

Regulation of podoplanin expression and function

Charlotte M. de Winde, Lindsey Millward, A. Christa Benjamin, Victor G. Martinez, Sophie E. Acton

Stromal Immunology Group, MRC Laboratory for Molecular Cell Biology, University College London, United Kingdom

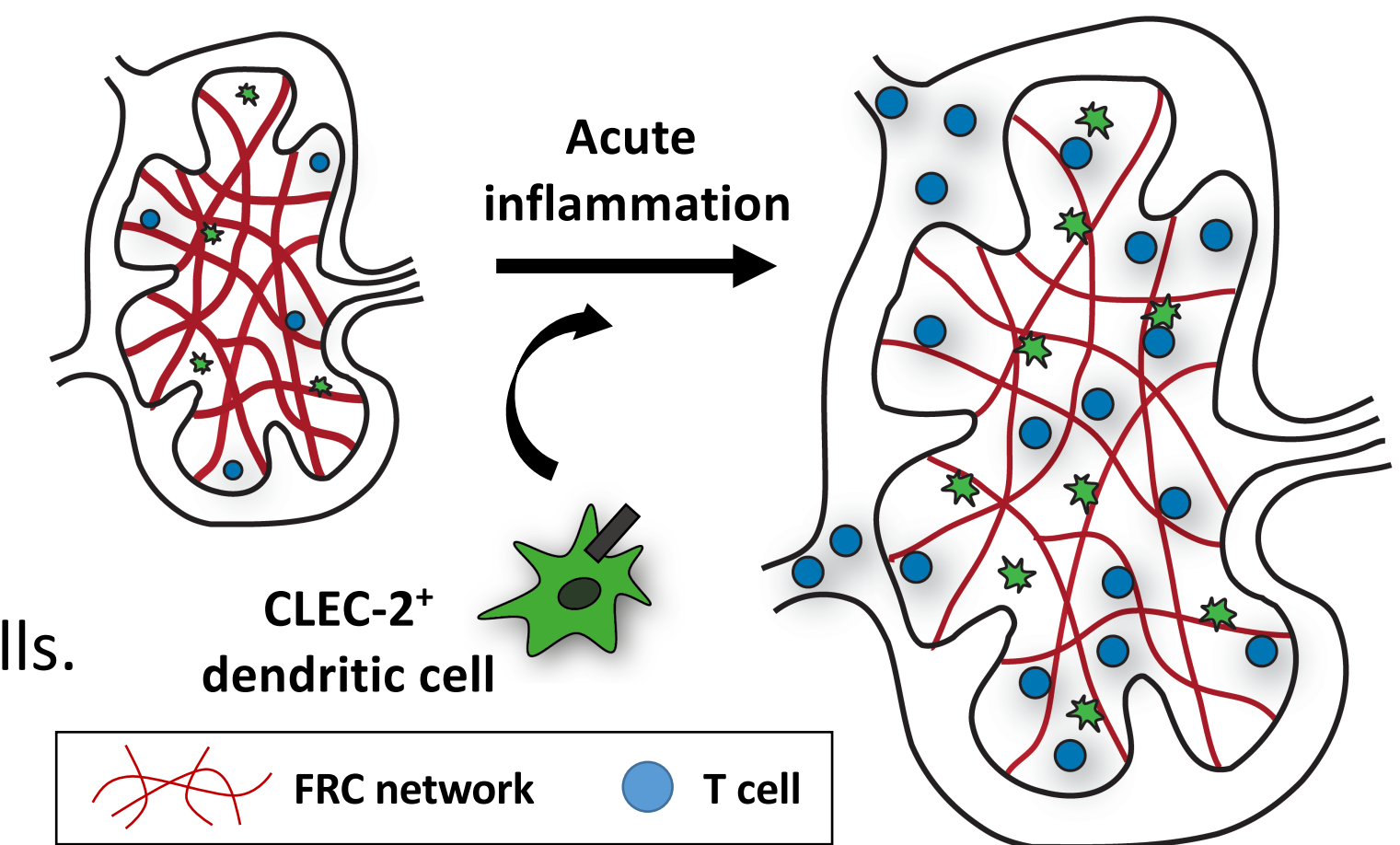
Find the author!



