



CAN THE CD43 MOLECULE BE CONSIDERED AS A THERAPEUTIC TAGET?

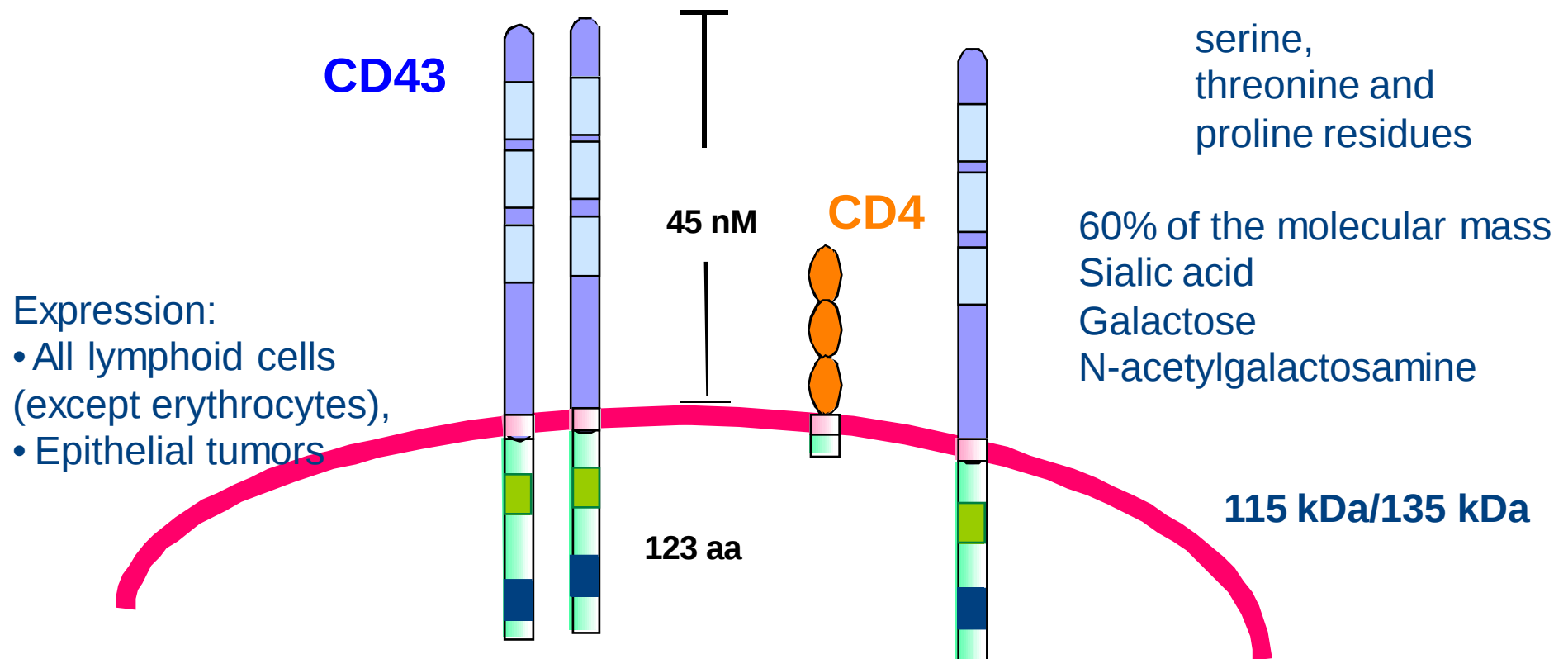
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UNAM**

CD43:

- the molecule and its signaling capacities
- favors a Th1 differentiation pattern and contributes to the decision making process of T lymphocytes
- participates in non-lymphoid tumors

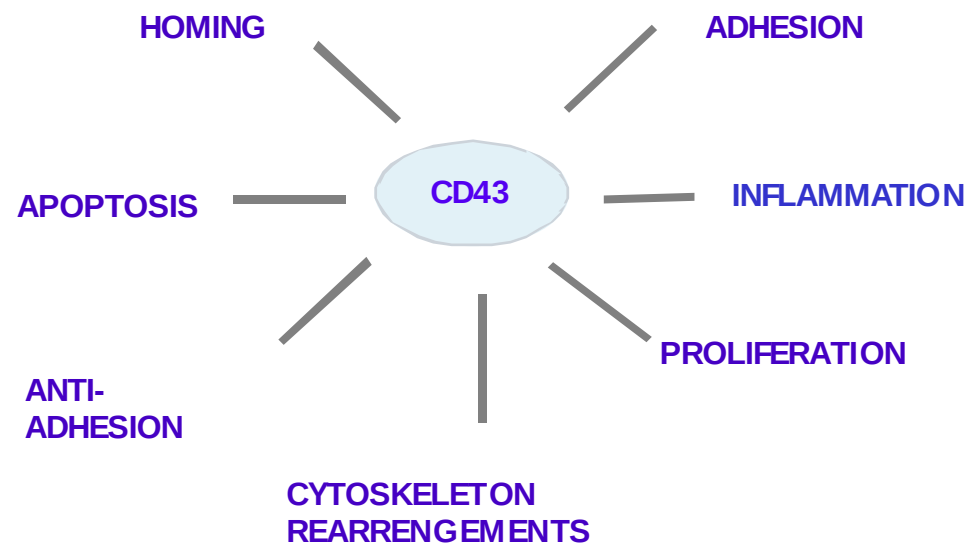
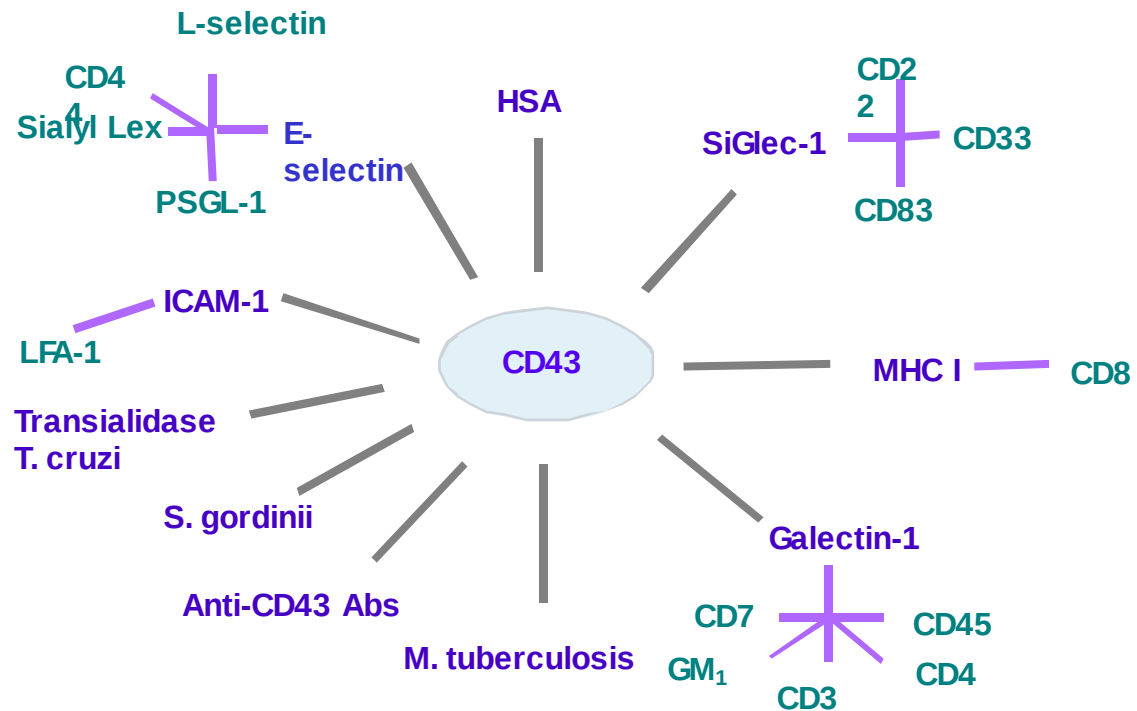
CD43:

