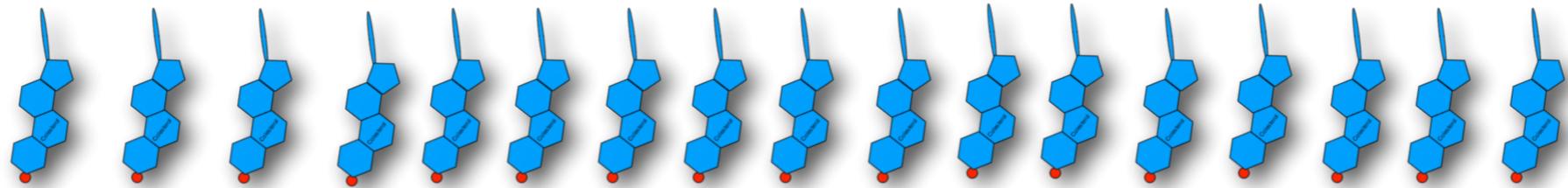


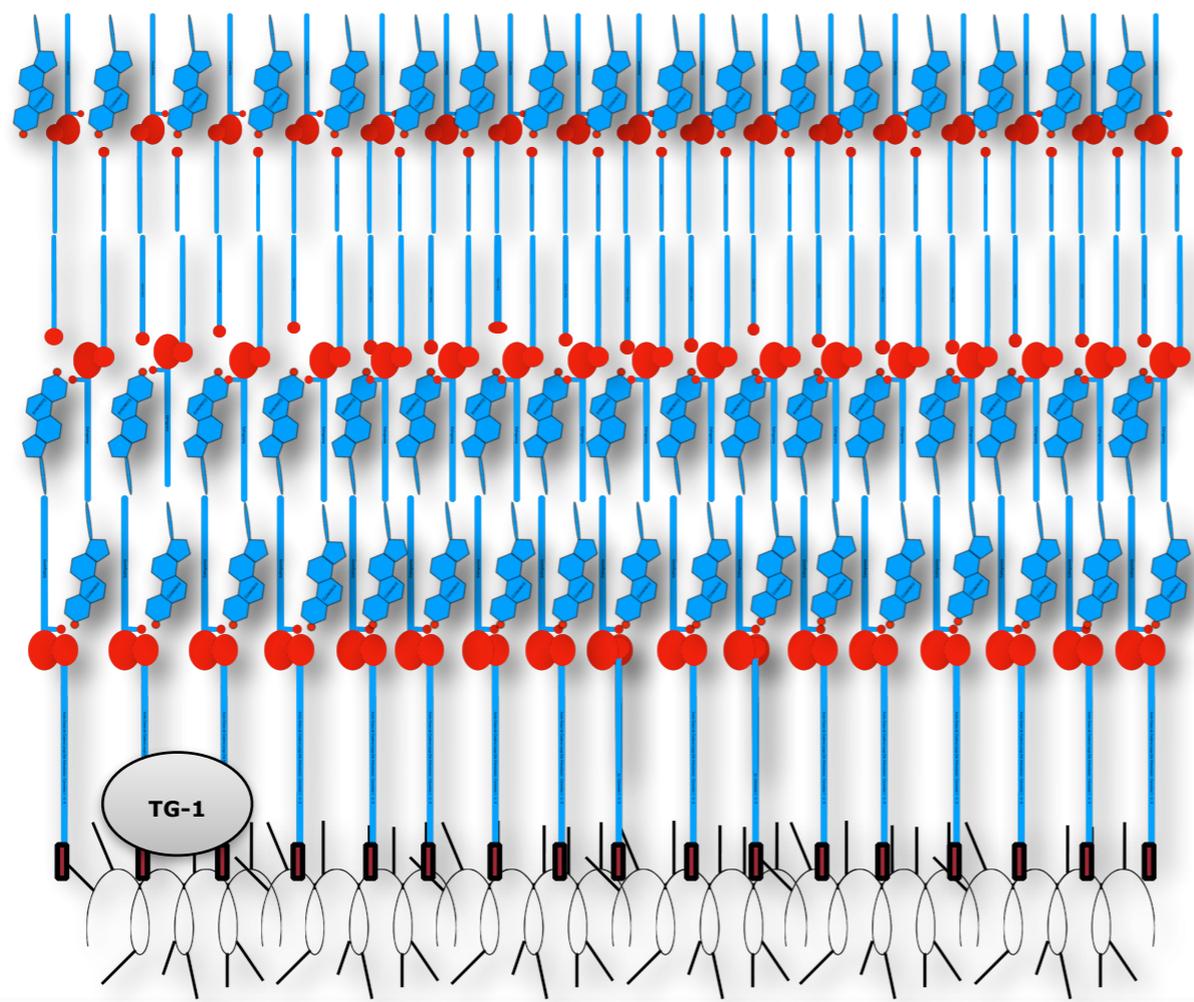
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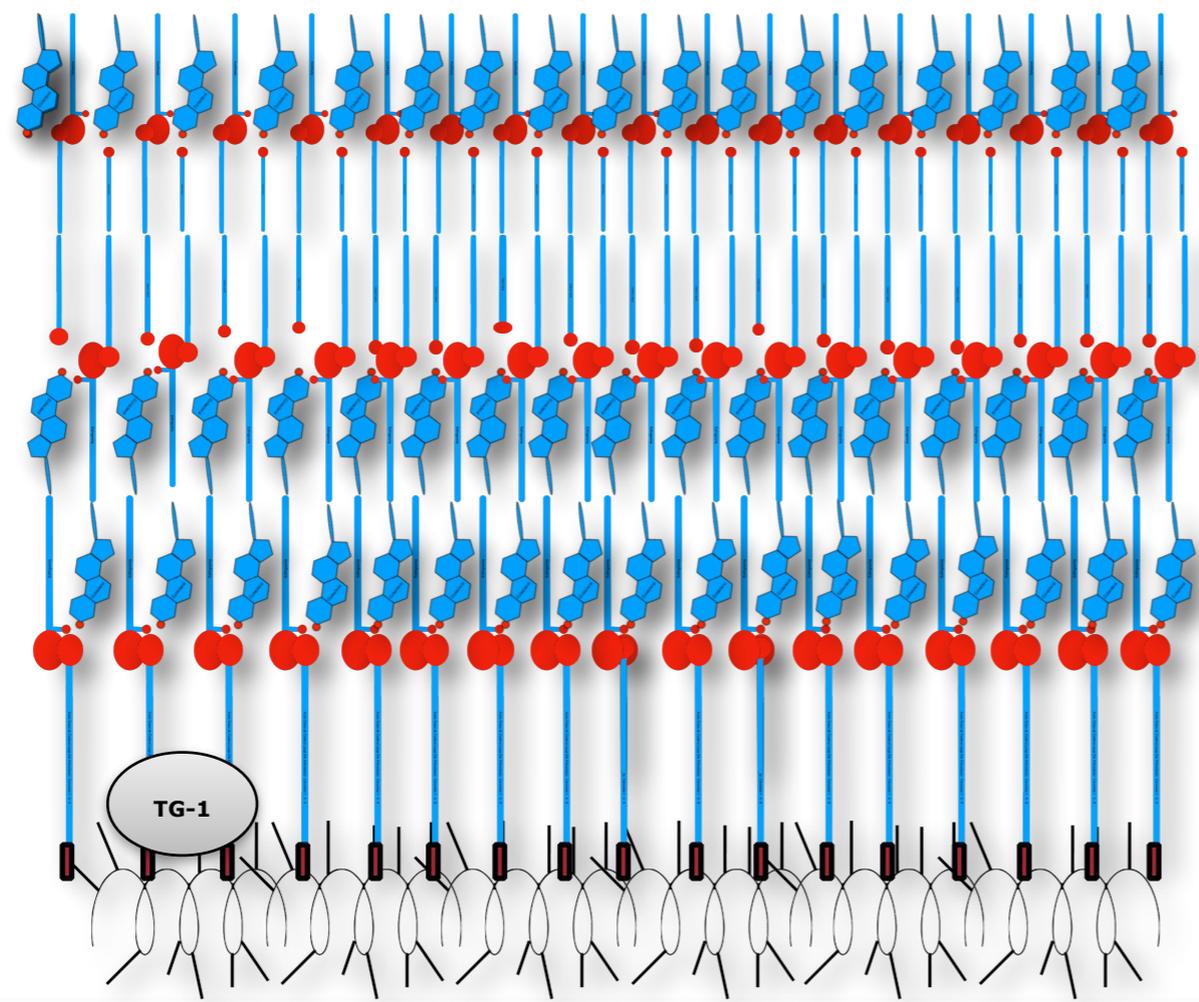


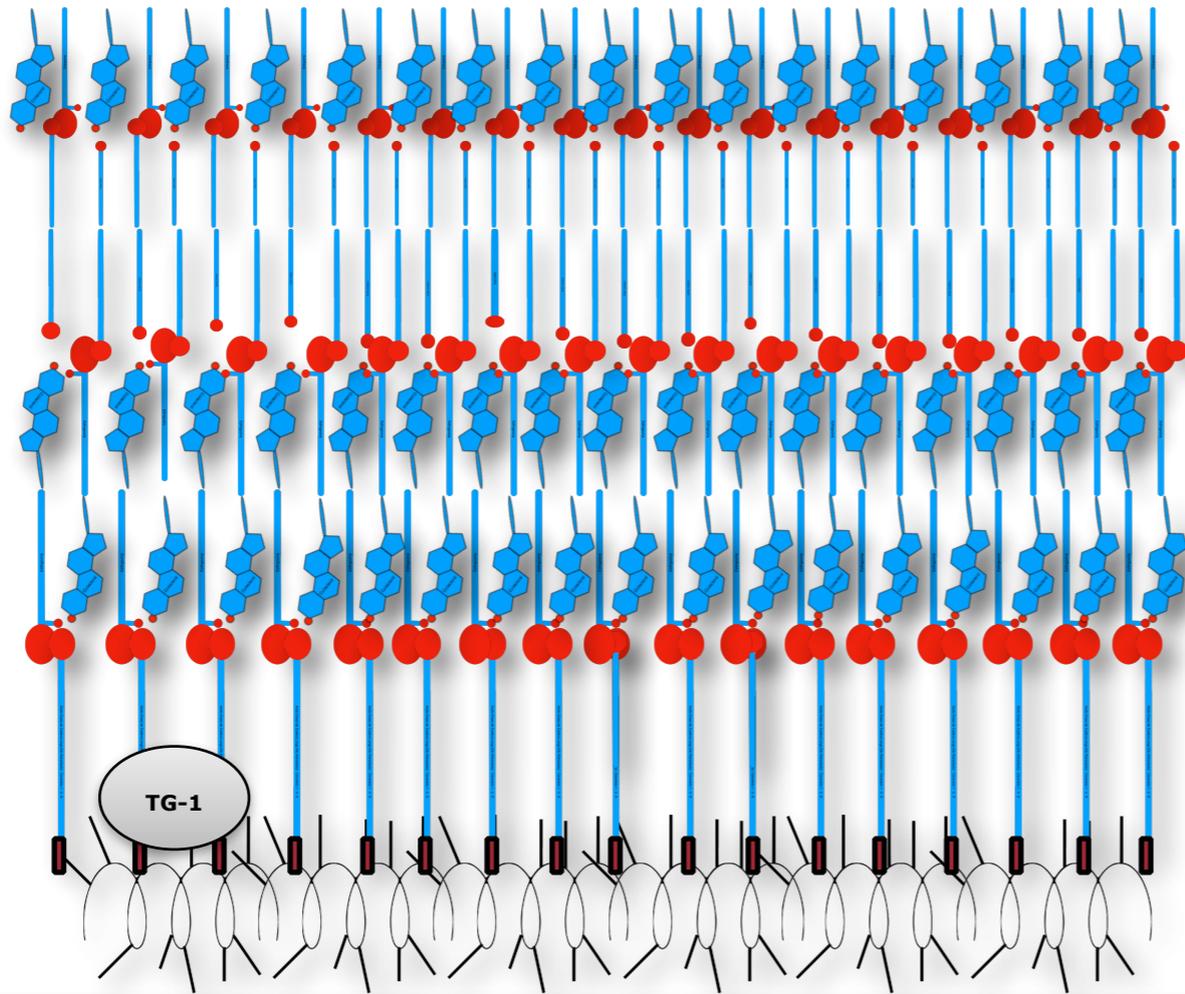
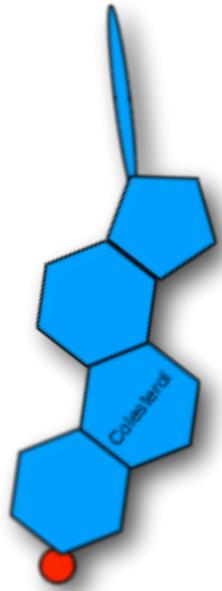


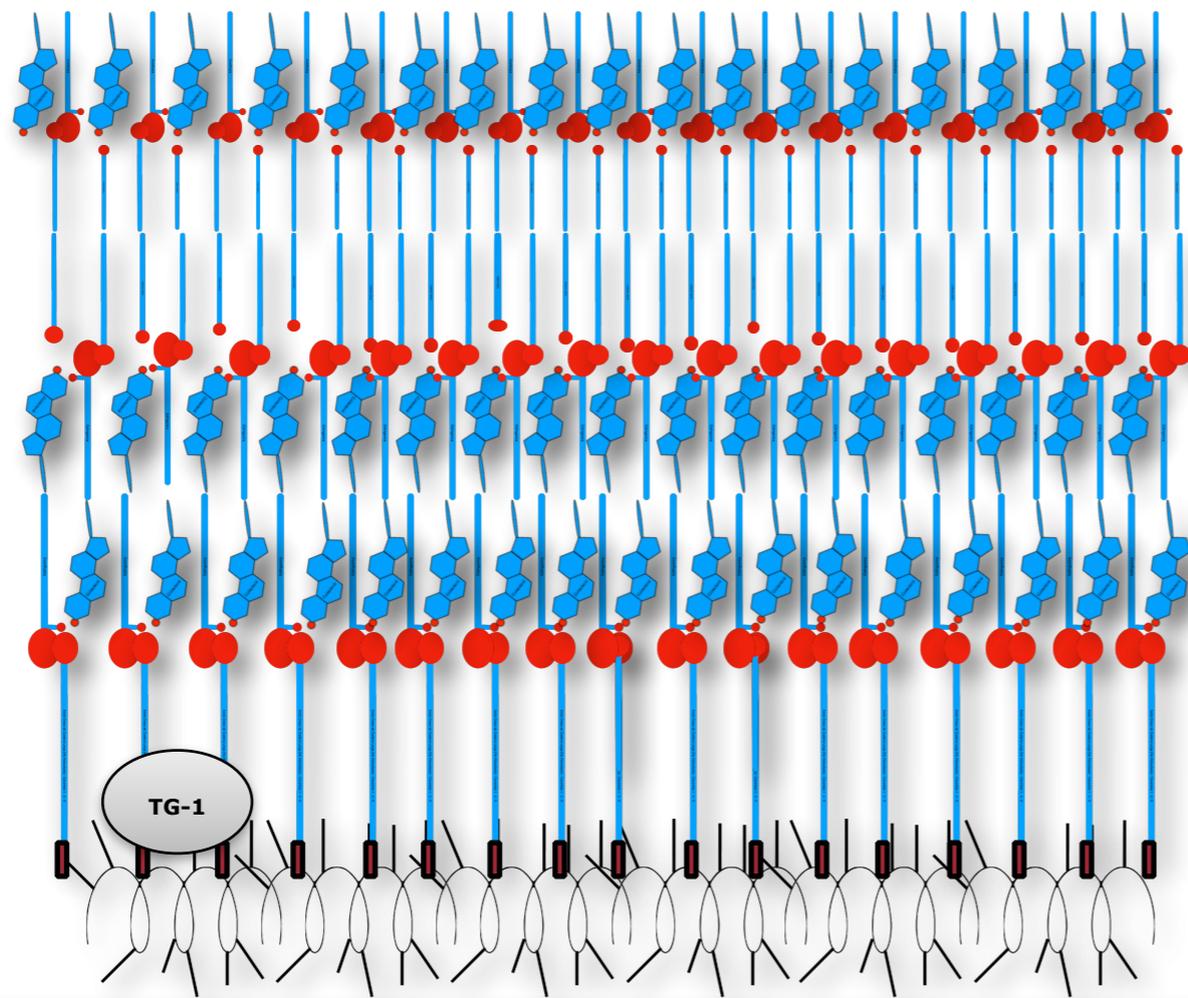
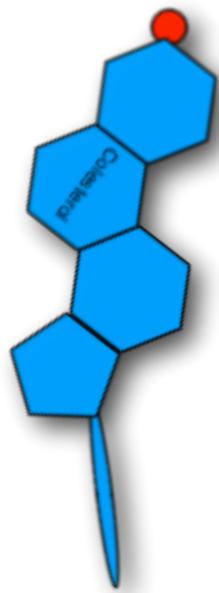


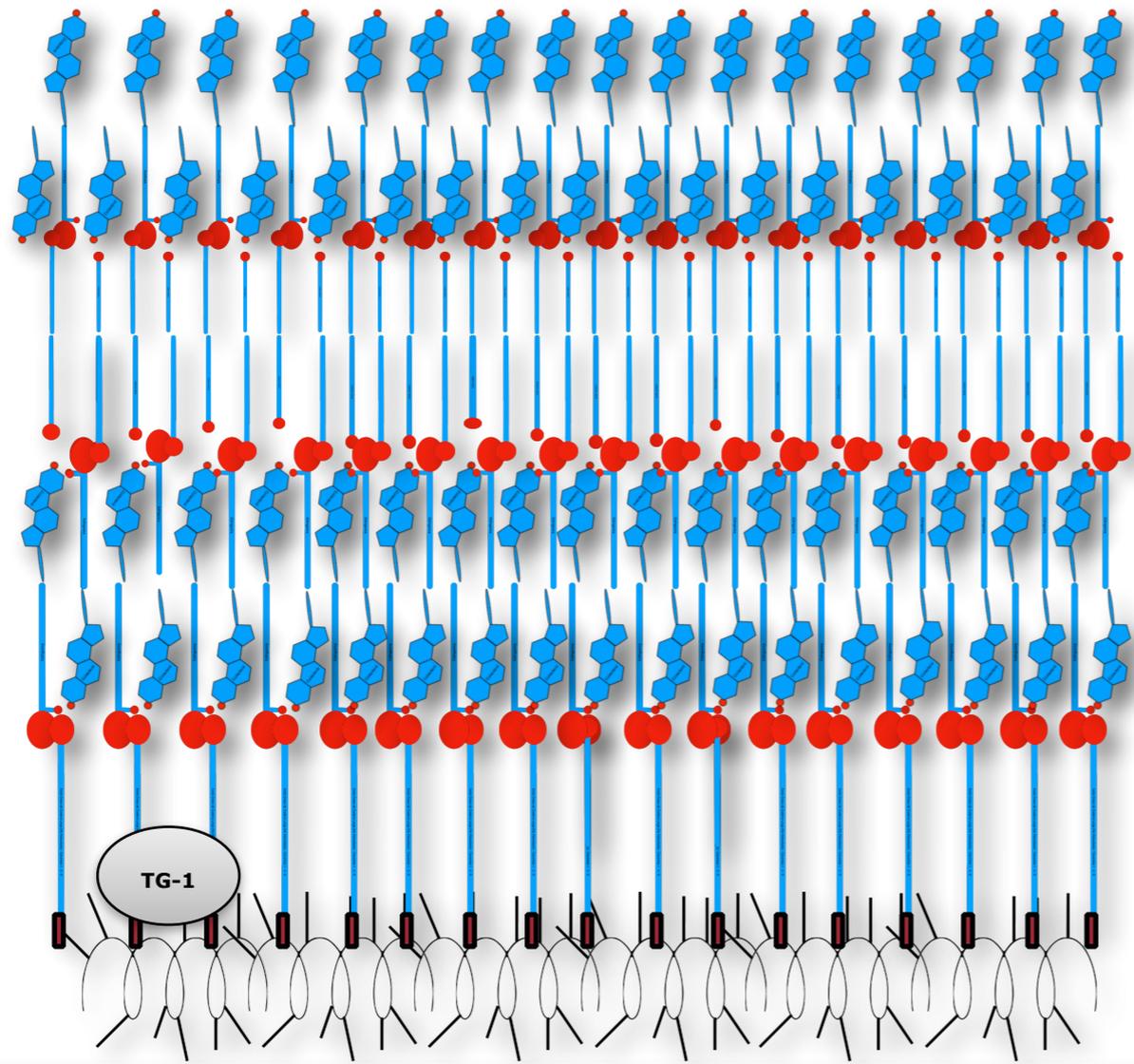


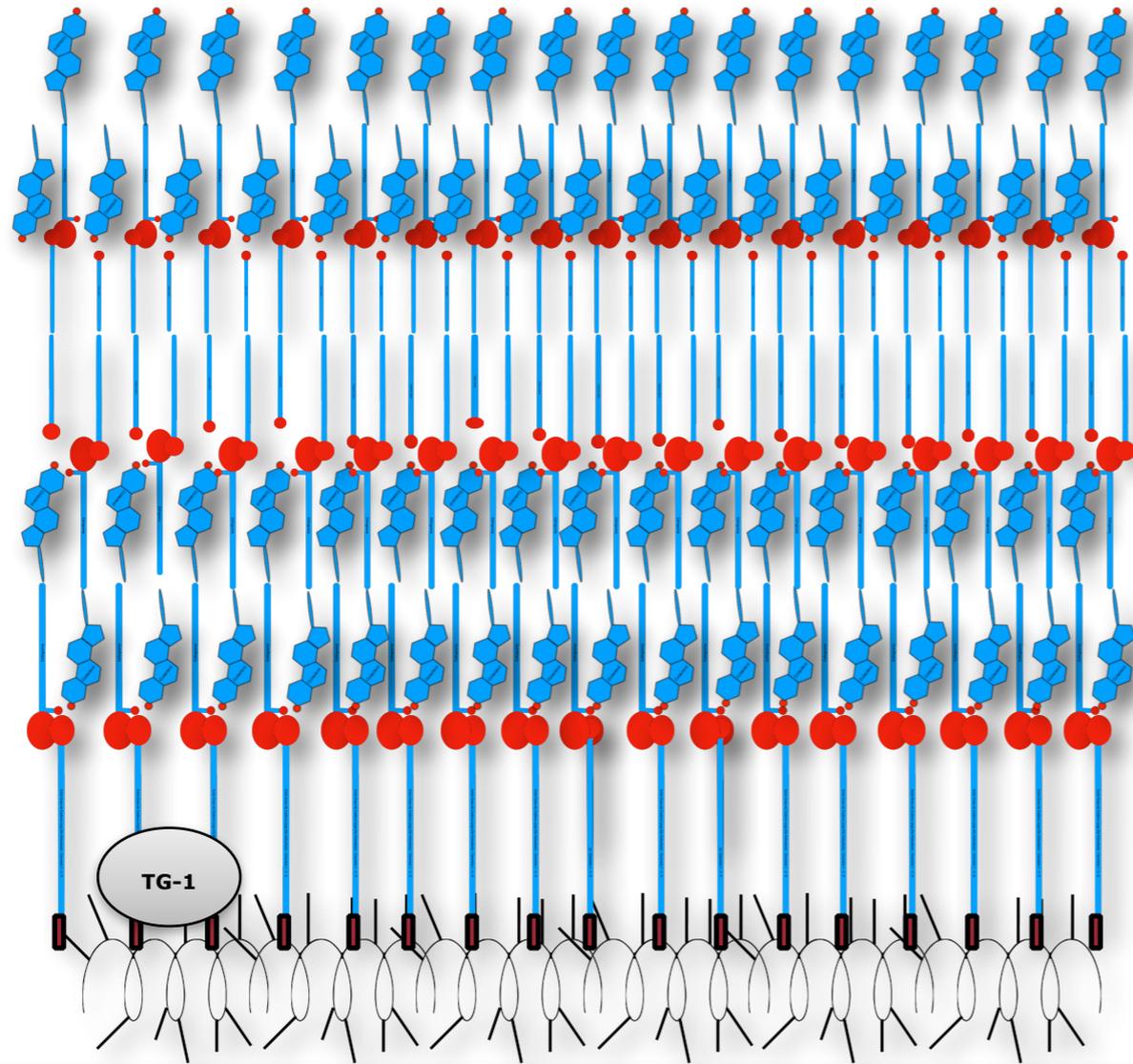


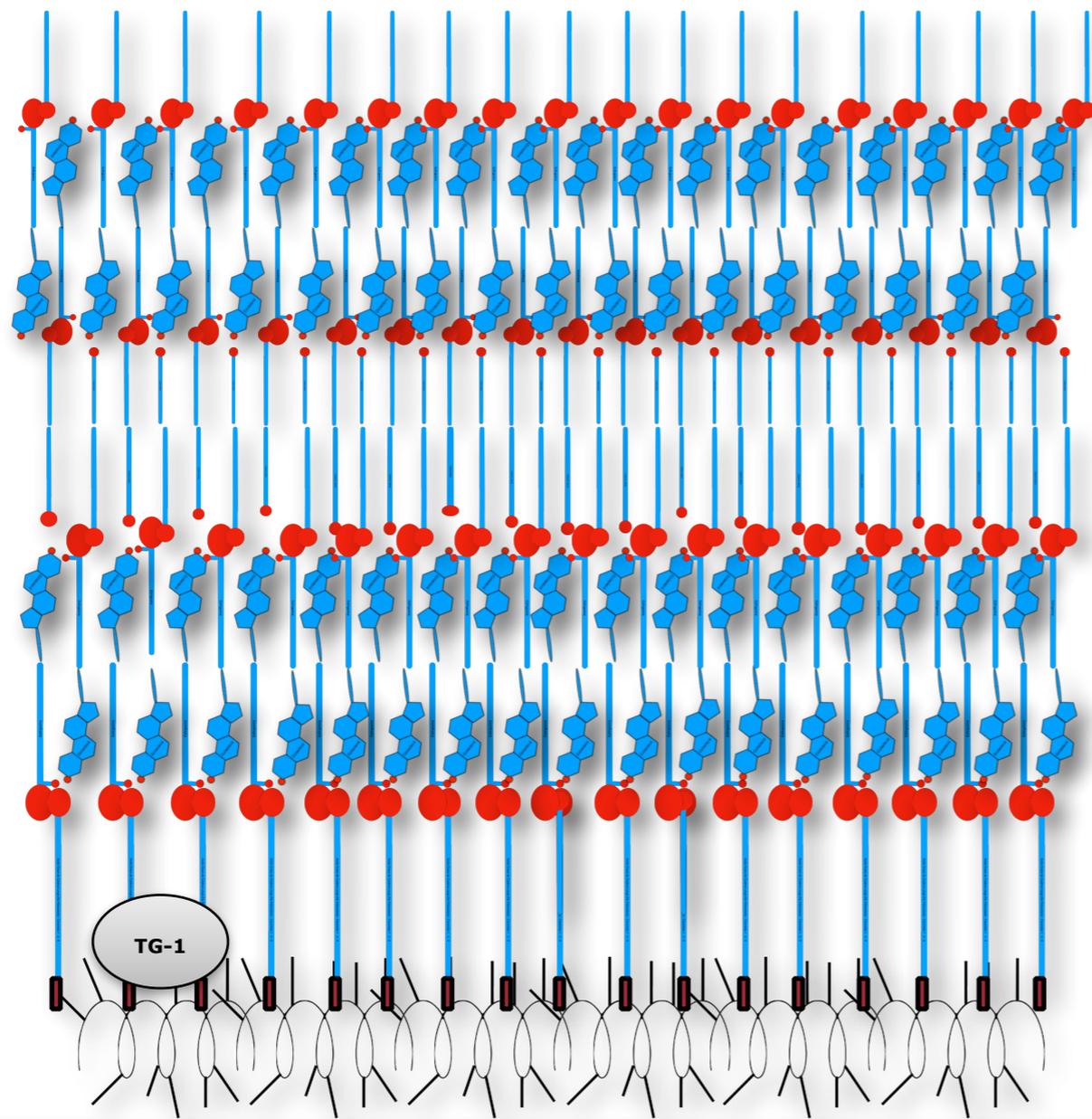


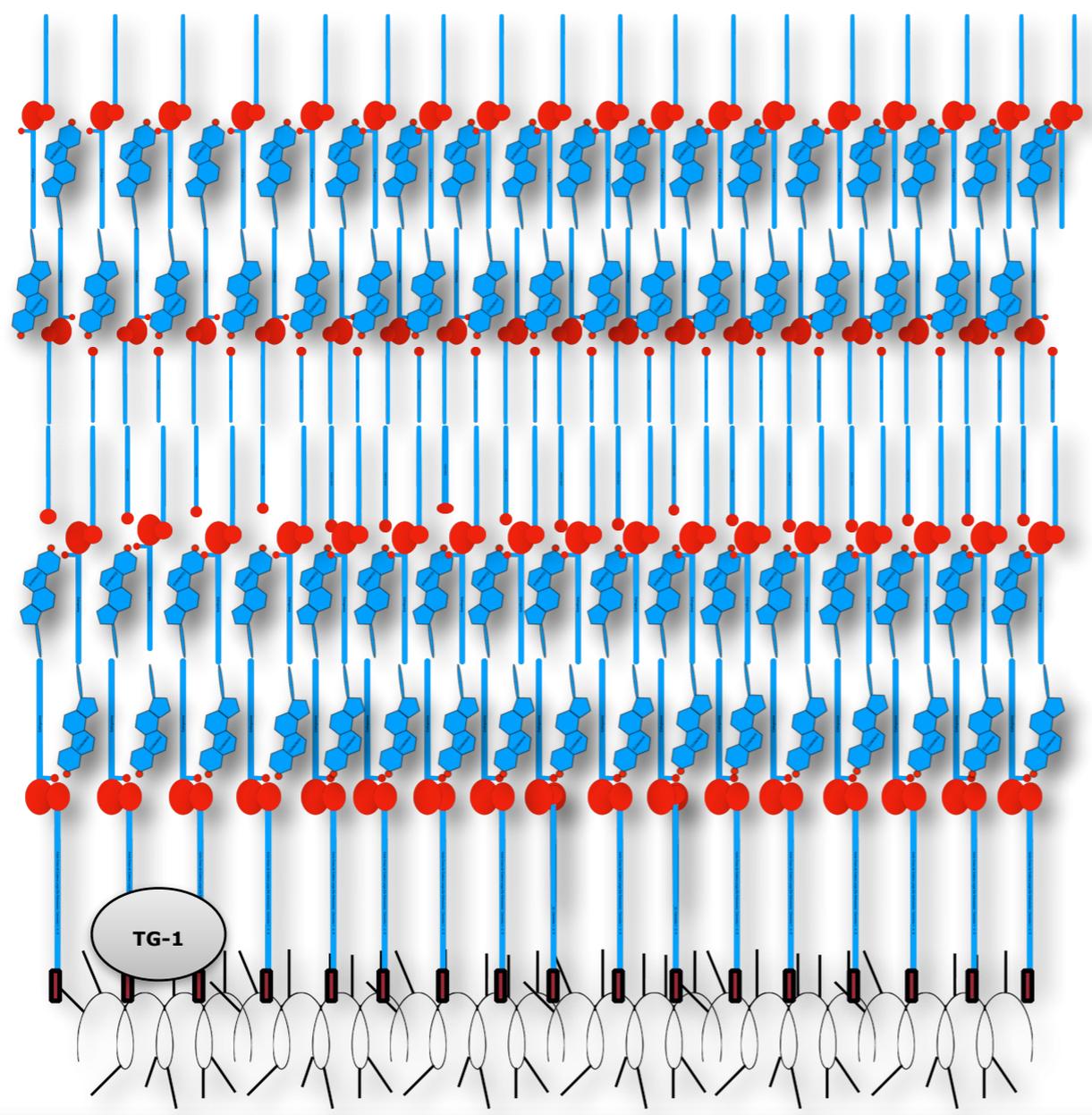
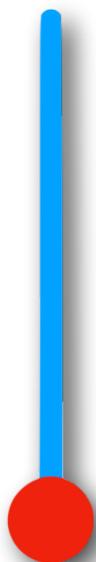


