CURSO DE BIOLOGÍA CELULAR 2021

Señalización celular I

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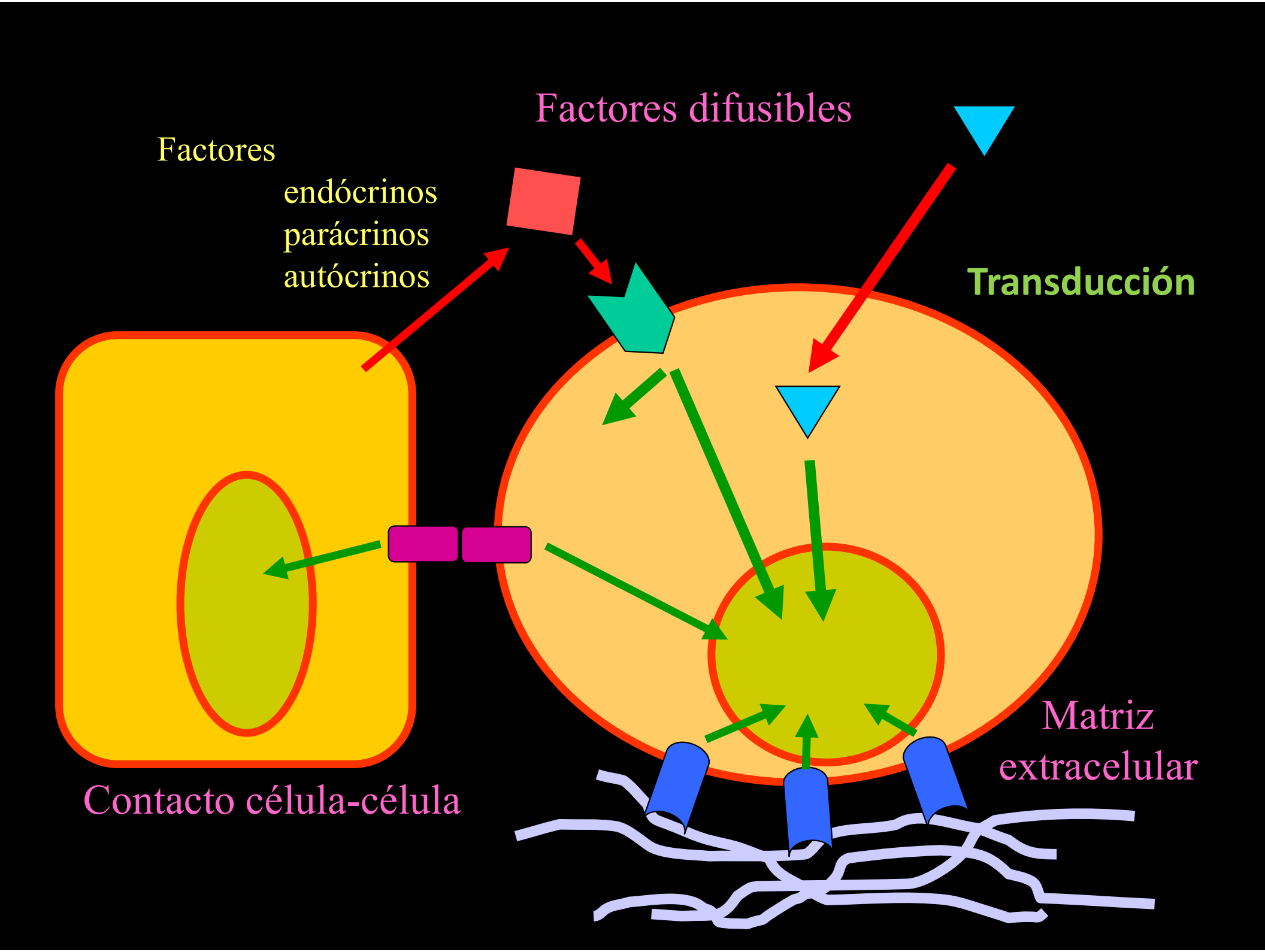
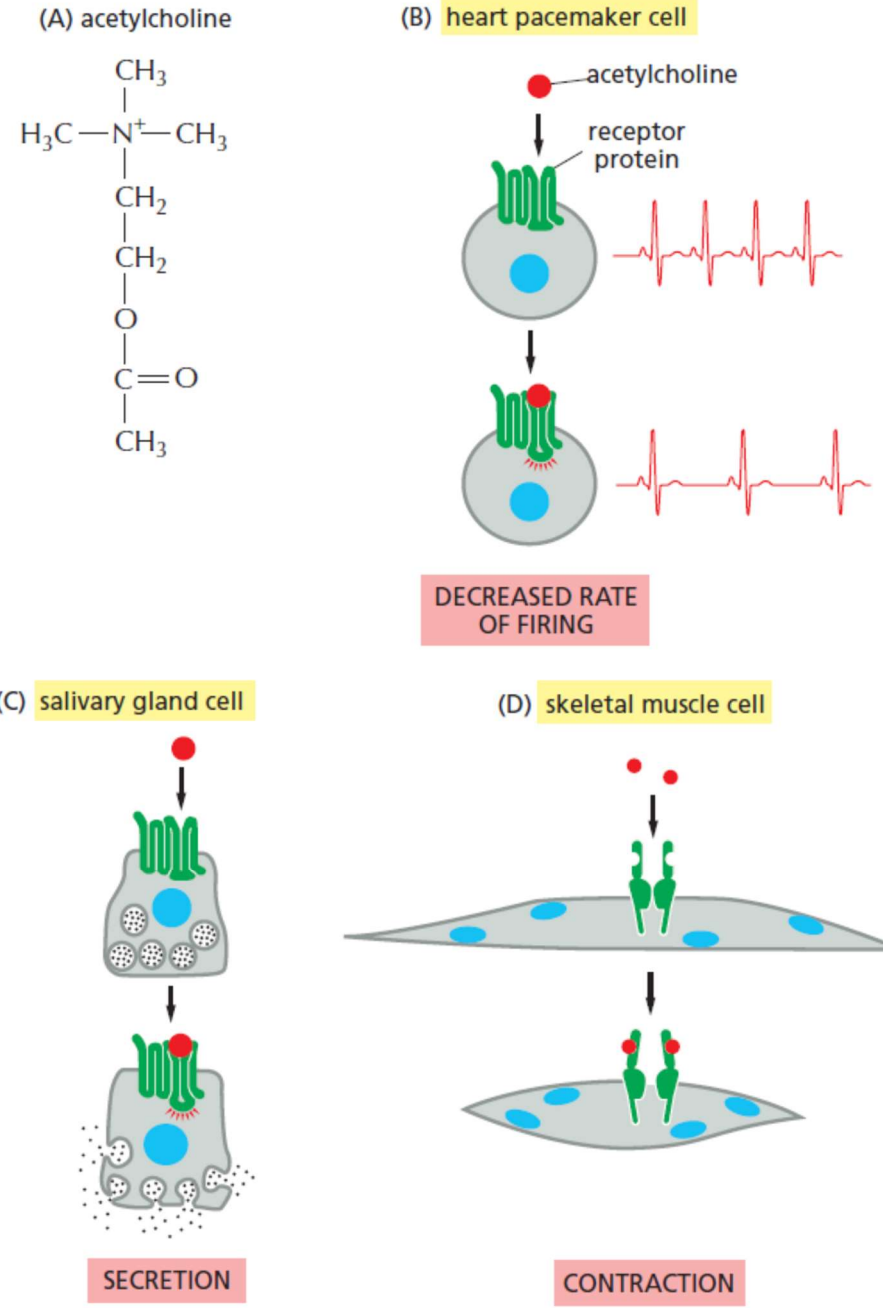
UNIVERSIDAD DE LA REPÚBLICA
URUGUAY