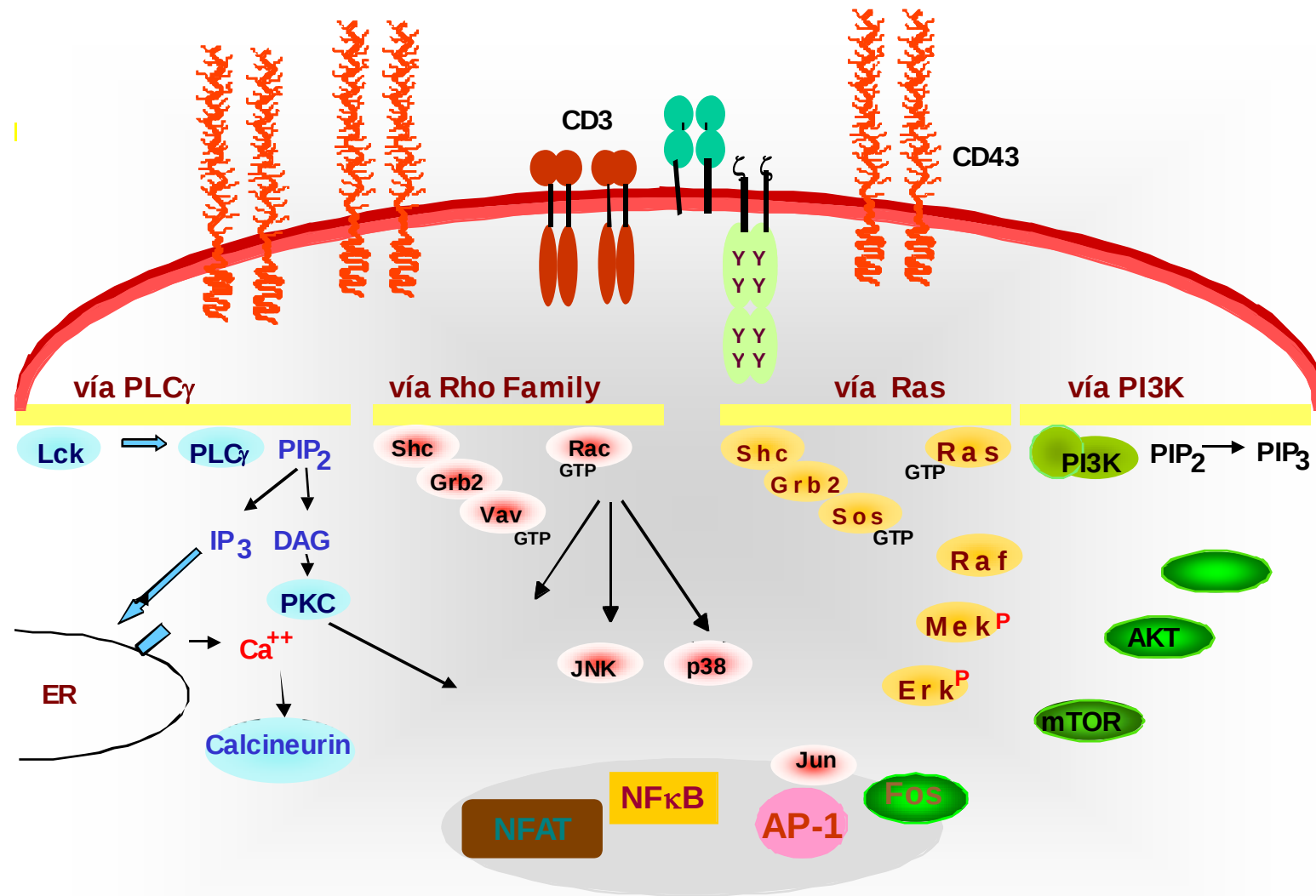
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Intracytoplasmic region:

- no enzymatic activity
- no tyrosine residues
- serine and threonine residues potentially phosphorylable
- Proline rich region
- ERMs binding region