Introduction

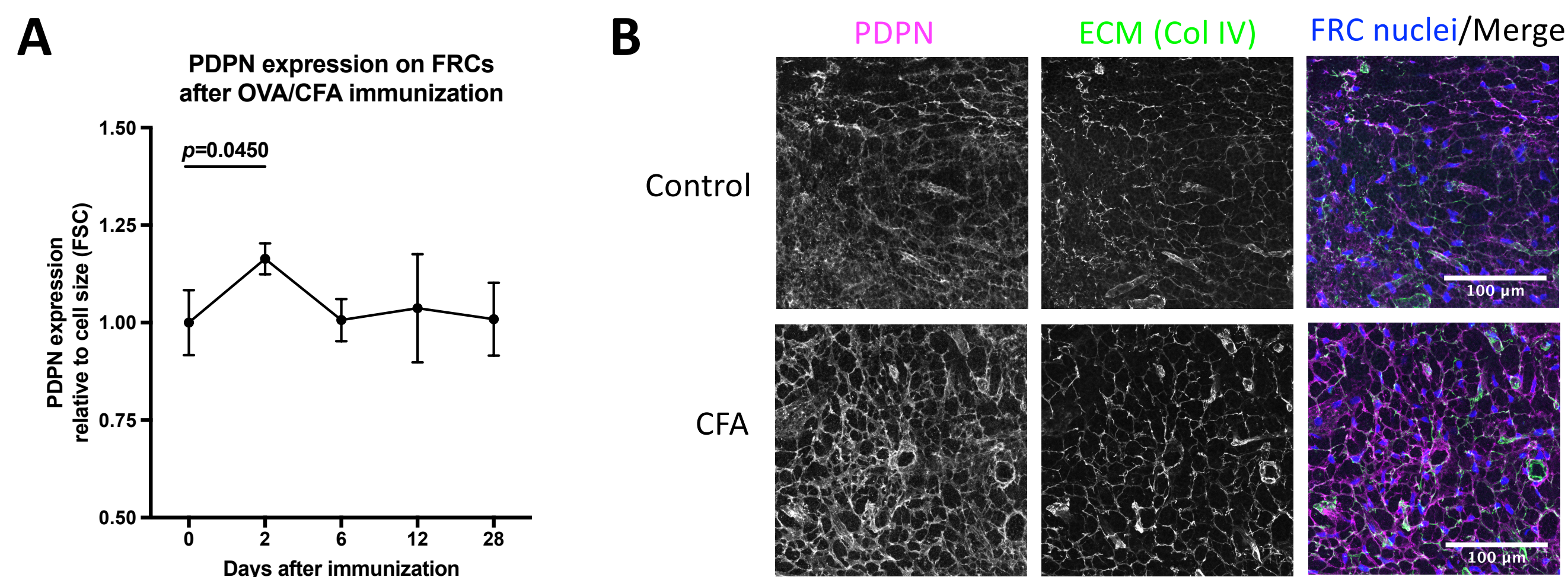
- Fibroblastic reticular cells (FRCs) are the most abundant stromal cells in the lymph node and express the glycoprotein podoplanin.
- The only known endogenous ligand of podoplanin is the C-type lectin receptor CLEC-2, expressed by migratory dendritic cells.
- The interaction between podoplanin and CLEC-2 inhibits contractility of the FRC network, allowing lymph node expansion.
- Upon CLEC-2 binding, podoplanin clusters into cholesterol-rich domains.
- Tetraspanin CD9 and the hyaluronic receptor CD44 are known binding partners of podoplanin in cancer cells and lymphatic endothelial cells.

→ What are the mechanisms underlying podoplanin expression and membrane localisation on FRCs during an immune response?

