SELECTED OPPORTUNITY IN OPHTALMOLOGY

FZD7 INHIBITORS FOR THE TREATMENT OF RETINAL NEOVASCULARIZATION (BIO17121)

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Product factsheet

stage

- **Target:**
  - Frizzled 7 receptor (Fzd7)
- **Application:**
  - Retinal neovascularization in ischemic retinopathies (e.g. diabetic retinopathy, age-related macular degeneration, neovascular glaucoma, and retinopathy of prematurity)
- **Technology:**
  - Neutralizing antibodies
  - Decoy receptor polypeptides
- **Rational / POC:**
  - Abrogation of Fzd7 protects against the development of pathological angiogenesis in ischemic retinopathy
- **Patent and publication:**
  - PCT/FR2018/050840 filed on 04/04/2018
  - Fzd7 (Frizzled-7) Expressed by Endothelial Cells Controls Blood Vessel Formation Through Wnt/β-Catenin Canonical Signaling. Peghaire *et al.* Arterioscler Thromb Vasc Biol. 2016.

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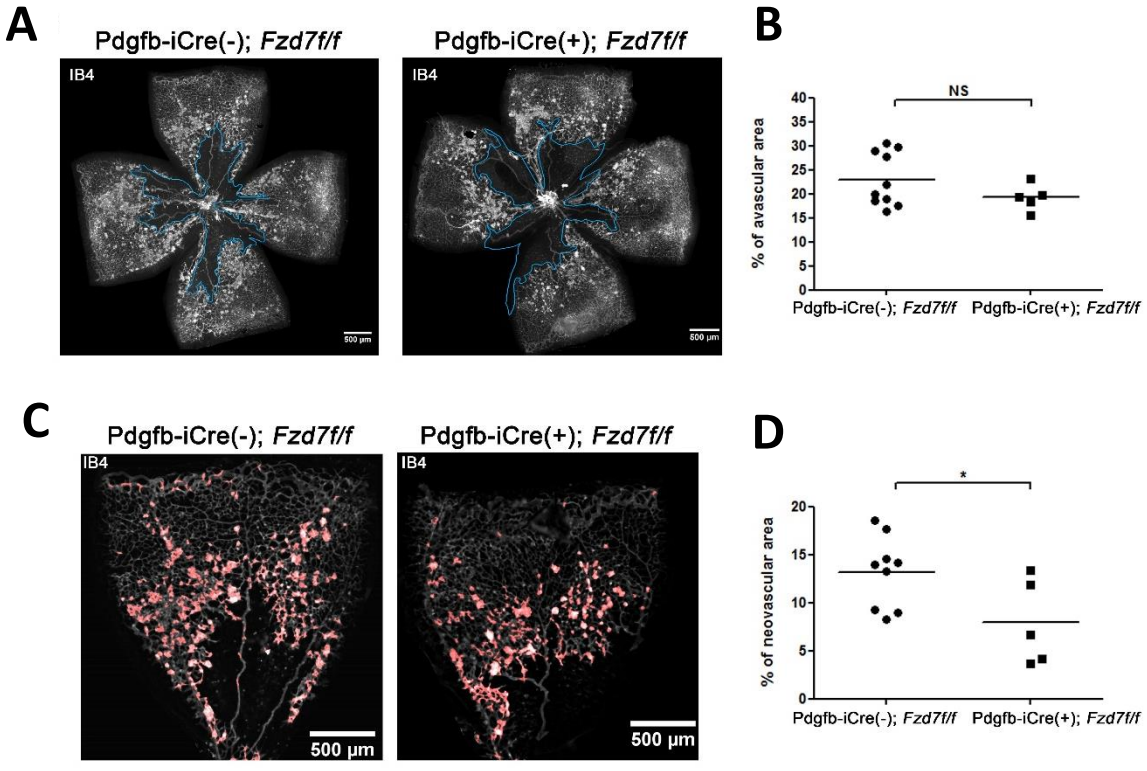
Proof of concept