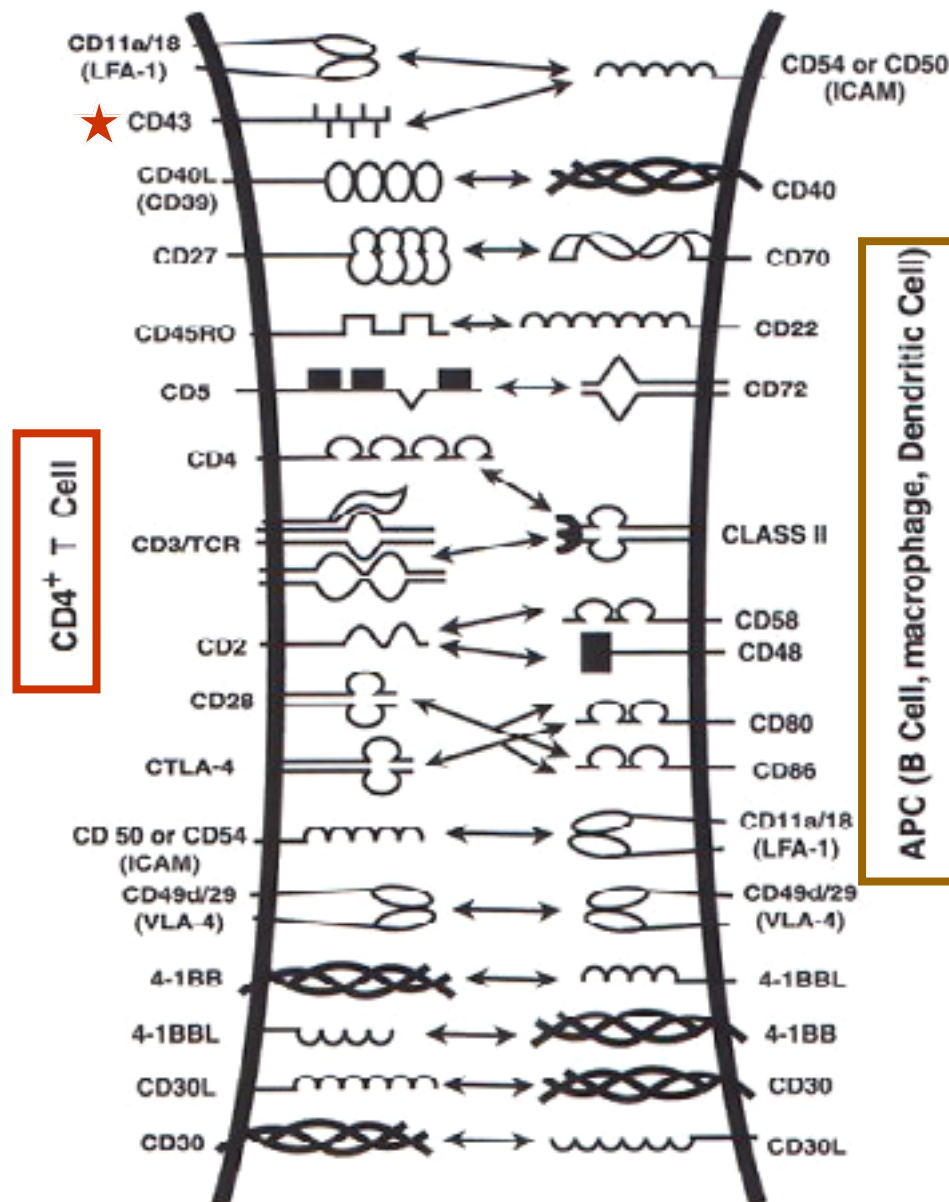




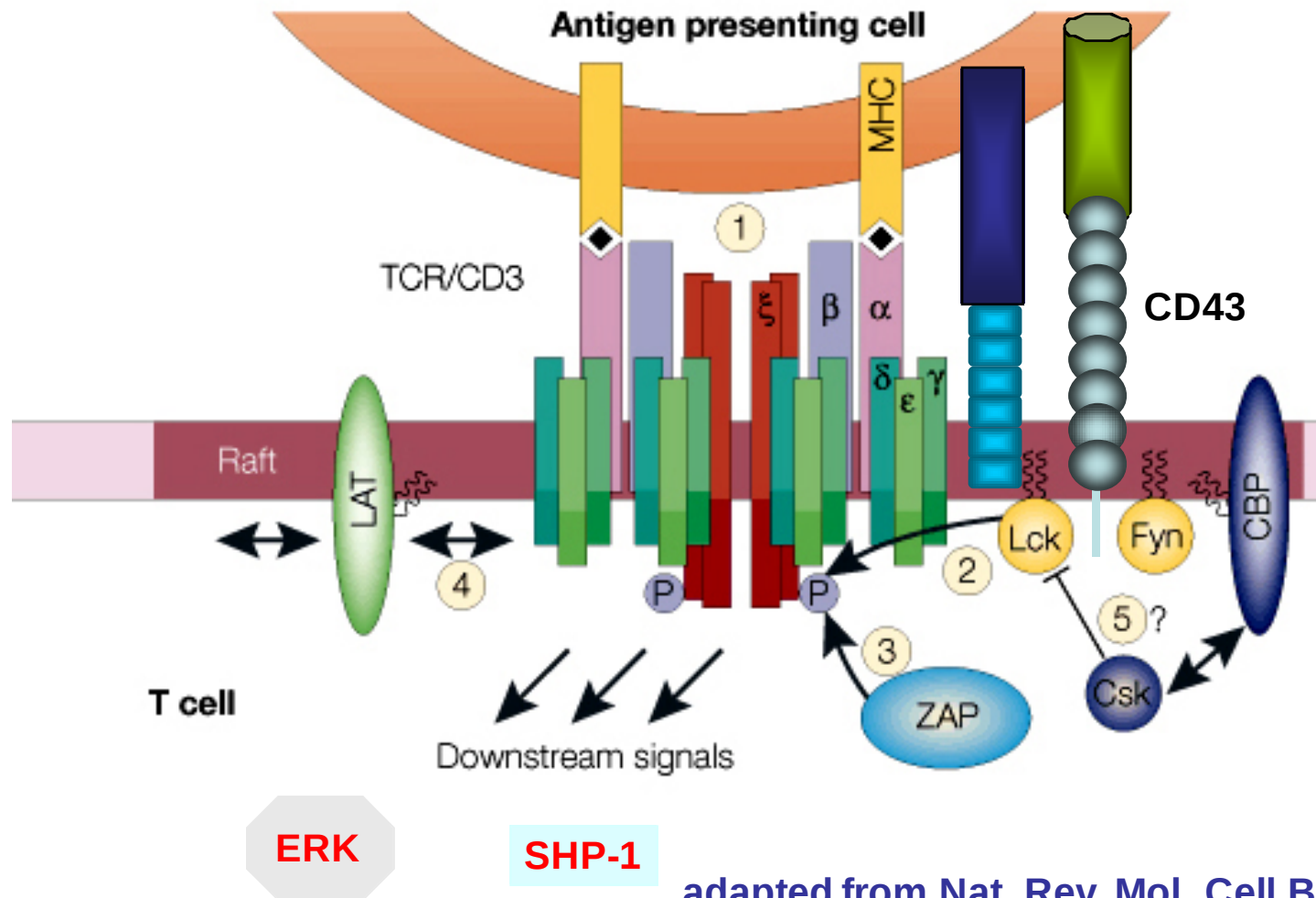
TRANSCRIPCIÓN DE GENES

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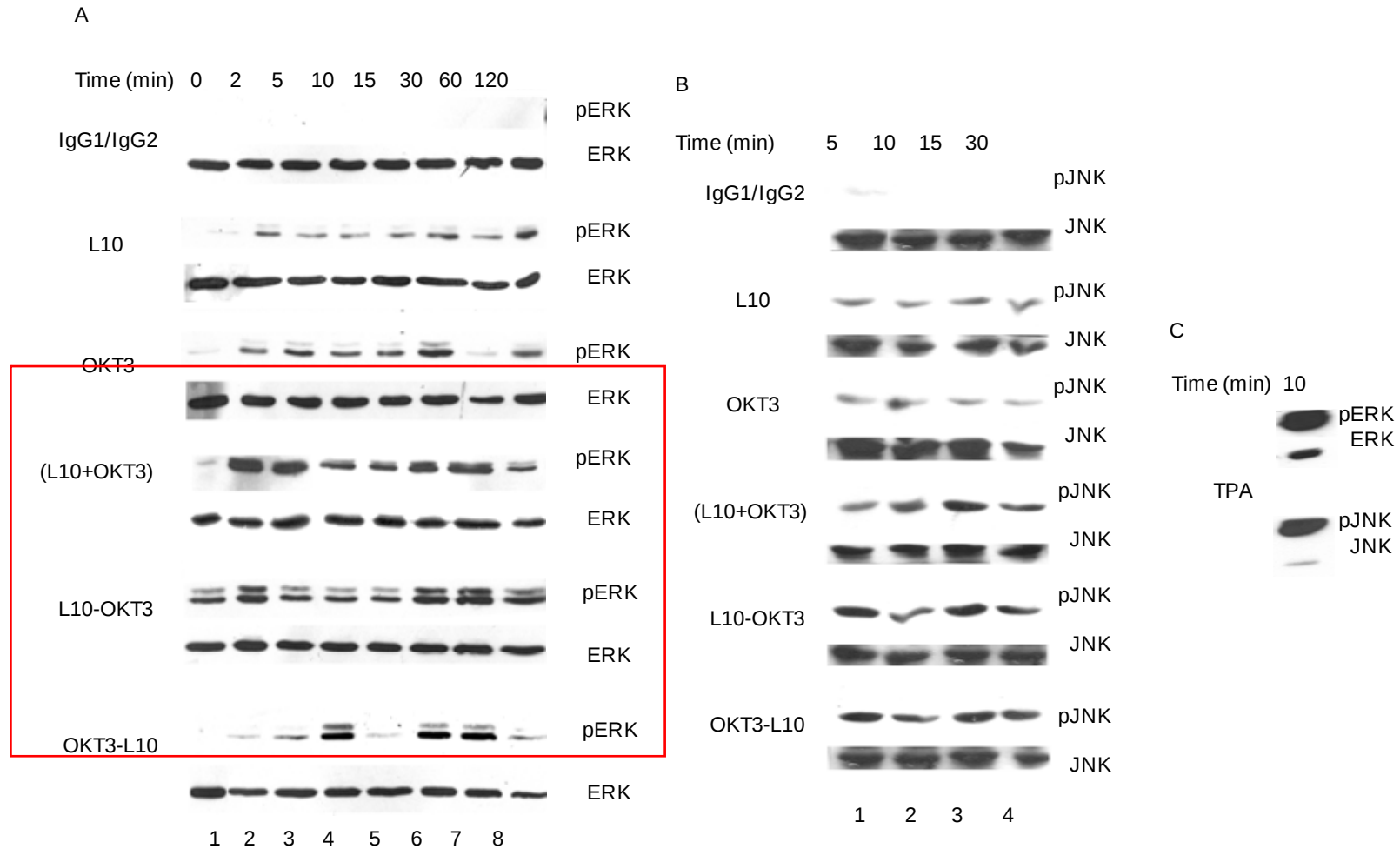


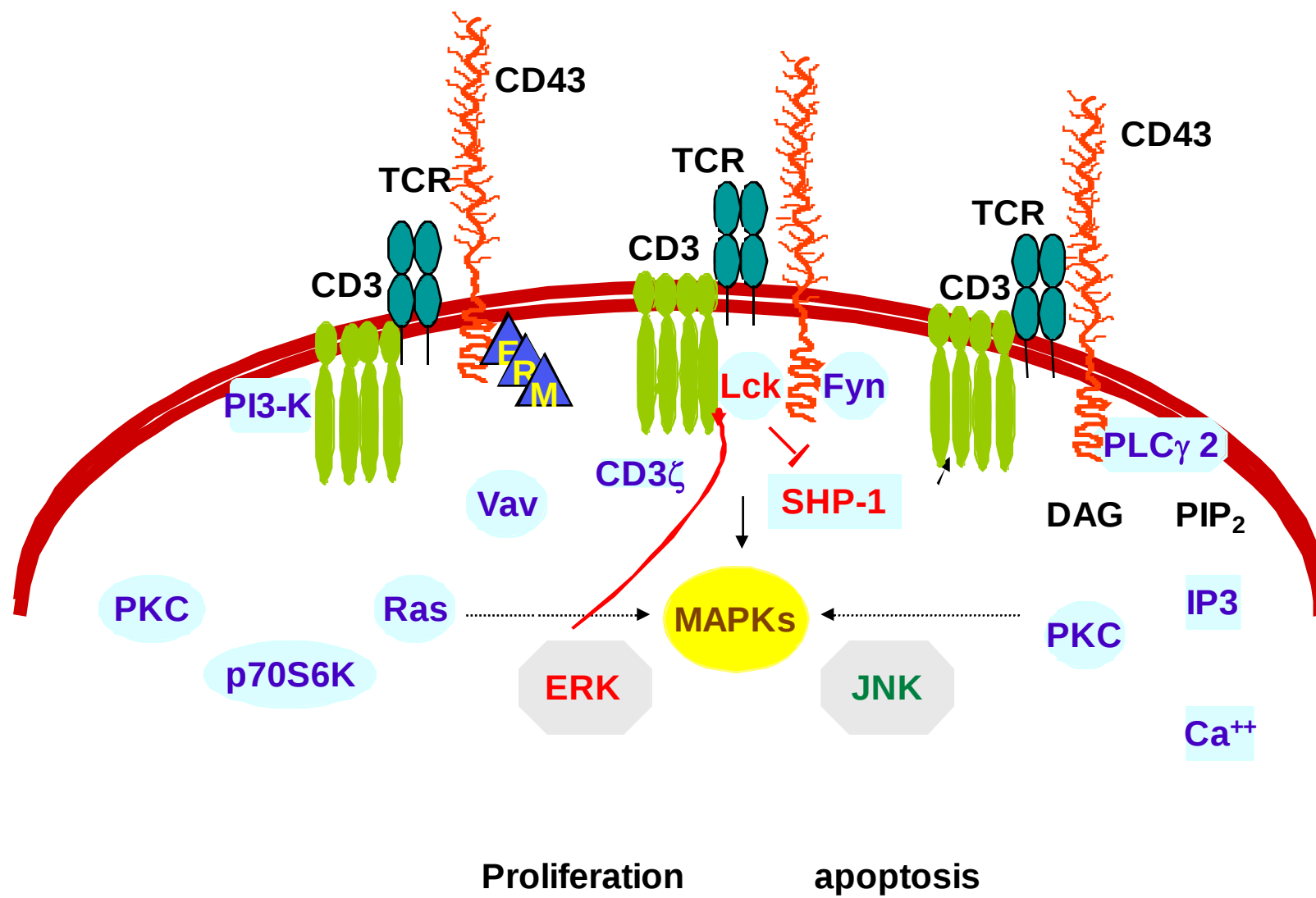
Is the order important?