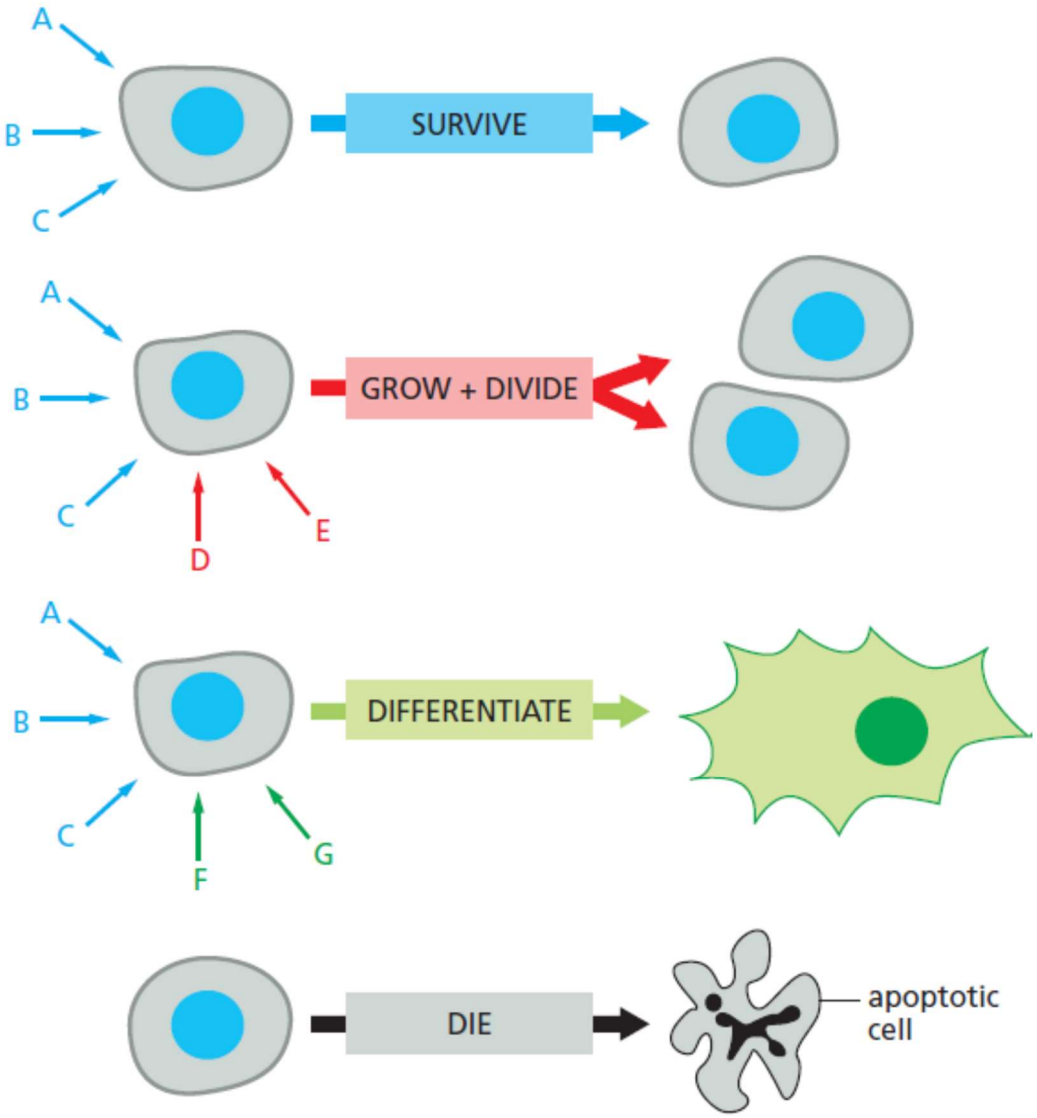

Factores difusibles
Factores
endócrinos
parácrinos
autócrinos
Transducción
Matriz
extracelular
Contacto célula-célula

Respuesta de la célula

COMPETENCIA



INTEGRACIÓN



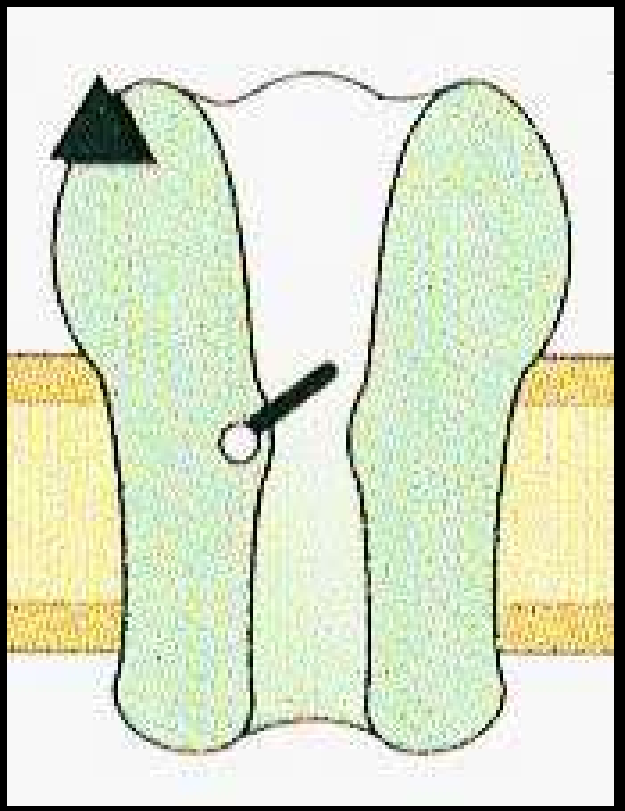
Receptores

A - Receptores canal (ionotrópicos)