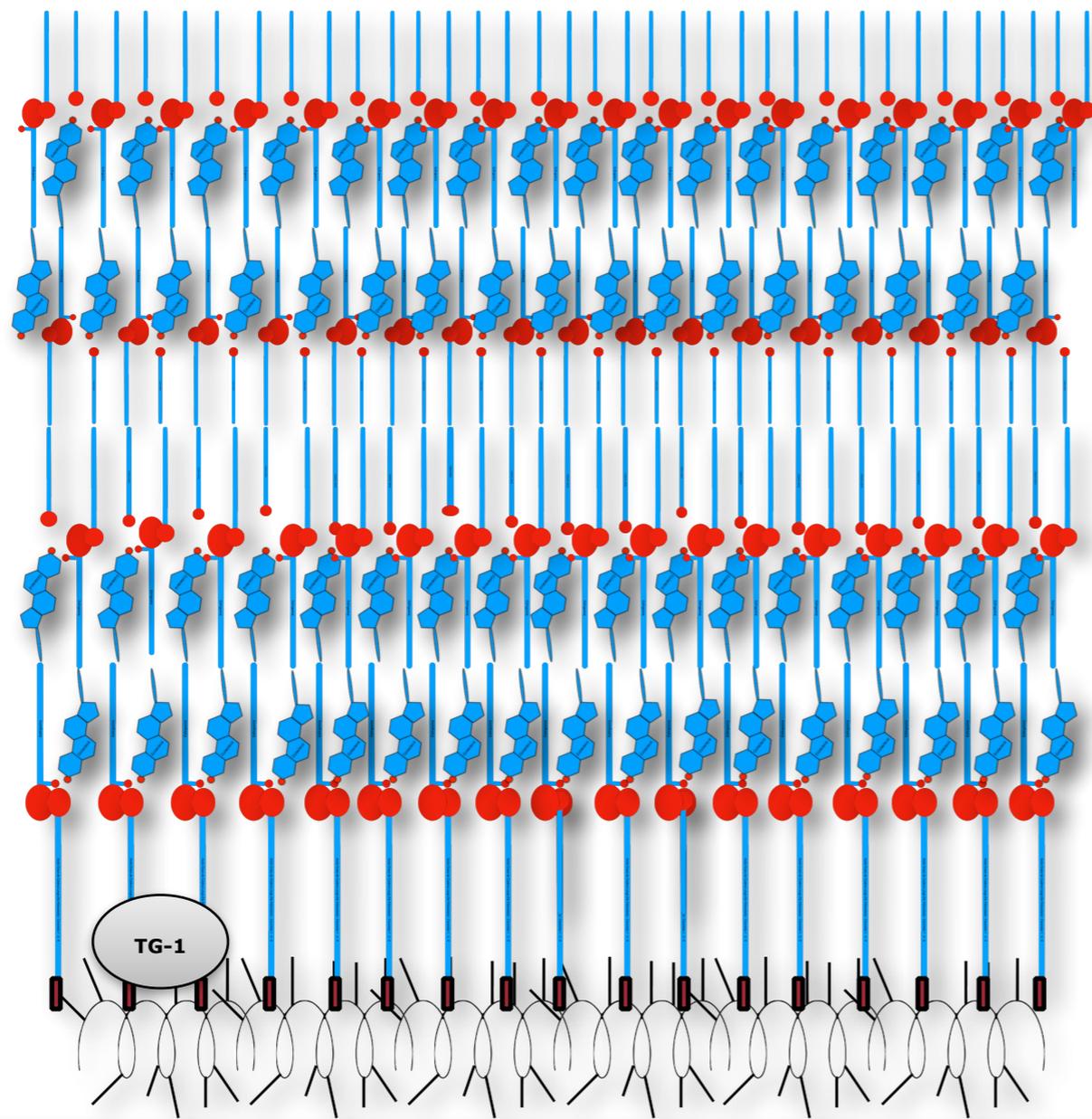


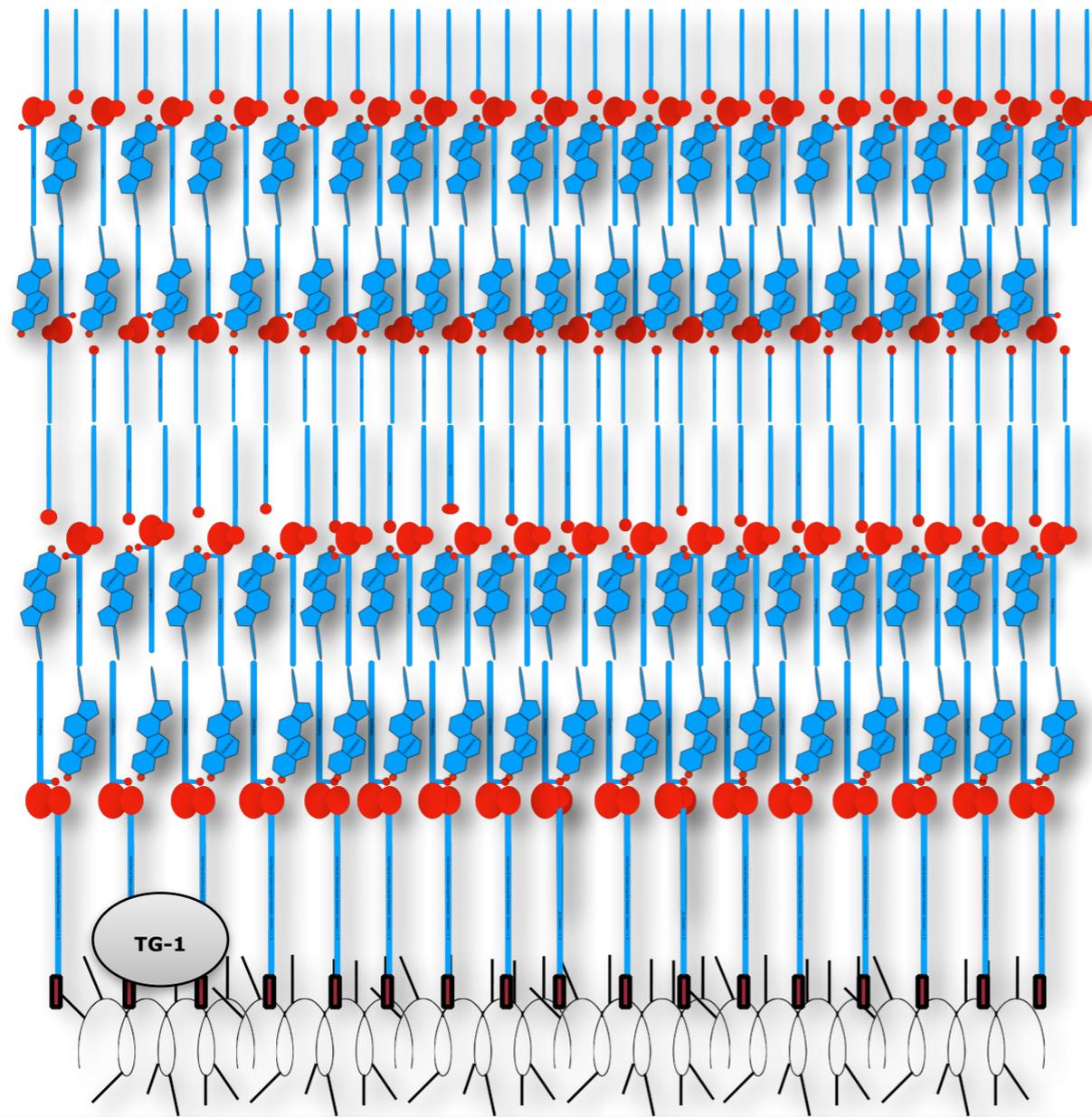
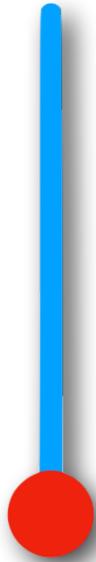


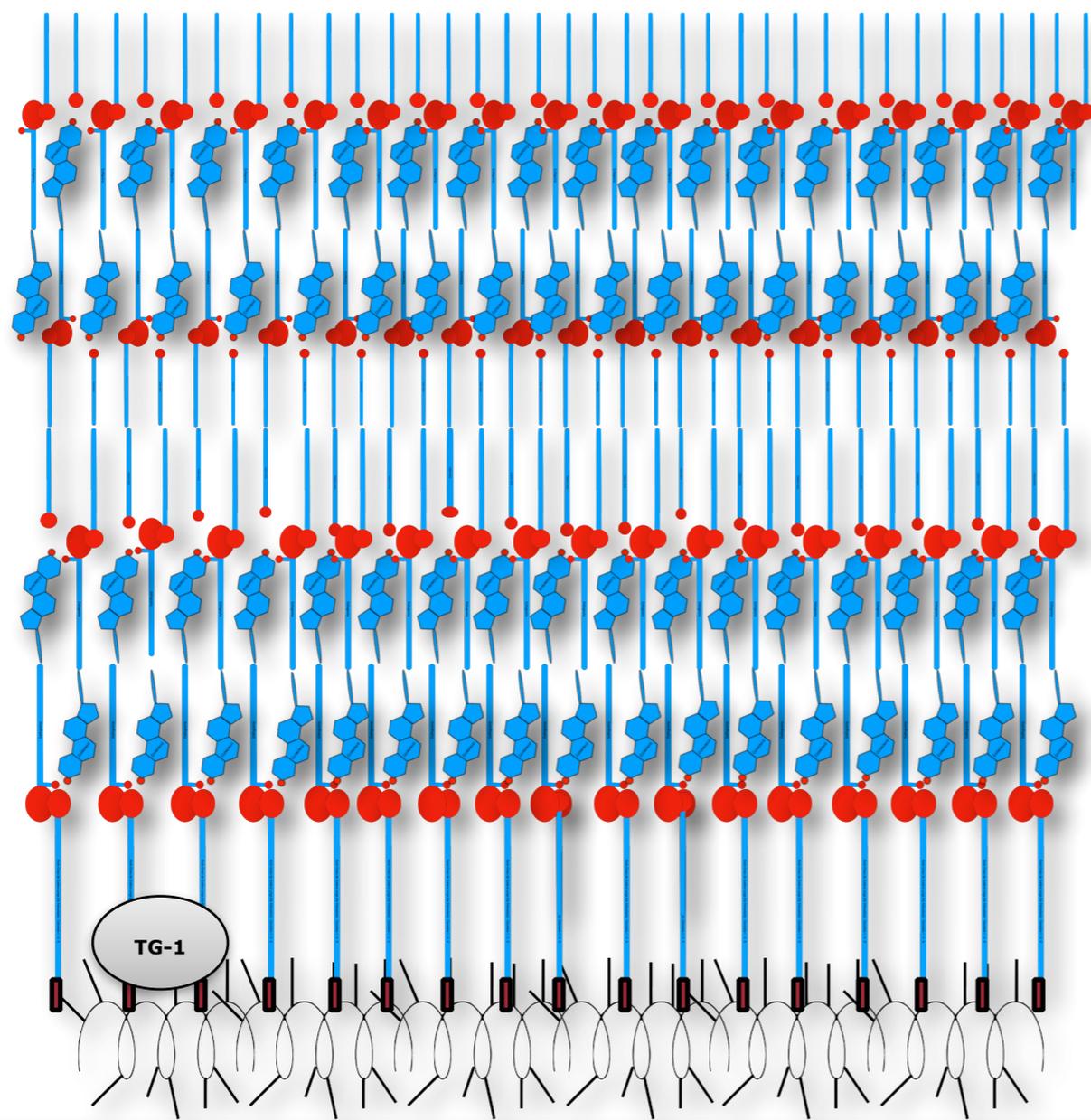


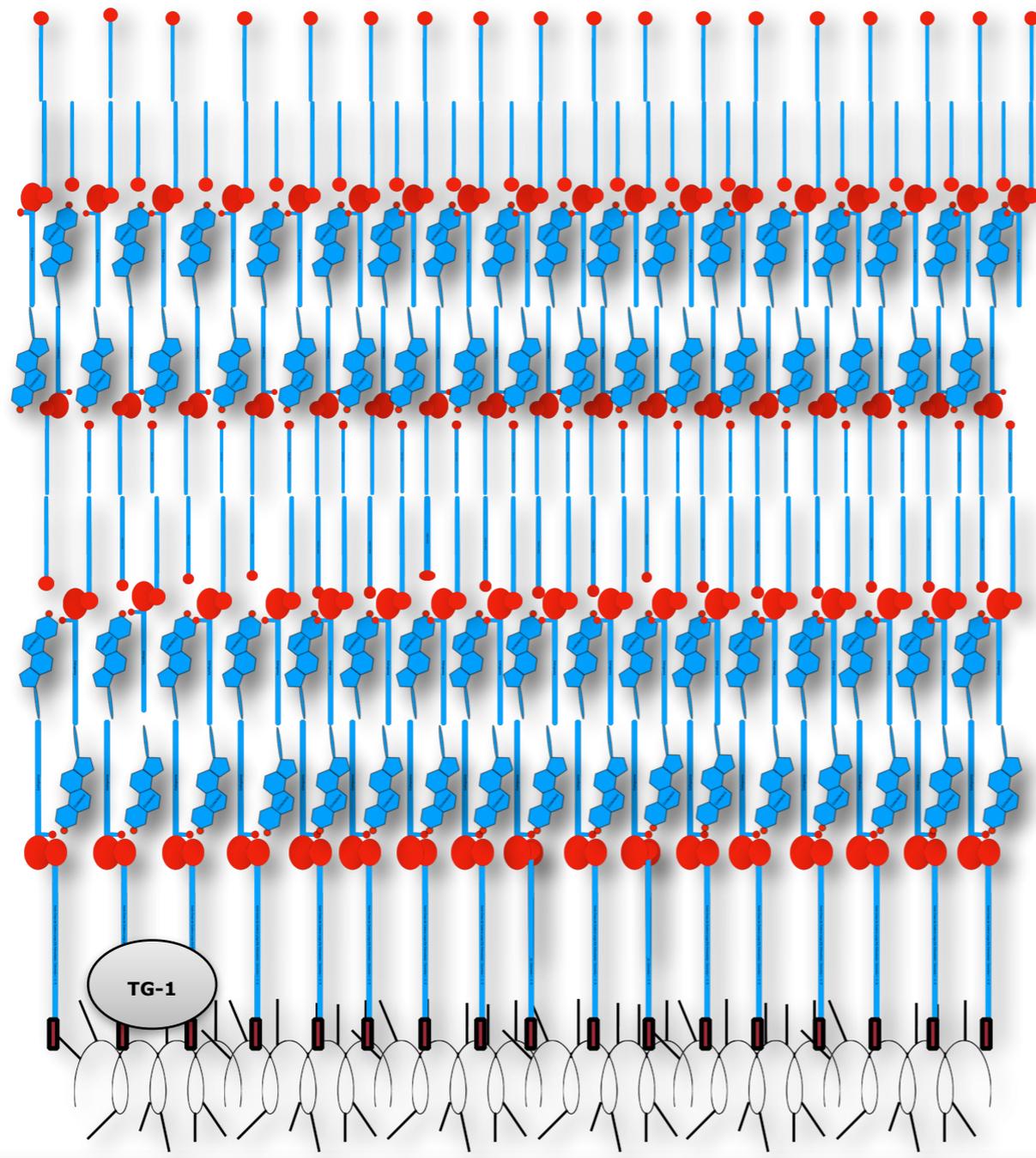


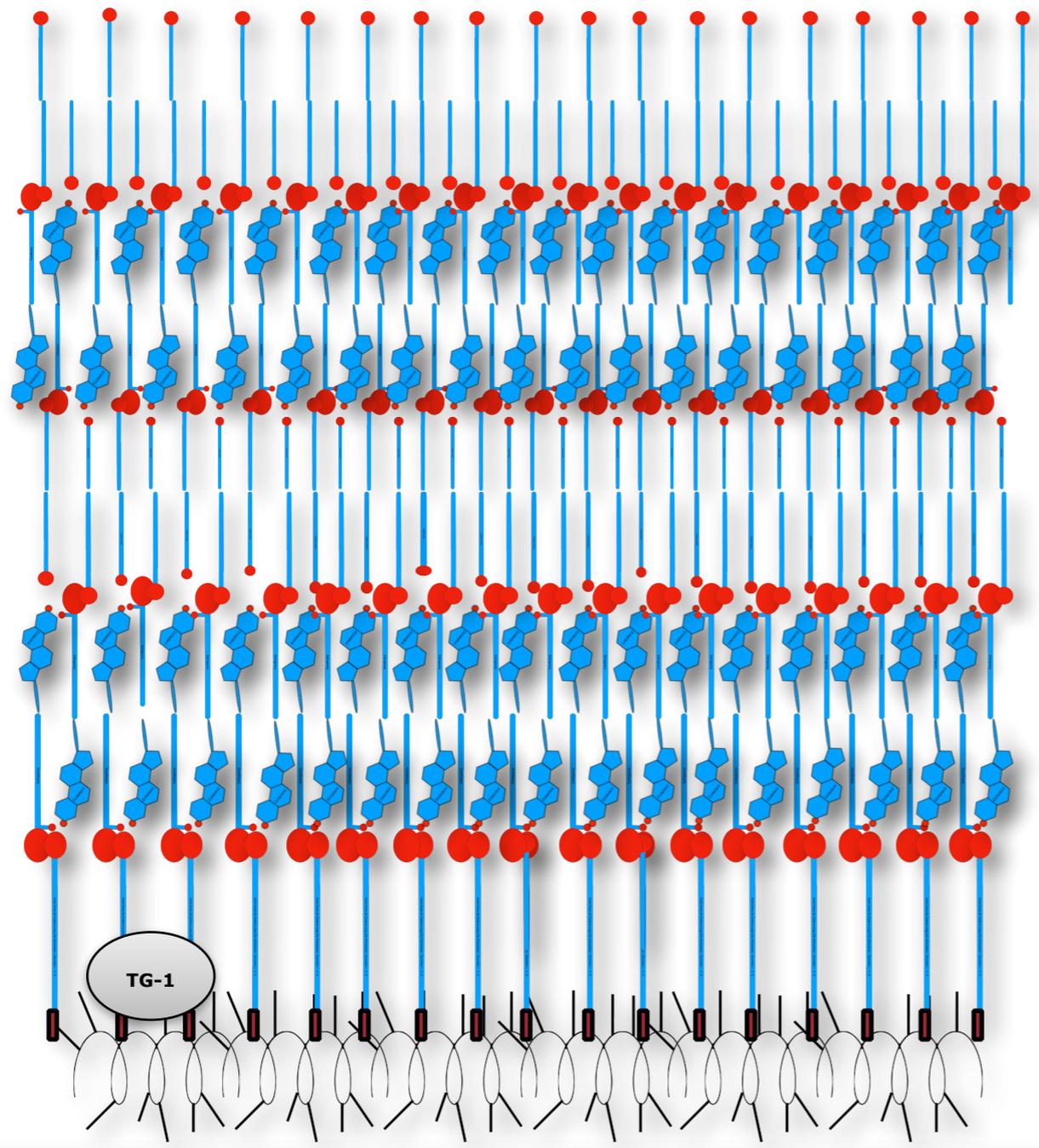
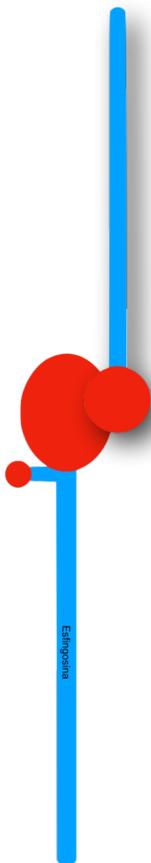