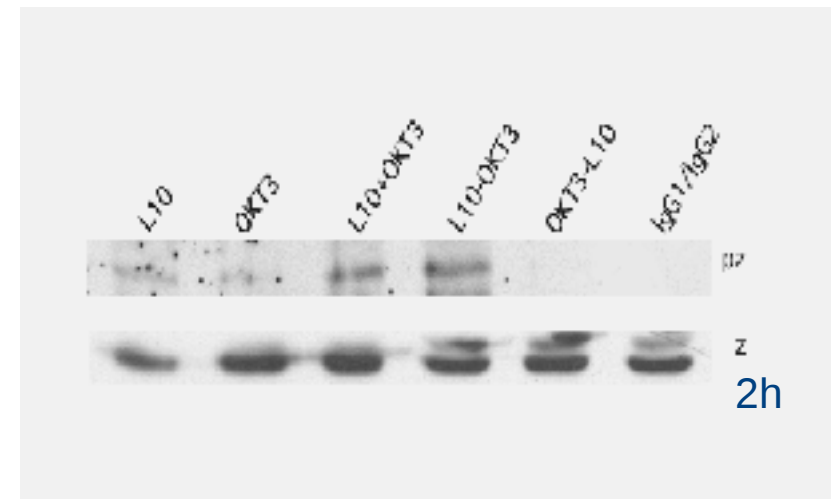
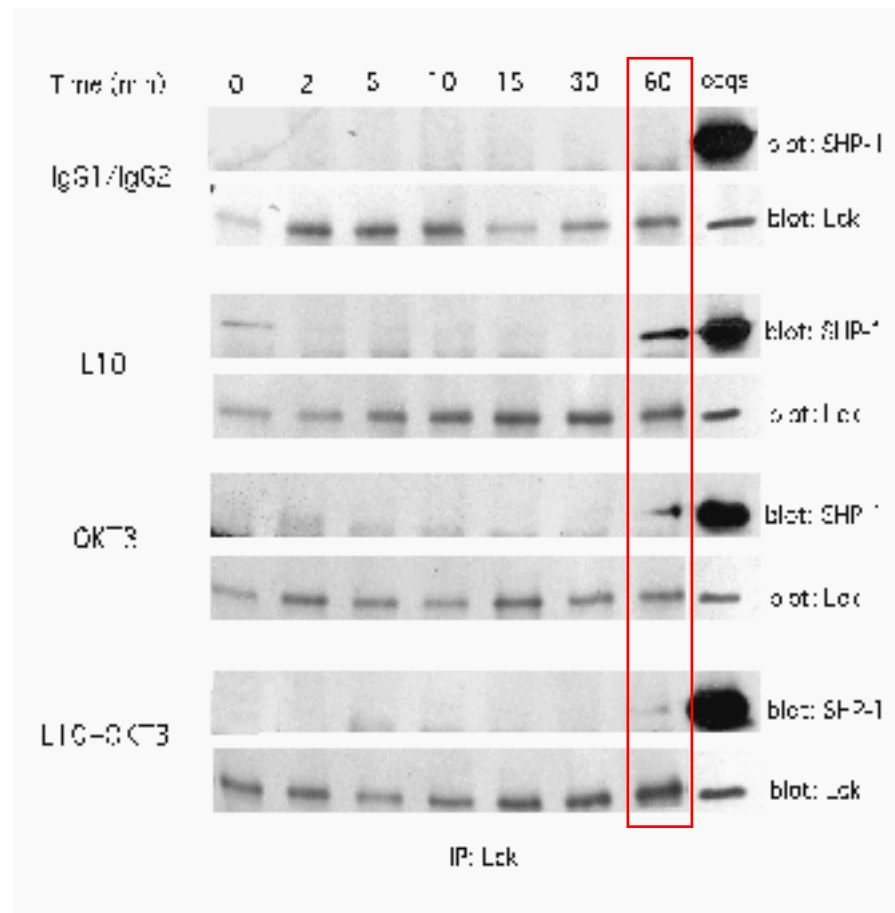
adapted from Nat. Rev. Mol. Cell Biol. 2000

CD43 engagement prior or at the same time as the TcR results in sustained ERK phosphorylation

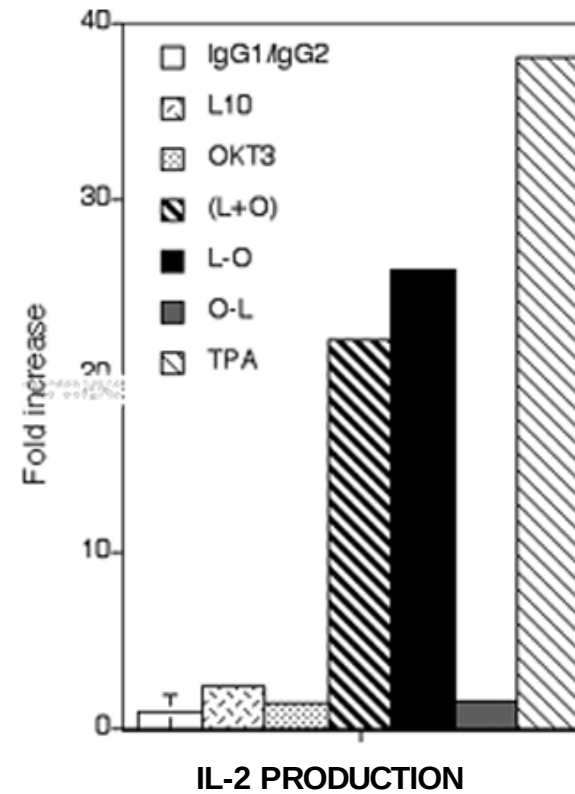
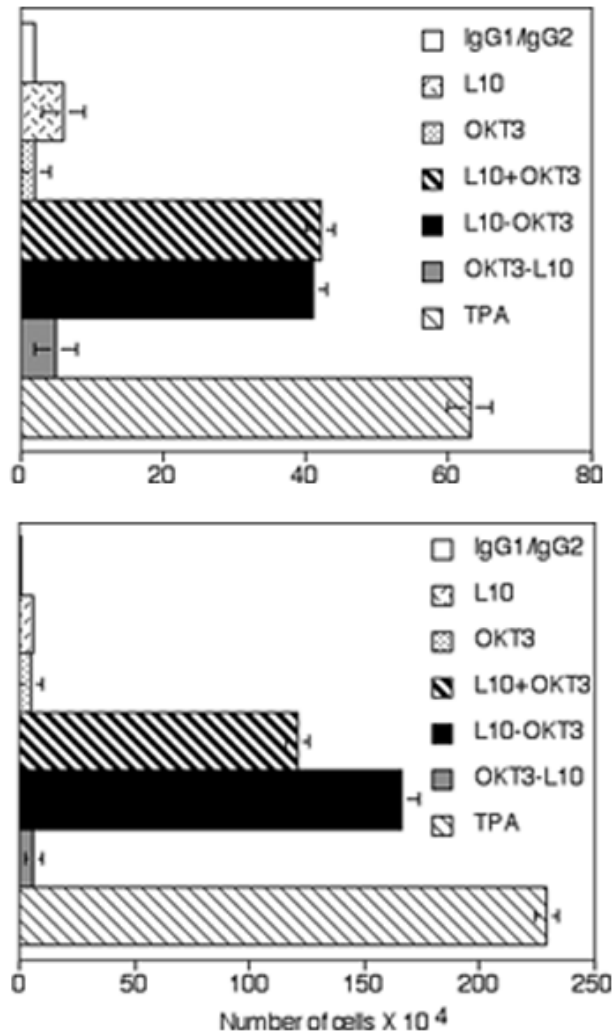