- **Specific endothelial deletion of Fzd7 during the vasoproliferative phase of OIR decreases the ectopic growth of neovessels by limiting EC proliferation in tufts.**



To explore how Fzd7 endothelial deletion could specifically affect the NV phase of OIR, gene deletion was obtained after intraperitoneal injections of Tamoxifen at P12 and P13, just after Pdgf-iCre; *Fzd* $^{f/f}$ pups returned to room air. At P17 as expected the percentage of avascular area was not modified in the both Fzd7 EC-WT mice (Pdgf-iCre(-); *Fzd* $^{f/f}$) and Fzd7 EC-deleted mice (Pdgf-iCre(+); *Fzd* $^{f/f}$) (**Fig. A&B**). In contrast, visual appearance of the blood vessel system clearly differed in the two groups of mice. Fzd7 EC-WT retinas appeared more severely affected than in Fzd7 EC-deleted retinas, with a larger number of clusters and disorganized, small-sized vascular tufts (**Fig. C&D)**.

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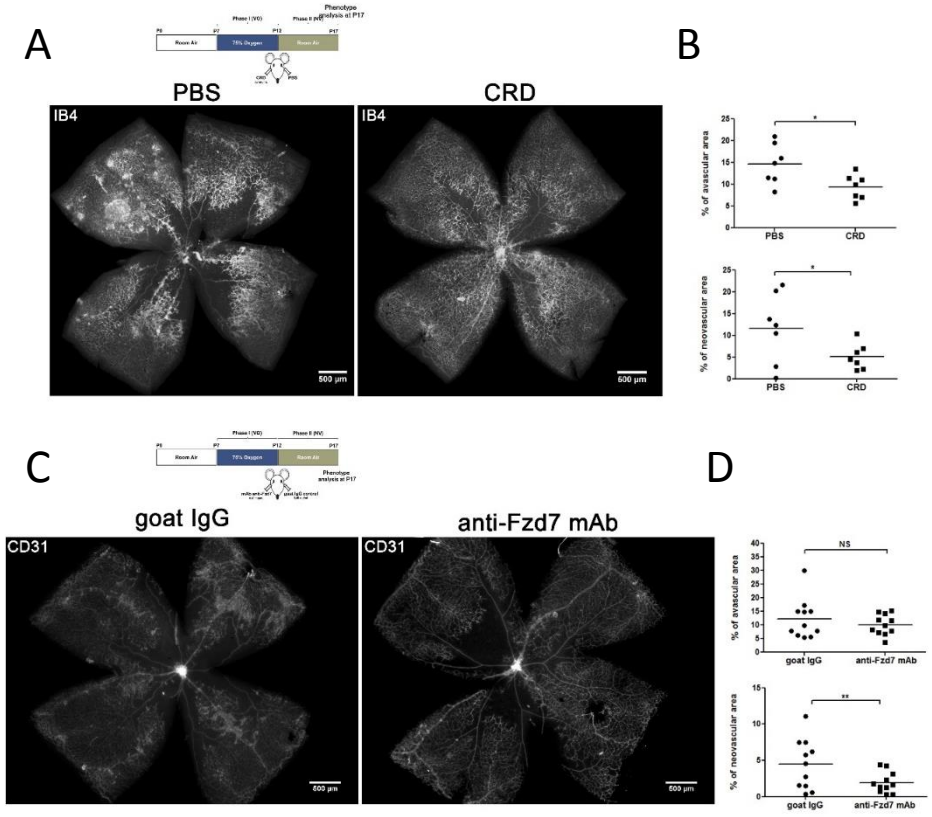