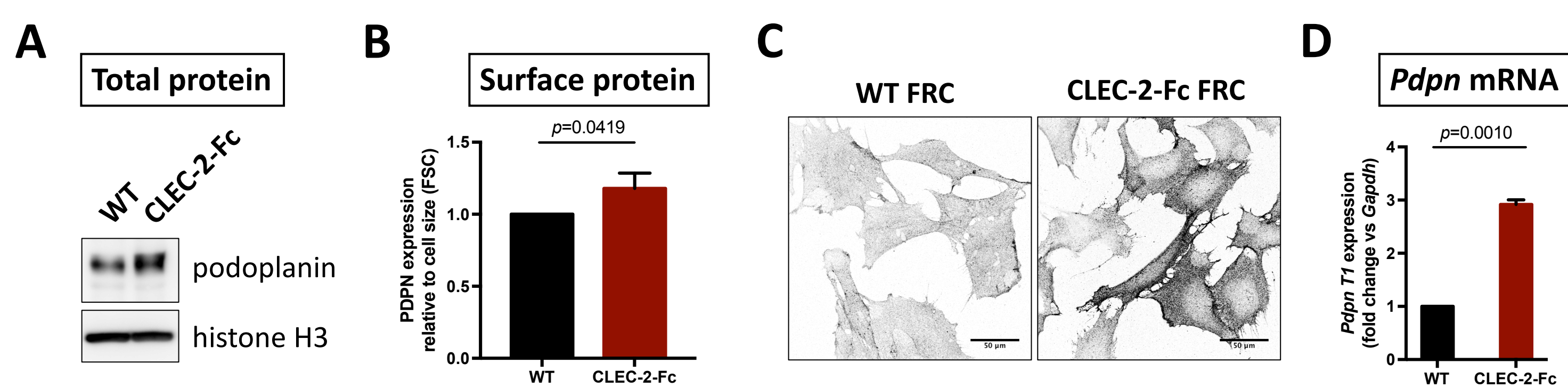


Results - I

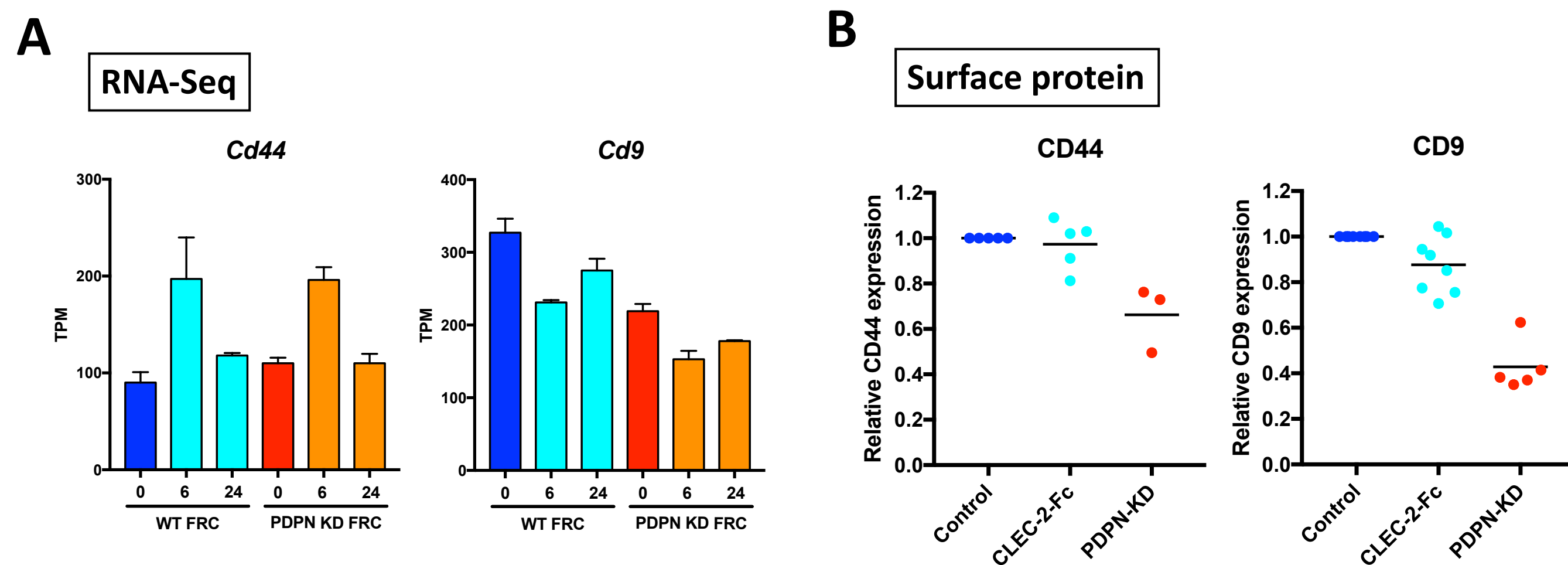
1) Podoplanin expression on FRCs in the lymph node is increased upon *in vivo* antigen (OVA/CFA) immunization



