Early Leukocyte Activation Antigen CD69 Limits Peritoneal Fibrosis by Regulating The Th17 / Regulatory T Cell Balance

Georgios Liappas[1]; Guadalupe T González-Mateo[1]; Raquel Sánchez-Díaz[2]; Sandra Lasarte[2]; Adela Matesanz-Martín[2]; Rafal Zur[3]; Evelina Ferrantelli[4]; Abelardo Aguilera[5]; Elena Fernández-Ruiz[5]; Robert H.J Beelen[4]; Rafael Selgas[6]; Francisco Sánchez-Madrid[2]; Pilar Martín[2]; Manuel López-Cabrera[1,$].

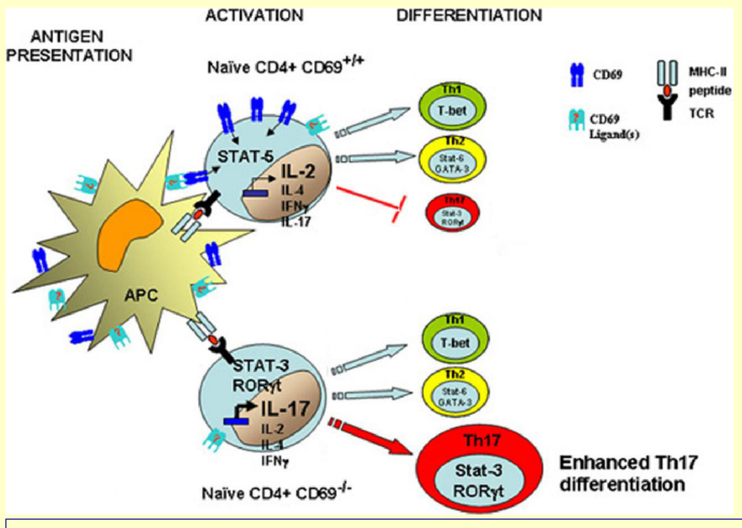
[1]Severo Ochoa Molecular Biology Center, Spanish Scientific Research Council (CSIC), Madrid, Spain
[2]Vascular Biology and Inflammation Department, National Cardiovascular Research Center (CNIC), Madrid, Spain
[3]National Center for Biotechnology, Madrid, Spain
[4]VU University Medical Center, Department of Immunology and cell Biology, Amsterdam, the Netherlands
[5]Molecular Biology Unit, University Hospital de la Princesa, Princesa Health Research Institute, Madrid, Spain
[6]Nephrology Department, La Paz University Hospital, La Paz Health Research Institute, Madrid, Spain

OBJECTIVES

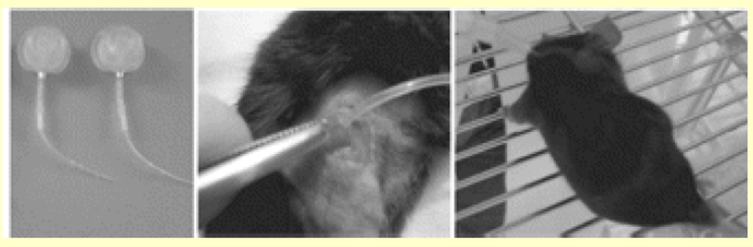
CD69 controls T helper (Th) 17/ T regulatory (Treg) cell balance in various inflammatory diseases. The mechanisms by which these T cell subsets regulate tissue fibrosis and the role of CD69 in this process remain largely unknown. **Herein, we explored the role of CD69 in peritoneal fibrosis induced by peritoneal dialysis fluid (PDF).**

