



SELECTED OPPORTUNITY IN NEUROSCIENCES

ROCK inhibitors to treat diabetic retinopathy (BIO15371)

ROCK INHIBITORS TO TREAT DIABETIC RETINOPATHY

Product factsheet

- ▶ **Product** : Rho-associated kinase (ROCK) inhibitor

- ▶ **Rational / PoC:**
 - ◆ membrane localization of ROCK-1 has been observed in human retina from diabetic but not from non-diabetic individual
 - ◆ ROCK-1 and ROCK-2 regulate junction proteins, but also contribute to cell polarity, mobility and apoptosis
 - ◆ ROCK-1 is abnormally expressed at the plasma membrane and is over-activated (increased phosphorylation of its substrates, MYPT1 and MLC) in the retinal pigment epithelium and in retinal vessels from GK rat (Goto Kakizaki murine model of type2 diabetes)
 - ◆ ROCK-1 inhibitor Fasudil injected into the vitreous of GK rats induces vasodilation of retinal vessels, and reduces hypoxic area and VEGF expression

- ▶ **Patent** : 13 Oct. 2015 PCT/EP2016/074468

- ▶ **Publication:**
 - ◆ Rothschild et al. Sci Rep. 2017 Aug 18;7(1):8834. *ROCK-1 mediates diabetes-induced retinal pigment epithelial and endothelial cell blebbing: Contribution to diabetic retinopathy*

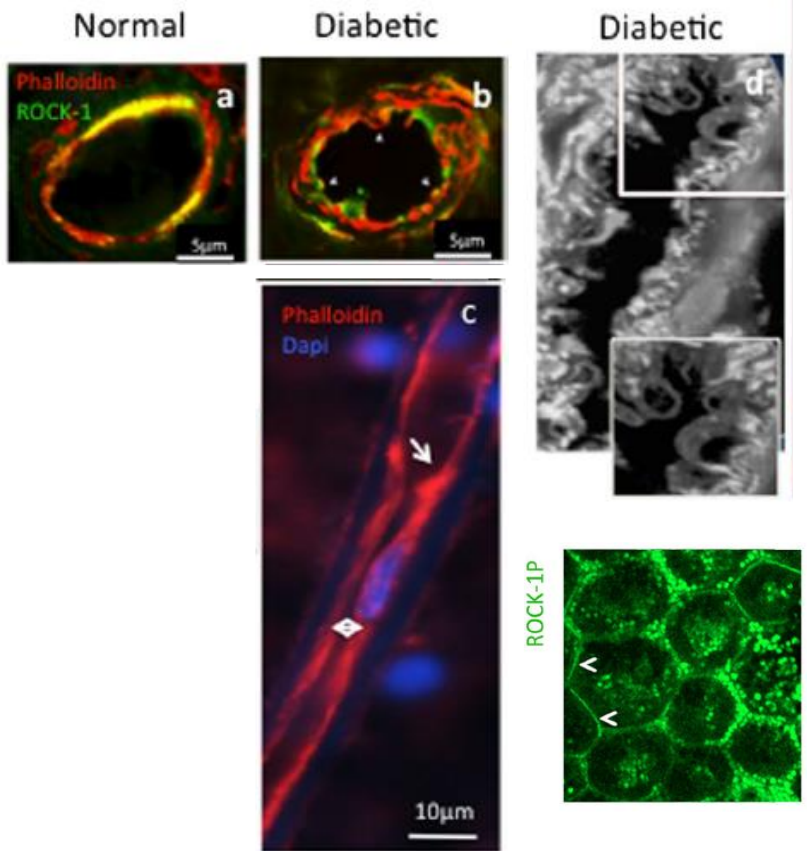
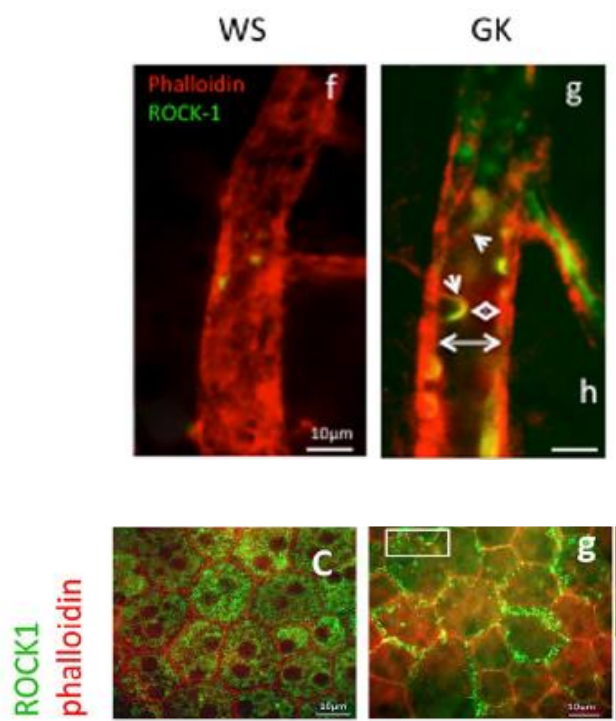
ROCK INHIBITORS TO TREAT DIABETIC RETINOPATHY