B - Receptores acoplados a proteínas G

C - Receptores acoplados a enzimas

F - Receptores nucleares



Receptores

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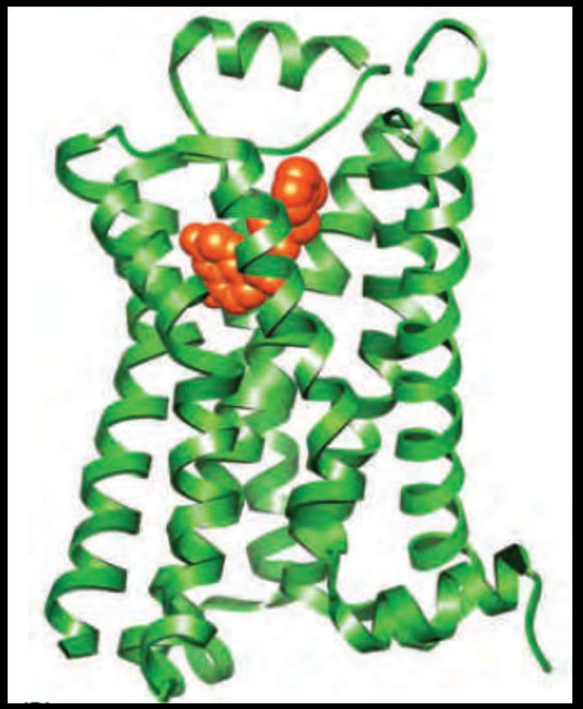
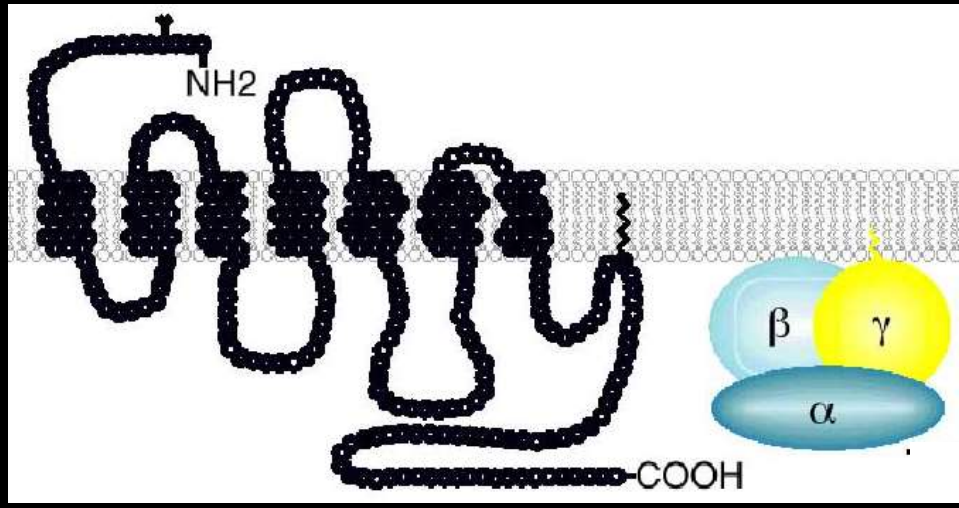


B - Receptores acoplados a proteínas G

C - Receptores acoplados a enzimas



F - Receptores nucleares

Receptores

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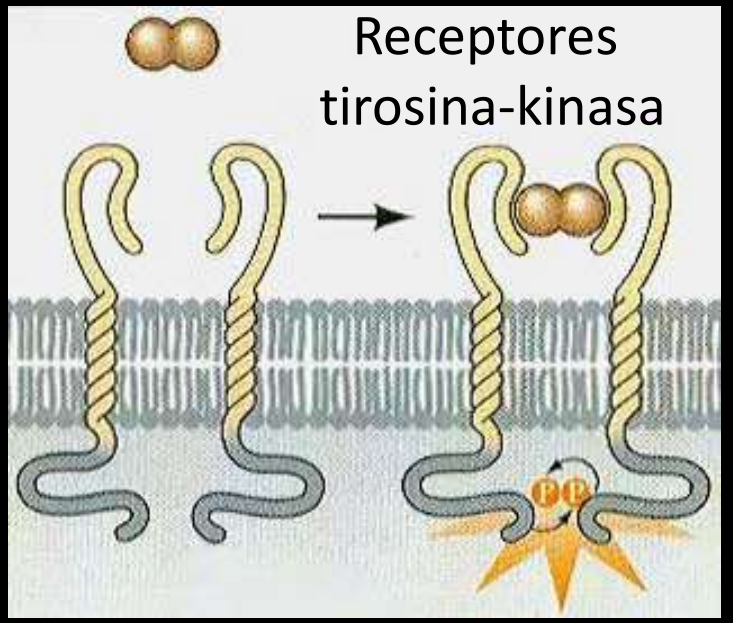
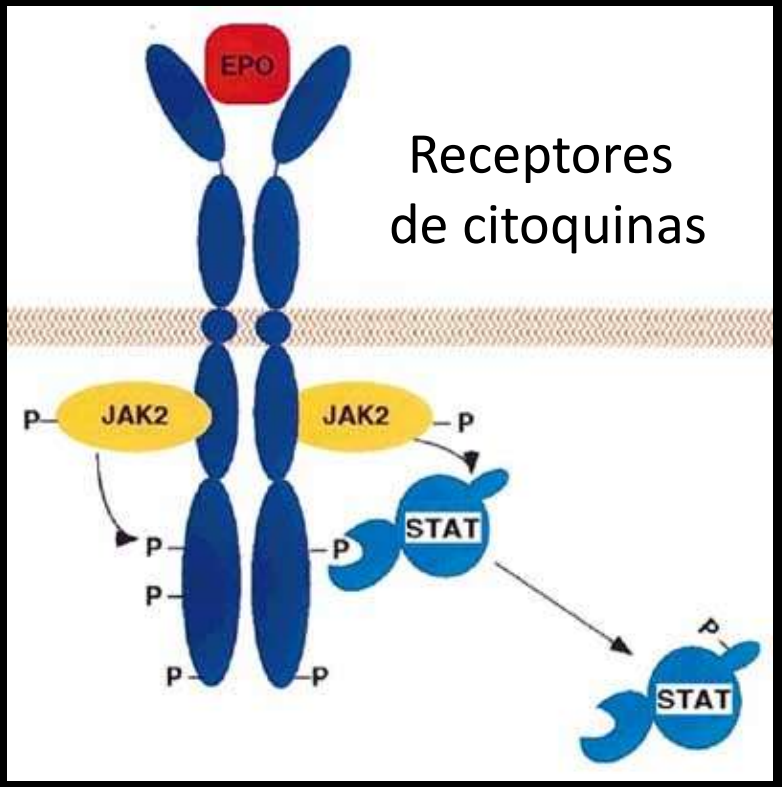