CD43 signals provided at the same time or prior to those of the TCR prevent the association of SHP-1 to Lck

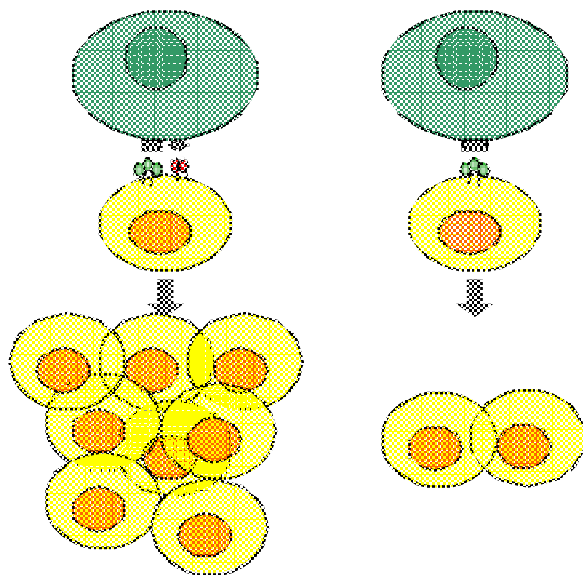


T cell proliferation vs anergy : the order matters ?



2h ↑
 48h — 7 d — Proliferation
 IL-2

CD43 prior or at the same time that the TCR prevents CTLA-4 expression

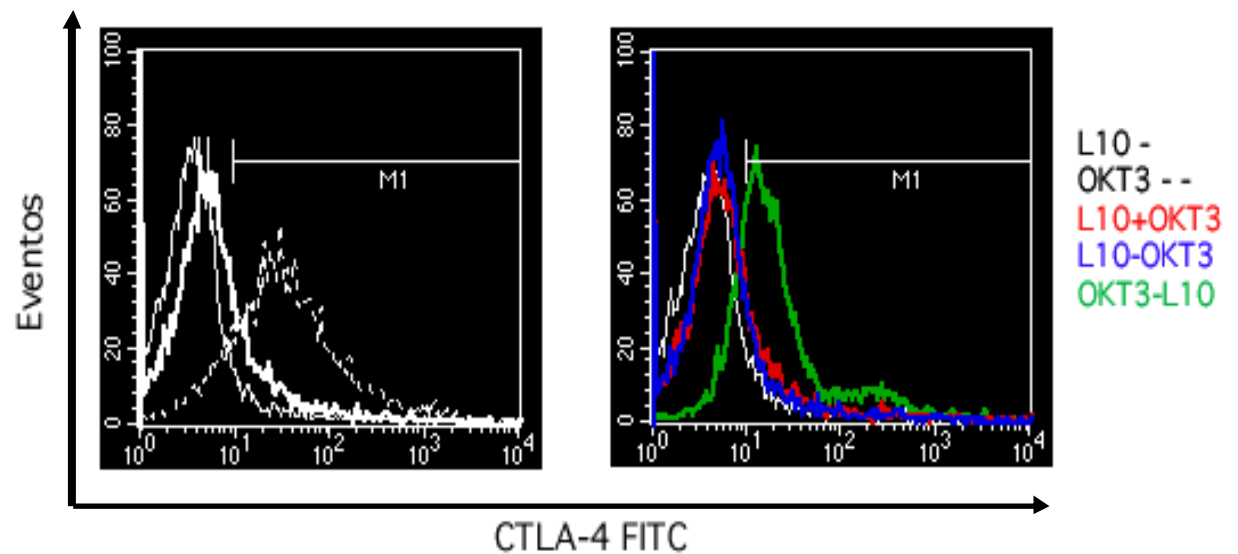


Proliferation

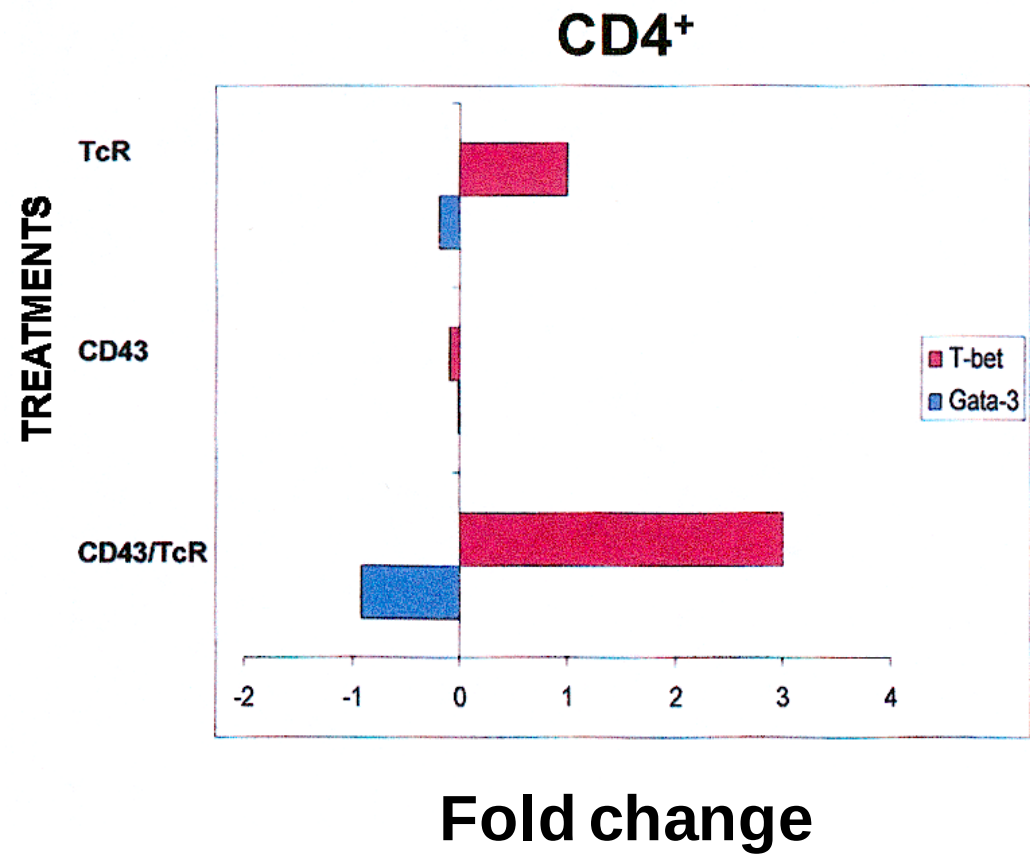
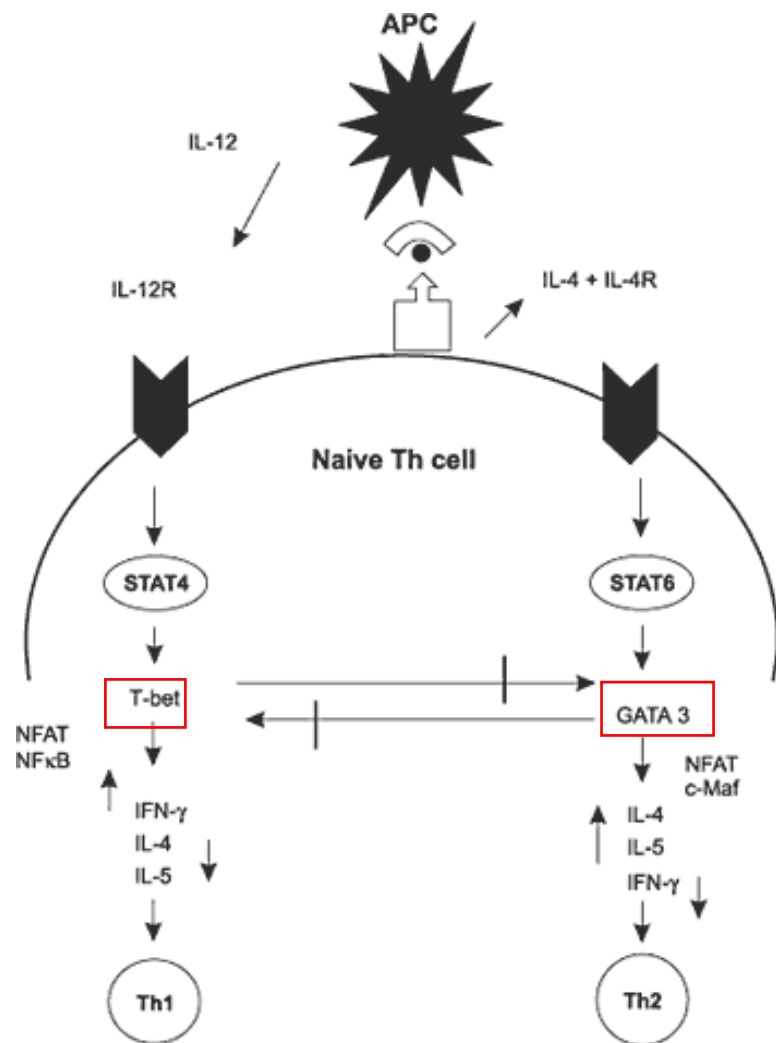
Anergy

