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Generation of a Novel Mouse Model to Visualise and Conditionally Modify Fibroblastic Stromal Cells

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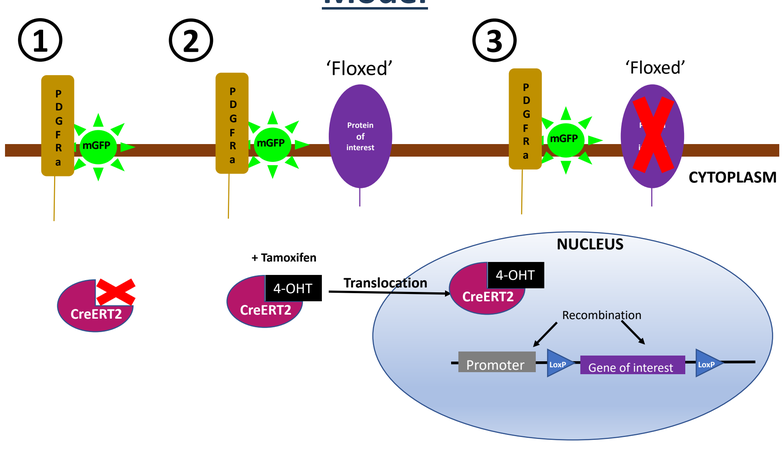
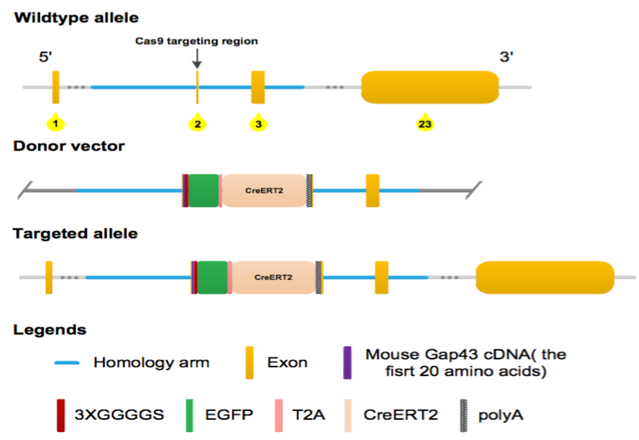
Summary

Fibroblastic reticular cells (FRCs) are the most abundant stromal cells in the lymph node (LN). They form a conduit network within the T cell zone area and play an important role in the flexibility of the LN structure whilst also facilitating the migration and interaction of dendritic cells and T-cells during an immune response. In order to study the role of FRCs in LNs a mouse model was designed in which platelet derived growth factor receptor alpha (PDGFRα (also known as CD140α)), an early marker of mesenchymal cells, will express membrane GFP and a tamoxifen inducible Cre recombinase (CreERT2), which is self-cleaved after translation. The aim of this model is to incorporate an inducible CreERT2 to allow knock-out of genes of interest within these fibroblasts whilst also enabling to visualise morphological changes. Preliminary data verify GFP expression in ear skin fibroblasts samples and in FRCs of LNs and Spleen. Further validation of conditional knock out is currently in progress where crossbreeding with floxed models of interest is being carried out.