VIEWPOINT: COVID-19

Cytokine release syndrome in severe COVID-19

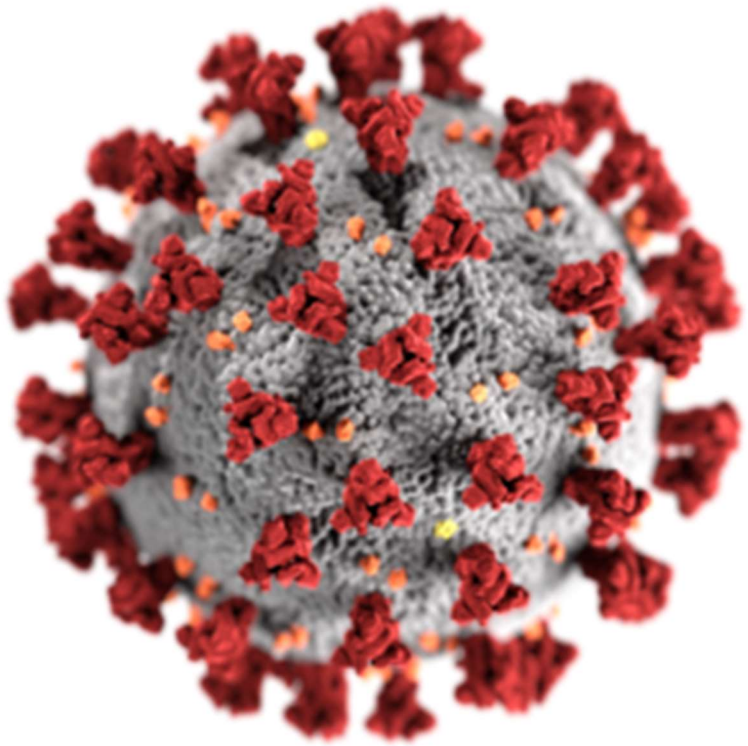
Lessons from arthritis and cell therapy in cancer patients point to therapy for severe disease

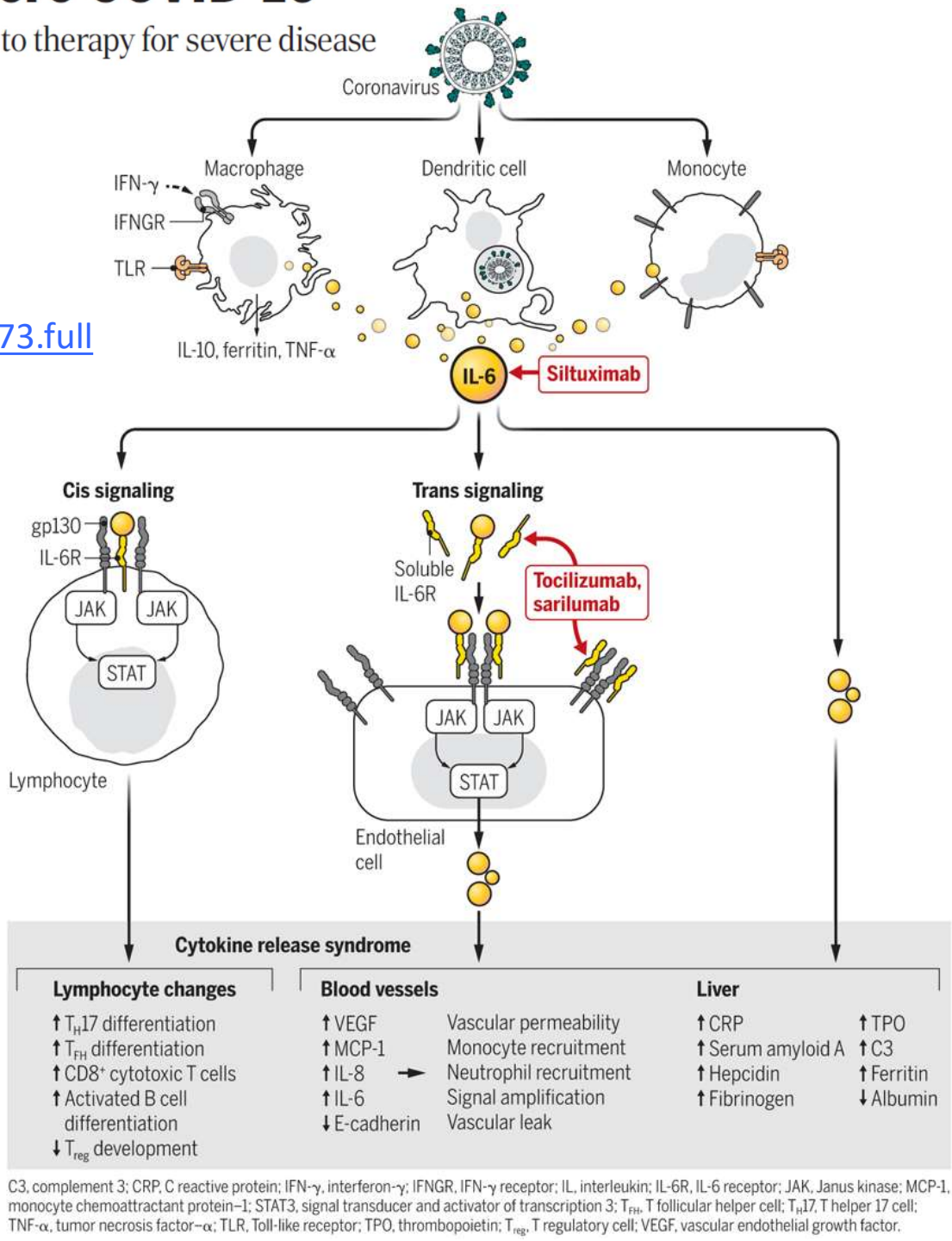
By **John B. Moore**[1] *and* **Carl H. June**[2]

SCIENCE sciencemag.org

1 MAY 2020 • VOL 368 ISSUE 6490

https://science.sciencemag.org/content/368/6490/473.full





C3, complement 3; CRP, C reactive protein; IFN-γ, interferon-γ; IFNGR, IFN-γ receptor; IL, interleukin; IL-6R, IL-6 receptor; JAK, Janus kinase; MCP-1, monocyte chemoattractant protein–1; STAT3, signal transducer and activator of transcription 3; T_{FH}, T follicular helper cell; T_H17, T helper 17 cell; TNF-α, tumor necrosis factor–α; TLR, Toll-like receptor; TPO, thrombopoietin; T_{reg}, T regulatory cell; VEGF, vascular endothelial growth factor.