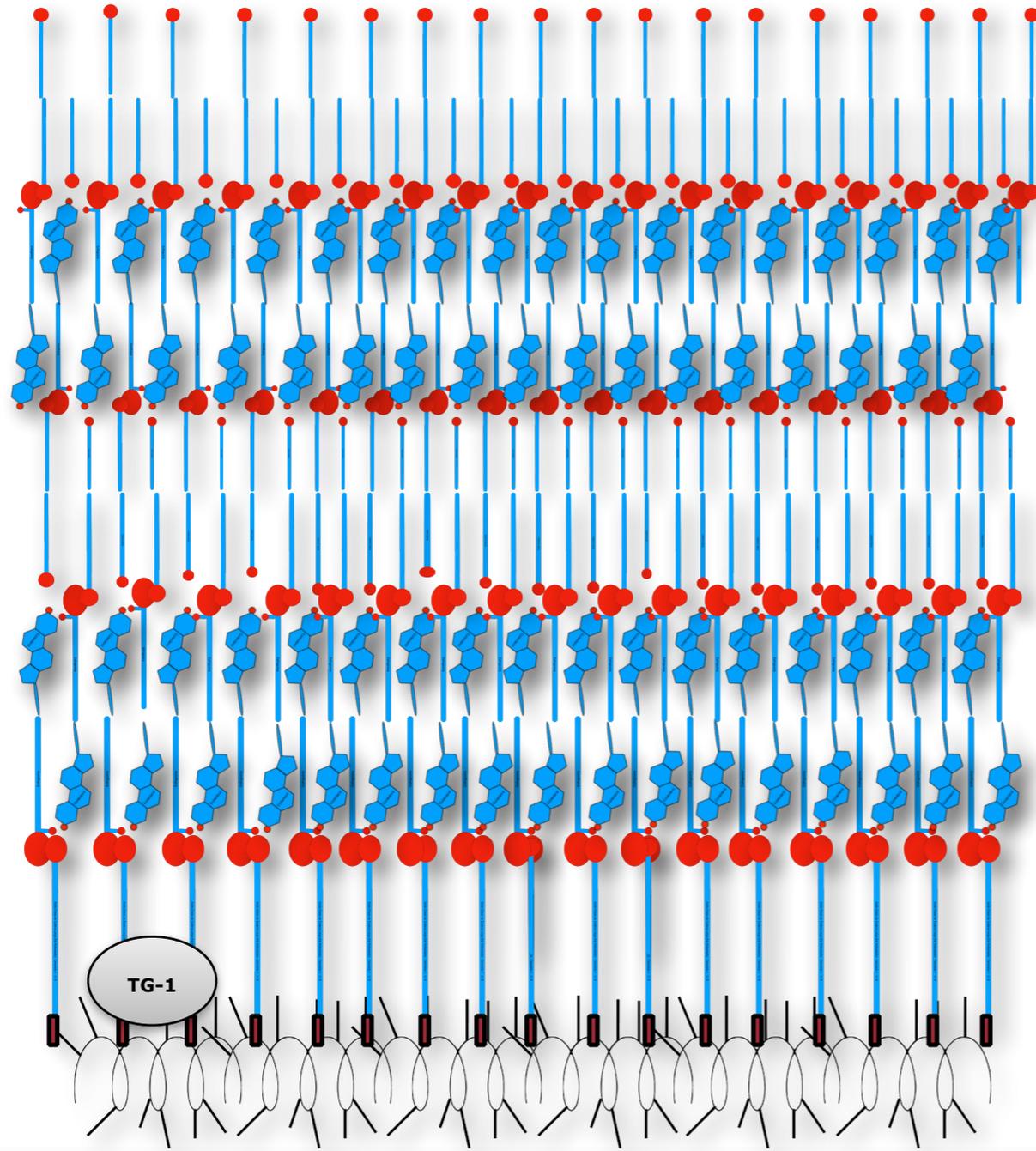


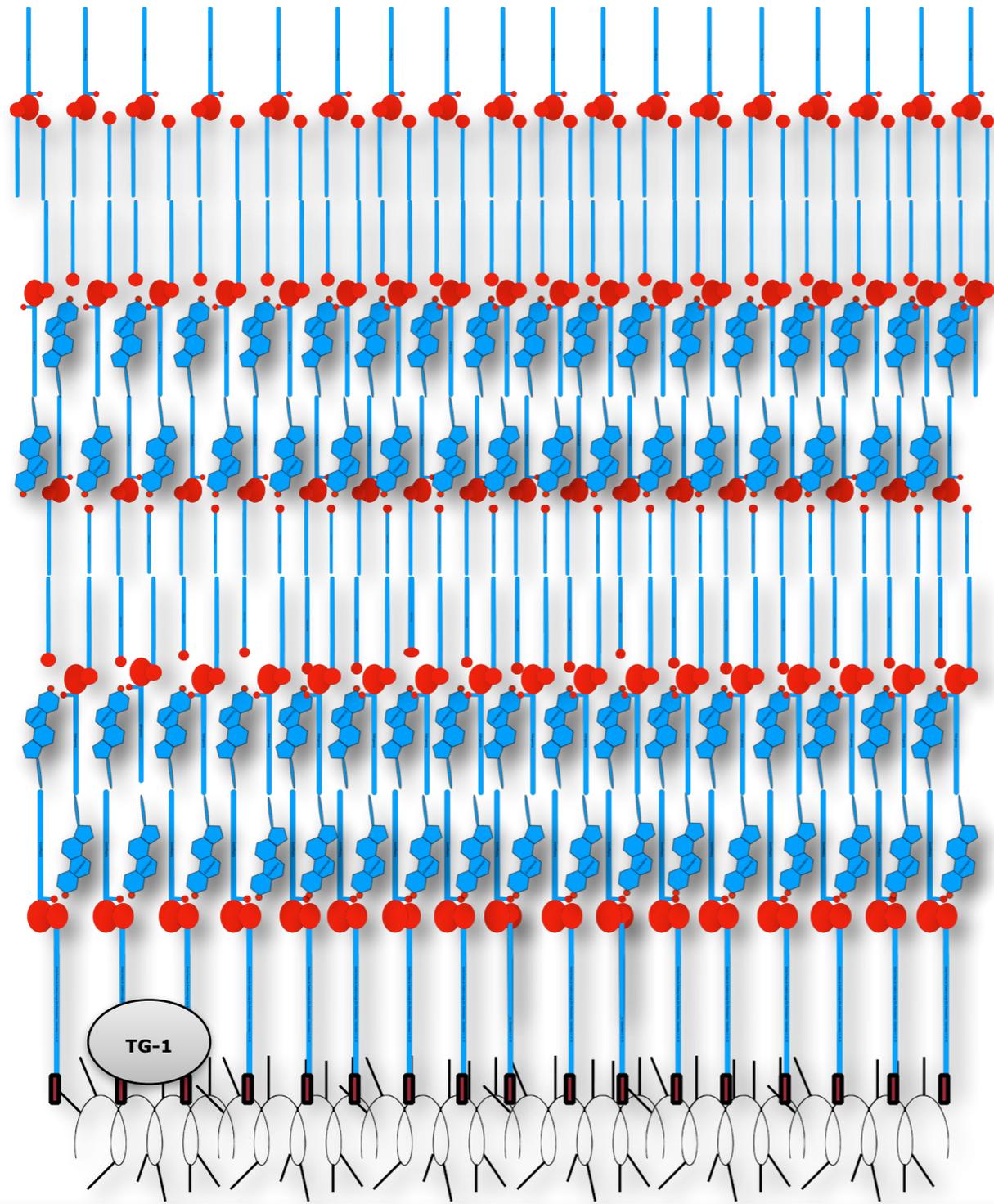


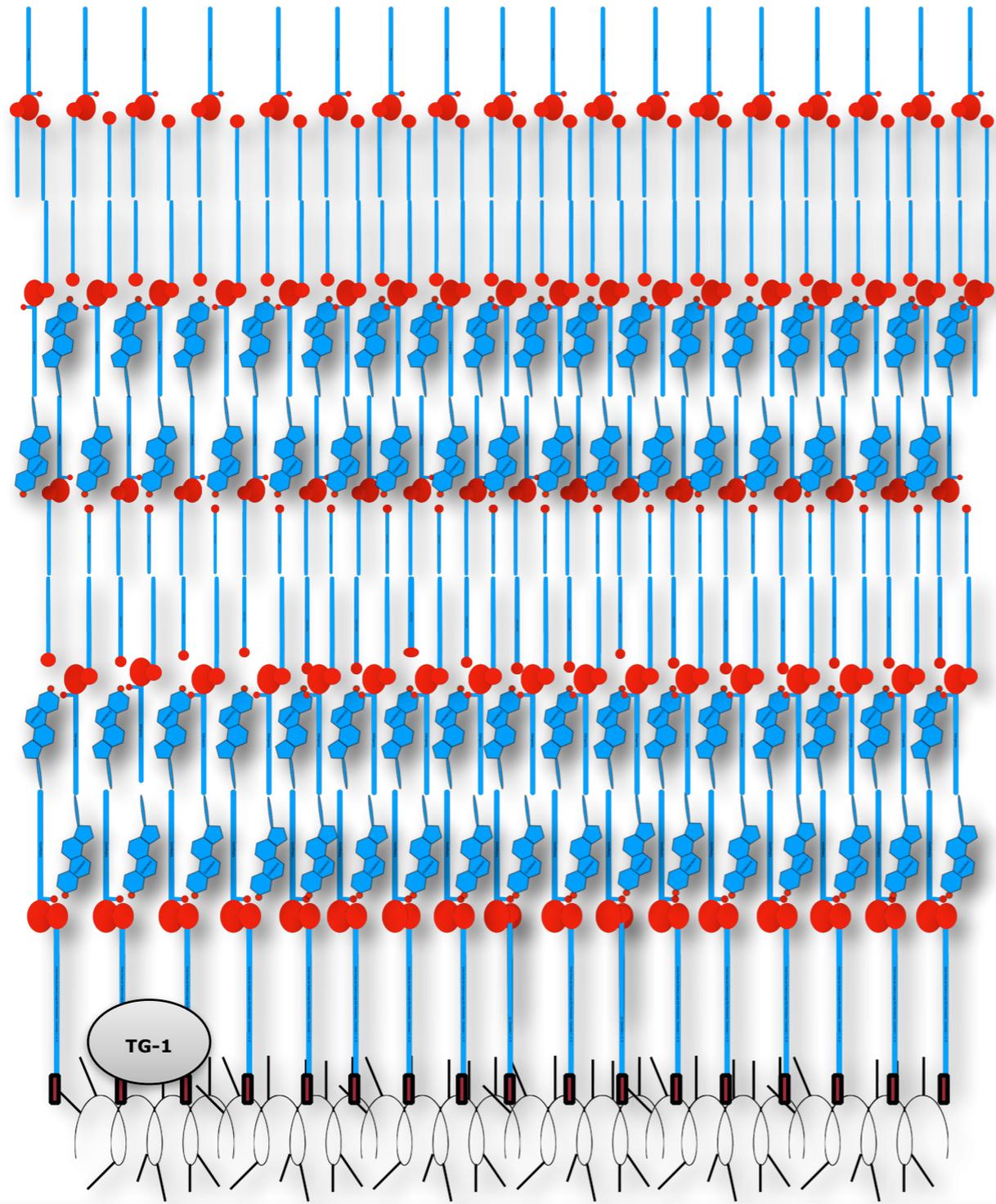


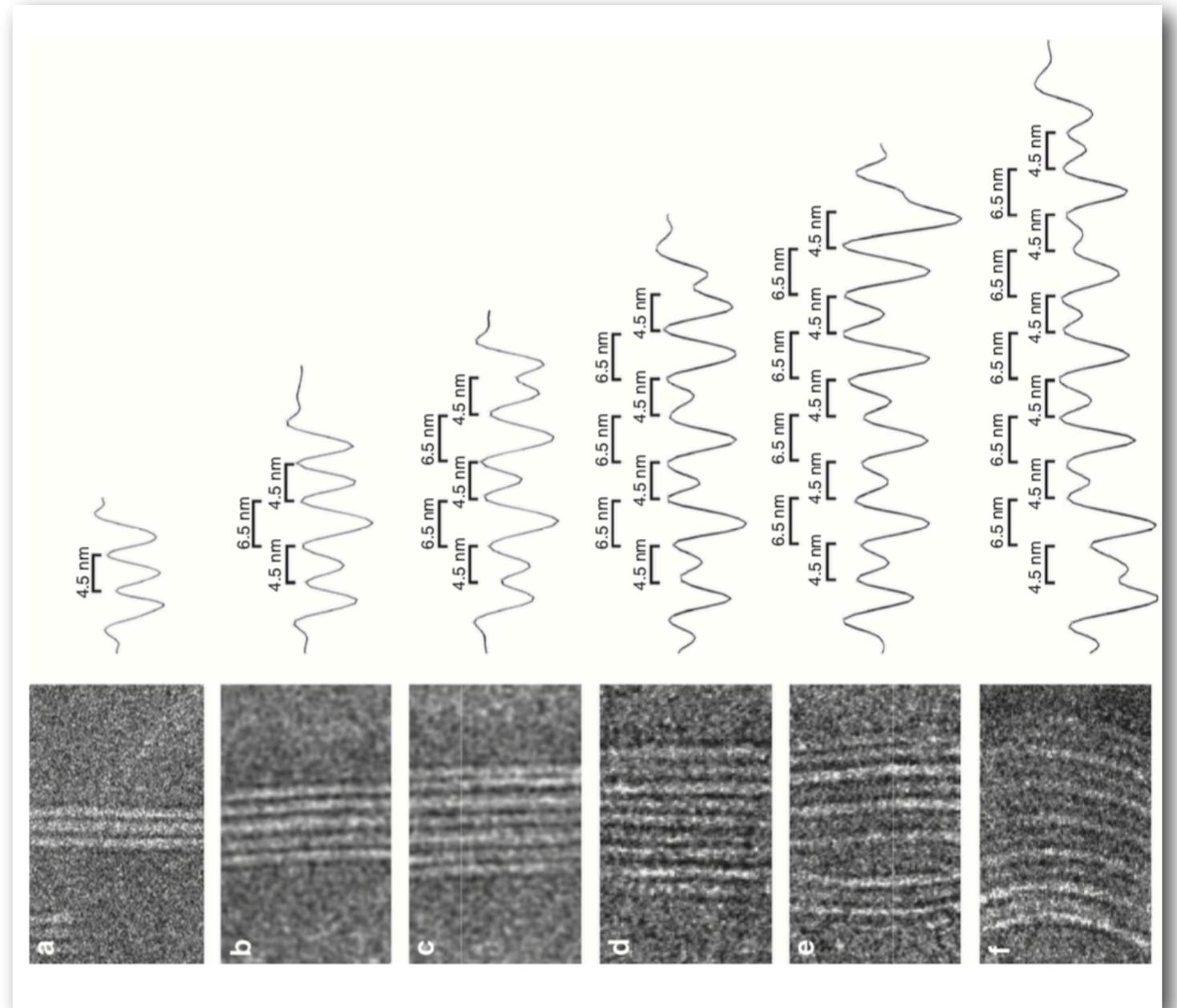
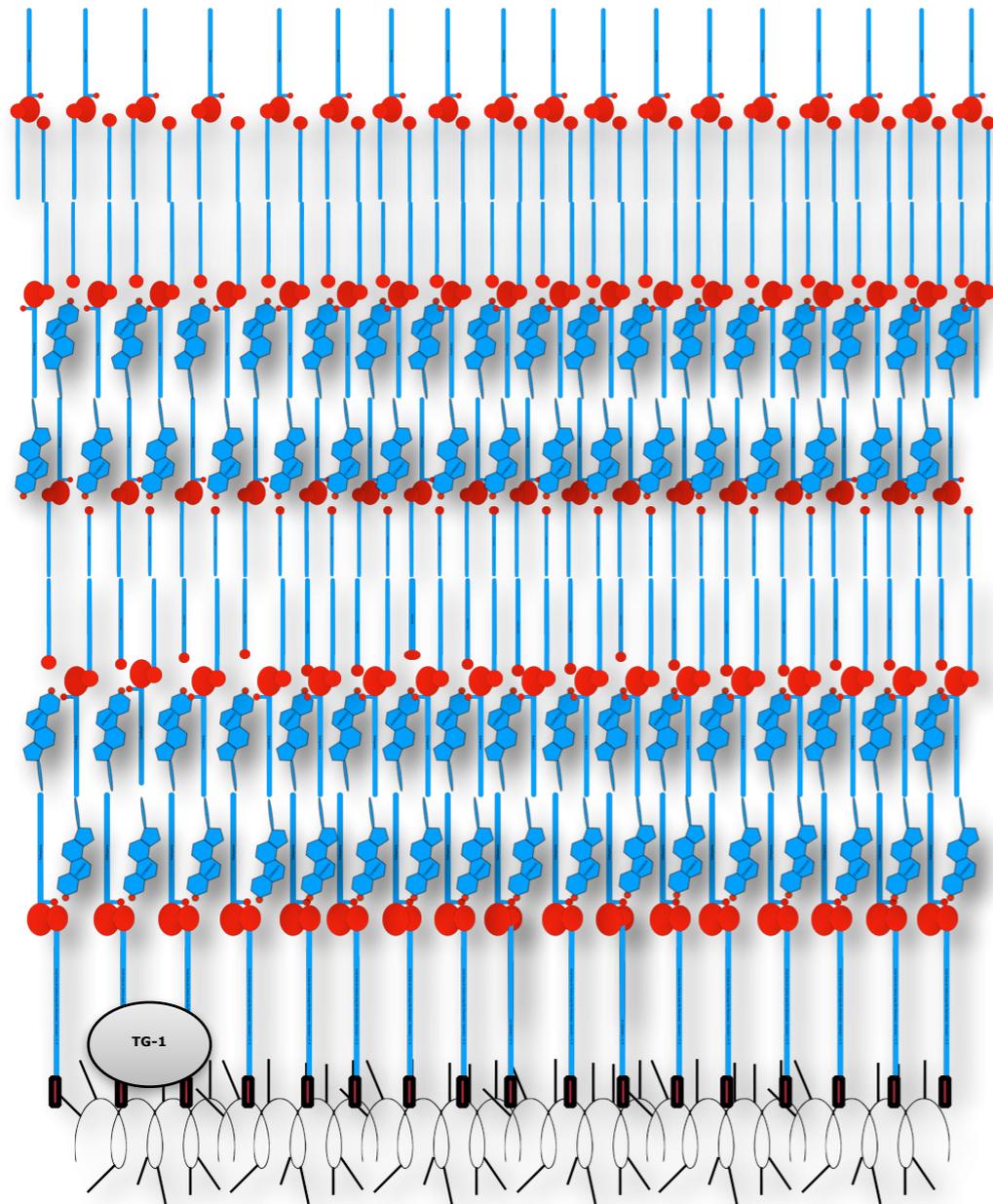


Esfingolipina









Iwai I "The human skin barrier is organized as stacked bilayers of fully extended ceramides with cholesterol molecules associated with the ceramide sphingoid moiety", *J Invest Dermatol.* 2012 Sep;132(9):2215-25

Barrera Cutánea

Partes de Estudio

- Síntesis y Liberación de Ceramidas

Barrera Cutánea

Partes de Estudio

✓ Fisiología y Formación de la Barrera Cutánea

- Formación de la Envoltura Cornea
- Síntesis y Liberación de Ceramidas
- Degradación de la Membrana Celular
- Colapso Controlado del Citoesqueleto
- Síntesis y Secreción de Cuerpos Laminares
- Maduración y Descamación del Estrato Corneo

Barrera Cutánea

Partes de Estudio

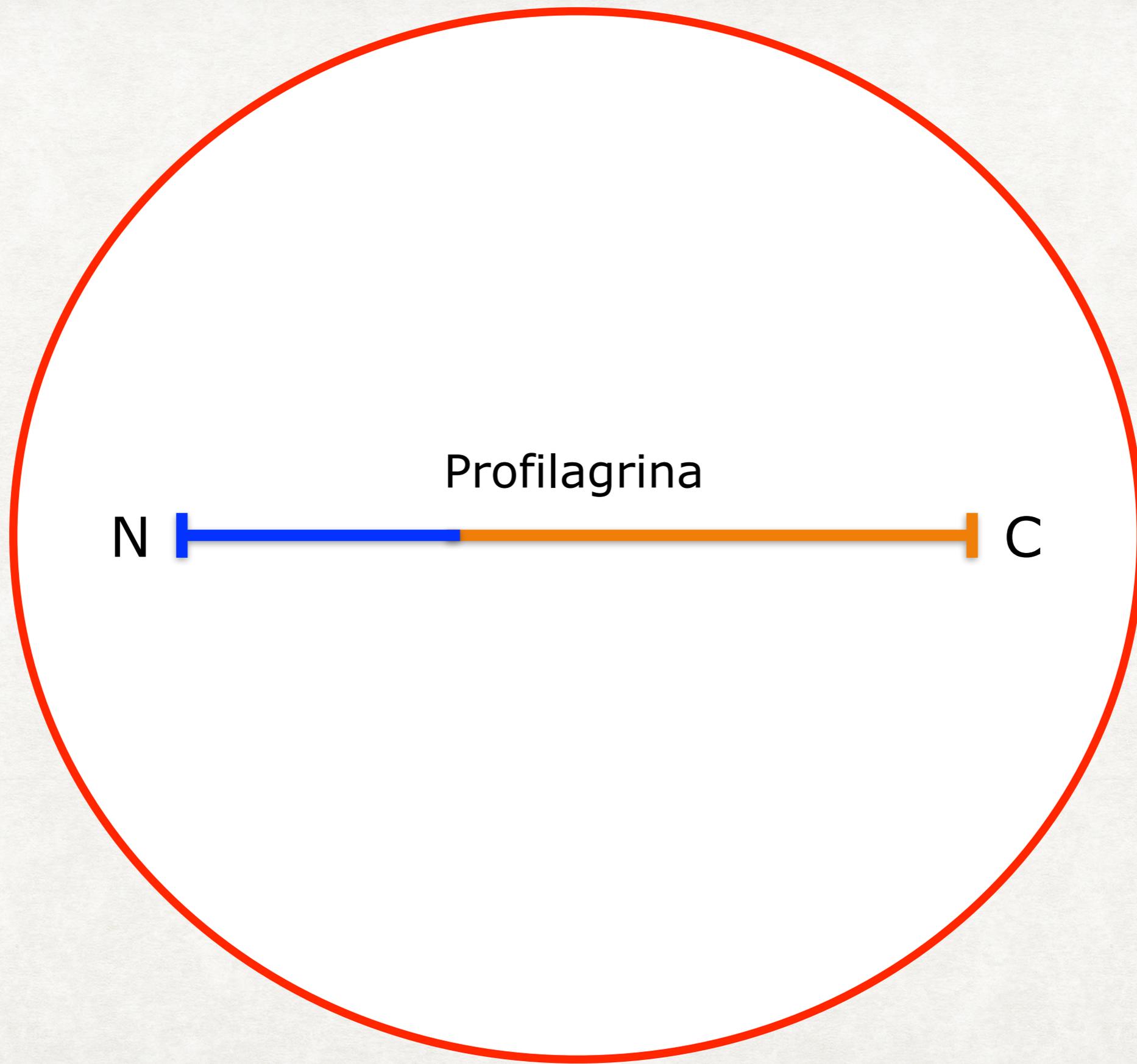
- Colapso Controlado del Citoesqueleto

- Desarrollo de Macrofilamentos de Keratina

- Profilagrina y Filagrina

- “Filaggrin” (filament- aggregating protein)*

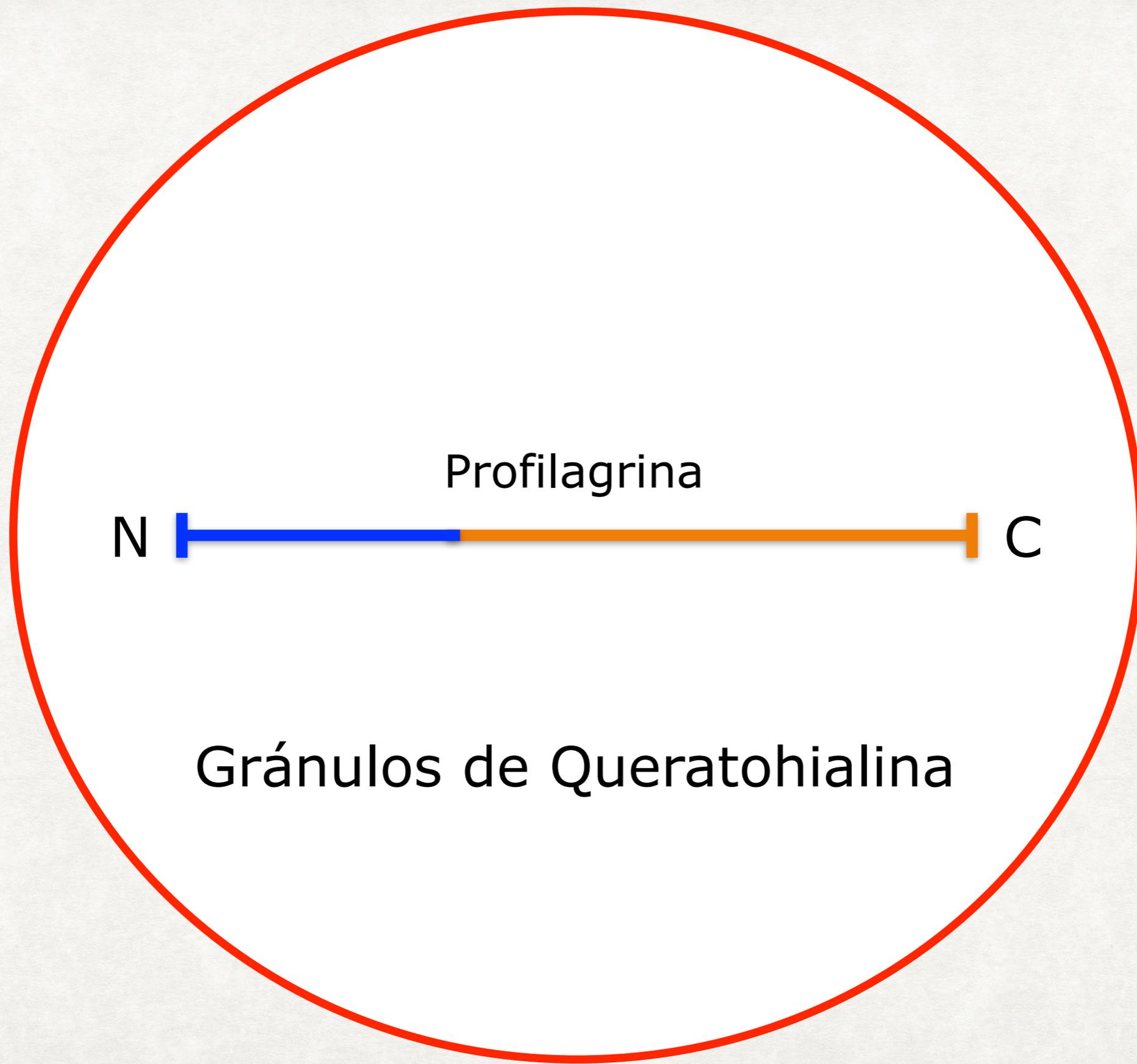




Profilagrina

N

C

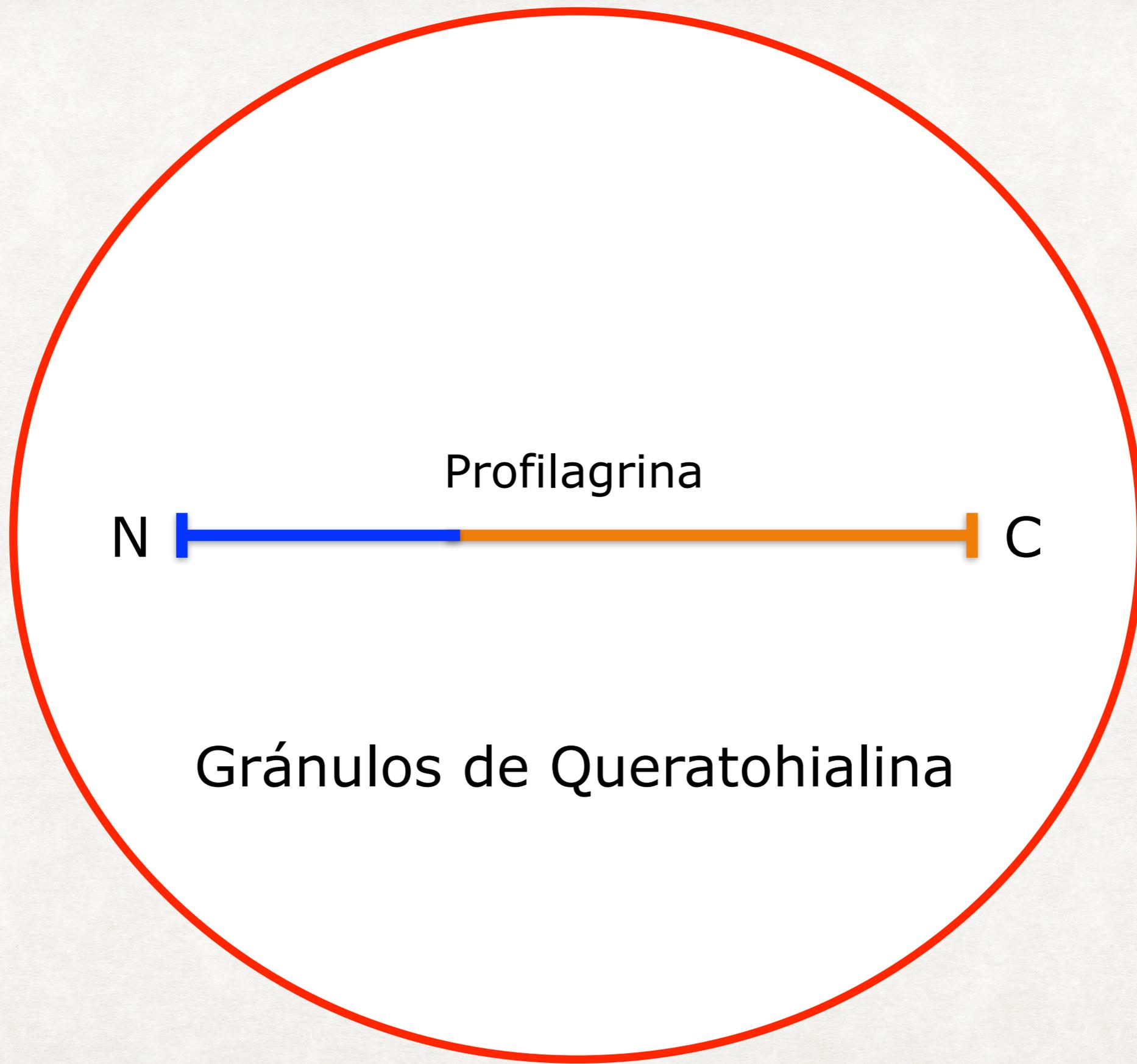


Profilagrina

N

C

Gránulos de Queratohialina

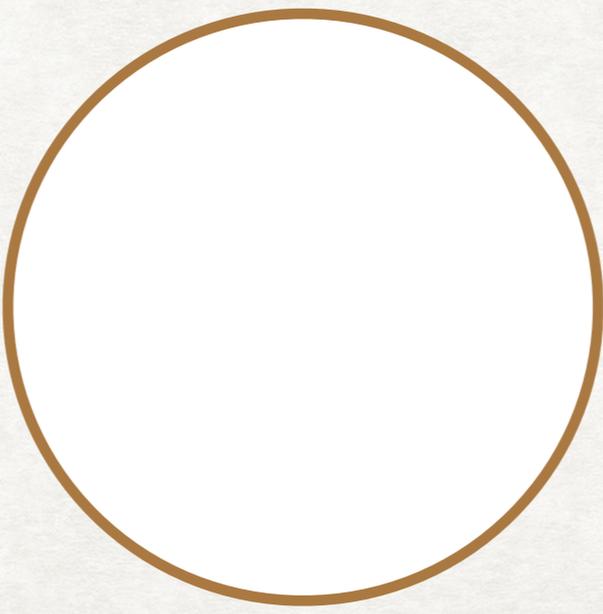
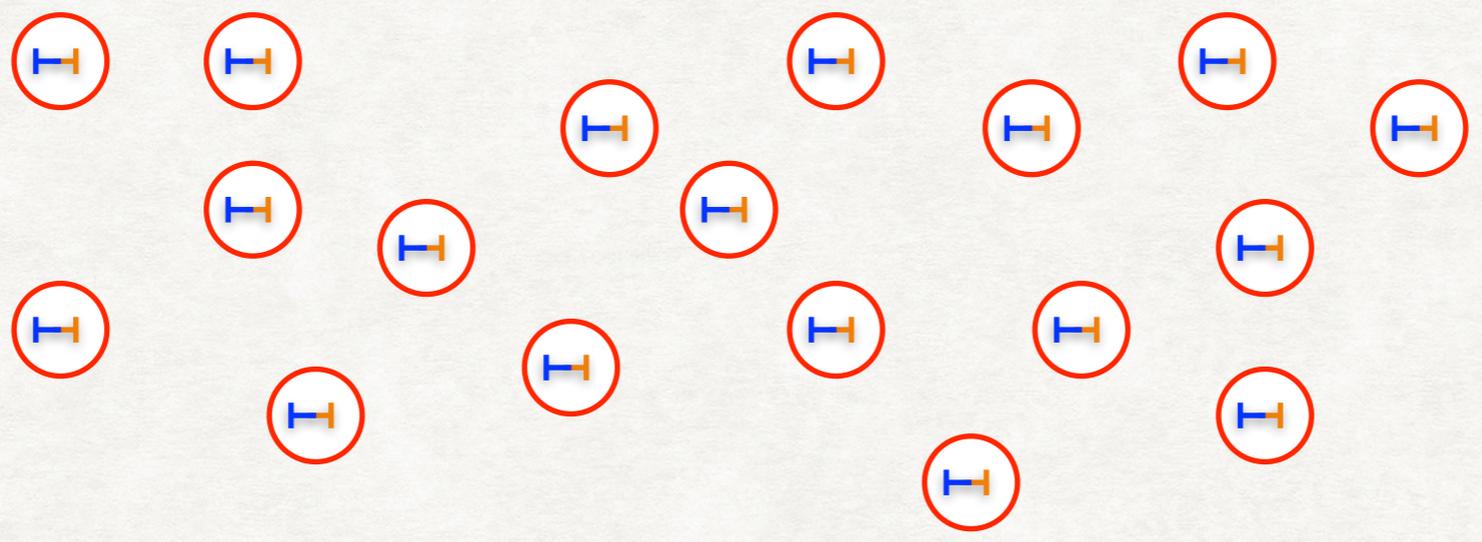