METHODS

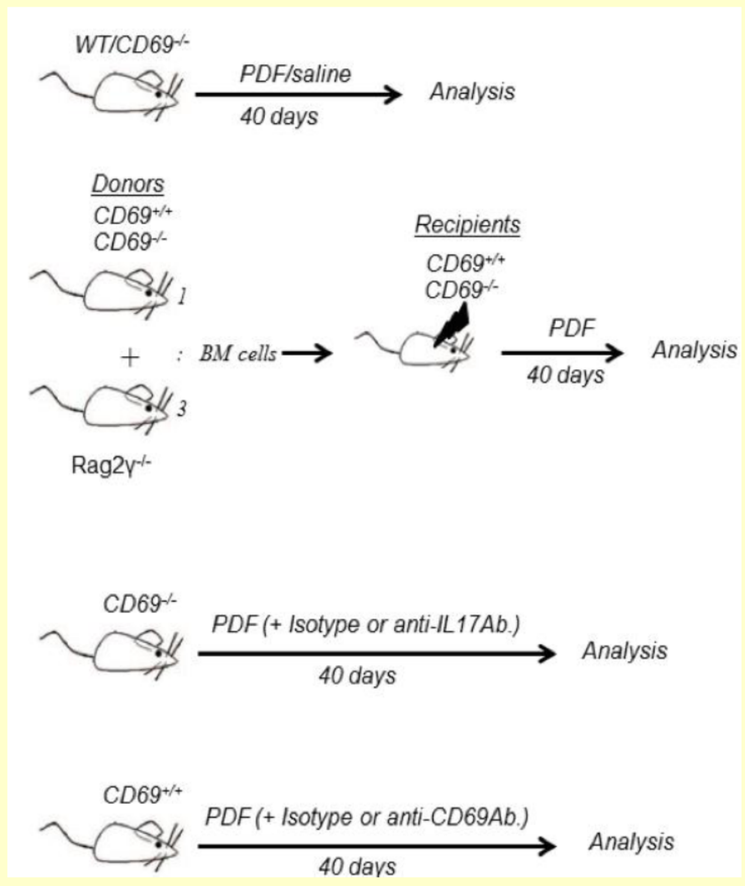
The CD69 role in peritoneal fibrosis was addressed by 40-day exposure to treatments with PDF in the following *in-vivo* models:
(I) bone marrow chimeras; (II) mice with blocked activity of the CD69 receptor; (III) mice with blocked IL-17.



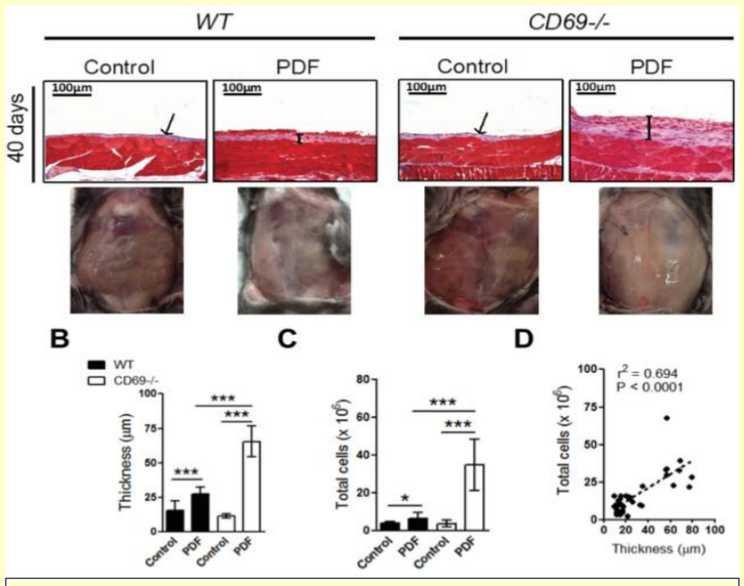
CD69 role in Th17/Treg differentiation (*)