Receptores

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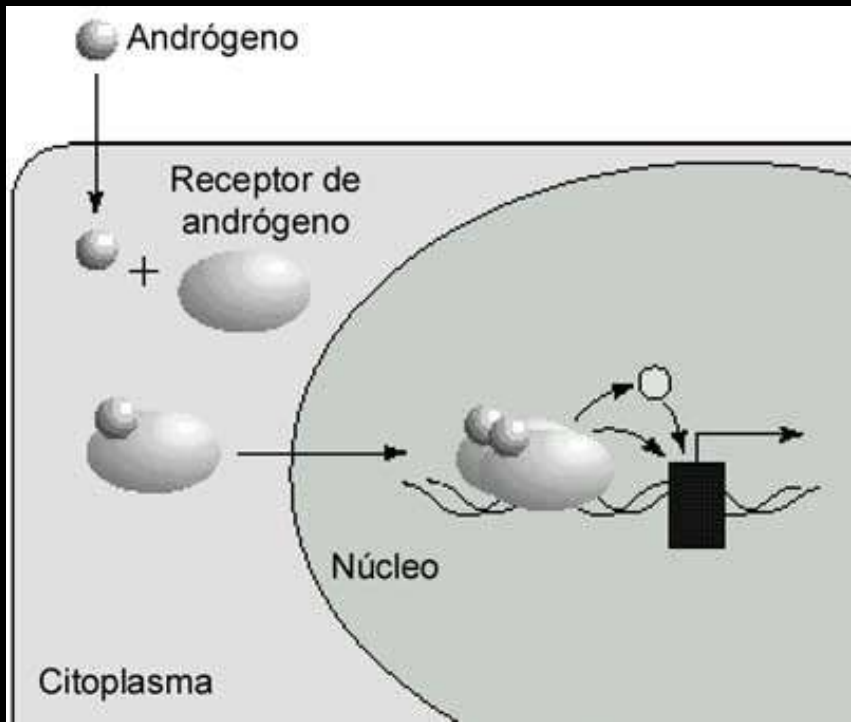
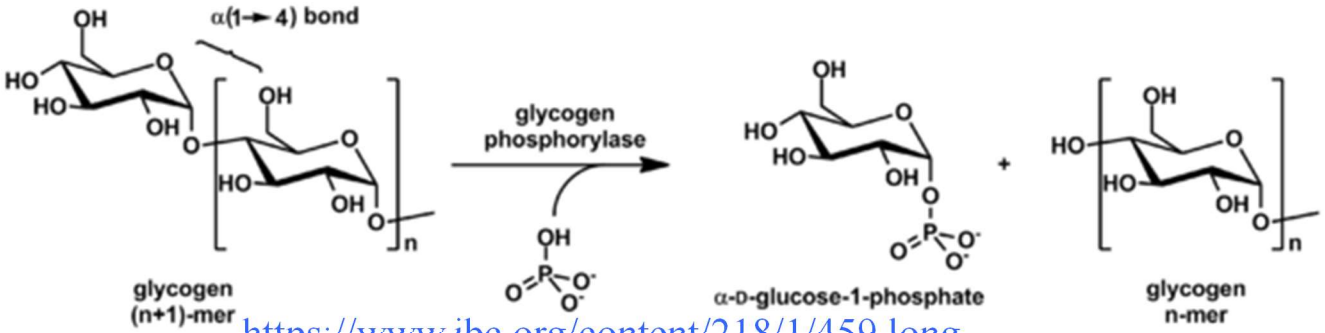


Earl W. Sutherland
(1915-1974)
Premio Nobel MedFis. 1971



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THE RELATIONSHIP OF EPINEPHRINE AND GLUCAGON TO LIVER PHOSPHORYLASE

I. LIVER PHOSPHORYLASE; PREPARATION AND PROPERTIES*

By EARL W. SUTHERLAND and WALTER D. WOSILAIT

(From the Department of Pharmacology, School of Medicine, Western Reserve University, Cleveland, Ohio)

(Received for publication, June 16, 1955)

https://www.jbc.org/content/218/1/469.long

THE RELATIONSHIP OF EPINEPHRINE AND GLUCAGON TO LIVER PHOSPHORYLASE

II. ENZYMATIC INACTIVATION OF LIVER PHOSPHORYLASE*

By WALTER D. WOSILAIT and EARL W. SUTHERLAND

(From the Department of Pharmacology, School of Medicine, Western Reserve University, Cleveland, Ohio)

(Received for publication, June 16, 1955)

THE RELATIONSHIP OF EPINEPHRINE AND GLUCAGON TO LIVER PHOSPHORYLASE

III. REACTIVATION OF LIVER PHOSPHORYLASE IN SLICES AND IN EXTRACTS*

By T. W. RALL, EARL W. SUTHERLAND, and WALTER D. WOSILAIT

(From the Department of Pharmacology, School of Medicine, Western Reserve University, Cleveland, Ohio)

(Received for publication, June 16, 1955)

https://www.jbc.org/content/218/1/483.long

THE RELATIONSHIP OF EPINEPHRINE AND GLUCAGON TO LIVER PHOSPHORYLASE

IV. EFFECT OF EPINEPHRINE AND GLUCAGON ON THE REACTIVATION OF PHOSPHORYLASE IN LIVER HOMOGENATES*

By T. W. RALL, EARL W. SUTHERLAND, and JACQUES BERTHET†

(From the Department of Pharmacology, School of Medicine, Western Reserve University, Cleveland, Ohio)

(Received for publication, July 16, 1956)

https://www.jbc.org/content/224/1/463.long

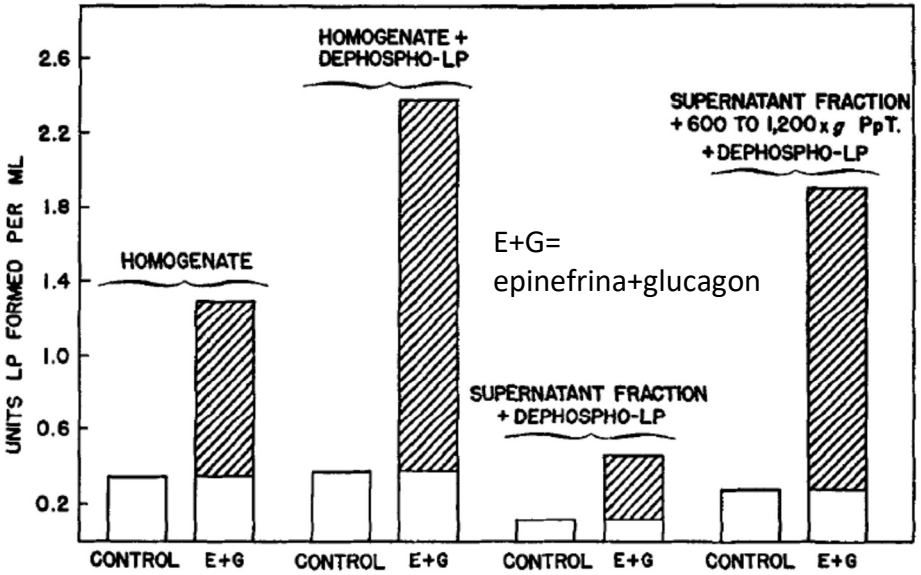


FIG. 1. The effect of epinephrine and glucagon on LP formation in a whole and fractionated cat liver homogenate. 0.14 ml. of homogenate or homogenate fraction was incubated with 2×10^{-2} M Tris buffer (pH 7.4), 2.5×10^{-3} M $MgSO_4$, and 1.7×10^{-3} M ATP in the presence and absence of 0.4 γ of *l*-epinephrine plus 1.0 γ of glucagon. The final volume was 0.20 ml. Dephospho-LP (4.2 units per ml.) was added where indicated. The supernatant fraction used in this experiment was the 1200 $\times$ *g* supernatant fraction. LP activity was assayed before and after 10 minutes incubation at 30°. The bars represent the amount of LP formed during the incubation period; the cross-hatched portions of the bars represent the increased LP formation above that of the control.

