Review of: "Single-cell characterization of neovascularization using hiPSC-derived endothelial cells in a 3D microenvironment"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

The manuscript investigated the differentially expressed genes and angiogenic signaling in the whole angiogenic process by applying single-cell transcriptomics, which gave more insights into the co-evolving cell clusters and various microenvironment. The sufficient analysis of single-cell transcriptomics may play a guiding role in optimizing the conditions of vascularization for vascular tissue engineering. It is an interesting topic in the area of tissue engineering and I have some questions as follows:

1. For velocity analysis of endothelial development, the author mentioned that the cell cycle regulator HMGA2 was in the turned-off state in angioblasts. However, previous publications illustrated that overexpression of HMGA2 could enhance vascular development and angiogenesis by regulating the secretion of VEGFA[1-3]. Please discuss about it.
2. The comparison of ECs differentiation in 2D and 3D culture format revealed the upregulated cell-cell interaction and stabilization of mural cell fraction in 3D suspension culture, but it also caused cell growth arrest of ECs. Can we draw a conclusion that 3D suspension culture is more suitable for early angiogenic induction of stem cells than 2D monolayer culture?
3. The author chose to induce EC maturation with ascorbic acid from day 12 to day 18 Matrigel cultures, how did the author determine the time period?

[1] Sakata J, Hirosue A, Yoshida R, Kawahara K, Matsuoka Y, Yamamoto T, Nakamoto M, Hirayama M, Takahashi N, Nakamura T, Arita H, Nakashima H, Nagata M, Hiraki A, Shinohara M, Nakayama H. HMGA2 Contributes to Distant Metastasis and Poor Prognosis by Promoting Angiogenesis in Oral Squamous Cell Carcinoma [J]. Int J Mol Sci, 2019, 20(10):

[2] Wang J, Chen Y, Zeng Z, Feng R, Wang Q, Zhang Q, Sun K, Chen A F, Lu Y, Yu Y. HMGA2 contributes to vascular development and sprouting angiogenesis by promoting IGFBP2 production [J]. Exp Cell Res, 2021, 408(1): 112831.

[3] Yan J, Dai P, Qin X, He Y, Zhang Y. HMGA2 promotes the migration and invasion of gallbladder cancer cells and HMGA2 knockdown inhibits angiogenesis via targeting VEGFA [J]. Mol Med Rep, 2022, 25(2):