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Supplementary Figure 1. UPARANT inhibits angiogenesis in HUVEC and chick embryo CAM assays. (A) HUVEC spheroids embedded in fibrin gel were incubated in the
presence of VEGF (30 ng·mL⁻¹) in combination with vehicle (PBS) or increasing concentrations of UPARANT. After 24 h, vessel sprouts were counted. (B, C) Representative images of HUVEC spheroids treated with VEGF in the presence of either vehicle or 0.01 nM UPARANT. (D) Chick embryo CAMs were implanted at day 11 after fertilization with alginate beads containing 0.1 µg VEGF in combination with vehicle or increasing amounts of UPARANT. After 3 days, newly-formed blood vessels converging versus the implant were counted. (E, F) Representative images of chick embryo CAMs treated with VEGF in the presence of either vehicle (E) or 0.1 µg UPARANT (F). UPARANT dose-dependently reduced angiogenesis in both the assays (*P < 0.05, **P < 0.01 and ***P < 0.001 versus vehicle-treated; ANOVA). Each histogram represents the mean ± SEM of data from 50 HUVEC spheroids or 8 implanted eggs. Scale bars, 150 µm (C) or 5 mm (F).

Supplementary Figure 2. PDR vitreous fluid does not affect the binding of UPARANT to endothelial cell surface and its consequent internalization. HUVECs were incubated in the
absence (A-C) or in the presence (D-F) of PDR vitreous fluid with 0.15 mM FITC-UPARANT (B, C, E, F) either in the absence (B, E) or in the presence (C, F) of 1.5 mM unlabelled UPARANT. After 60 min, cell binding and internalization of FITC-UPARANT (in *green*) was assessed. Nuclei were counterstained with DAPI (*in blue*). Representative images from three independent experiments, each performed in triplicate. Scale bar, 50 µm.