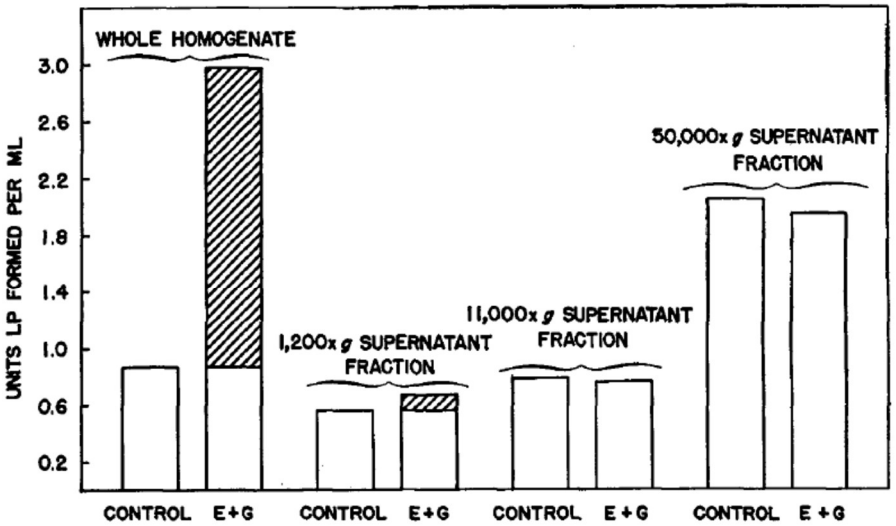
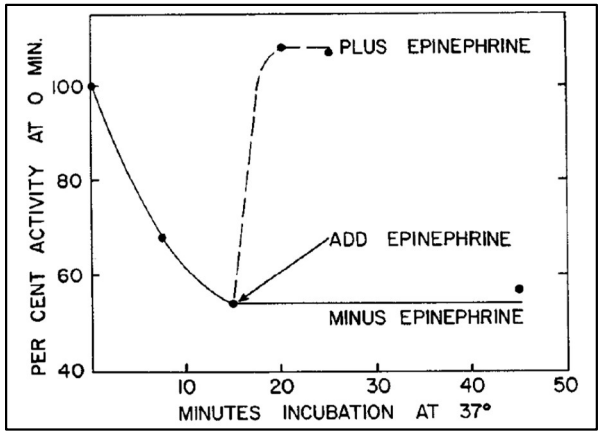


FIG. 3. The effect of epinephrine and glucagon on LP formation in fractions of a cat liver homogenate. 0.14 ml. of homogenate or homogenate fraction was incubated 10 minutes at 30° with 4×10^{-2} M Tris buffer (pH 7.4), 2.5×10^{-3} M $MgSO_4$, 1.7×10^{-3} M ATP, and 4.2 units per ml. of dephospho-LP in the presence and absence of 0.4 γ of *l*-epinephrine plus 2.0 γ of glucagon. The final volume was 0.20 ml.



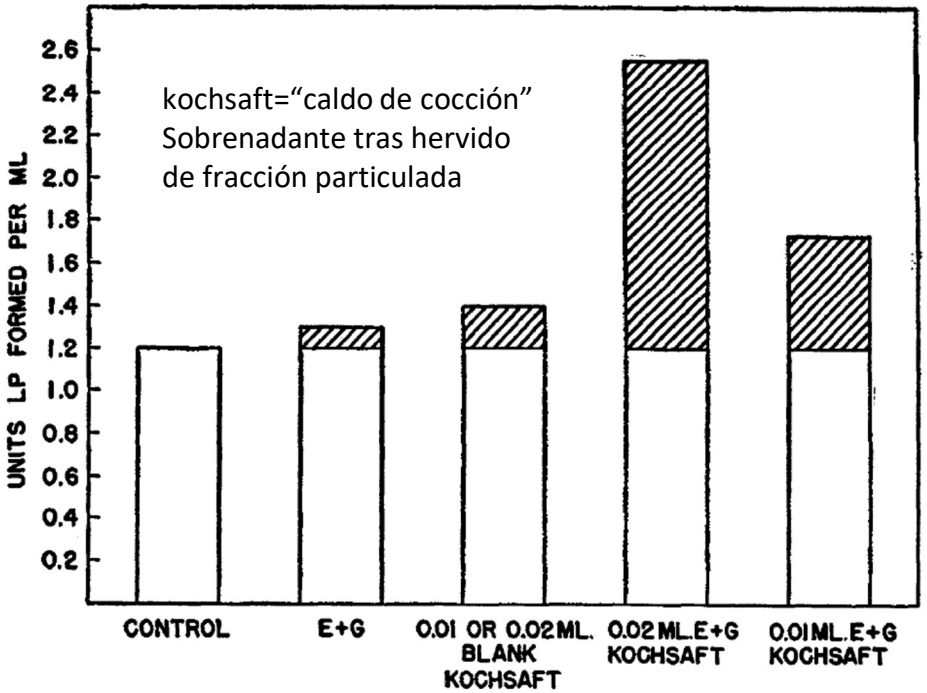


FIG. 4. The effect of preparations of the boiled extract on the formation of LP. Two 25 ml. portions of a suspension of washed particles in 0.25 M sucrose, derived from about 25 gm. of cat liver slices, were incubated with 2×10^{-2} M Tris buffer (pH 7.4), 2.5×10^{-3} M $MgSO_4$, and 1.7×10^{-3} M ATP in a final volume of 30 ml. One vessel contained 150 γ of both *l*-epinephrine and glucagon (E + G), while the other contained no added hormones (blank). After shaking for 5 minutes at 30°, the flasks were heated in boiling water for 3 minutes and then chilled to 0°. The flask contents were centrifuged at 15,000 $\times$ *g* for 15 minutes in the cold. 0.02 ml. and 0.01 ml. aliquots of the supernatant fluids (boiled extracts) were incubated with 0.13 ml. of an 11,000 $\times$ *g* supernatant fraction of a dog liver homogenate in 4×10^{-2} M Tris buffer (pH 7.4), 2.5×10^{-3} M $MgSO_4$, and 1.7×10^{-3} M ATP. The final volume was 0.20 ml. Control experimental vessels contained either water or 1.2 γ of both *l*-epinephrine and glucagon in place of the boiled extracts. LP activity was assayed before and after 5 minutes incubation at 30°, and the bars represent the amount of LP formed during this incubation period.