Proof of concept

ROCK-1 is expressed in retina at the endothelial cell membrane and surrounds the endoluminal blebs in diabetic subjects

Rat Retina

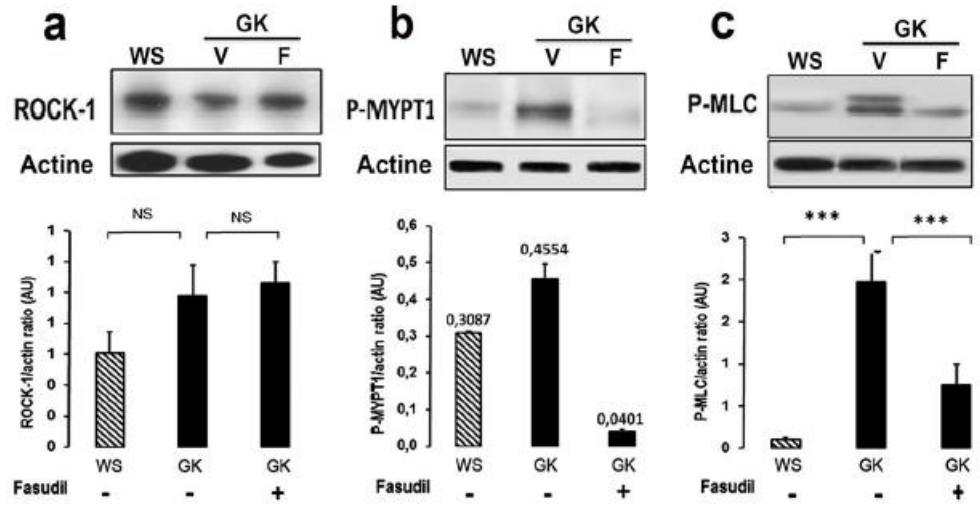
Human retina



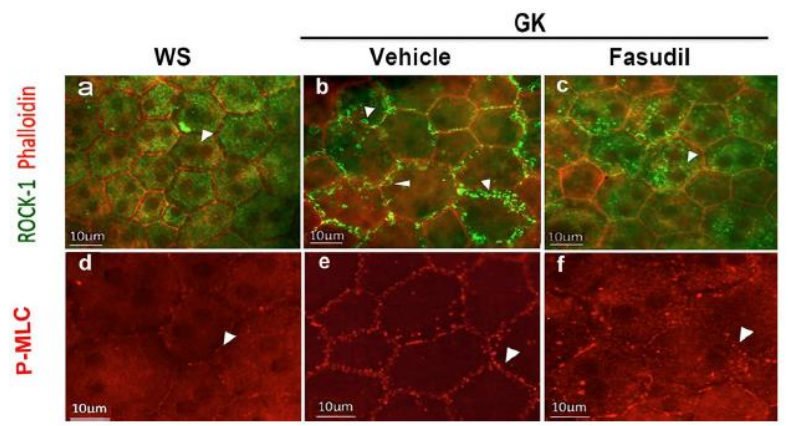
ROCK INHIBITORS TO TREAT DIABETIC RETINOPATHY

Proof of concept

Intravitreal injection of ROCK-1 inhibitor fasudil affects expression and localization of downstream effectors