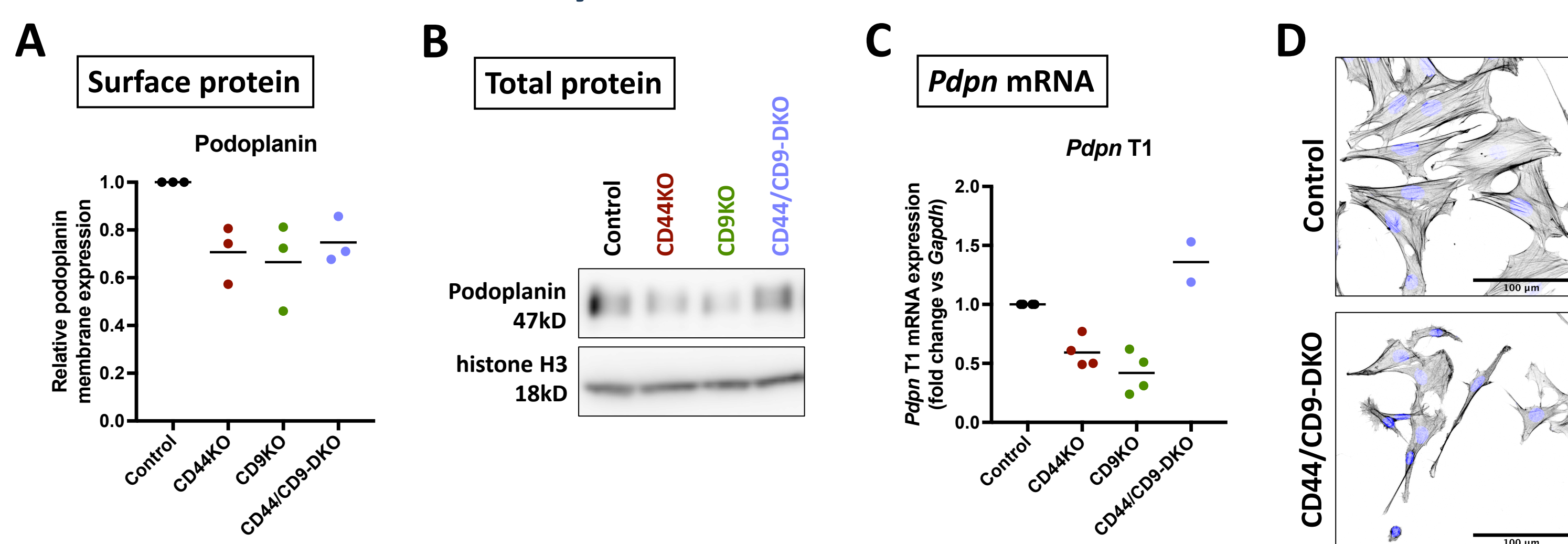
2) CLEC-2 stimulation *in vitro* increases podoplanin expression on FRCs



