In this work, Ong et al studied the effects of colorectal cancer cells-overexpressed cellular prion protein (PrP^C) and γ-Synuclein (γ-Syn) in angiogenesis of endothelial cells (ECs). Using various methods authors identified that overexpression of PrP^C and γ-Syn reduced proliferation, invasion, migration and hetero-cell adhesion of ECs, but induced the tube formation, increased nitric oxide (NO) secretion, decreased secretion of matrix metalloproteases (MMP-2 and MMP-9) and decreased secretion of pro-angiogenic factors to extracellular environment. Based on the observations authors conclude that PrP^C and γ-Syn overexpressed in colorectal cancer cells can induce angiogenesis of endothelial cells possibly by regulating NO secretion.

This paper is well written and, results and discussion are explained elaborately. Although several aspects of the work are conceptually not novel, but the observation that factor(s) overexpressed in one-cell type can control tumor microenvironment by modulating morphology of nearby cell type. This work could consider for publication after the following concerns have been addressed.

1. This reviewer suggests to emphasize (in the figure legend) how the relative intensity was calculated in Fig 1A. Like, doing ratio over actin.
2. In Fib 2B & C, it is suggested to mention how the expression and / or secretion level of MMP-2 and MMP-9 was normalized.