Profilagrina

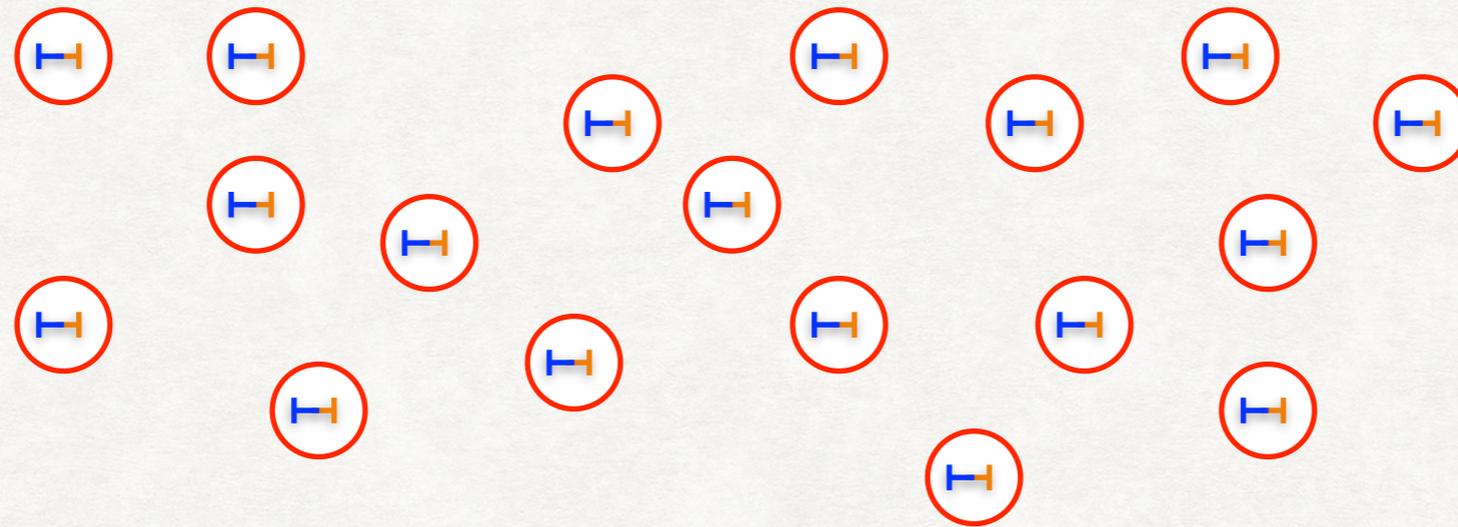
N

C

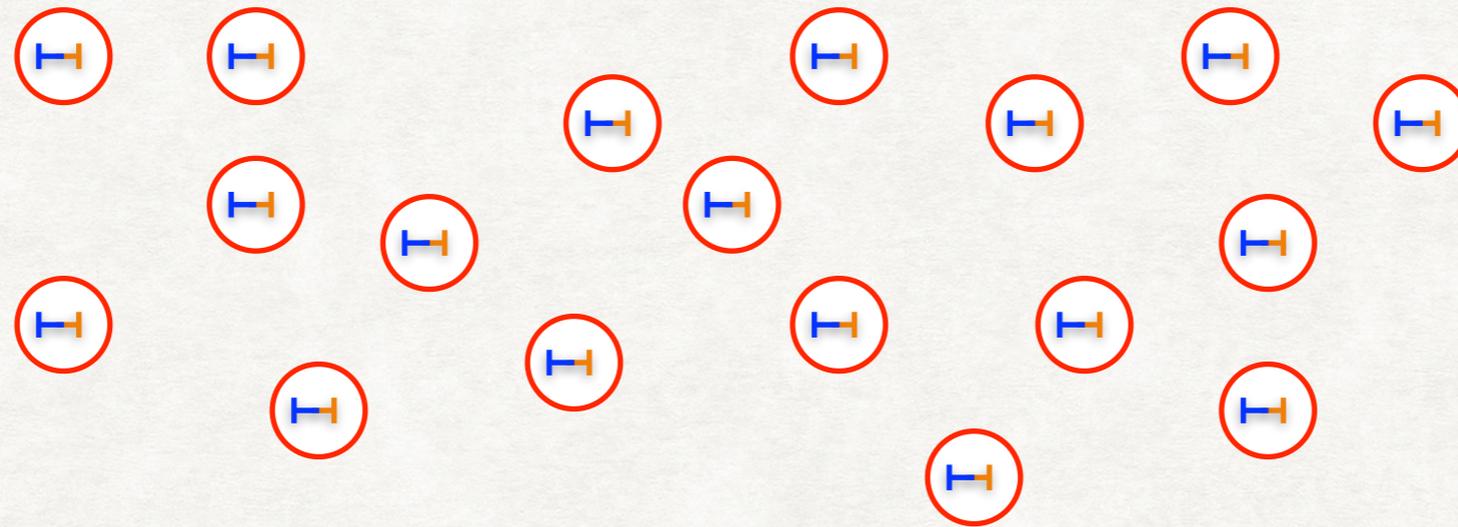
Gránulos de Queratohialina

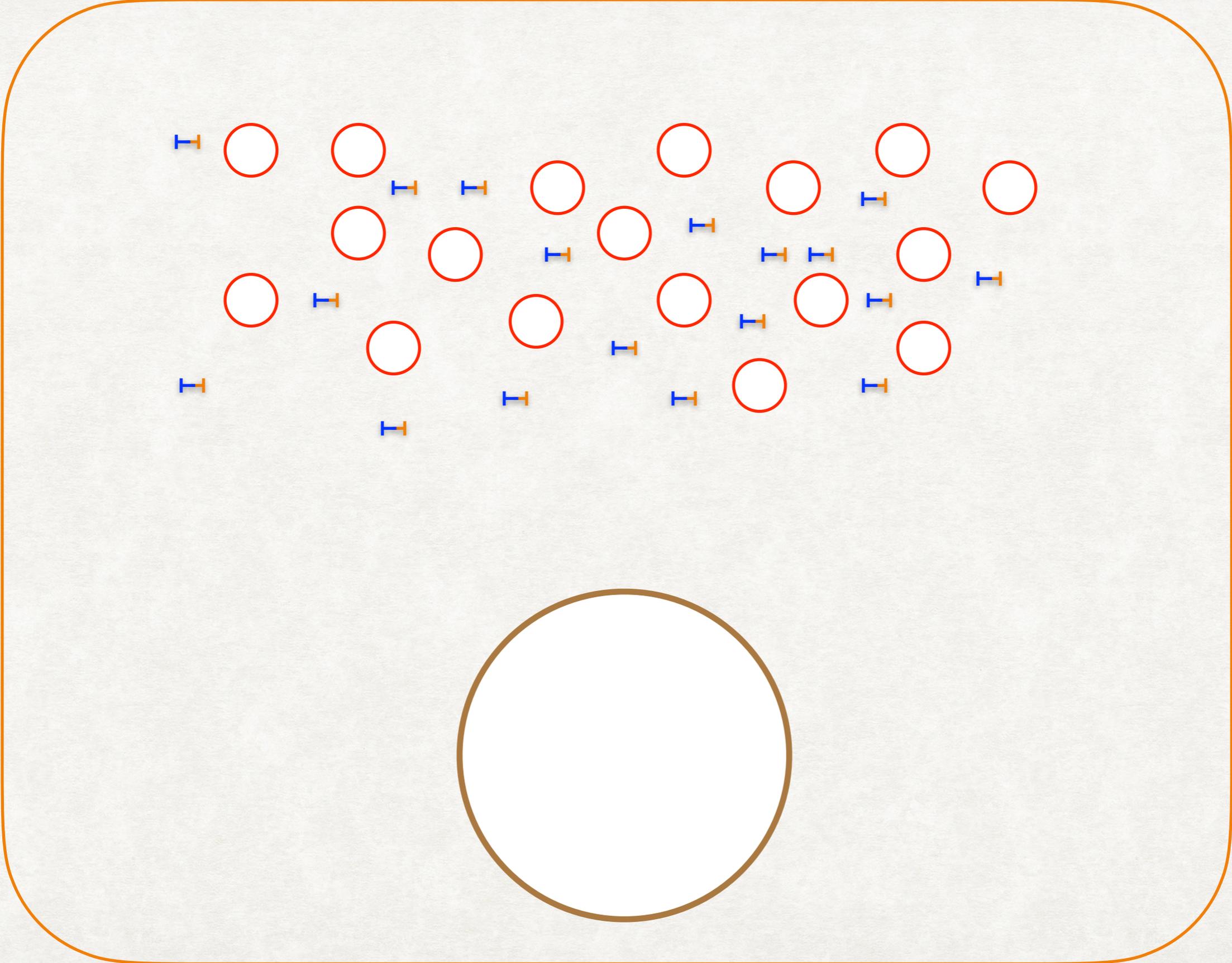


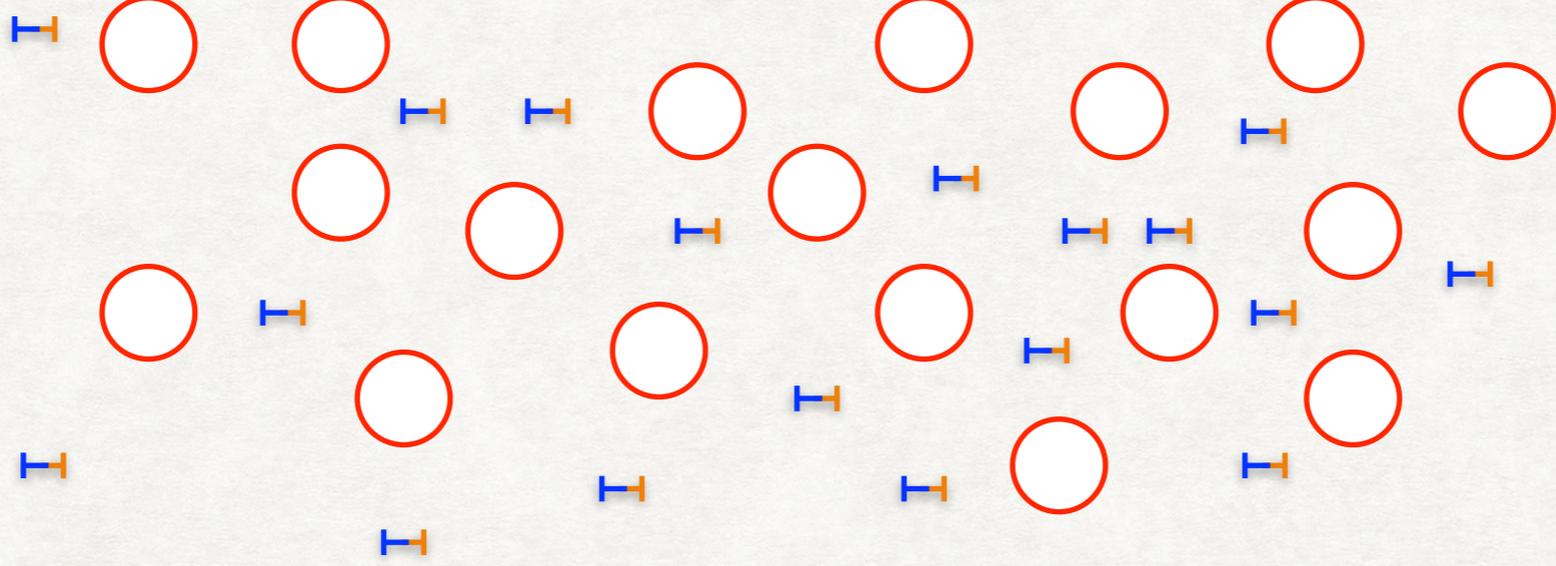
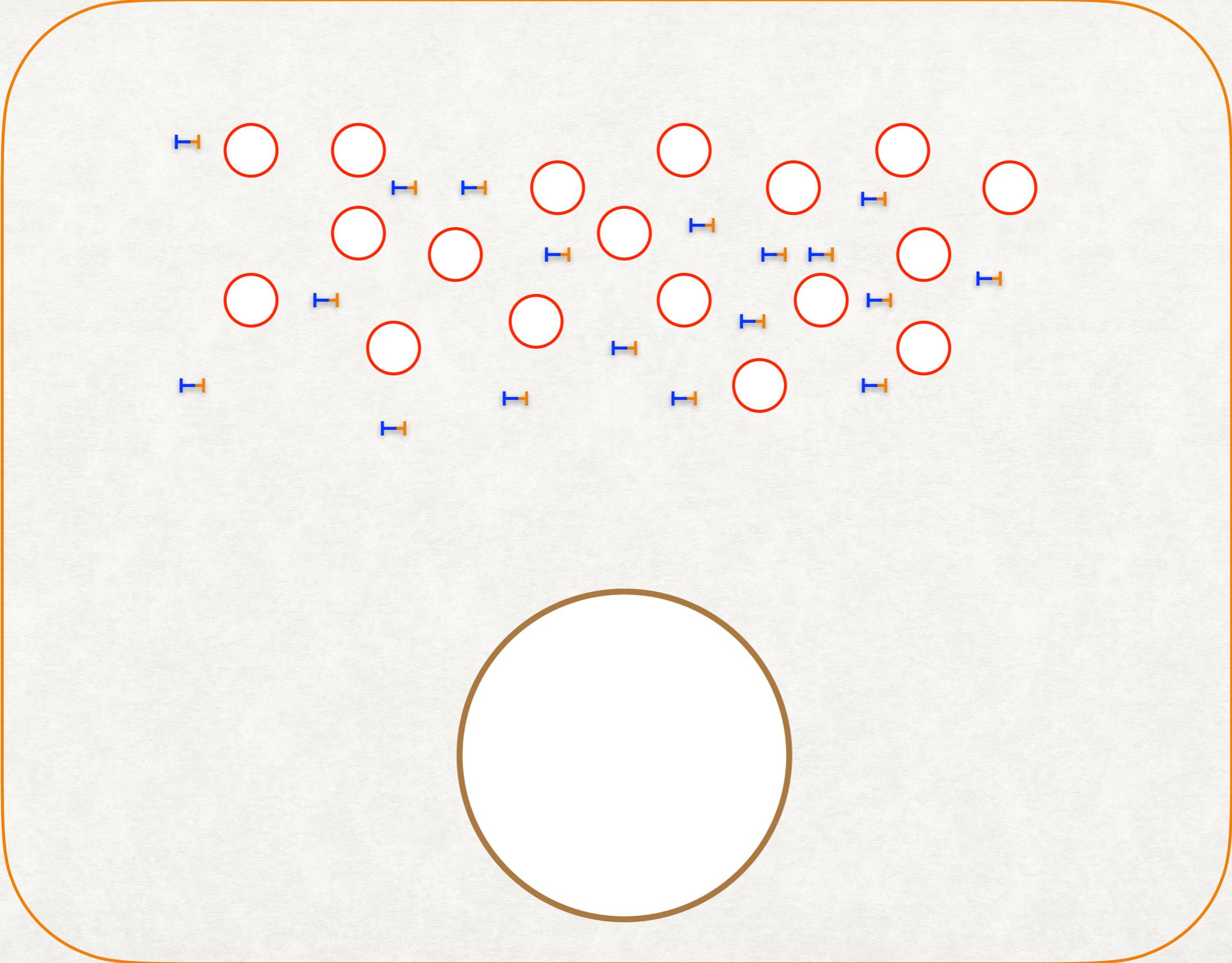
Ca^{+2} ↑



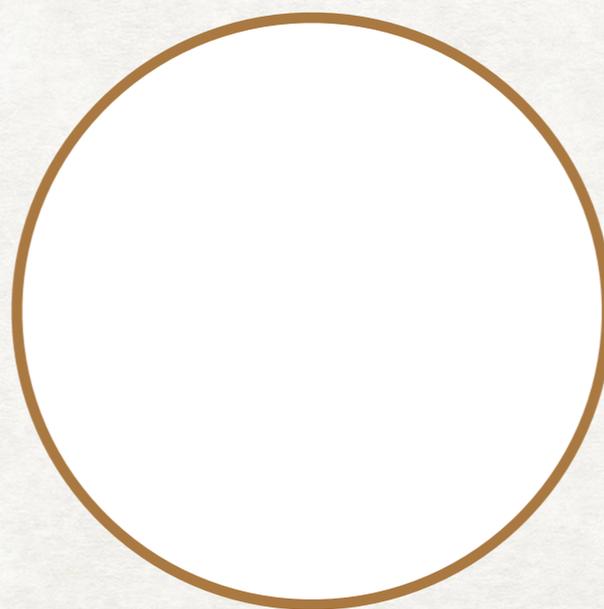
Ca^{+2} ↑



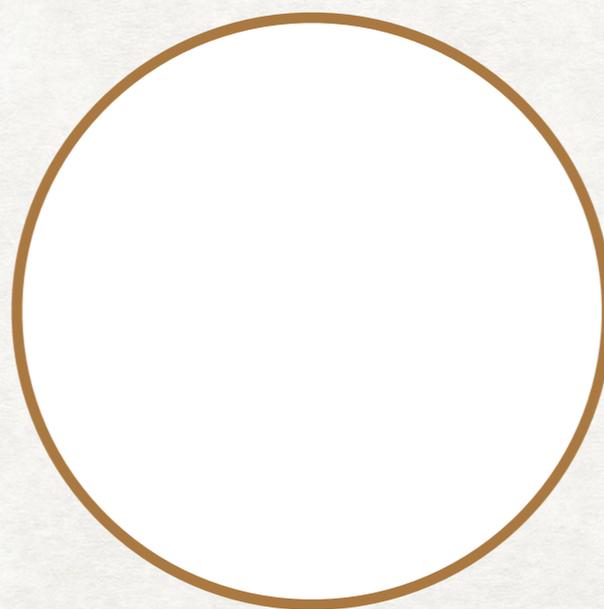




Profilagrina



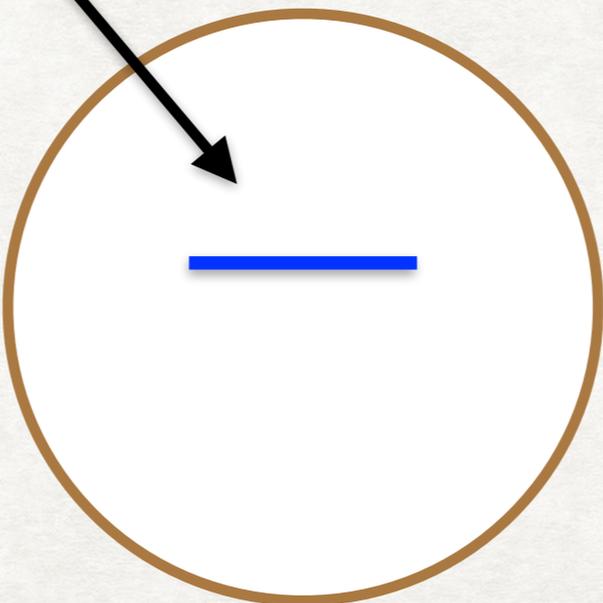
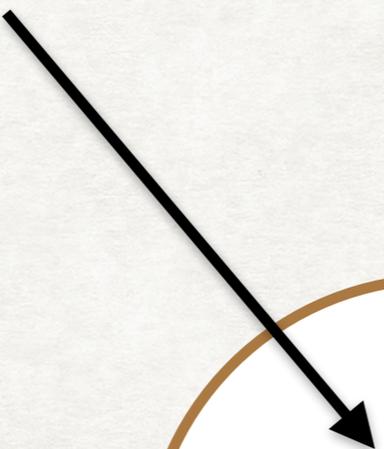
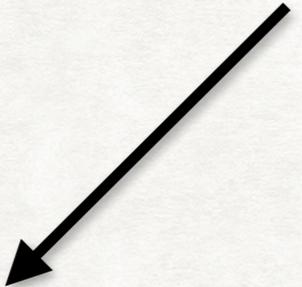
Profilagrina



Profilagrina



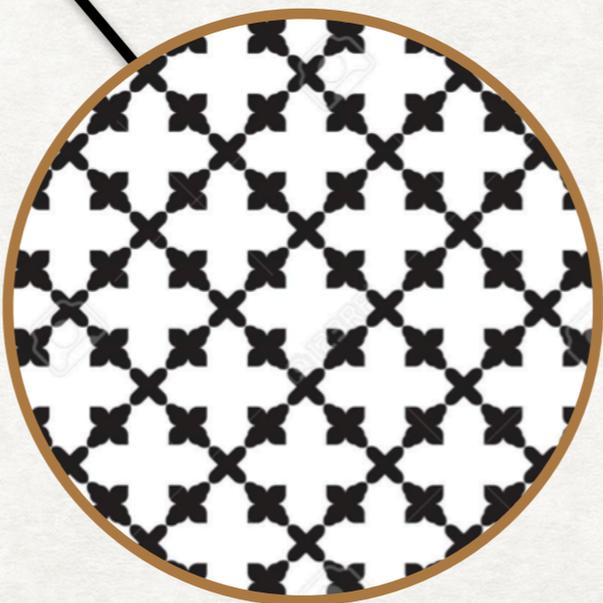
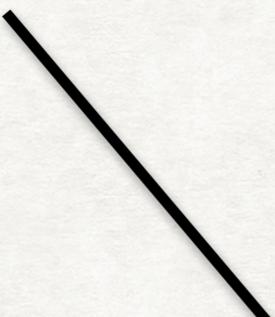
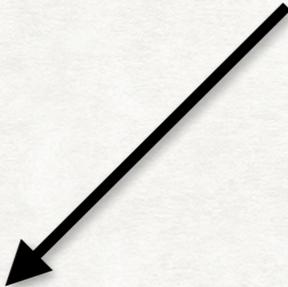
Prostasin
Maltriptasa
Fosfatasas



Profilagrina



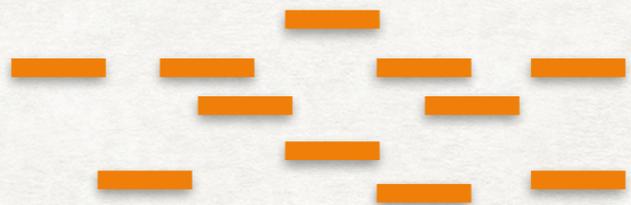
Prostasin
Maltriptasa
Fosfatasas



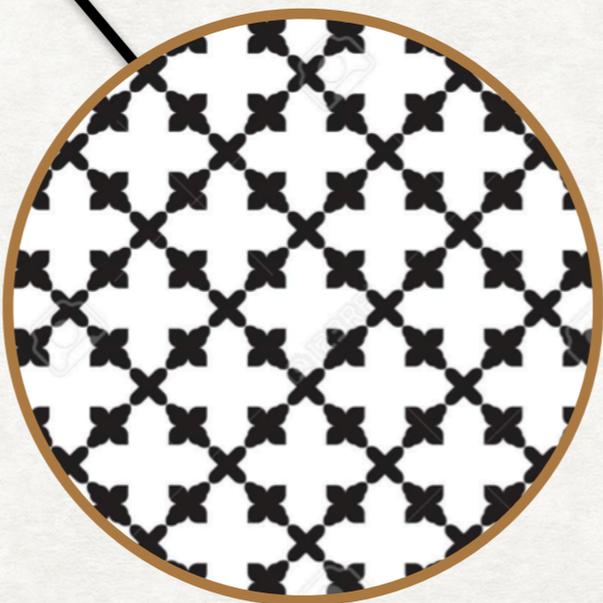
Profilagrina

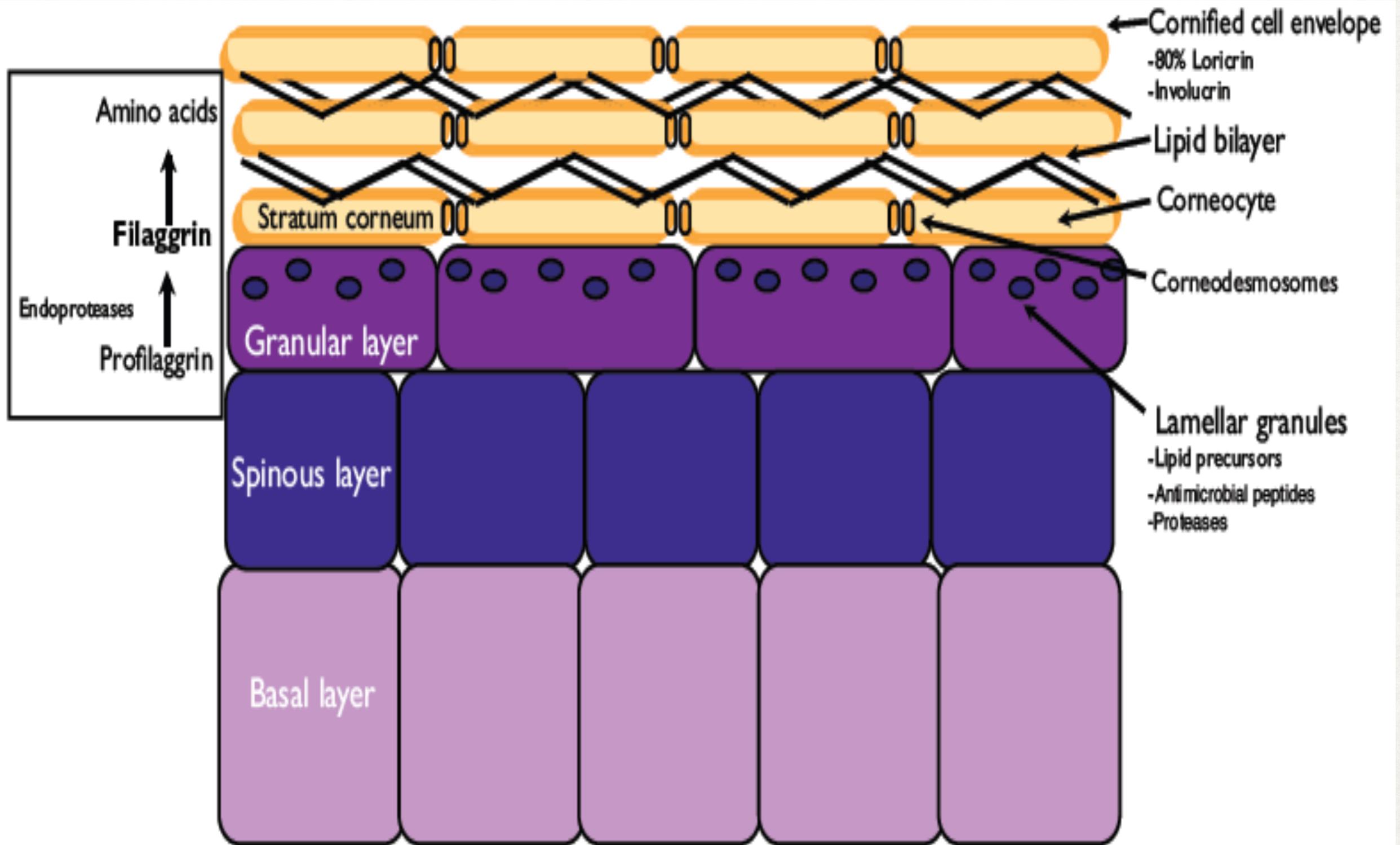


Prostasin
Maltriptasa
Fosfatasas



Filaggrina

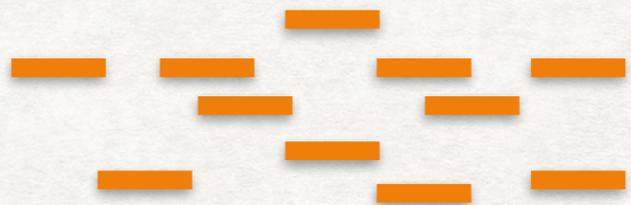
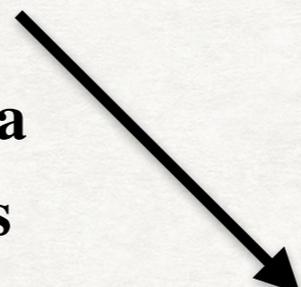