Dinámica de grupos

Consigna

- Analizar los resultados en su conjunto
- Extraer conclusiones generales
- Especular sobre el mecanismo molecular de activación de la fosforilasa mediado por hormonas

Cada grupo nombrará 1 o 2 voceros para comunicar sus conclusiones

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(Received for publication, July 16, 1956)

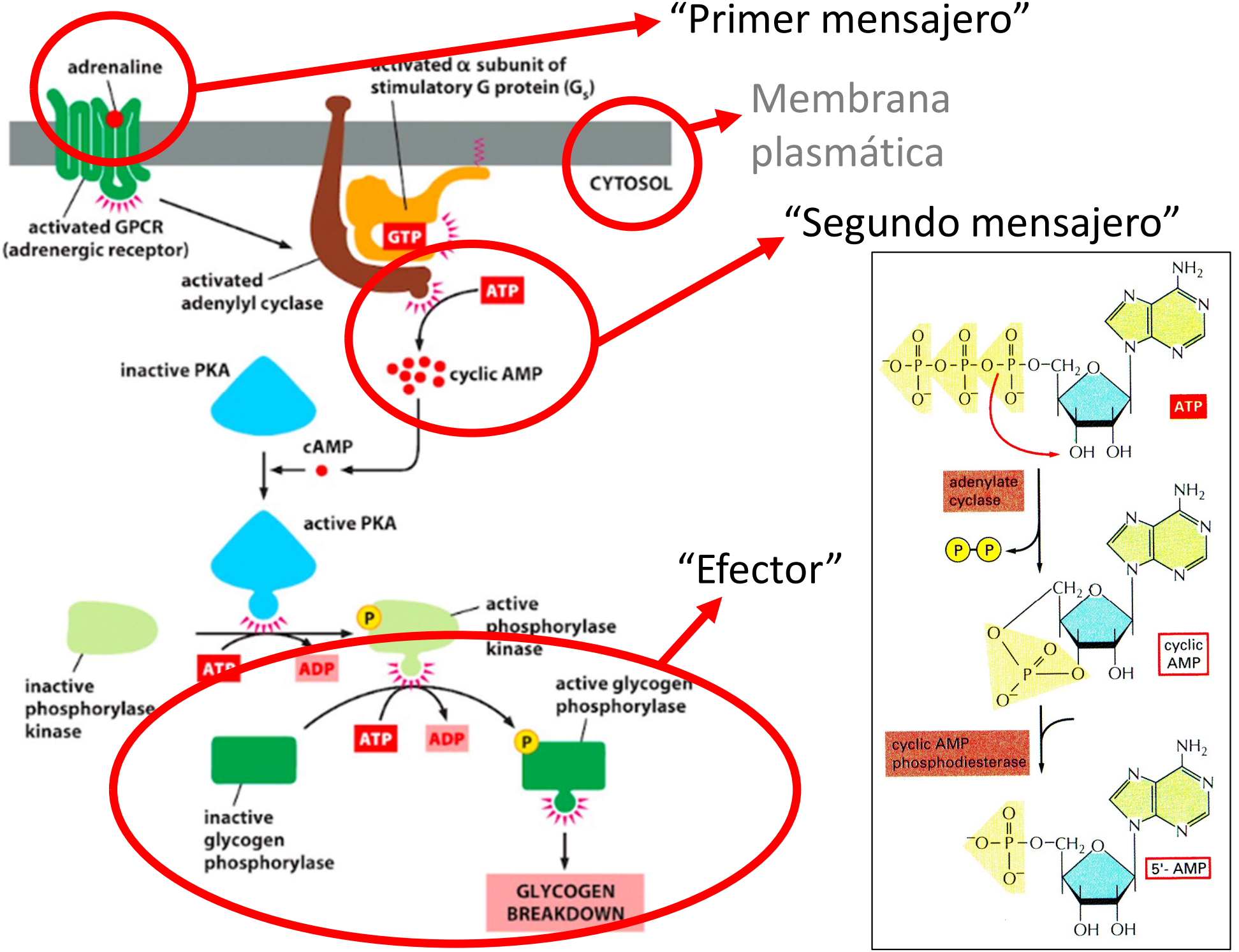
SUMMARY

1. The formation of liver phosphorylase from dephosphophosphorylase in cell-free homogenates of dog and cat liver was increased markedly in the presence of either epinephrine or glucagon in low concentration.

2. The relative activities of sympathomimetic amines in homogenates were similar to those observed in liver slices and in the intact animal.

3. The response to the hormones in liver homogenates was separated into two phases: first, the formation of an active factor in particulate fractions in the presence of the hormones and, second, the stimulation by the factor of liver phosphorylase formation in supernatant fractions of homogenates in which the hormones themselves had no effect.

4. The active factor was heat-stable, dialyzable, and was purified considerably by chromatography on anion and cation exchange resins.