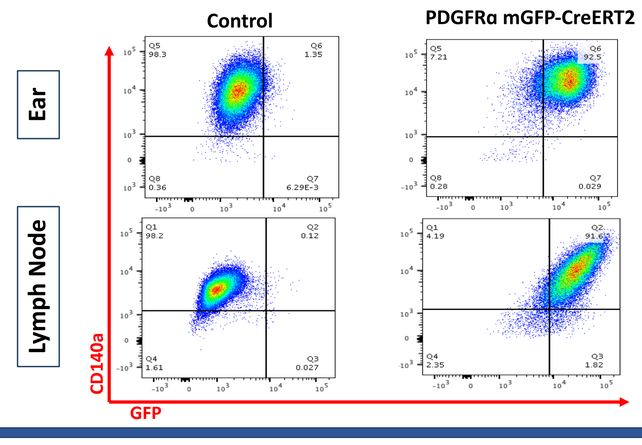
Model



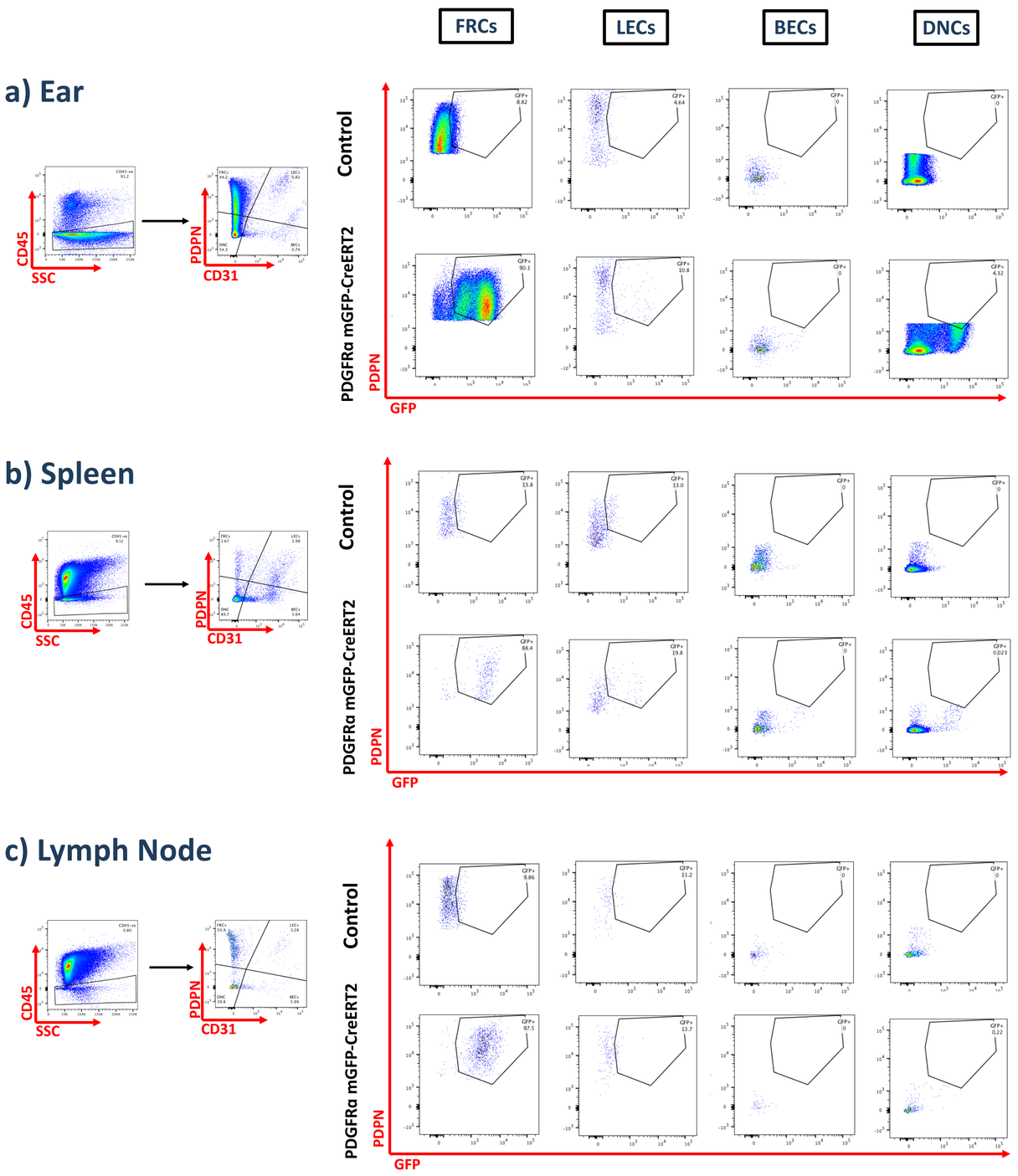
Genetic Strategy