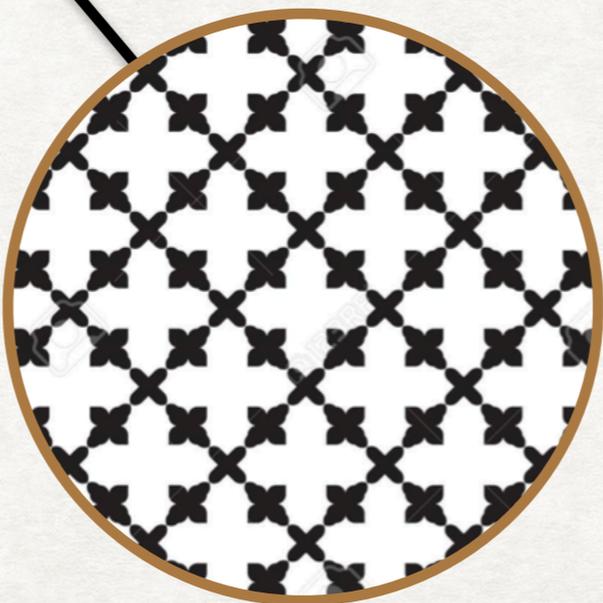
Profilagrina

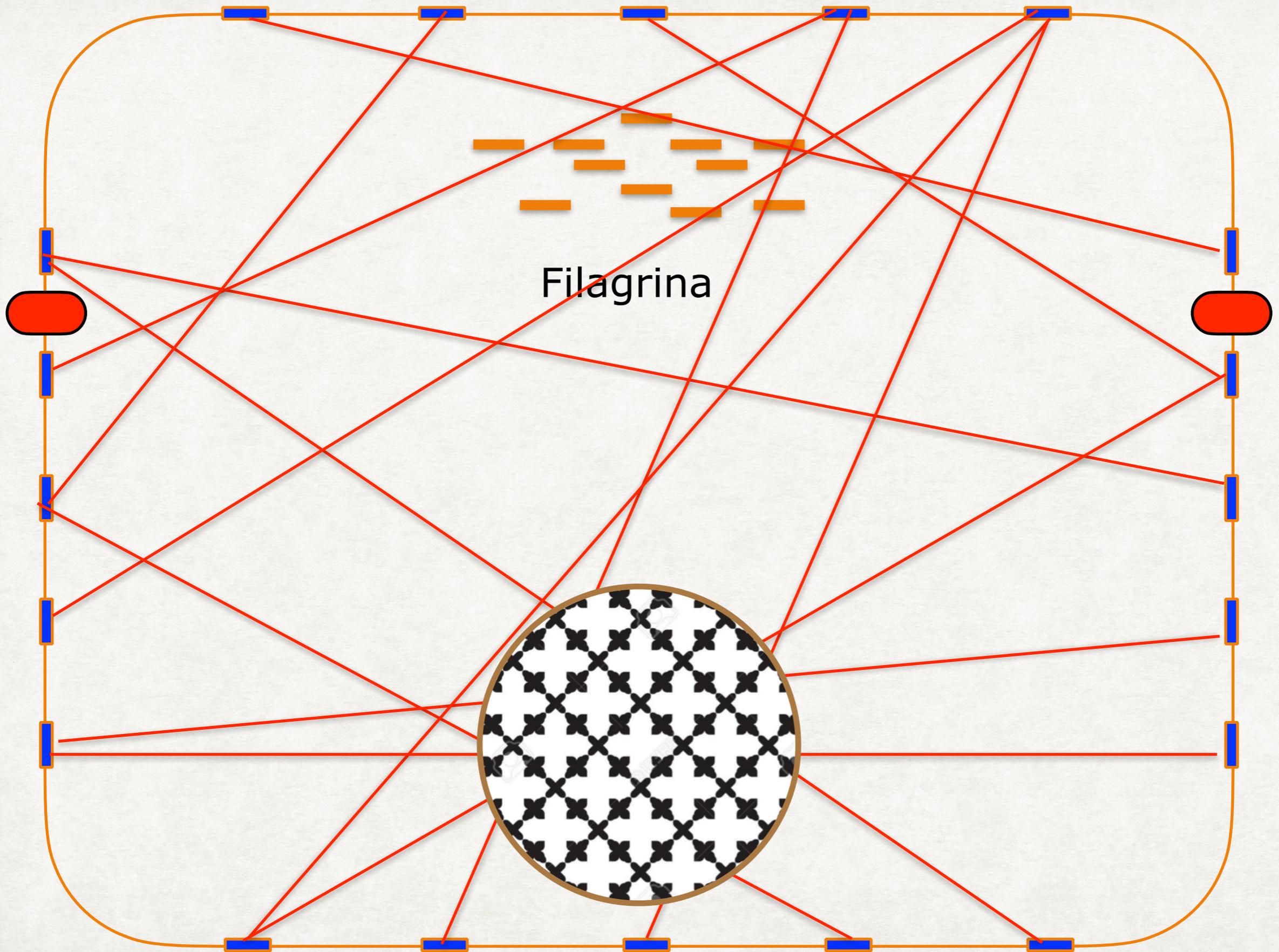


Prostasin
Maltriptasa
Fosfatasas

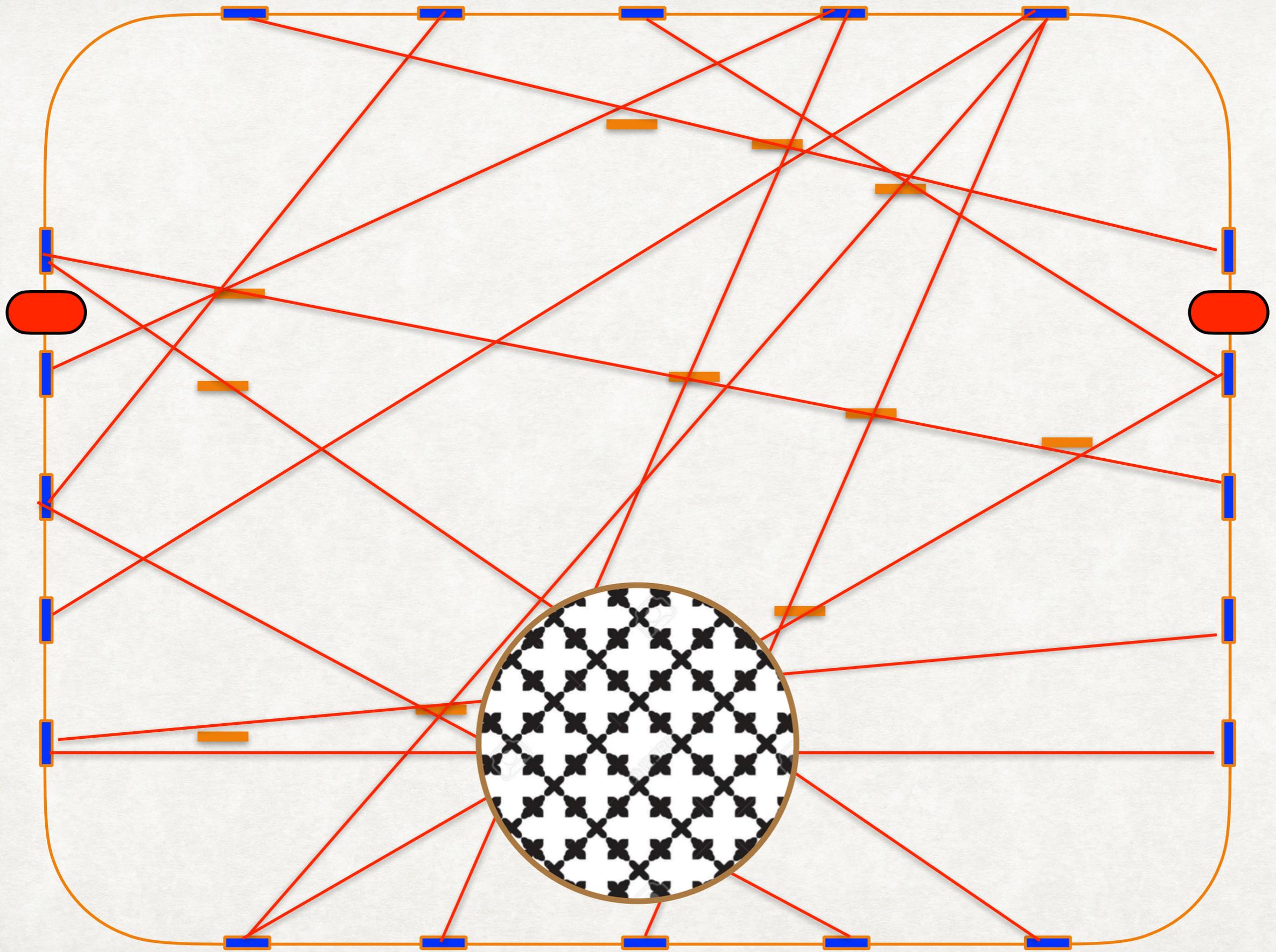


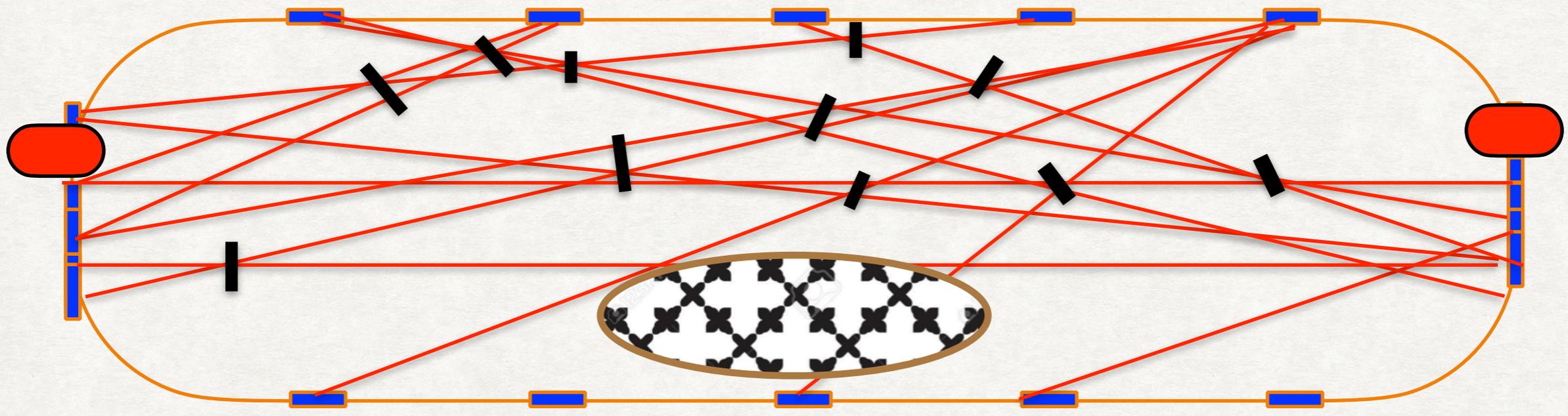
Filaggrina

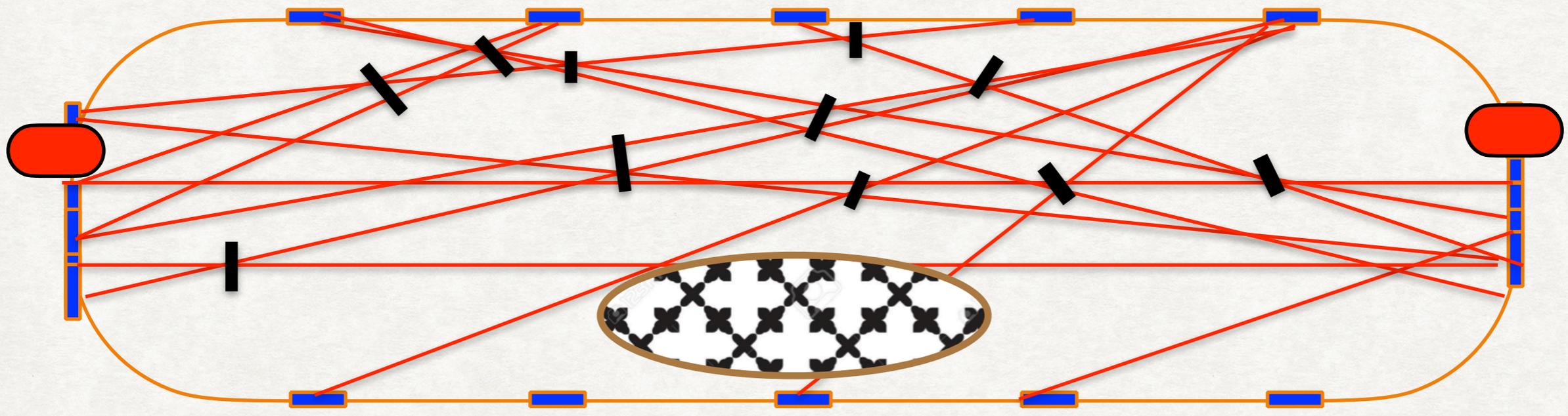




Filagrina







Barrera Cutánea

Partes de Estudio

- Colapso Controlado del Citoesqueleto

- Desarrollo de Macrofilamentos de Keratina

- Profilagrina y Filagrina

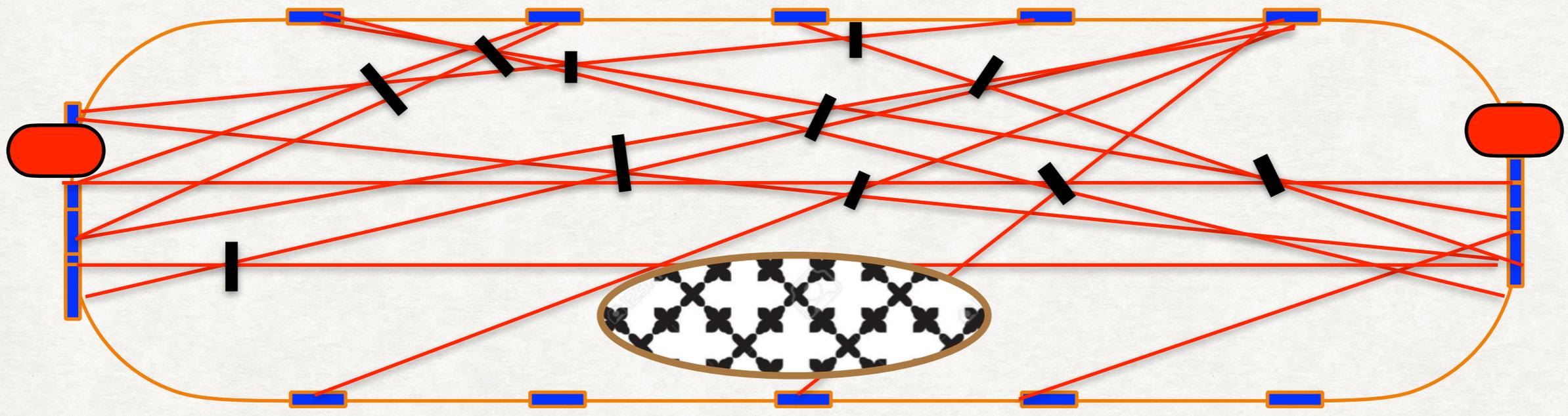
- “Filaggrin” (filament- aggregating protein)*



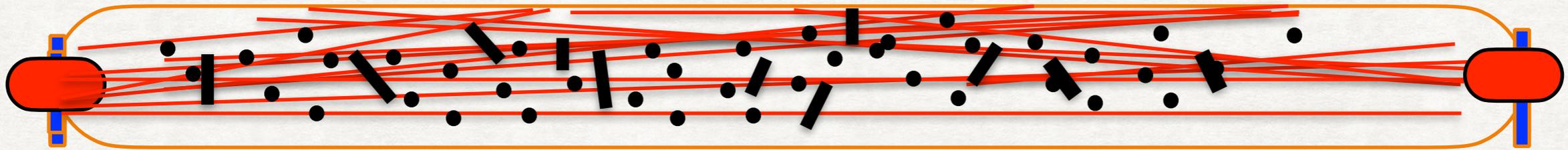
Barrera Cutánea

Partes de Estudio

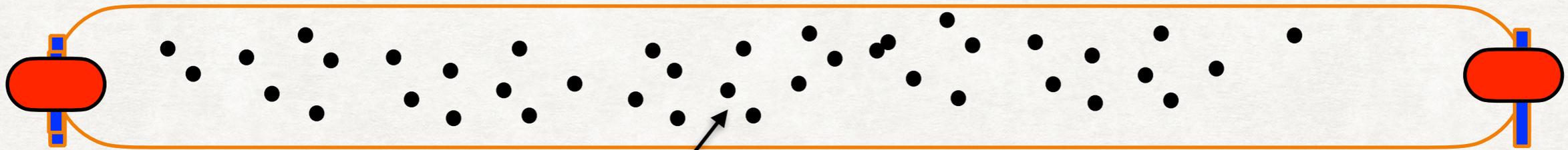
- ◉ Colapso Controlado del Citoesqueleto
 - ➔ Desarrollo de Macrofilamentos de Keratina
 - Profilagrina y Filagrina
 - Funciones de la Filagrina
- ✓ *Formar los Macrofilamentos de Queratina*
- ✓ *Hidratación del Estrato Corneo*
- ✓ *Control del pH*



Caspasa 14



Caspasa 14



✓ **Aminoácidos Libres**

✓ **Ácido Urocánico**

Higroscópicos

Bajan pH

Proteje luz UV

Barrera Cutánea

Partes de Estudio

- Colapso Controlado del Citoesqueleto
 - Desarrollo de *Macrofilamentos de Keratina*

Barrera Cutánea

Partes de Estudio

✓ Fisiología y Formación de la Barrera Cutánea

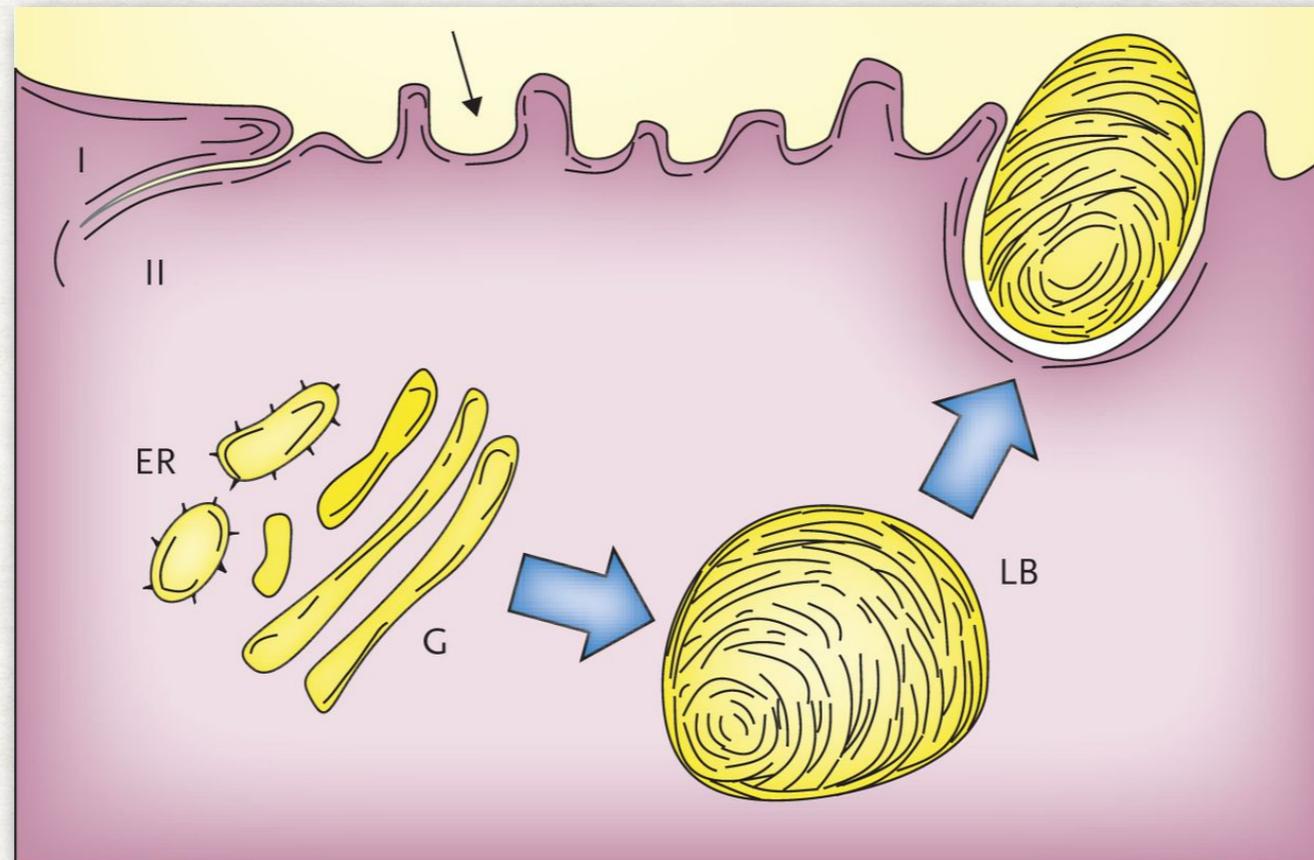
- Formación de la Envoltura Cornea
- Síntesis y Liberación de Ceramidas
- Degradación de la Membrana Celular
- Colapso Controlado del Citoesqueleto
- Síntesis y Secreción de Cuerpos Laminares
- Maduración y Descamación del Estrato Corneo

Barrera Cutánea

Partes de Estudio

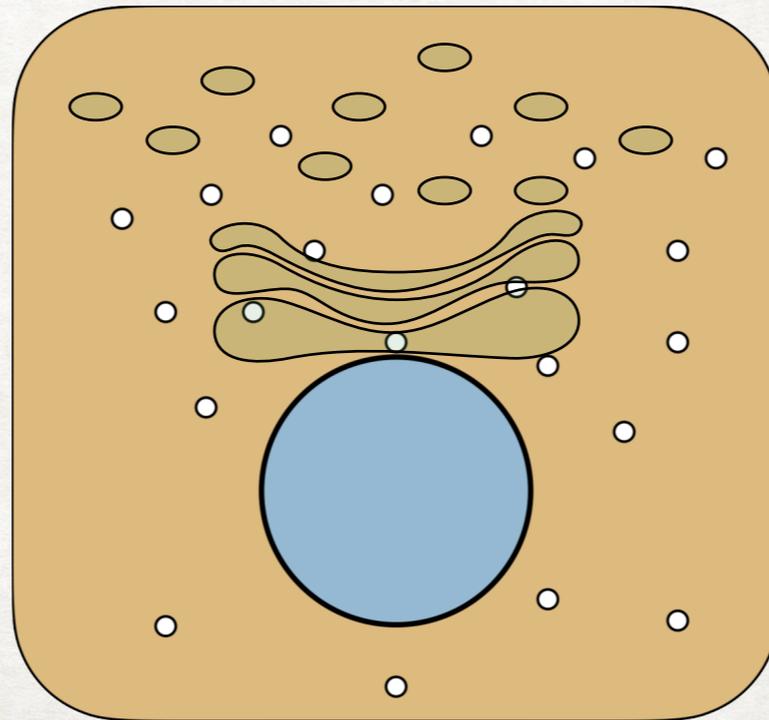
- Síntesis y Secreción de Cuerpos Laminares

→ Estructura de los Cuerpos Laminares



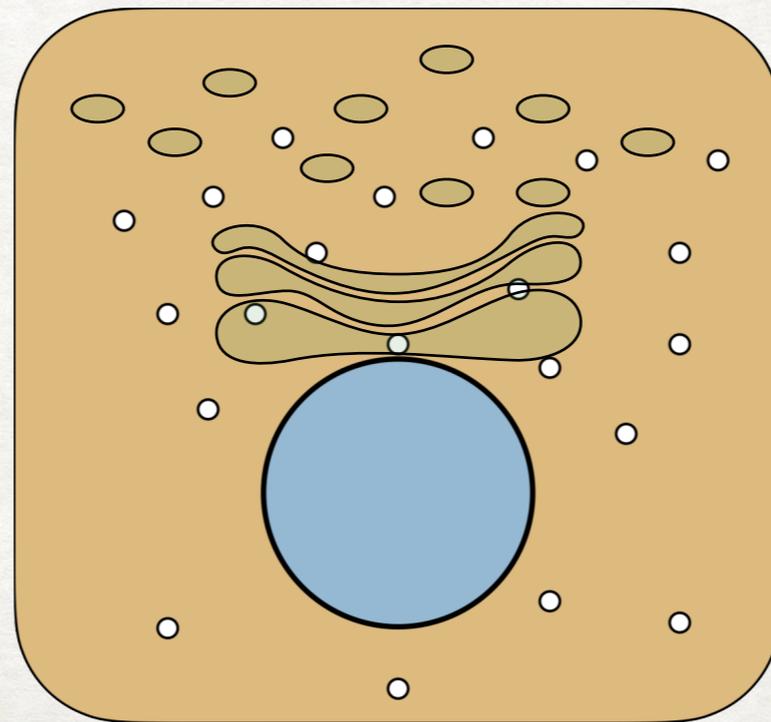
Barrera Cutánea

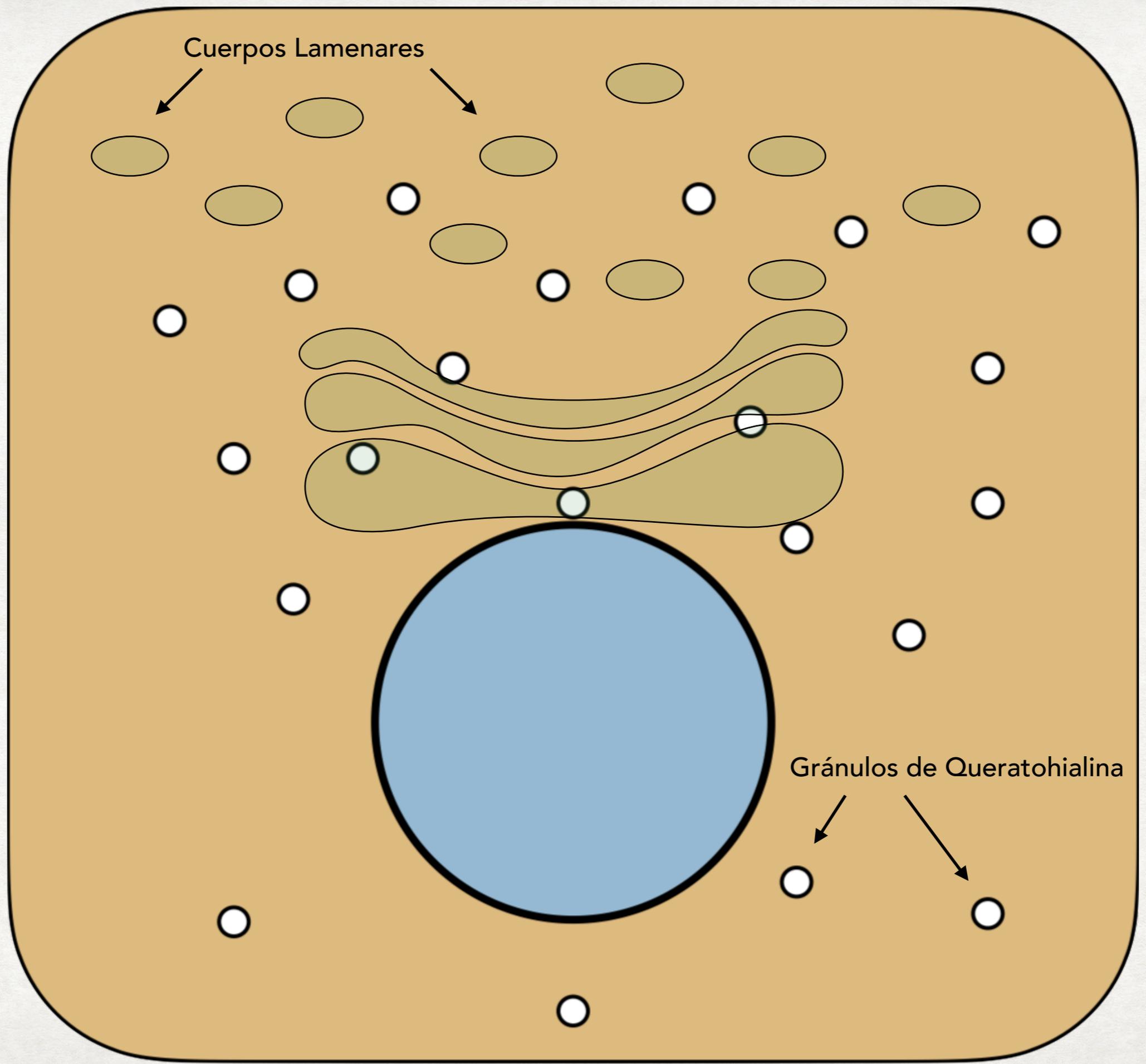
Síntesis y Secreción de Cuerpos Laminares