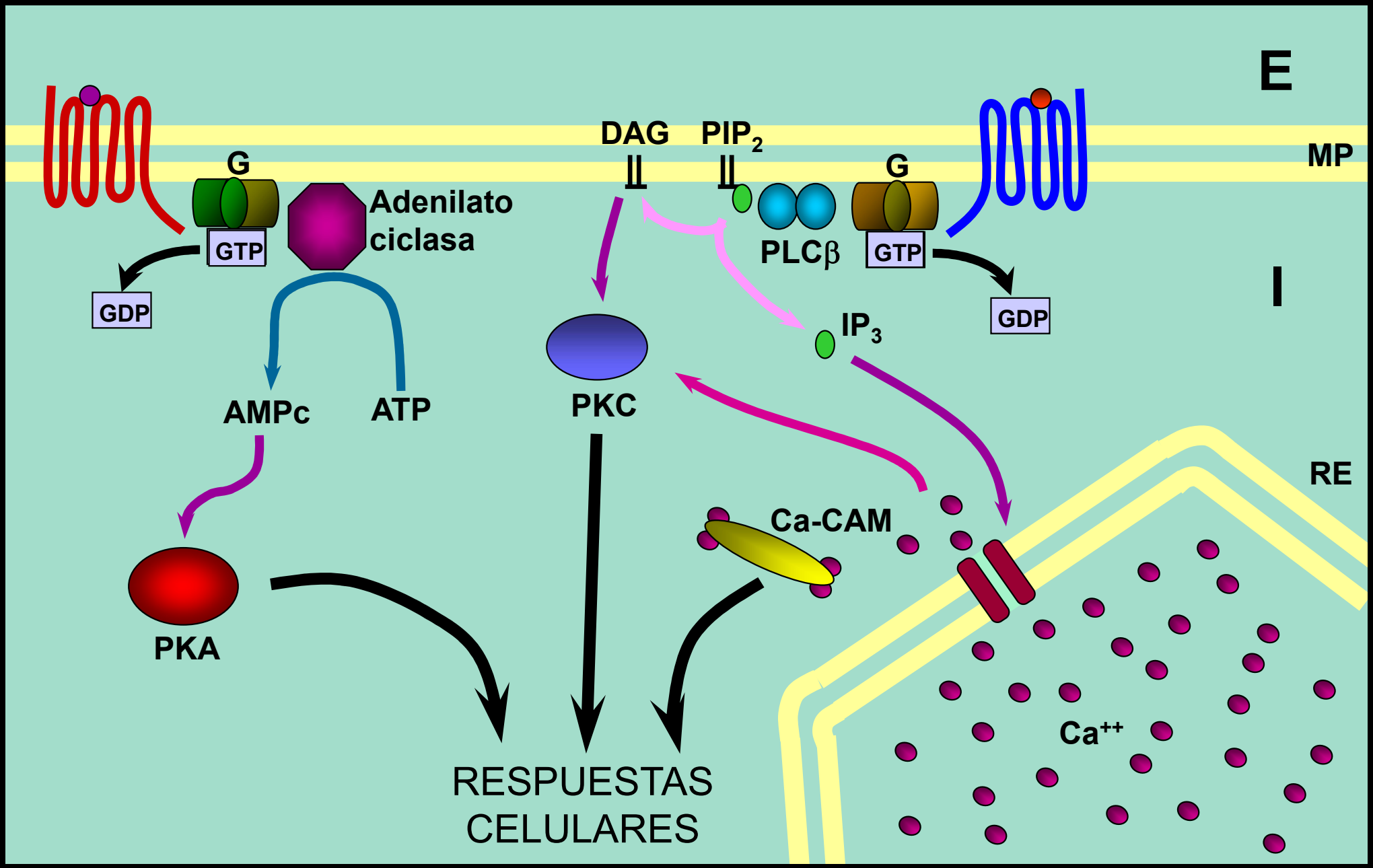

"Primer mensajero"
adrenaline
activated α subunit of stimulatory G protein (G_s)
Membrana plasmática
CYTOSOL
activated GPCR (adrenergic receptor)
GTP
activated adenylyl cyclase
ATP
"Segundo mensajero"
cyclic AMP
inactive PKA
cAMP
active PKA
"Efector"
active phosphorylase kinase
inactive phosphorylase kinase
ATP
ADP
P
active glycogen phosphorylase
inactive glycogen phosphorylase
GLYCOGEN BREAKDOWN
adenylate cyclase
cyclic AMP phosphodiesterase
5'- AMP

A - Activación de proteínas G

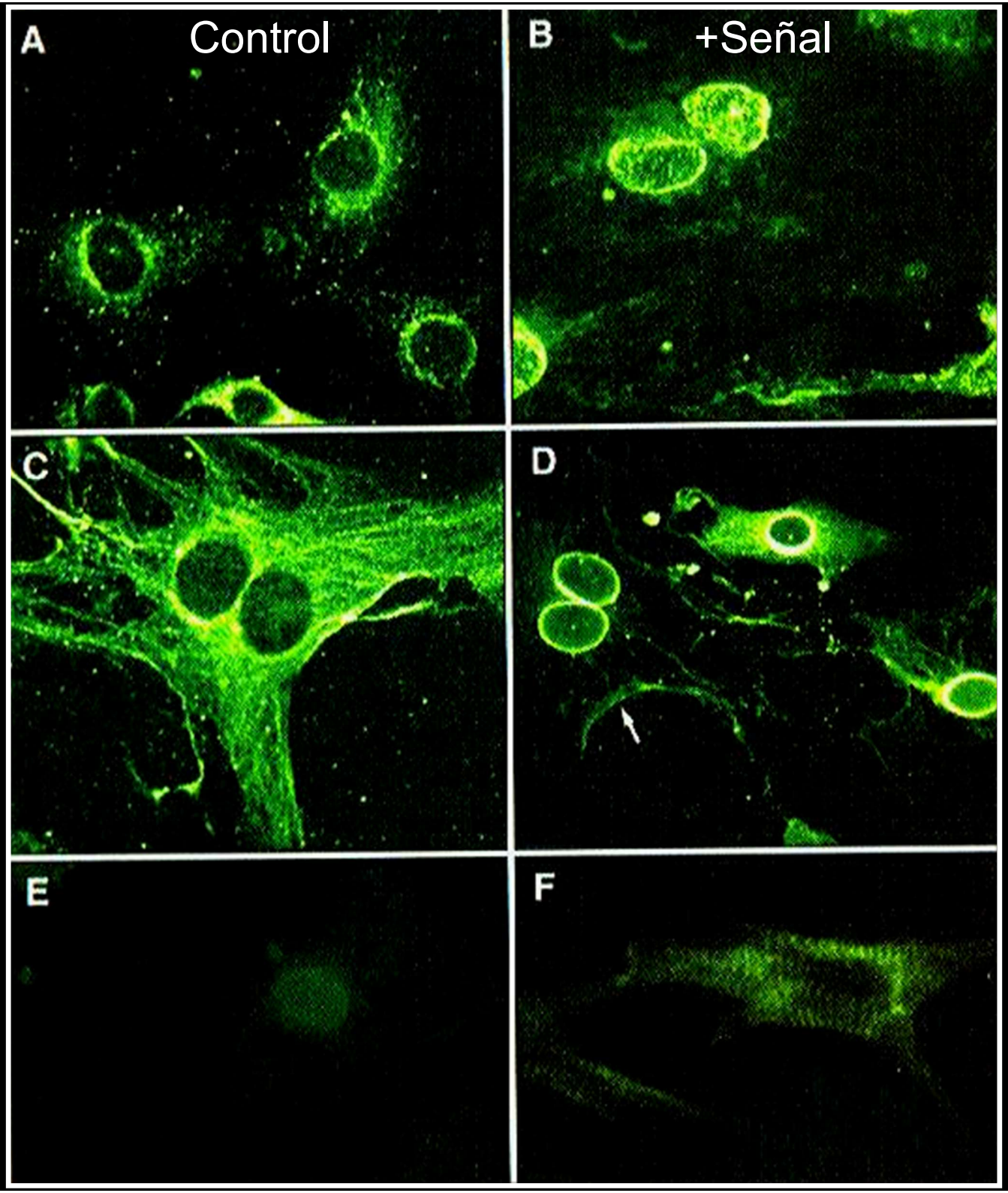
B - Interacciones moleculares

C - Segundos mensajeros

D - Fosforilación de proteínas



E - Localización subcelular de proteínas



Mochly-Rosen, 1995

Propiedades de los segundos mensajeros:

- Son moléculas pequeñas, difunden rápido

- Son producidos rápidamente (precursores o stock abundantes)

- Son eliminados rápidamente (degradación o remoción)

- Interactúan con proteínas efectoras