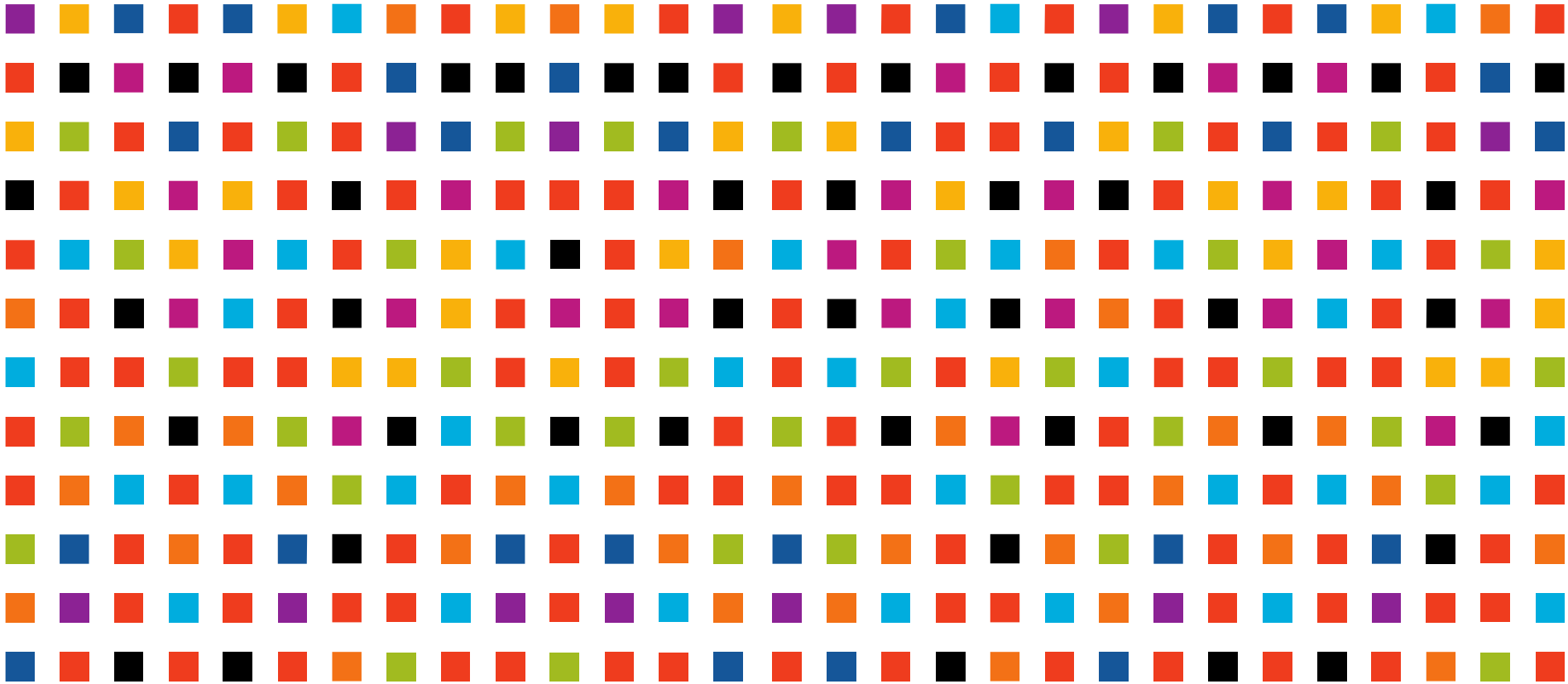
Proof of concept

- **Blocking Fzd7 signaling by antibody or soluble receptor prevents the development of aberrant neovascularization.**



(A and C) Schematic representations of Fzd7 pharmacological blocking in retinas from C57BL/6 mice at P12 after OIR. Immediately upon mice returned to room air, the right eye was injected intravitreally with 0.7 mg/mL of CRD (C) or 0.4 mg/mL of monoclonal anti-Fzd7 antibody, while the left eye was injected with equivalent doses of either PBS or goat IgG control , respectively. (B and D) Results of quantification of the % of avascular area and neovascular tufts area in P17 OIR retinas. In retinas treated with CRD, the relative % of both the avascular areas and those of neovascular areas significantly decreased compared with the control OIR eye; *p<0.05; paired Student's t test (n=7)



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