Barrera Cutánea

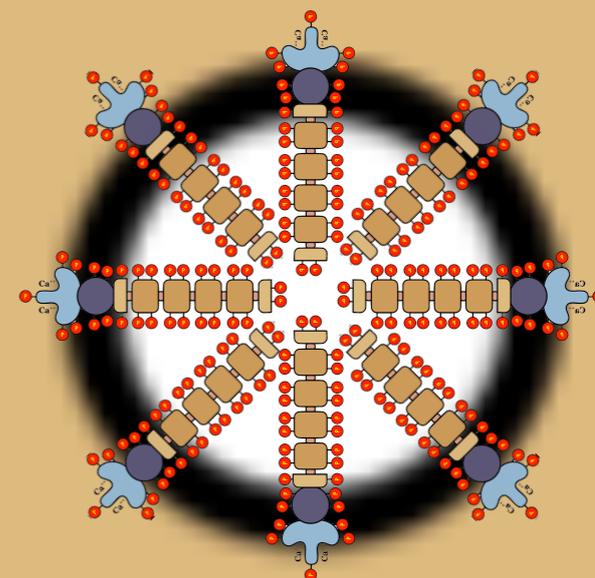
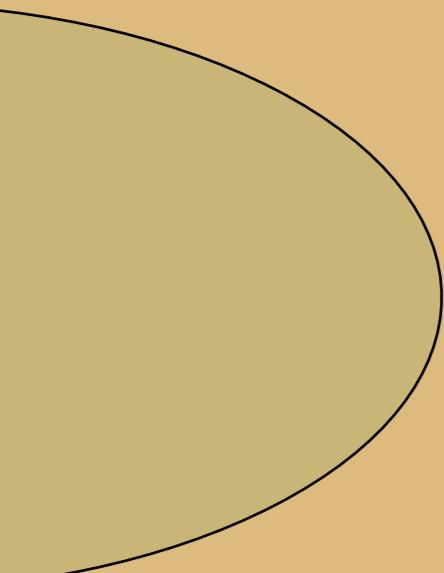
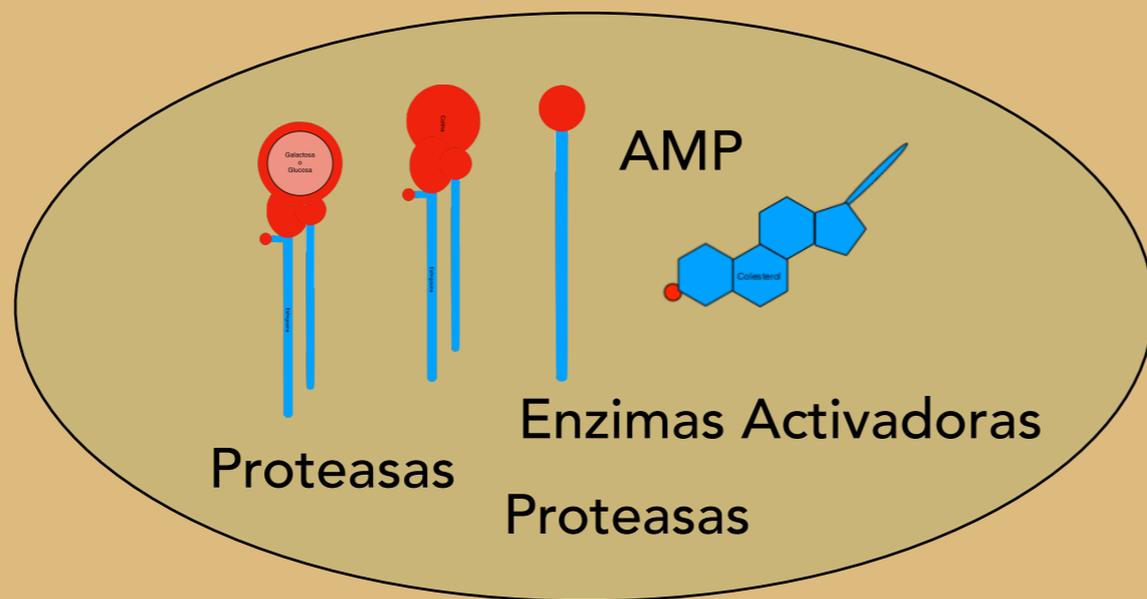
Síntesis y Secreción de Cuerpos Laminares





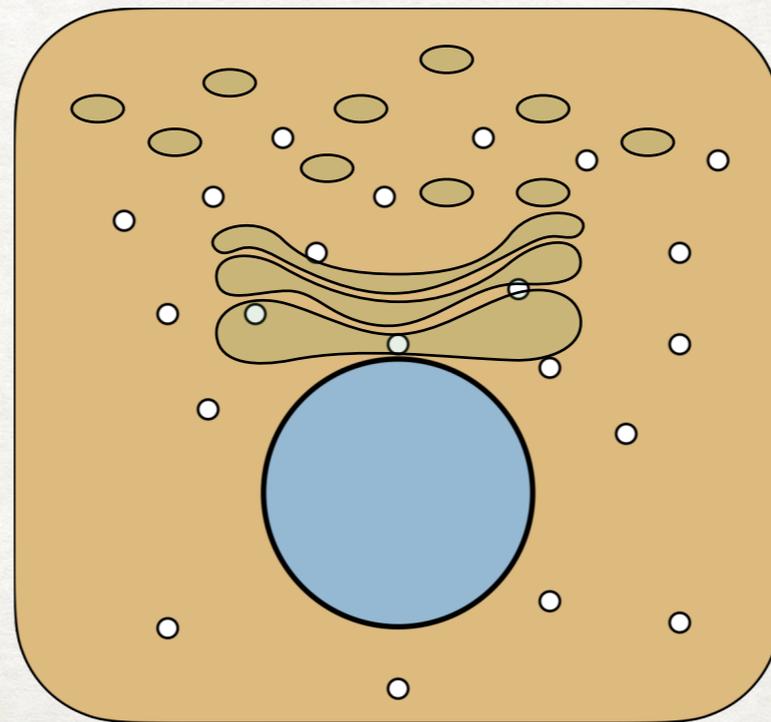
Cuerpos Laminares

Gránulos de Queratohialina



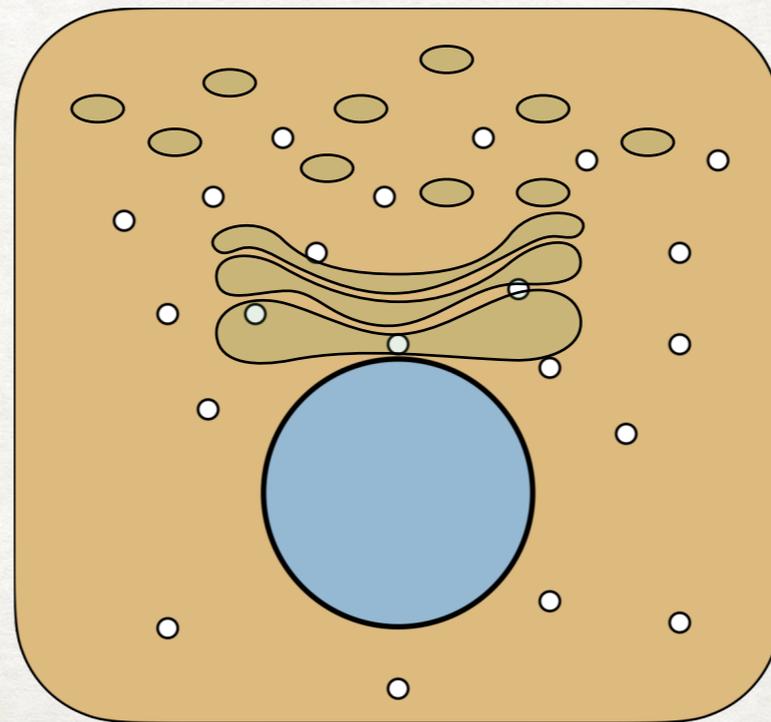
Barrera Cutánea

Síntesis y Secreción de Cuerpos Laminares



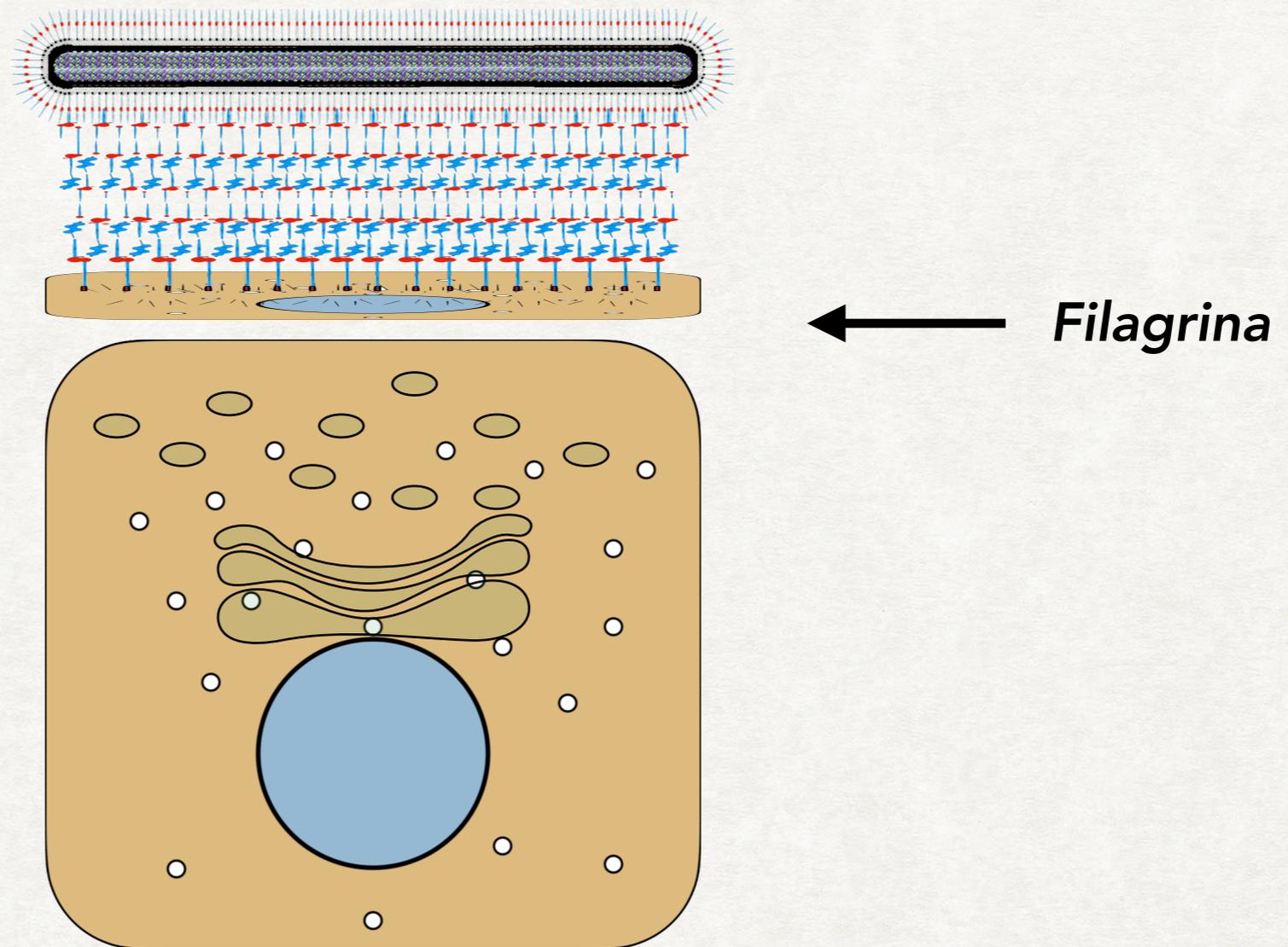
Barrera Cutánea

Síntesis y Secreción de Cuerpos Laminares



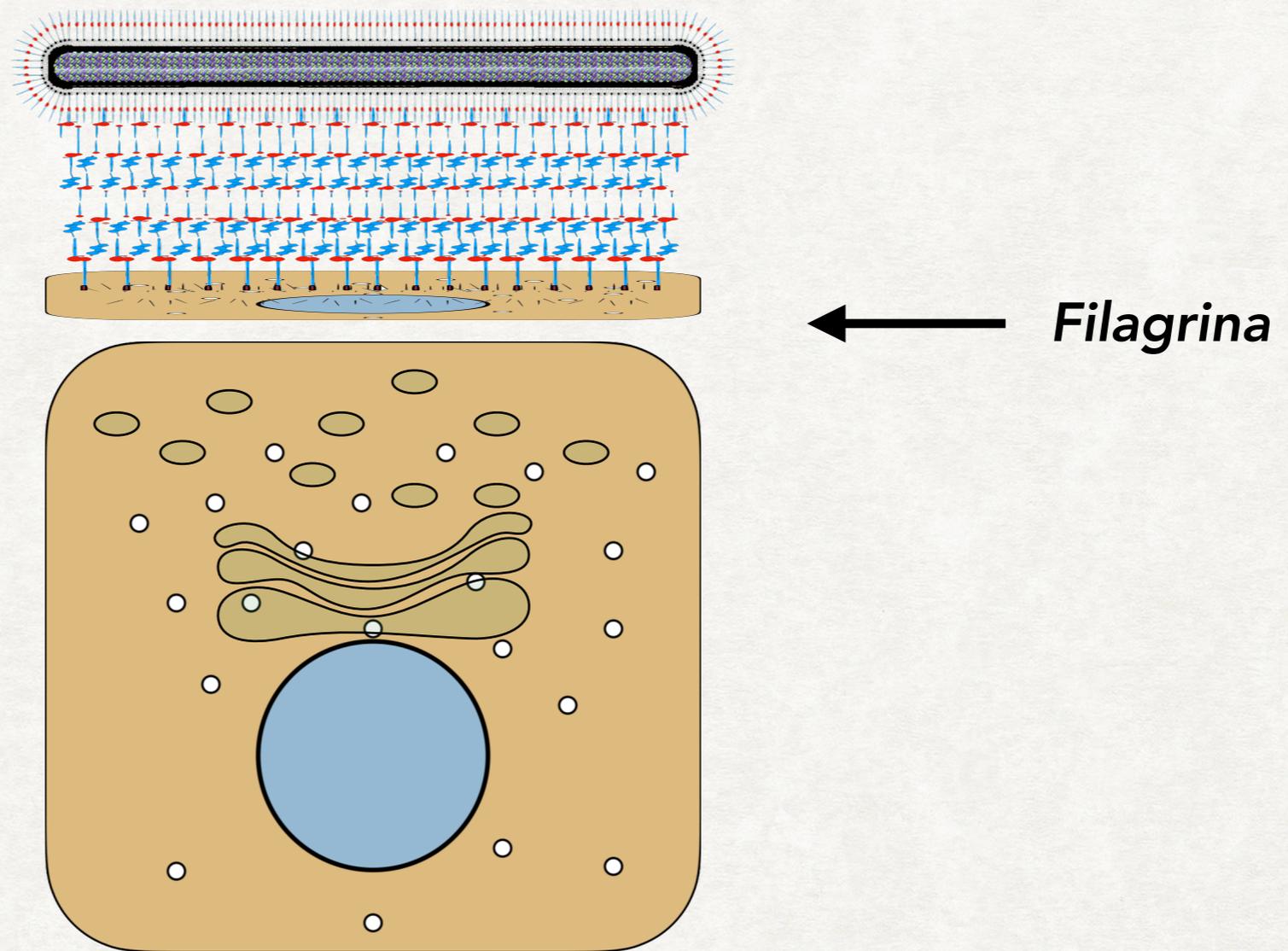
Barrera Cutánea

Síntesis y Secreción de Cuerpos Laminares



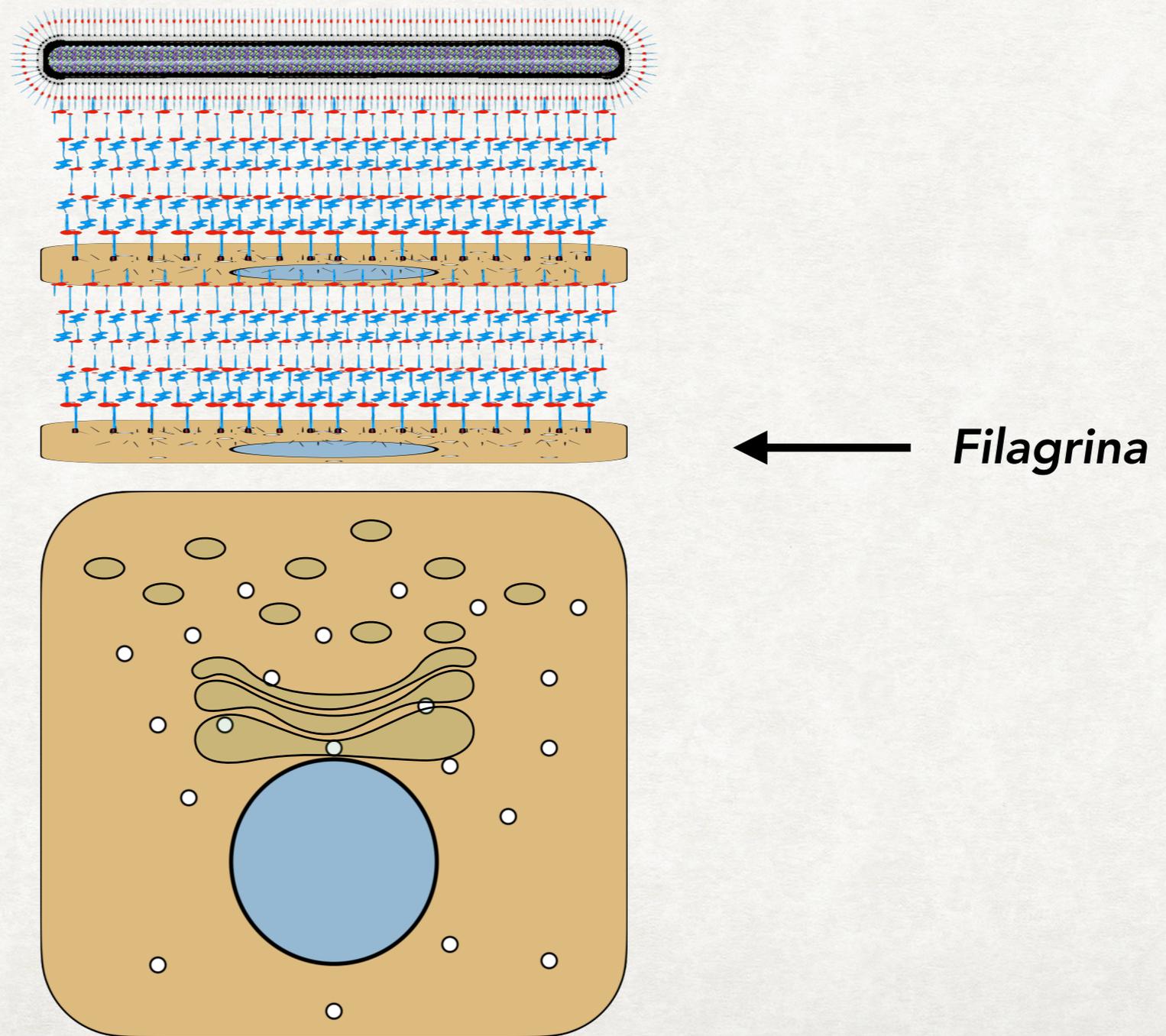
Barrera Cutánea

Síntesis y Secreción de Cuerpos Laminares



Barrera Cutánea

Síntesis y Secreción de Cuerpos Laminares

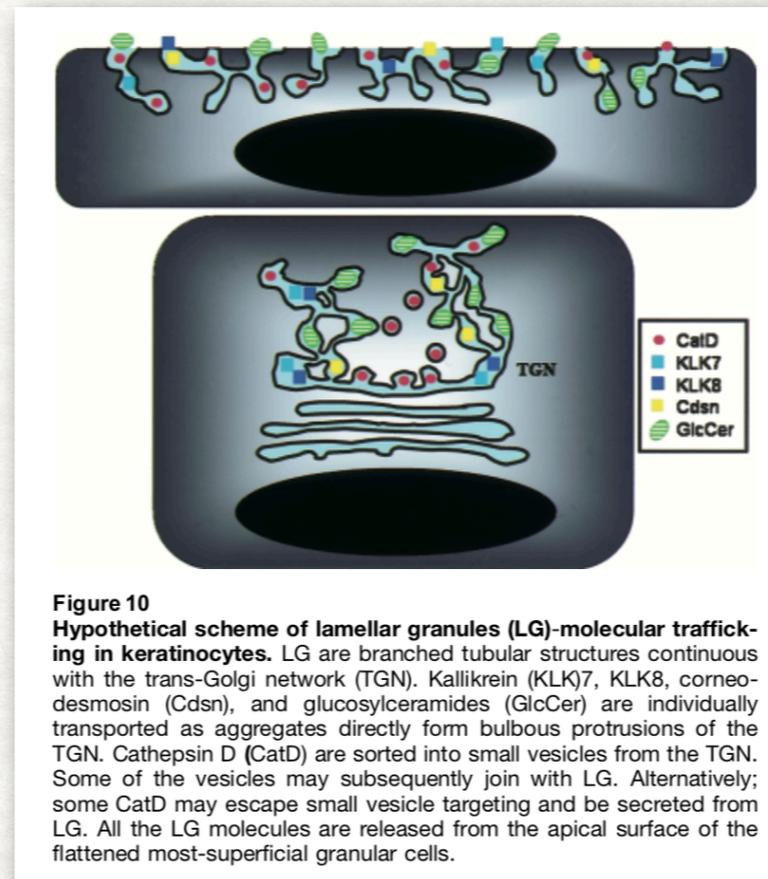


Barrera Cutánea

Partes de Estudio

● Síntesis y Secreción de Cuerpos Laminares

→ Estructura de los Cuerpos Laminares



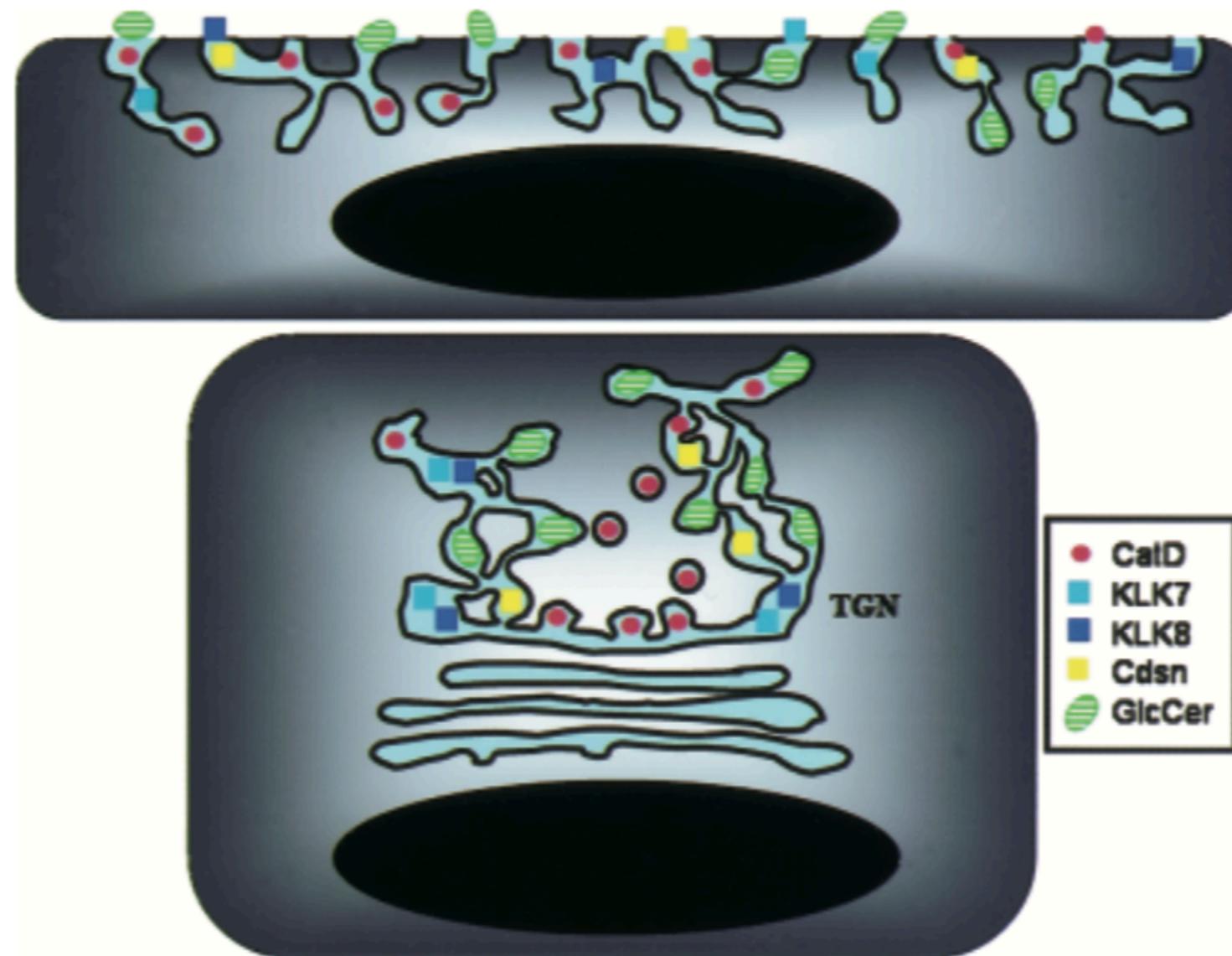


Figure 10

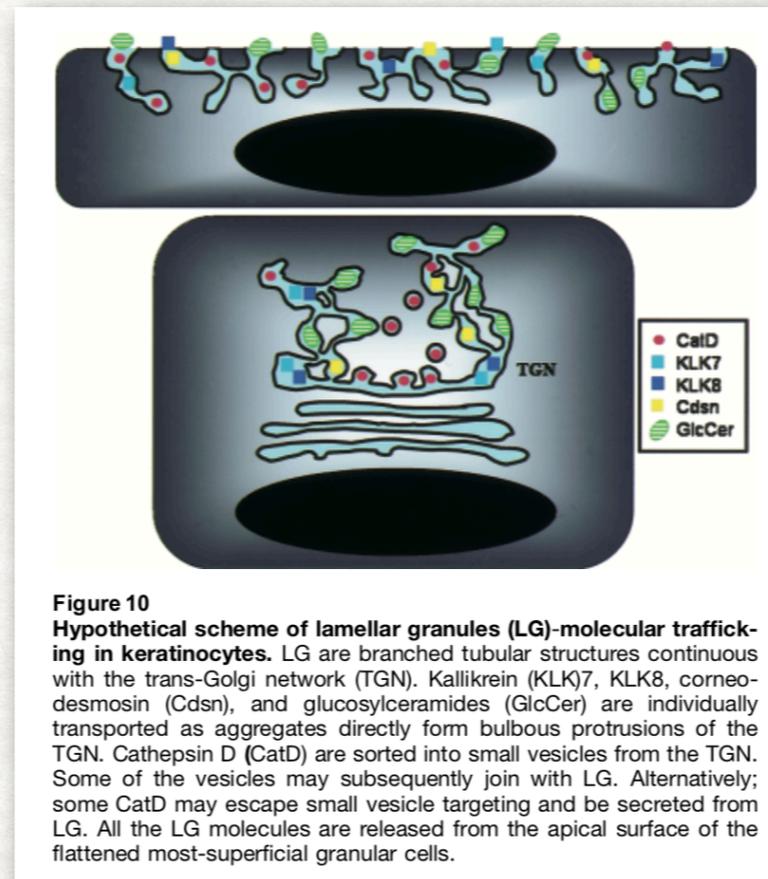
Hypothetical scheme of lamellar granules (LG)-molecular trafficking in keratinocytes. LG are branched tubular structures continuous with the trans-Golgi network (TGN). Kallikrein (KLK)7, KLK8, corneodesmosin (Cdsn), and glucosylceramides (GlcCer) are individually transported as aggregates directly from bulbous protrusions of the TGN. Cathepsin D (CatD) are sorted into small vesicles from the TGN. Some of the vesicles may subsequently join with LG. Alternatively; some CatD may escape small vesicle targeting and be secreted from LG. All the LG molecules are released from the apical surface of the flattened most-superficial granular cells.