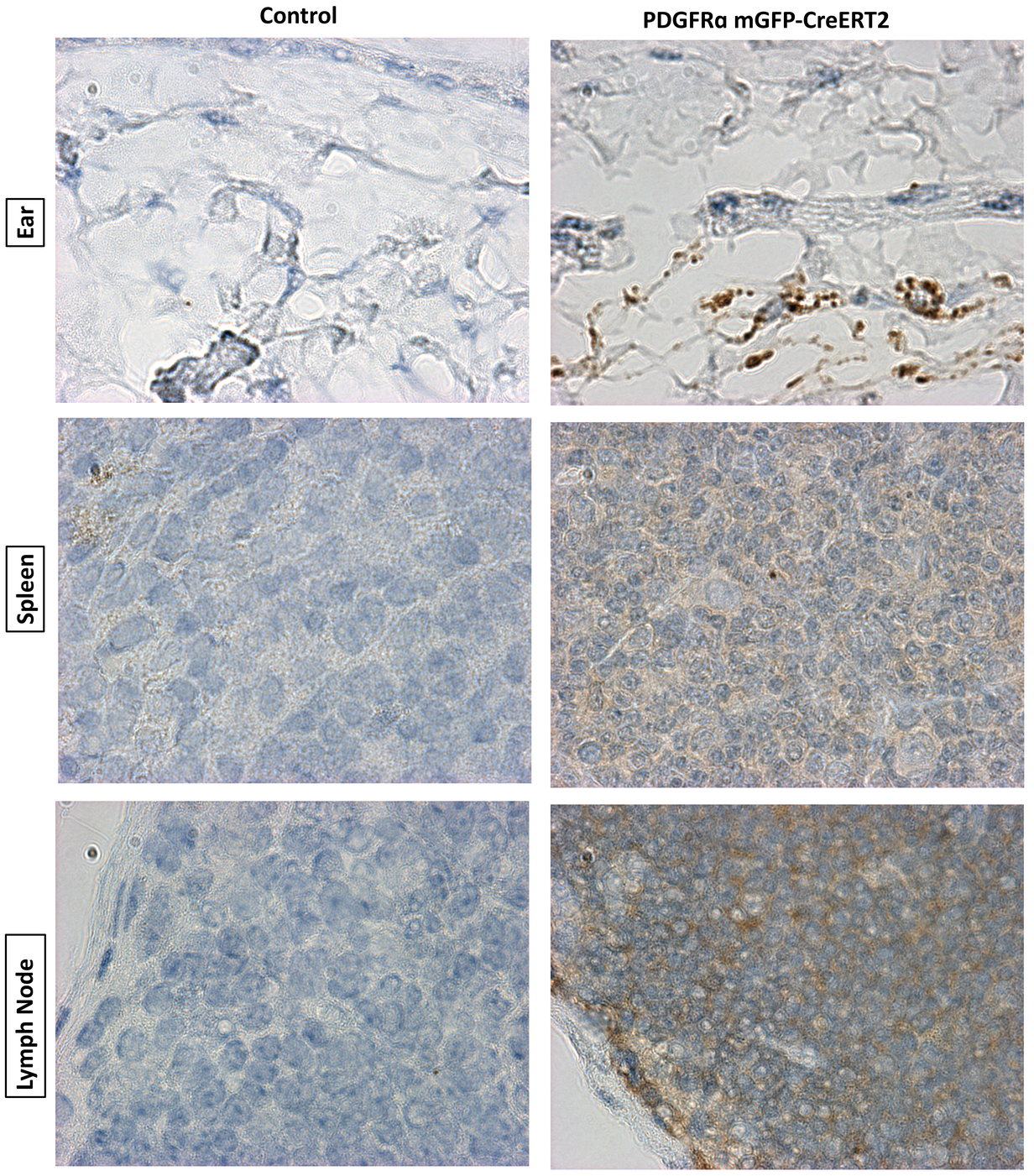
1) Validation of co-expression of CD140α and GFP in ear and lymph node stromal cells