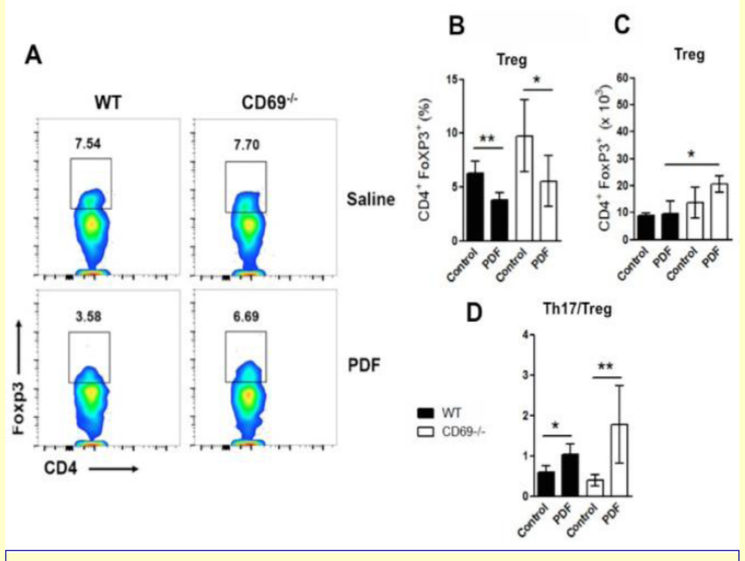
PD model in WT and CD69-/- mice (**)



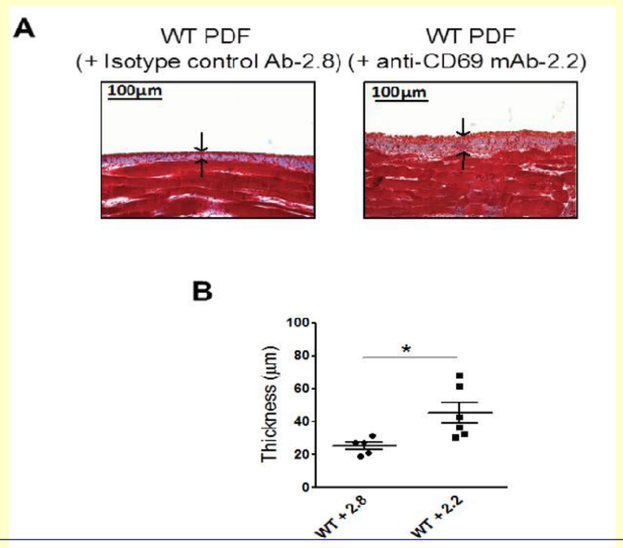
Experimental procedures



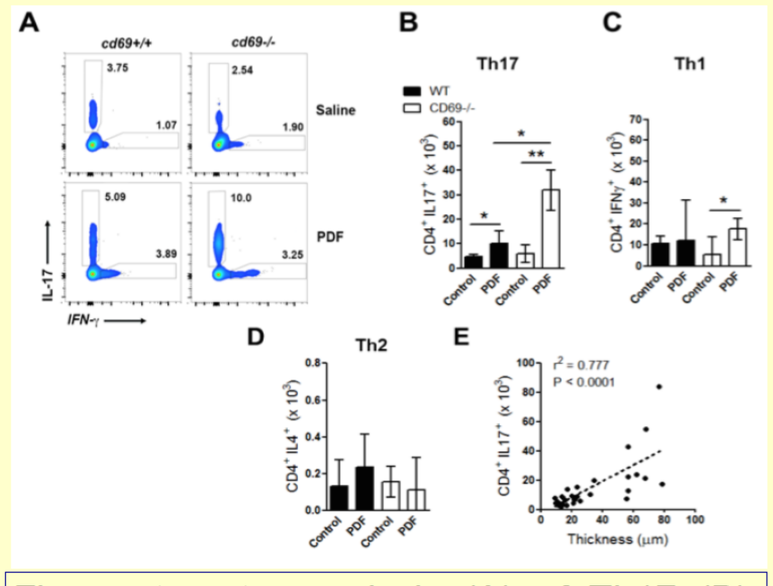
Peritoneal fibrosis (A, B), total peritoneal cells (C) and correlation (D) between thickness and total cells in WT and CD69-/- mice.