-CTLA-4

-No IL-2

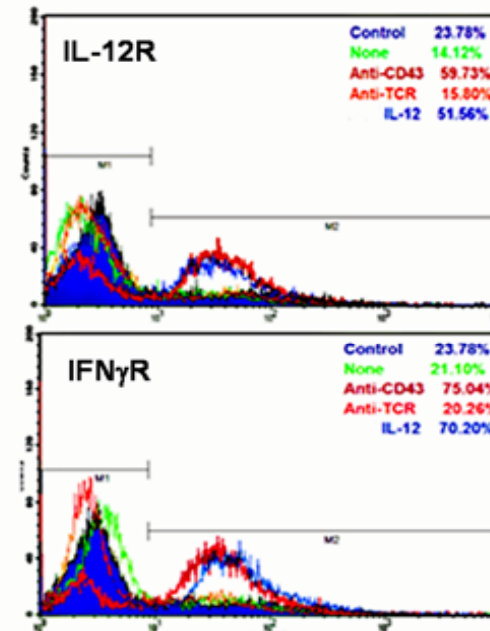
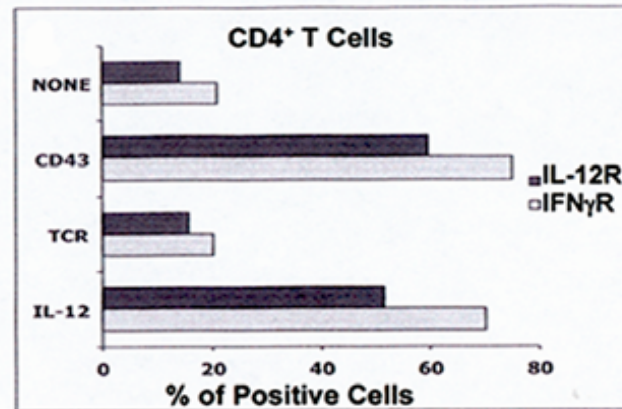


2h
48h
CTLA-4

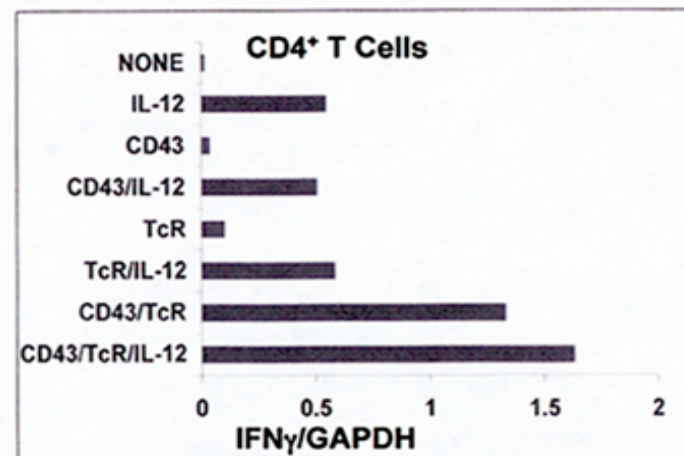


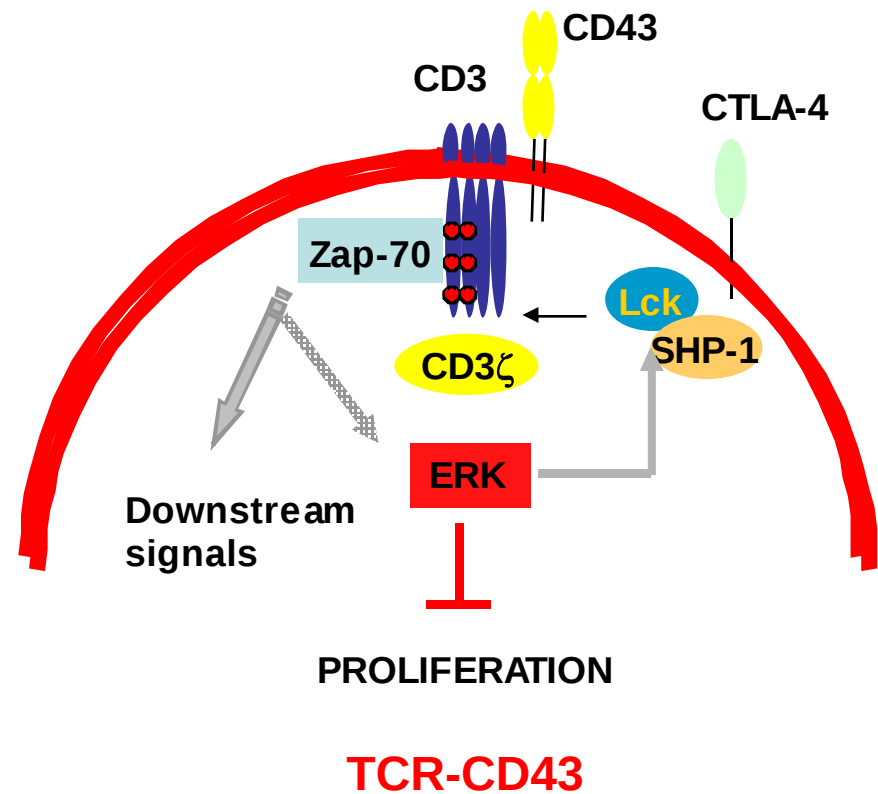
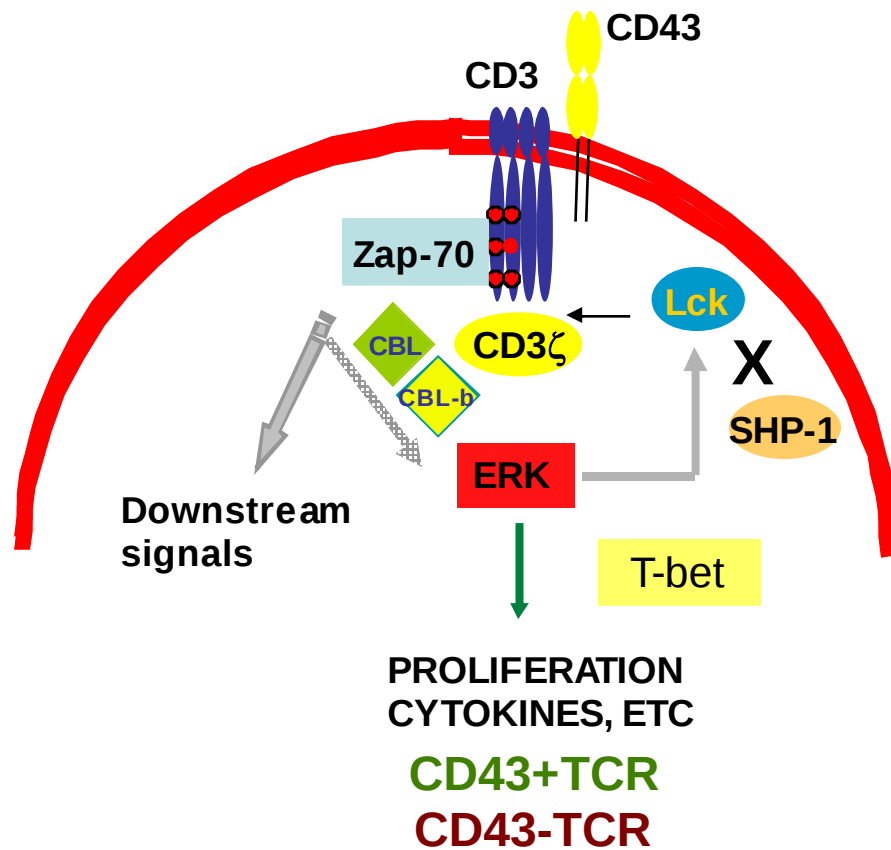
CD43 signals induce IL-12R , IFN γ R and IFN γ expression

