



The Impact of vGPCR Expression in Lymphatic Vessels on Vessel Identity and Density

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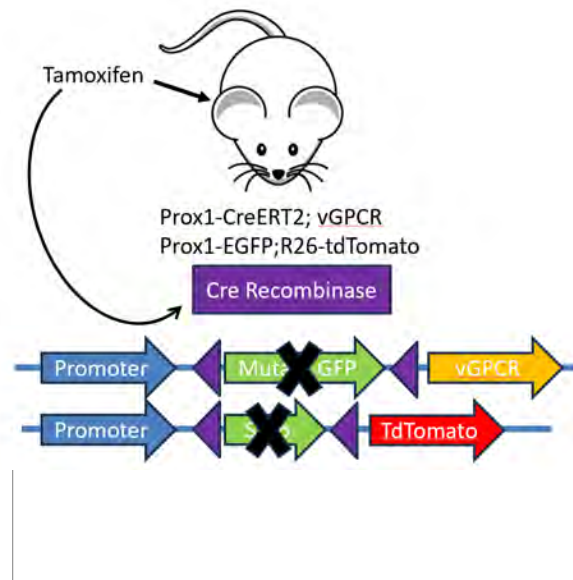
Abstract

Kaposi Sarcoma-associated herpesvirus (KSHV) is a human oncogenic virus and is a primary cause to Aids malignancies. The virus consists of a linear, double stranded DNA genome and belongs to the Herpesviridae family. KSHV was originally identified from Kaposi Sarcoma (KS) lesions in AIDS patients. Following the discovery of KSHV, primary effusion lymphoma (PEL) and a variant of multicentric Castleman's disease (MCD), which are neoplastic disorders, were learned to be linked to KSHV. KSHV has many genes that contribute to its ability to replicate and cause human disease. One of the most important genes that KSHV uses to cause disease is viral G-protein coupled receptor (vGPCR). Since signaling through vGPCR can promote cell survival, KSHV can manipulate vGPCR to its benefit. Within our project, we examined the changes caused by expressing vGPCR in lymphatic vessels in the mouse ear.

Objective

- Characterize the expression pattern of GFP and TdTomato in control and vGPCR expressing mouse lines
- Quantify changes in vessel density and fluorescent vessel expression

Methods



Methods Continued

- We used transgenic mice that express Cre recombinase protein in Prox1-expressing vessels when exposed to tamoxifen. The experimental mouse line contains vGPCR which is only expressed after Cre-driven recombination. These mouse lines also expressed green fluorescent protein (EGFP) in Prox1+ cells and TdTomato in cells expressing Cre.
- Three weeks after tamoxifen exposure, ears from control (PRD) mice and vGPCR-expressing (PBRD) mice were collected. The ears were fixed in paraformaldehyde and then frozen. Frozen sections were made using cryotome and mounted onto glass slides. The tissue were imaged using a fluorescent microscope at 10x magnification.
- For quantification, imageJ was used to measure the fluorescent area per total region of interest and expressed as a percentage. Mean percentage area for GFP and TdTomato were compared between control and experimental group. T-test was performed to statistically compare mean percentage area between the control and experimental group. Statistical significance was considered $p < 0.05$.

Conclusion

- vGPCR expression in lymphatic cells leads to increased lymphatic vessel density and ear thickening compared to control mice.
- We see vessels that no longer express GFP in vGPCR-expressing cells, which suggests that there is a change in the identity of these former lymphatic vessels.

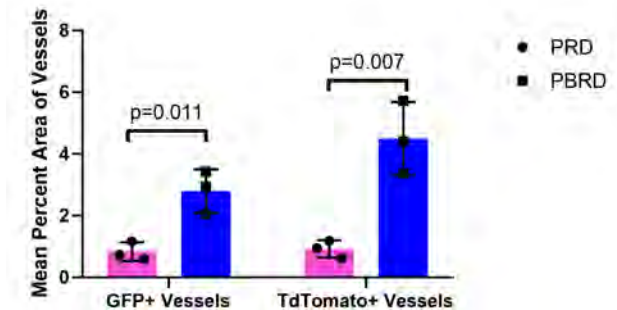
Results

Mouse Ear Tissue:

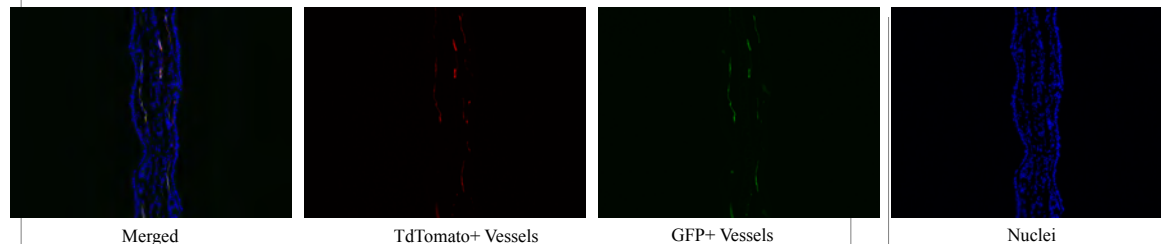


PRD: Normal and healthy ears

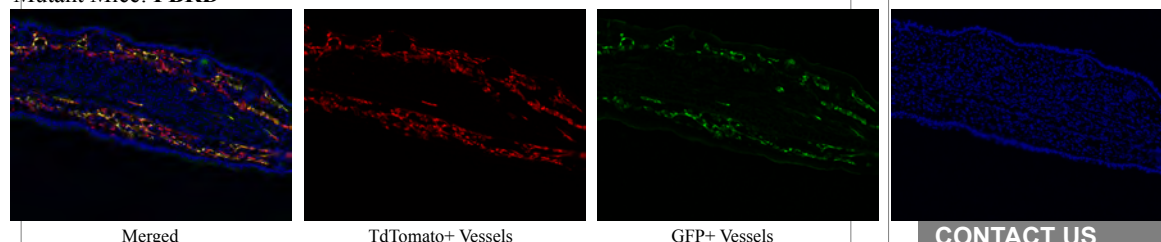
PBRD: Malformation and inflammation



Control Mice: PRD



Mutant Mice: PBRD



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