Barrera Cutánea

Partes de Estudio

● Síntesis y Secreción de Cuerpos Laminares

→ Estructura de los Cuerpos Laminares

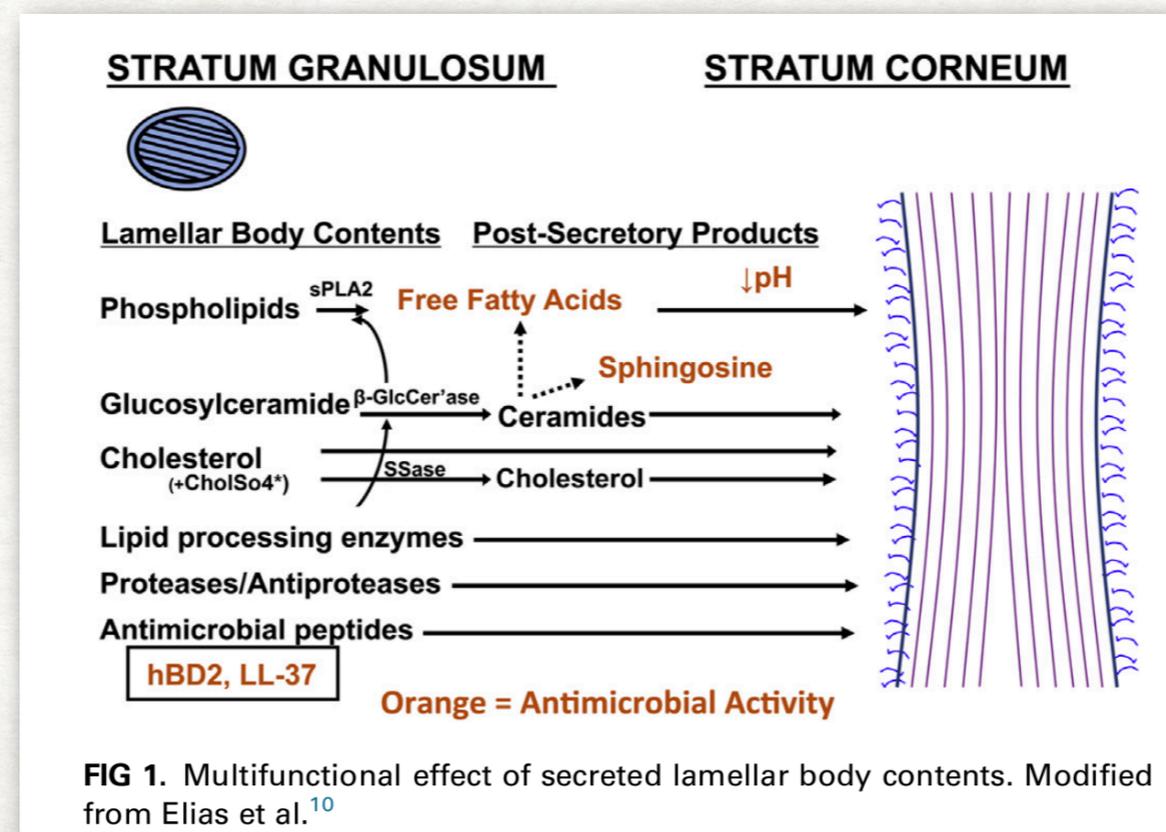


Barrera Cutánea

Partes de Estudio

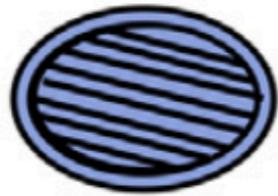
● Síntesis y Secreción de Cuerpos Laminares

→ Estructura de los Cuerpos Laminares



STRATUM GRANULOSUM

STRATUM CORNEUM



Lamellar Body Contents

Post-Secretory Products

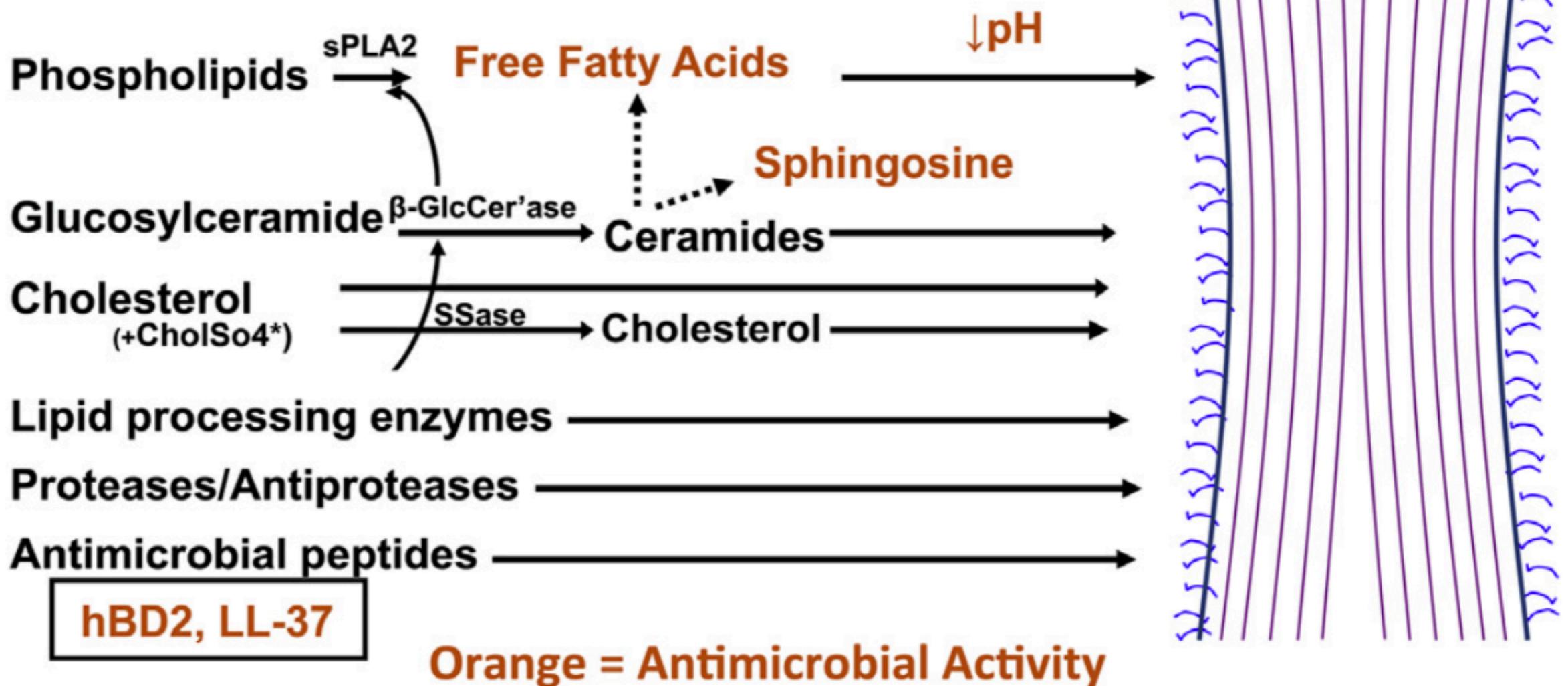


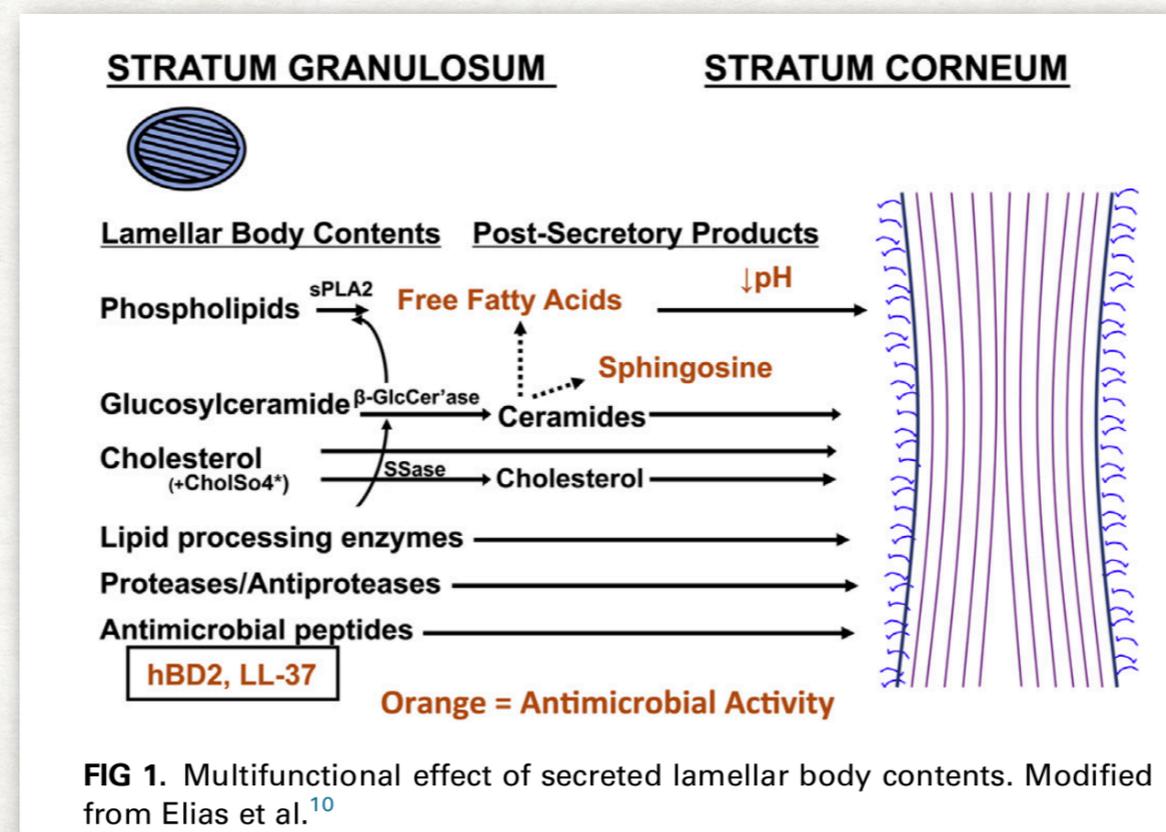
FIG 1. Multifunctional effect of secreted lamellar body contents. Modified from Elias et al.¹⁰

Barrera Cutánea

Partes de Estudio

● Síntesis y Secreción de Cuerpos Laminares

→ Estructura de los Cuerpos Laminares



Barrera Cutánea

Partes de Estudio

- ◉ Síntesis y Secreción de Cuerpos Laminares
 - Estructura de los Cuerpos Laminares
 - Composición
 - Glucosil Ceramida y Esfingomielina
 - Acidos Grasos
 - Colesterol
 - Enzimas Múltiples
 - Péptidos Antimicrobianos

Barrera Cutánea

Partes de Estudio

✓ Fisiología y Formación de la Barrera Cutánea

- Formación de la Envoltura Cornea
- Síntesis y Liberación de Ceramidas
- Degradación de la Membrana Celular
- Colapso Controlado del Citoesqueleto
- Síntesis y Secreción de Cuerpos Laminares
- Maduración y Descamación del Estrato Corneo

Barrera Cutánea

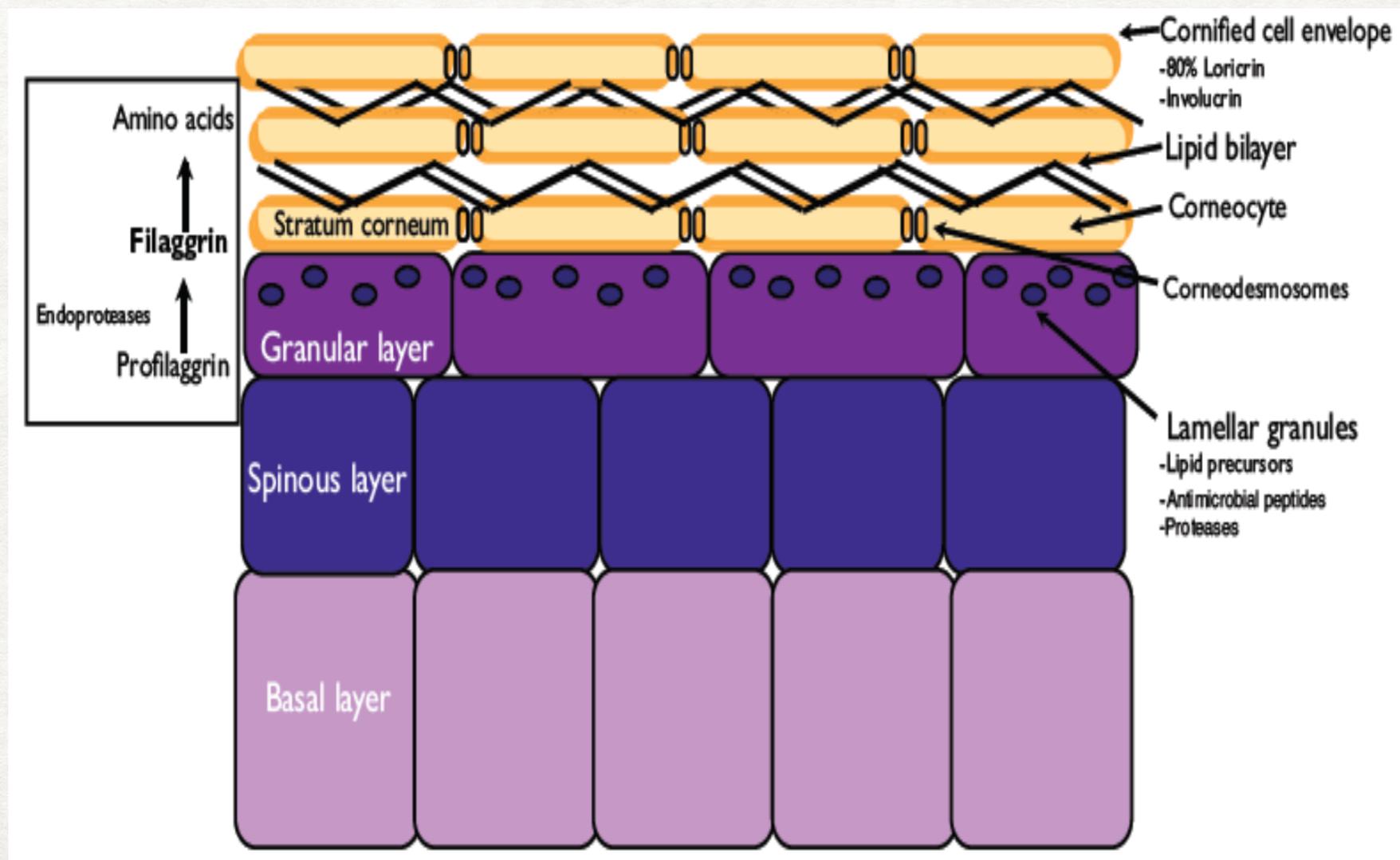
Partes de Estudio

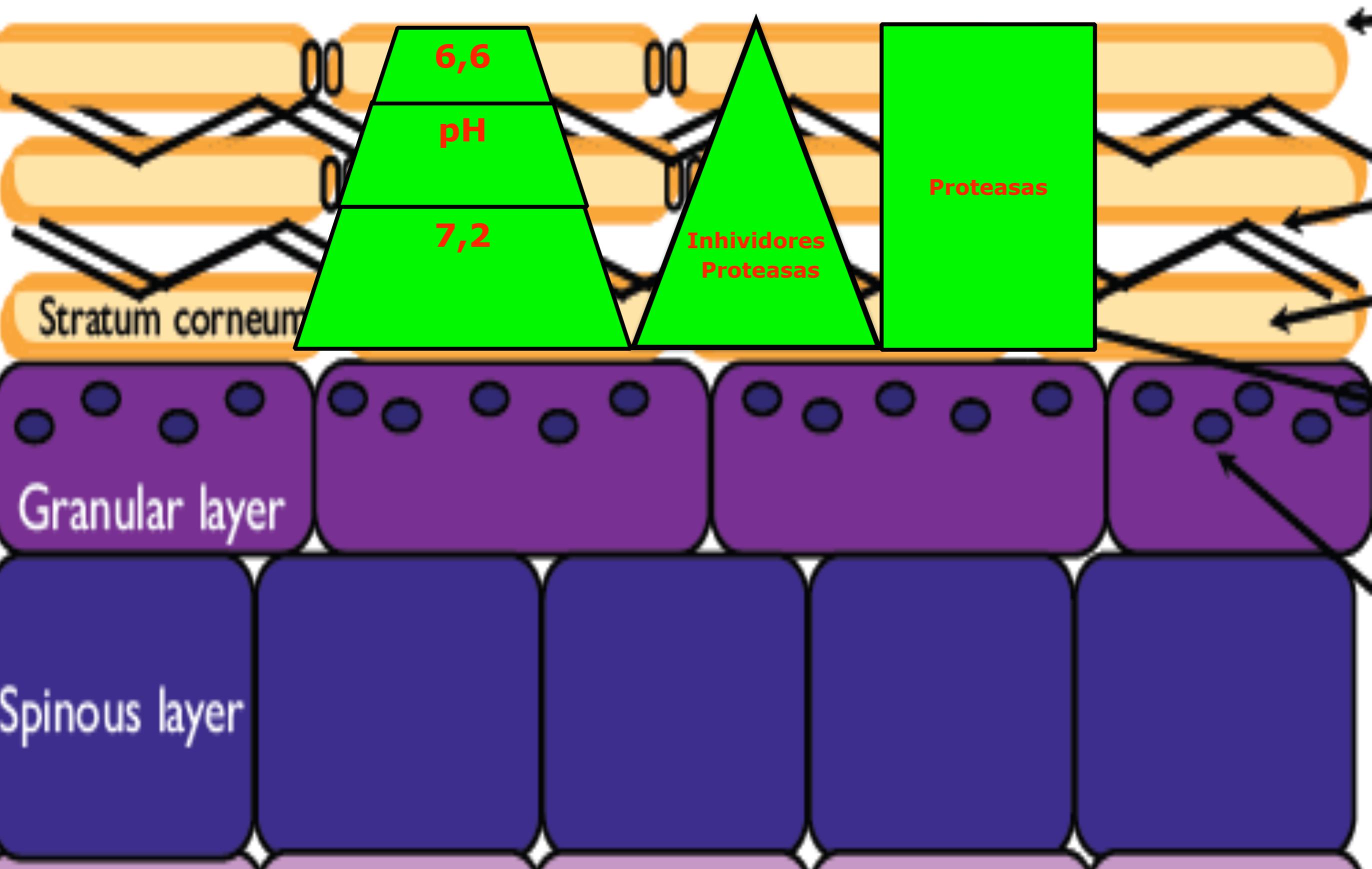
- Maduración y Descamación del Estrato Corneo
 - ✓ Degradación de Filagrina (Factor Humectante Natural)
 - ✓ Degradación de Corneodesmosomas (Kalikreina 5 y 7) - **pH Acido y Neutro**
 - ✓ Lympho-epithelial Kazal-type-related inhibitor (LEKTI) - **pH Neutro**
 - ✓ Rol del gradiente de pH en el Estrato Corneo

Barrera Cutánea

Partes de Estudio

● Maduración y Descamación del Estrato Corneo





6,6

pH

7,2

Proteasas

Inhividores
Proteasas

Stratum corneum

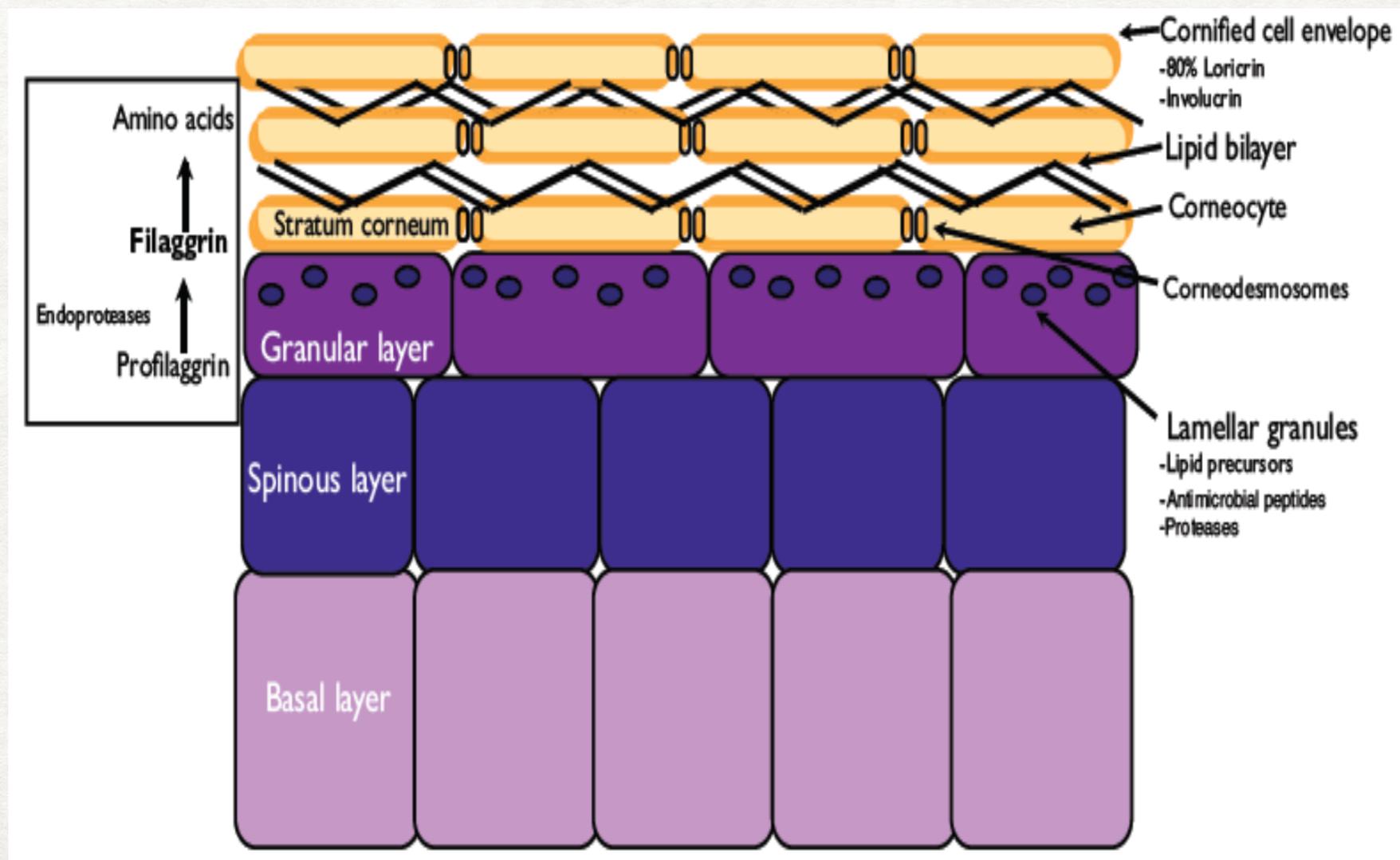
Granular layer

Spinous layer

Barrera Cutánea

Partes de Estudio

- Maduración y Descamación del Estrato Corneo



Barrera Cutánea

Partes de Estudio

Rol del gradiente de pH en el Estrato Corneo

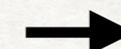
Pacientes
con DA



Menos Ceramidas (Menos AG Libres)

Menos Aminoácidos

Menos Acido Urocánico



Incremento
en pH

pH in Skin Pathophysiology

Surber C, Abels C, Maibach H (eds): pH of the Skin: Issues and Challenges.
Curr Probl Dermatol. Basel, Karger, 2018, vol 54, pp 95–107 (DOI: 10.1159/000489523)

pH in Atopic Dermatitis

Simon G. Danby^a • Michael J. Cork^{a-c}

^aSheffield Dermatology Research, The University of Sheffield Medical School, ^bThe Paediatric Dermatology Clinic, Sheffield Children's Hospital, and ^cDepartment of Dermatology, Royal Hallamshire Hospital, Sheffield, UK

Veterinary Dermatology

Vet Dermatol 2019; **30**: 121–e34

DOI: 10.1111/vde.12723

Pilot study using five methods to evaluate skin barrier function in healthy dogs and in dogs with atopic dermatitis

Danielle Cobiella, Linda Archer, Mary Bohannon and Domenico Santoro 

Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, 2015 SW 16th Ave, Gainesville, FL 32610, USA

Correspondence: Domenico Santoro, Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, 2015 SW 16th Ave, Gainesville, FL 32610, USA. E-mail: dsantoro@ufl.edu

Perros con DA tienen un pH mayor en su superficie cutánea

Barrera Cutánea

Partes de Estudio

Rol del gradiente de pH en el Estrato Corneo

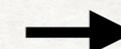
Pacientes
con DA



Menos Ceramidas (Menos AG Libres)