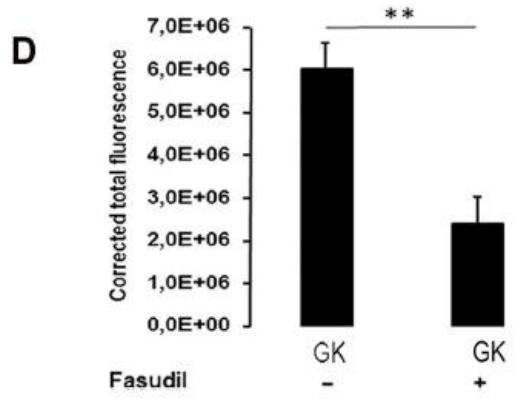
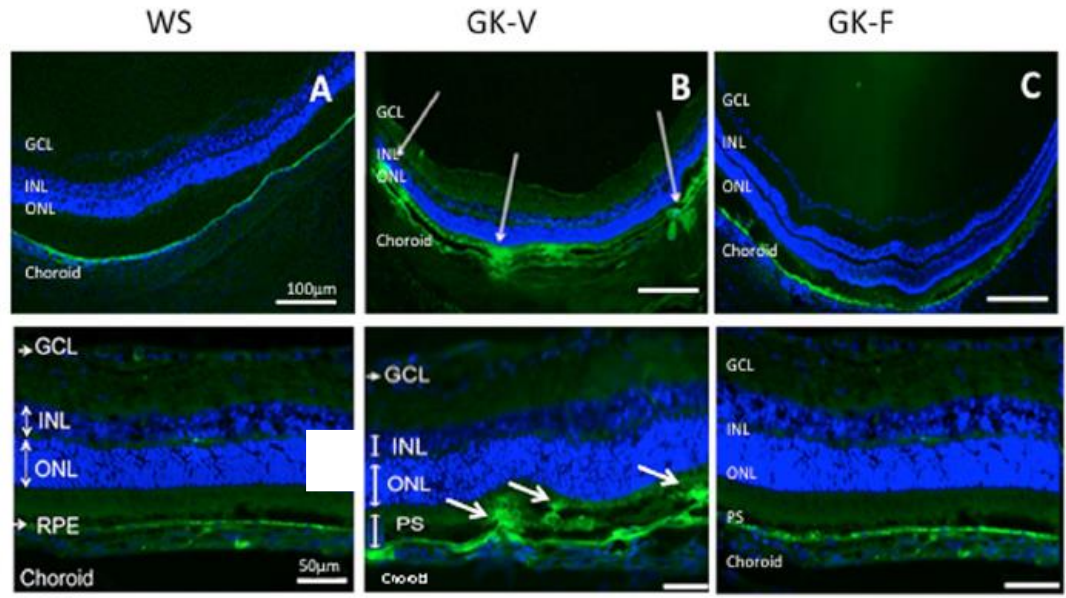
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ROCK INHIBITORS TO TREAT DIABETIC RETINOPATHY

Proof of concept

Intravitreal injection of ROCK-1 inhibitor fasudil restores GK rat outer retinal barrier permeability

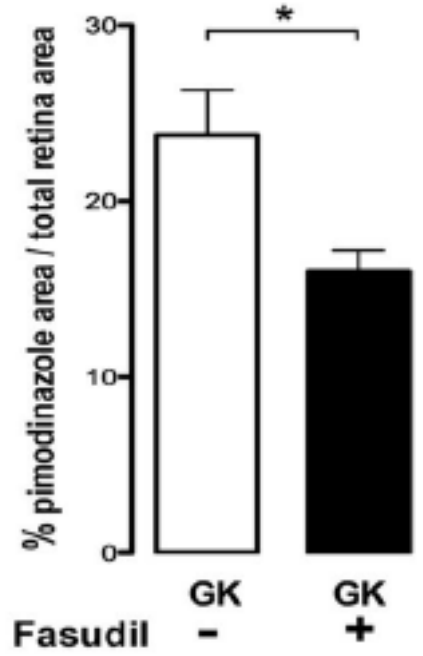
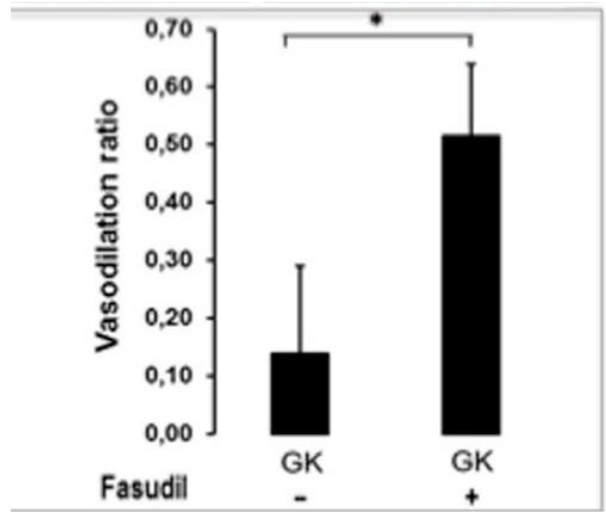