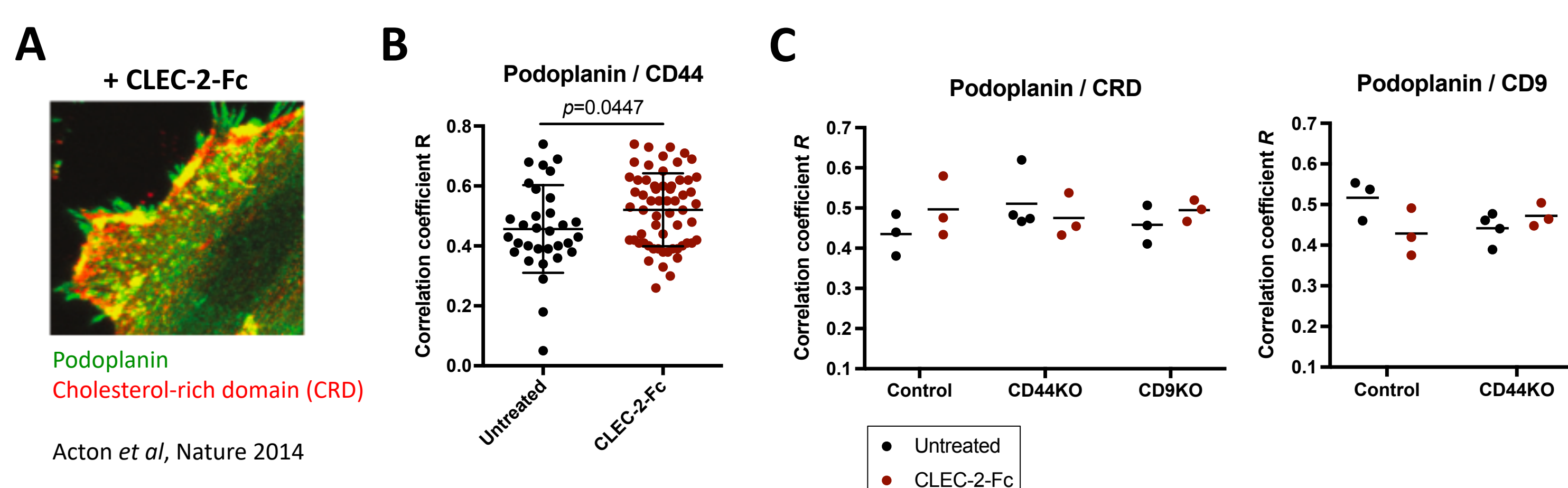
3) Podoplanin/CLEC-2 binding coregulates mRNA expression of podoplanin binding partners CD44 and tetraspanin CD9



4) CD44 and CD9 control podoplanin expression and podoplanin-driven FRC contractility