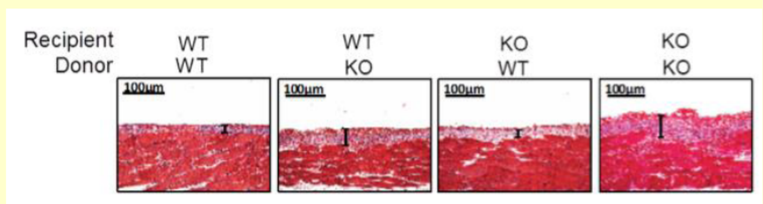
Flowcytometry analysis (A) of the % (B) and total (C) Treg cells in the peritoneal cavity of WT and CD69-/- mice. Ratio between Th17 and Treg cells (D).



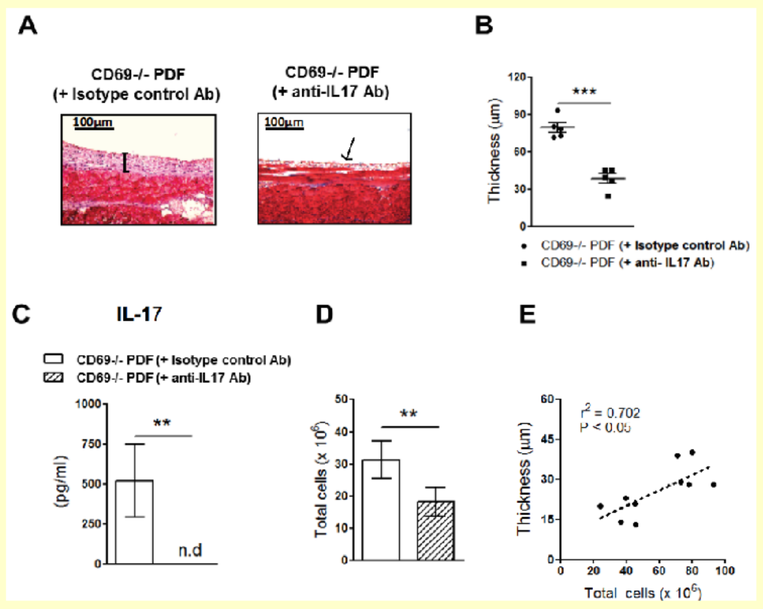
Peritoneal fibrosis (A) staining and quantification (B) when blocking CD69 receptor in WT mice.



Flow cytometry analysis (A) of Th17 (B), Th1 (C) and Th2 (D) responses. Correlation between Th17 cells and thickness (E).



Peritoneal fibrosis staining in chimeric groups.



Staining of fibrosis (A), quantification of fibrosis (B), IL-17 (C), total peritoneal cells (D) and correlation between thickness and and total cells (E), when blocking with anti-IL-17 antibody.

RESULTS

CD69$^{-/-}$ mice showed enhanced fibrosis and Th17 cell infiltration, decreased Treg responses and increased the ratio Th17/Treg when treated with PDF for a total period of 40 days.

Mixed bone marrow from CD69$^{-/-}$ and Rag2gc$^{-/-}$ transplanted into WT mice reproduced the disease in CD69$^{-/-}$ mice, thus CD69 exerts its function within the lymphocyte compartment.

Conversely, an IL-17 blockade in CD69$^{-/-}$ mice reduced the Th17 response and decreased peritoneal fibrosis.

CD69 blockade in WT mice mimicked the fibrotic response observed in CD69$^{-/-}$ mice.

CONCLUSIONS

CD69 modulates Th17-mediated responses and negatively regulates peritoneal fibrosis.

REFERENCES

* *Martin et al 2011;*
**Guadalupe T. Gonzalez-Mateo et al 2009;*

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