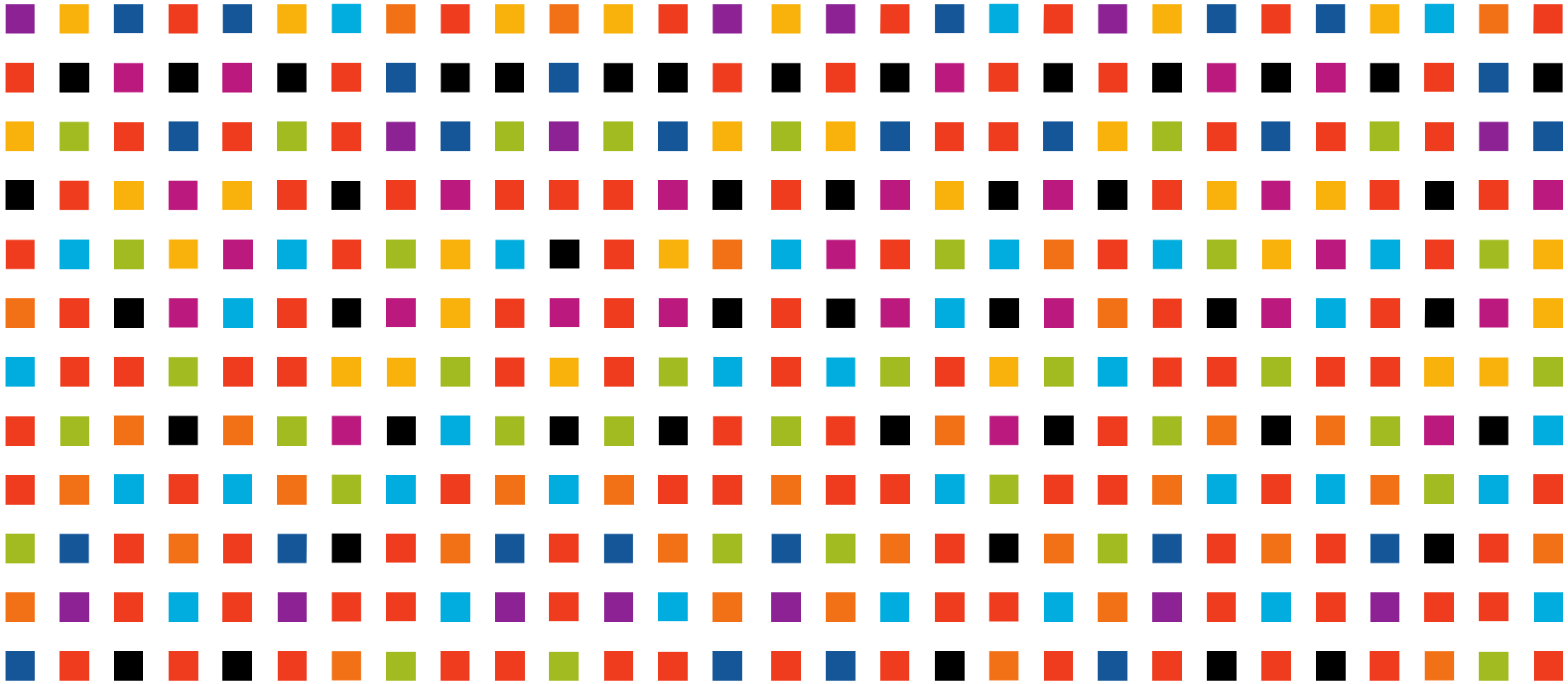
GK rats are treated either with Vehicle (GK-V) or with fasudil (GK-F)
Green FITC-dextran IV injected in rats highlights vessels permeability
Quantification of total retinal leakage was performed by the measurement of neural retina corrected total fluorescence (CTF)

ROCK INHIBITORS TO TREAT DIABETIC RETINOPATHY

Proof of concept

Fasudil reduces vasoconstriction and reduces retinal hypoxia of the diabetic rat retina





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