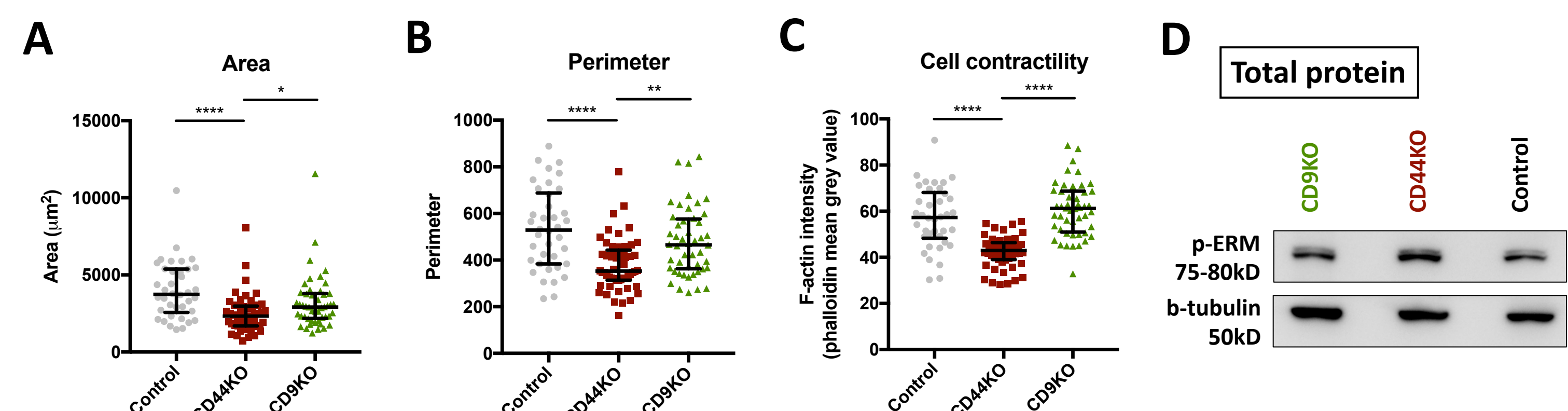


5) Podoplanin is present in different membrane domains

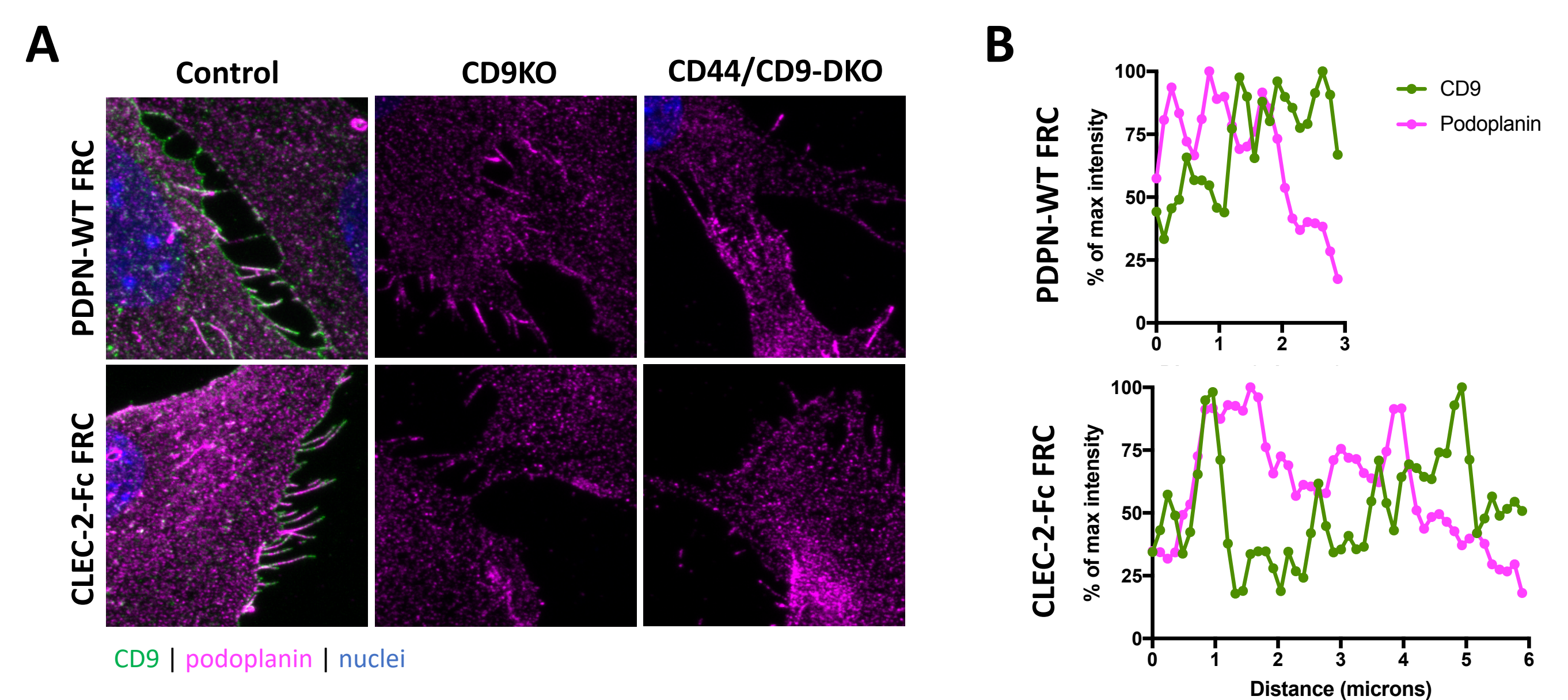


Results - II

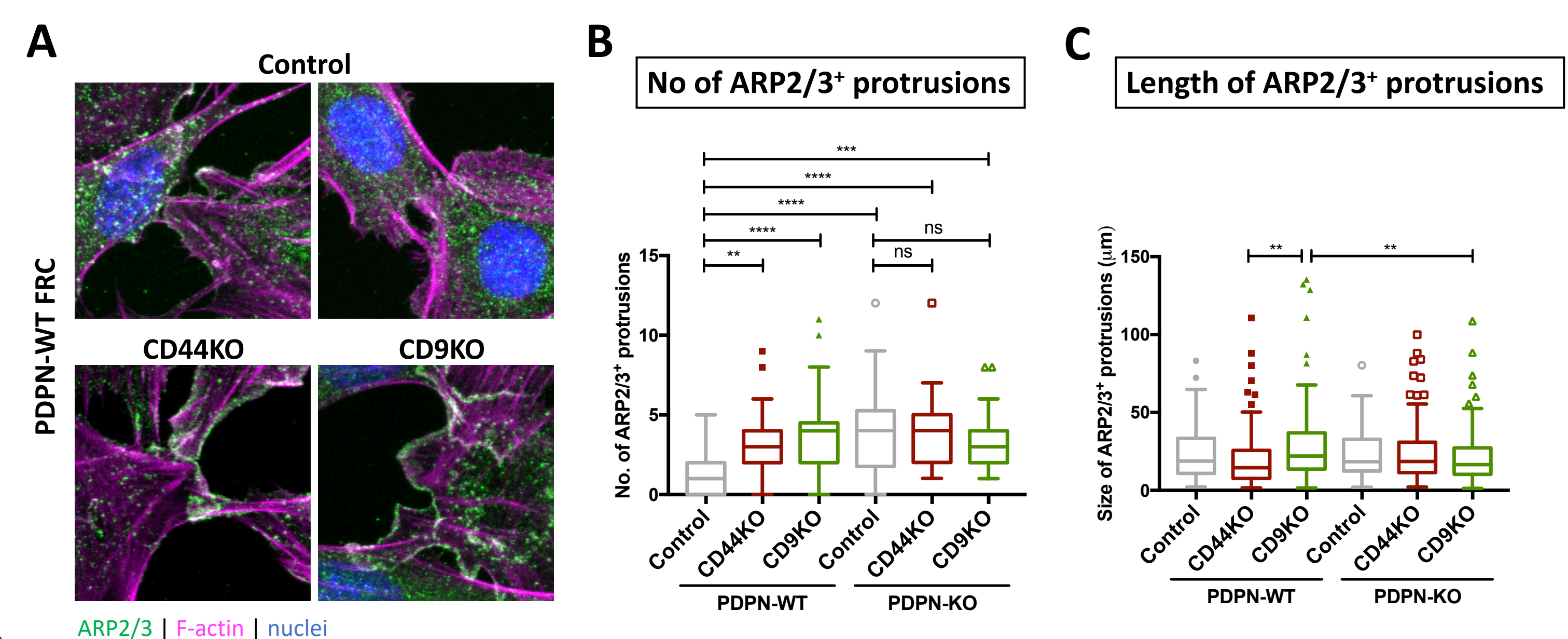
6) CD44 KO decreases FRC area, perimeter and actomyosin contractility



7) Podoplanin and CD9 are both localized in cell protrusions



8) Loss of CD44 or CD9 drives changes in ARP2/3⁺ cell protrusions



Model: Podoplanin has different functions on FRCs