Menos Aminoácidos

Menos Acido Urocánico



Incremento
en pH

Barrera Cutánea

Partes de Estudio

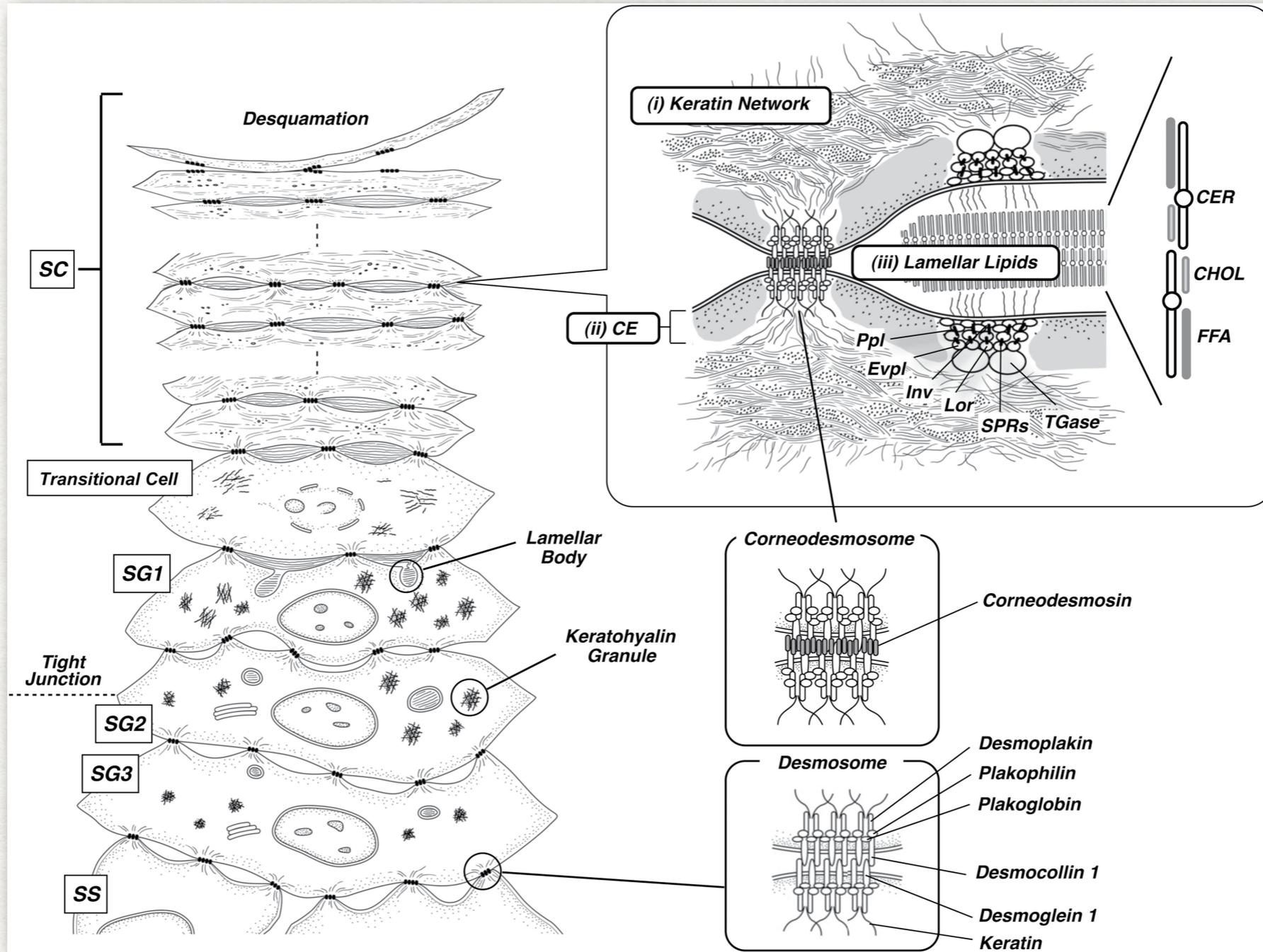
- Maduración y Descamación del Estrato Corneo
 - ✓ Degradación de Filagrina (Factor Humectante Natural)
 - ✓ Degradación de Corneodesmosomas (Kalikreina 5 y 7) - pH Acido y Neutro
 - ✓ Lympho-epithelial Kazal-type-related inhibitor (LEKTI) - pH Neutro
 - ✓ Rol del gradiente de pH en el Estrato Corneo

Barrera Cutánea

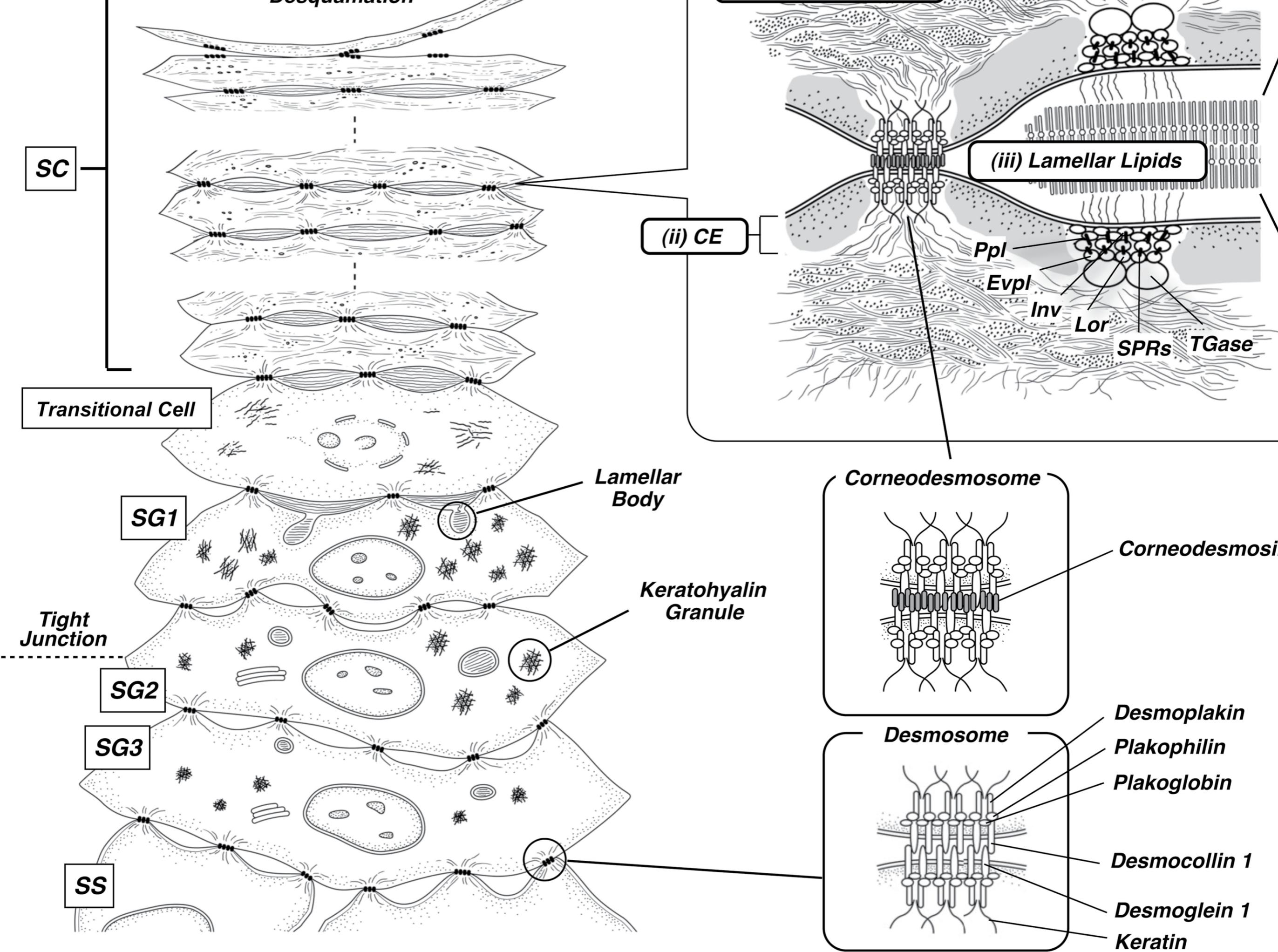
Partes de Estudio

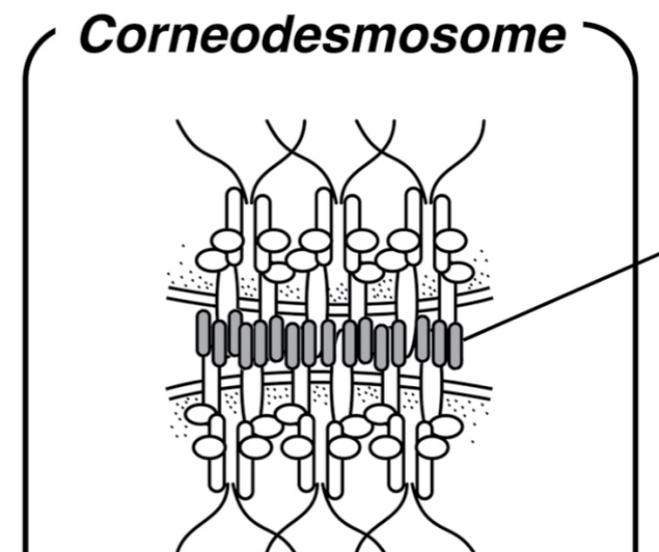
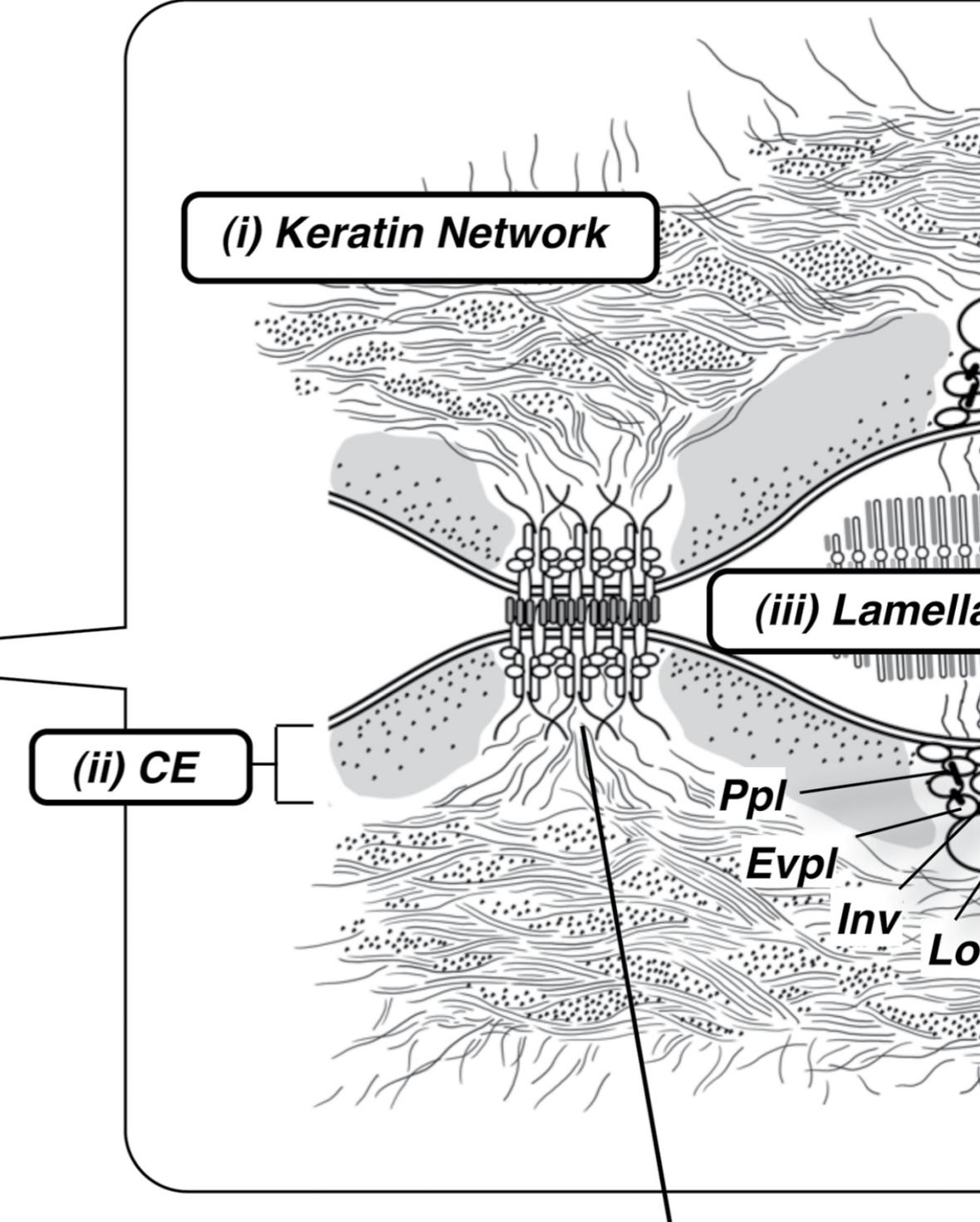
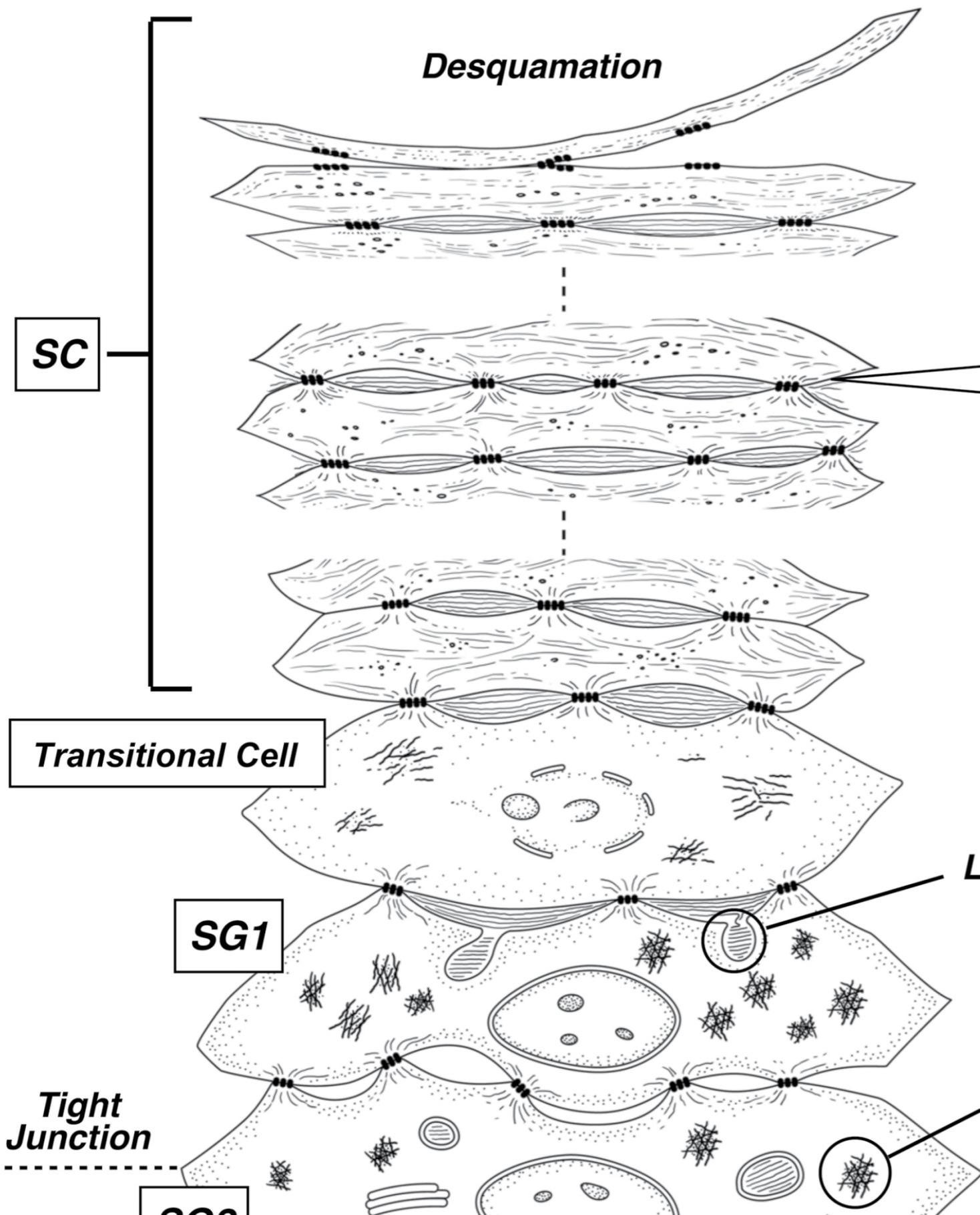
✓ Fisiología y Formación de la Barrera Cutánea

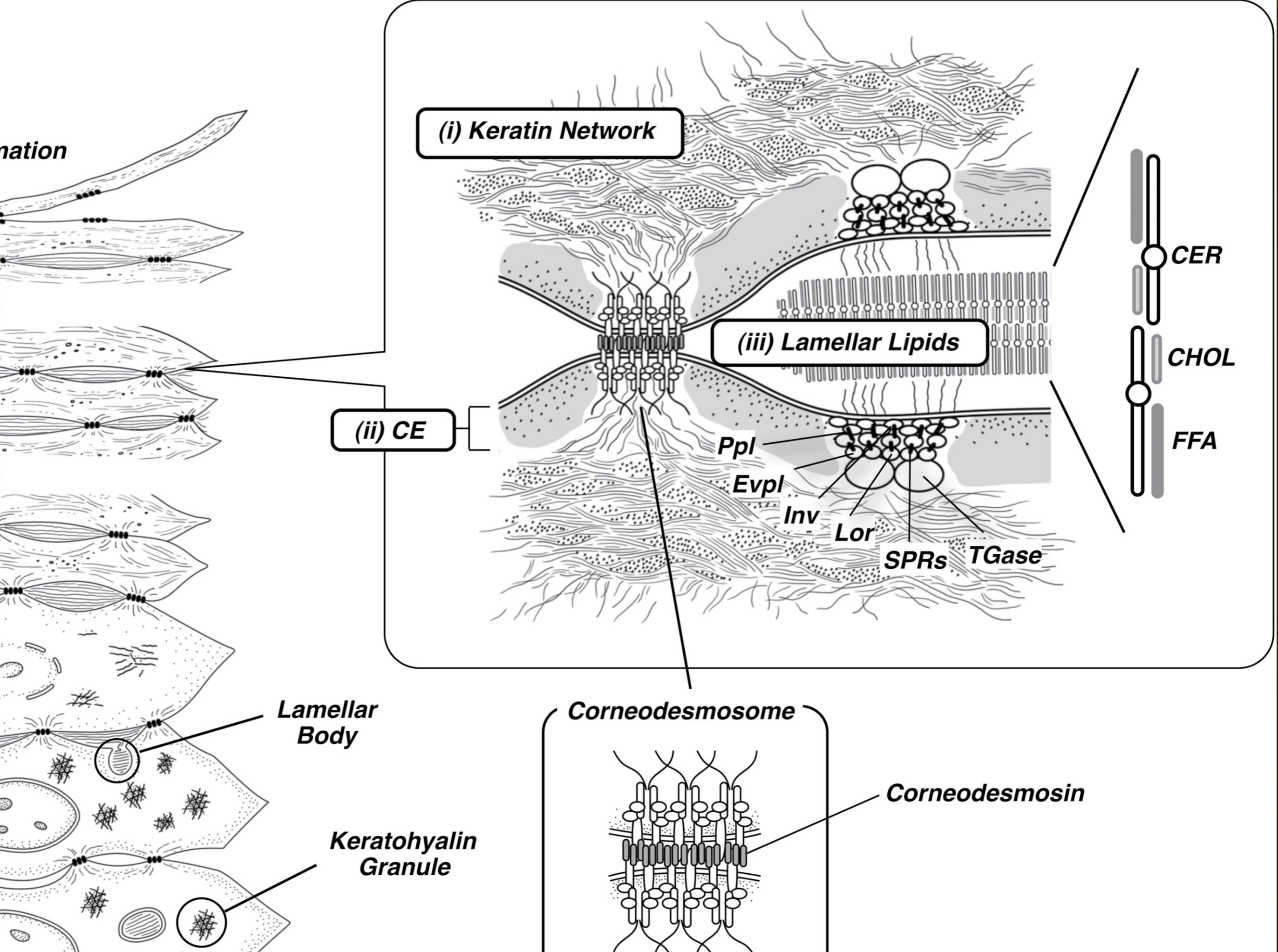
- Formación de la Envoltura Cornea
- Síntesis y Liberación de Ceramidas
- Degradación de la Membrana Celular
- Colapso Controlado del Citoesqueleto
- Síntesis y Secreción de Cuerpos Laminares
- Maduración y Descamación del Estrato Corneo

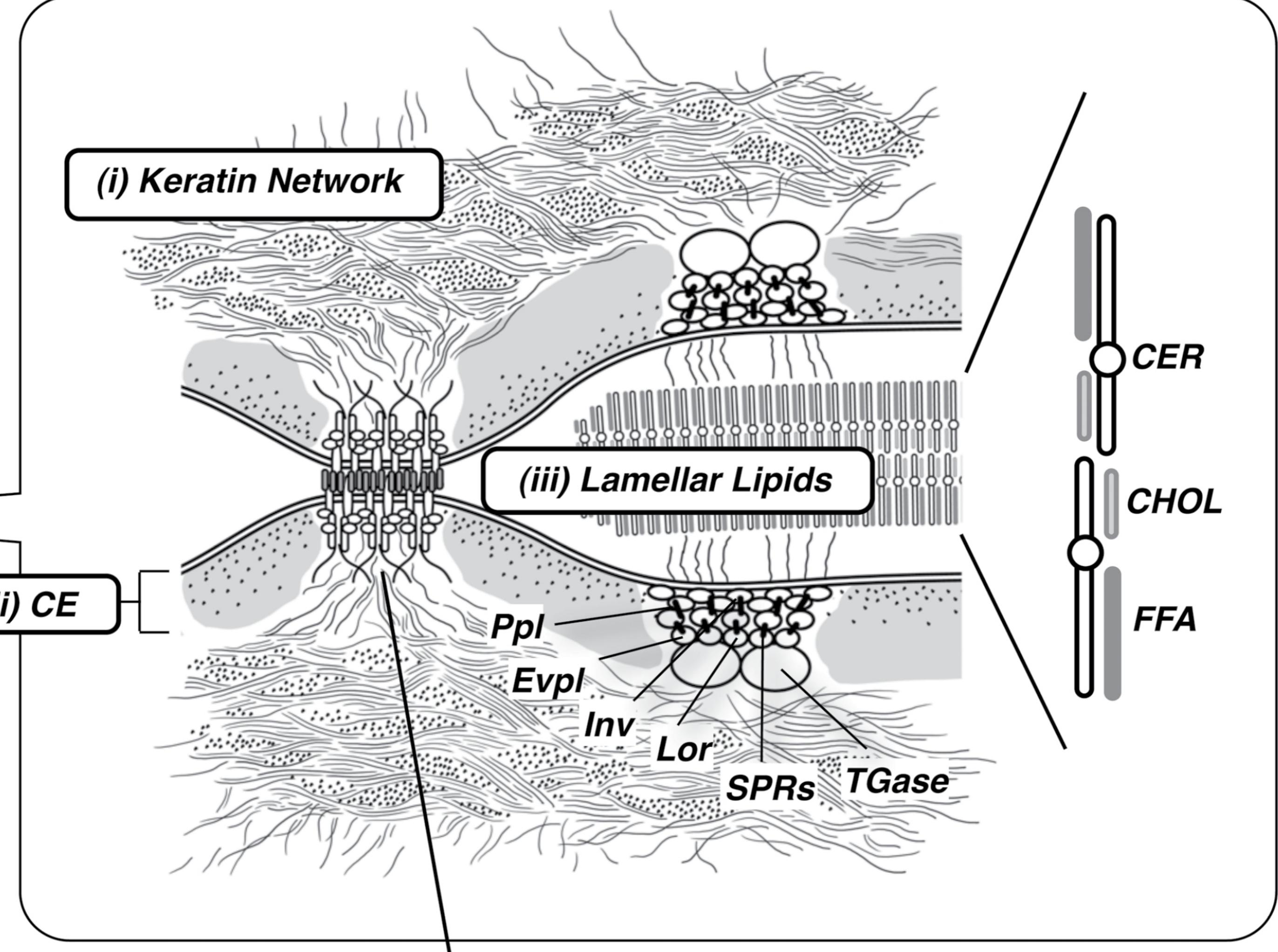


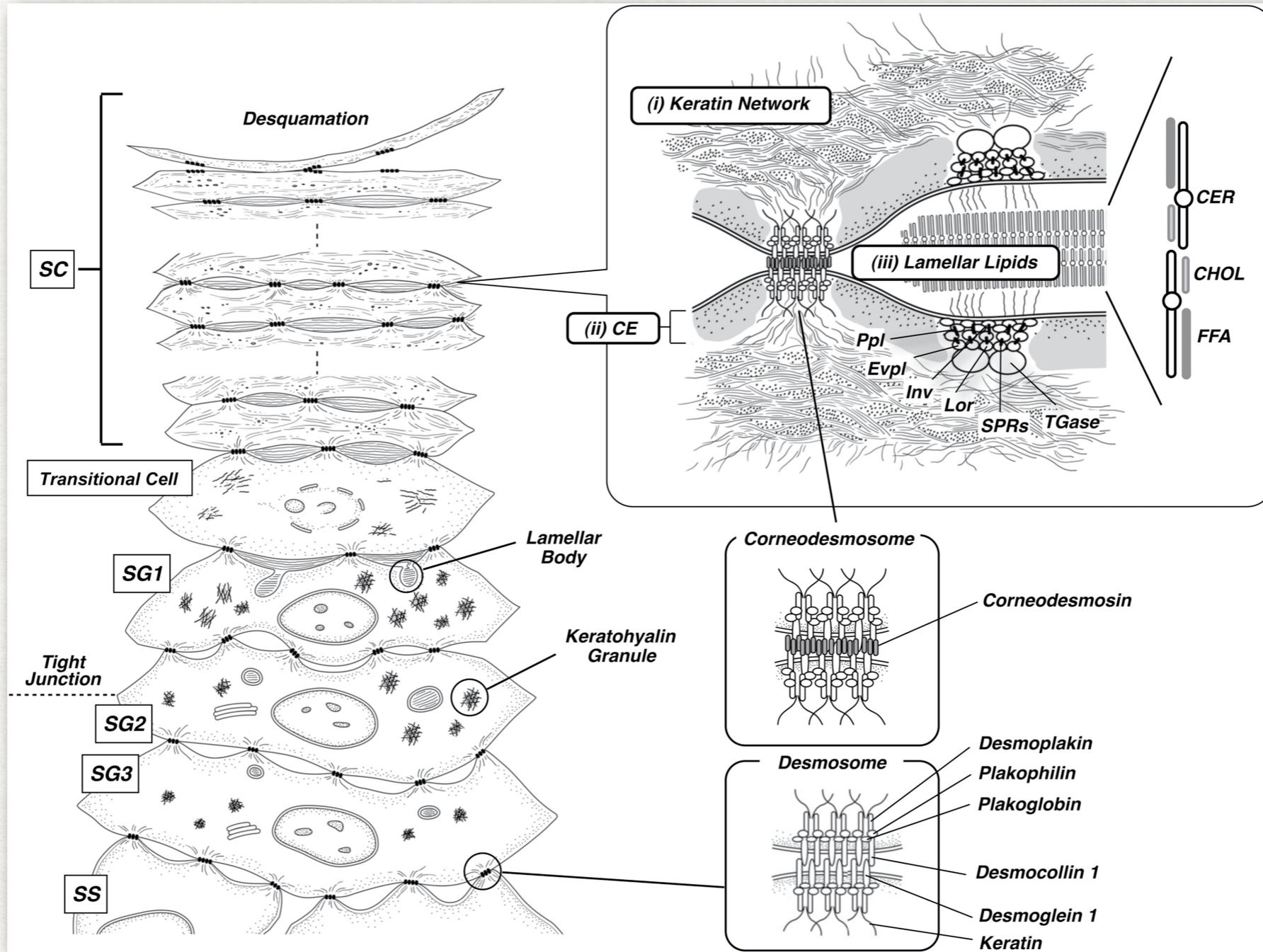
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Matsui, T., & Amagai, M. (2015). Dissecting the formation, structure and barrier function of the stratum corneum. *International Immunology*, 27(6), 269–280.



Final

1ra Parte



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