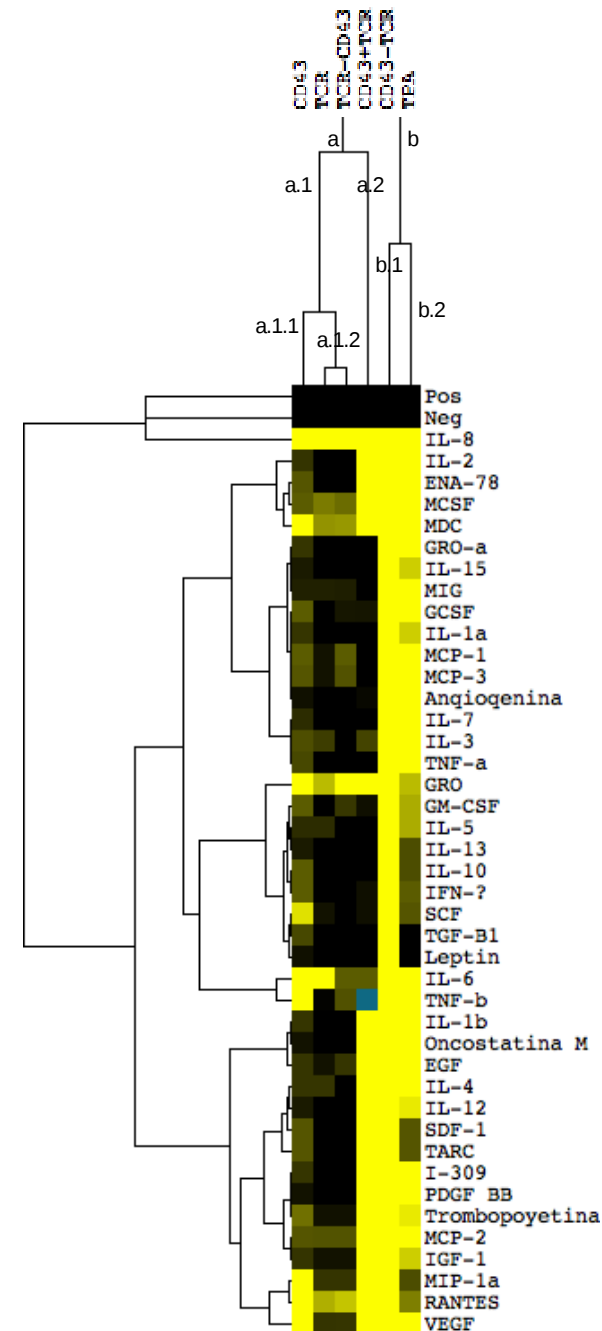
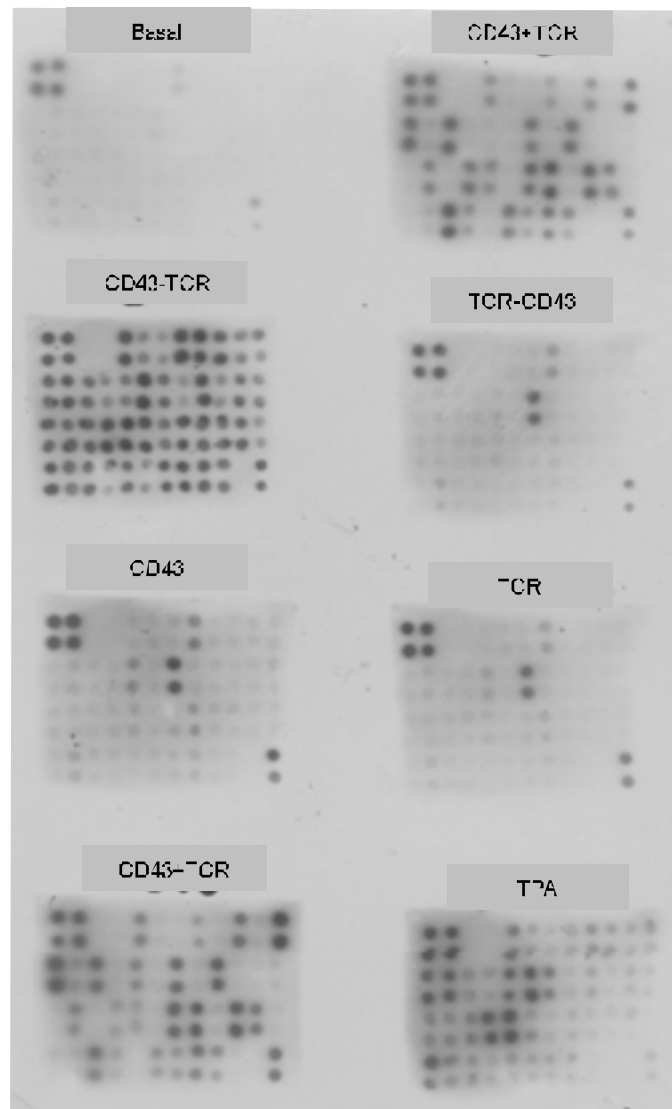
A



B





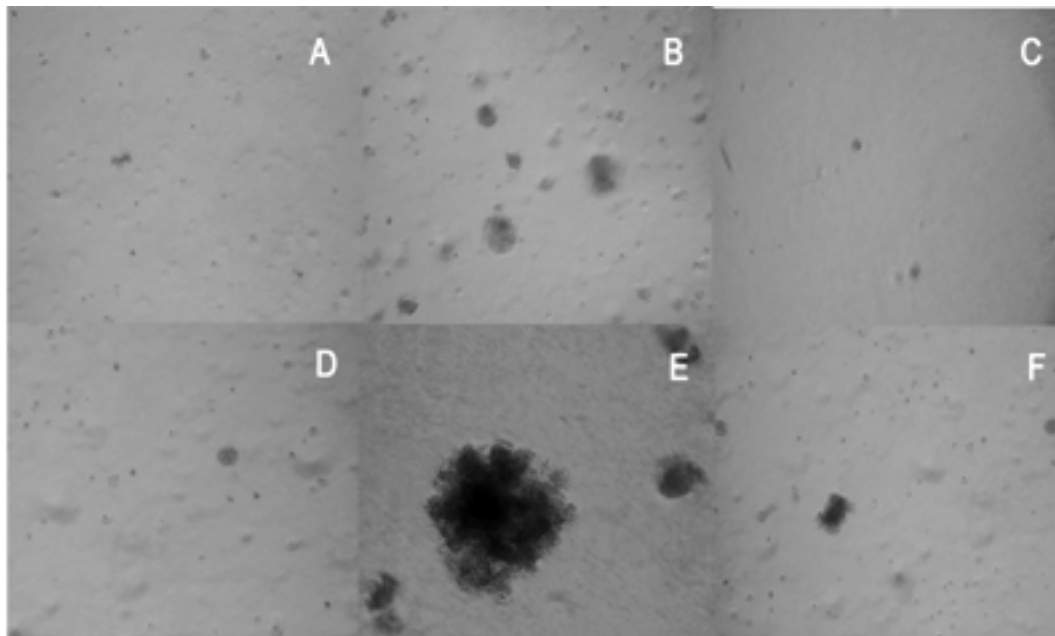
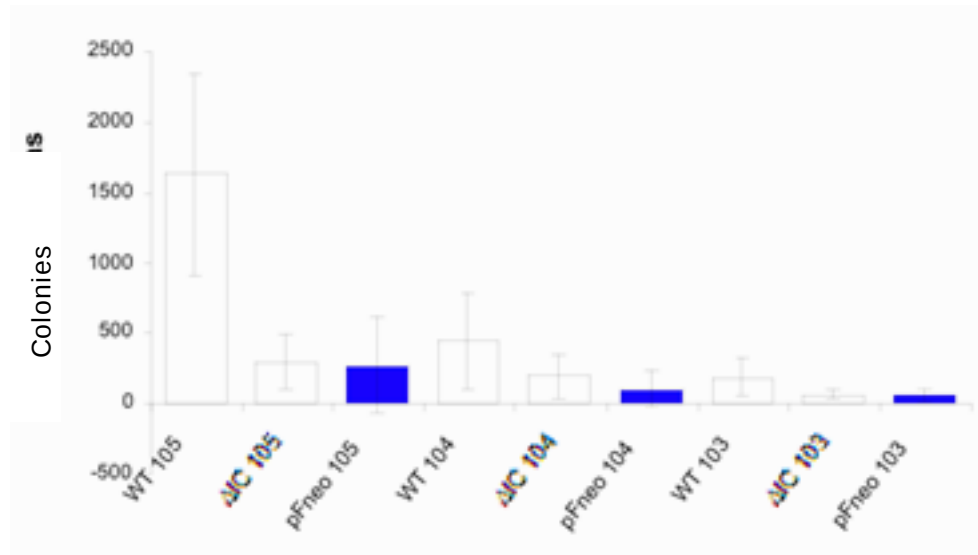