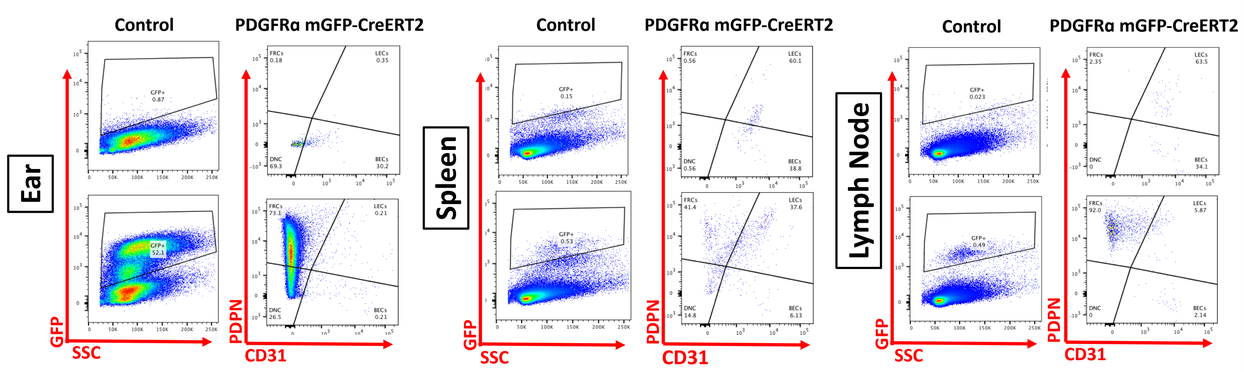
2) CD45⁻CD31⁻PDPN⁺ fibroblasts express GFP



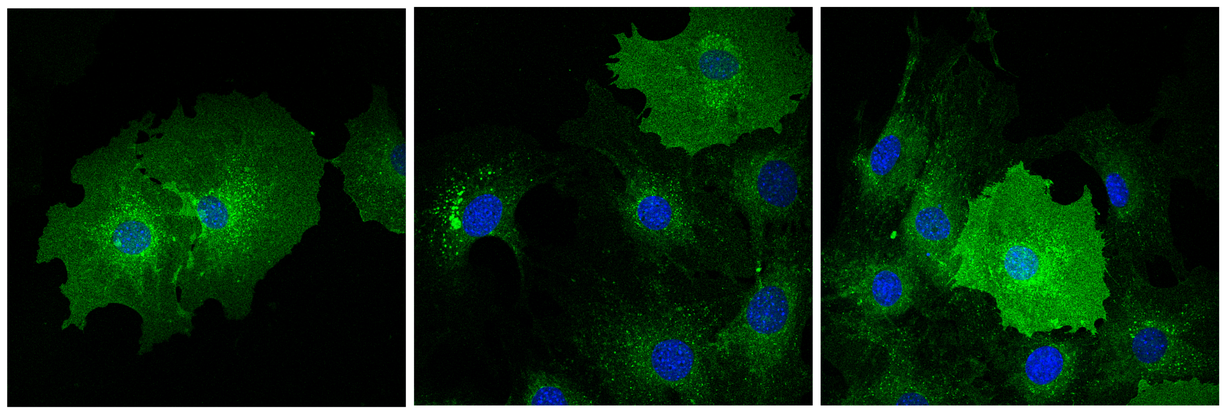
4) Ear, spleen and lymph node tissue sections show GFP expression



3) GFP is predominantly expressed in fibroblastic populations



5) Ear fibroblasts show endogenous GFP expression



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