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<i>Trminos de la búsqueda (PubMed)</i>	<i># de entradas</i>
CD43	997
CD43 & tumor cells	386
CD43 & lymphomas	261
CD43 & skin	88
CD43 & lung	35
CD43 & breast	15
CD43 & colon	13
CD43 & ovary	10
CD43 & cervix	5
CD43 & thyroid	3
CD43 & metastasis	12

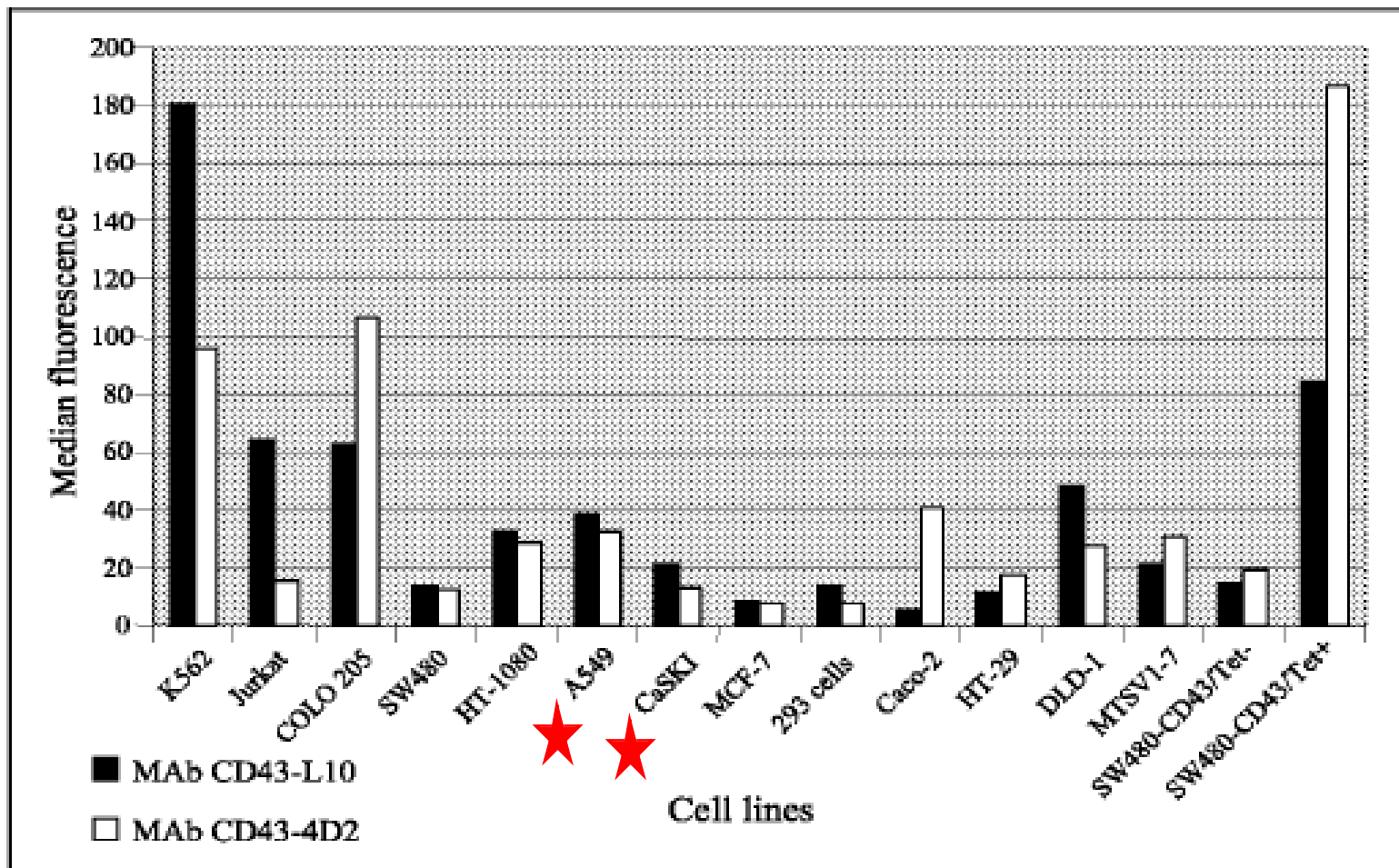
CD43 promotes cell transformation



A and D. NIH-3T3 mock cells.

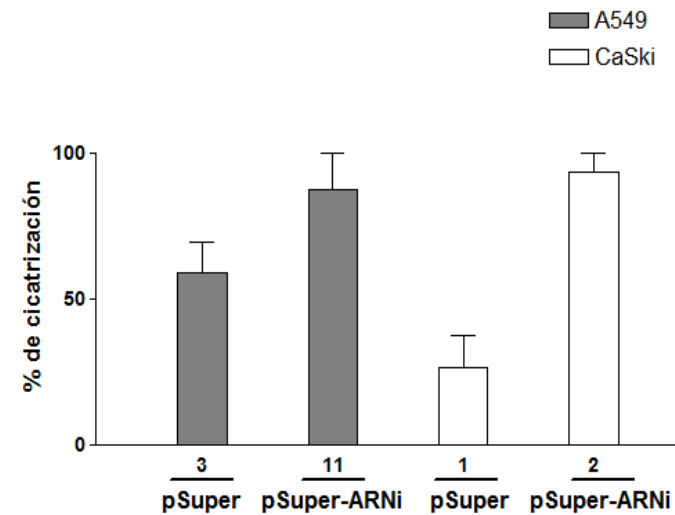
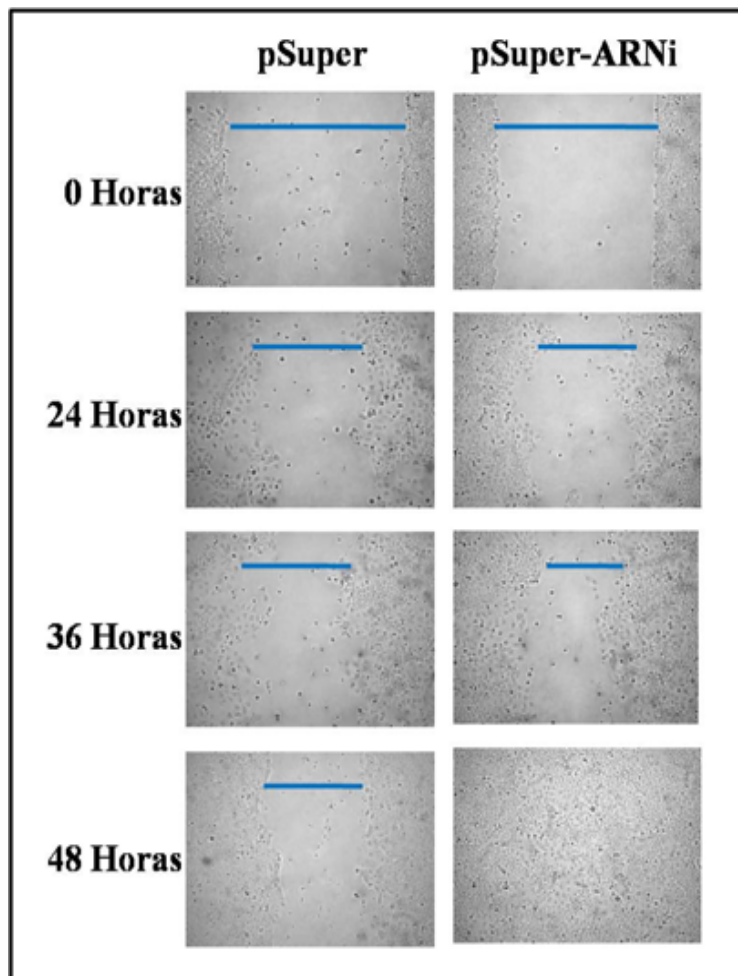
B and E. NIH-3T3-CD43WT.

C and F. NIH-3T3-CD43ΔIC.



Baeckstrom *et al.*, 1995; Santamaria *et al.*, 1996; Sikut *et al.*, 1997; Kadaja *et al.*, 2004; Ziprin *et al.*, 2004

CD43 enhances wound-healing



Conclusions

- CD43 senses the cell's environment
- The quality of the cell's response can reflect the order with which a cell perceives different signals
 - Cbl c pSer vs Cblc pY & SHP-1 dependent mechanism
- CD43 promotes a Th1 response
- CD43-mediated signals lead to the synthesis of numerous cytokines, chemokines and growth factors, both in normal human T cells and in non-lymphoid human tumor cells
- CD43 favors transformation/proliferation/locomotion of non lymphoid tumor cells

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