Study on Vascular Formation in a Cellular Spheroid by Using Selective Plane Illumination Microscopy (SPIM)

Bishnubrata Patra,1,2* Yu-Sheng Peng,1,2 Wei-Hao Liao,3 Keng-Hui Lin,4 Yi-Chung Tung,3 and Chau-Hwang Lee1,2,3

1Institute of Biophotonics, National Yang-Ming University, Taipei 11221, Taiwan
2Biophotonics & Molecular Imaging Research Center (BMIRC), National Yang-Ming University, Taipei 11221, Taiwan
3Research Center for Applied Sciences, Academia Sinica, Taipei 11529, Taiwan
4Institute of Physics, Academia Sinica, Taipei 11529, Taiwan
*E-mail: bishnubrata.patra@gmail.com

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ABSTRACT: Anti-angiogenic therapy targets vascular formation in tumors to suppress the tumor growth and metastasis. In recent years investigations indicate that anti-angiogenics may act through vascular normalization and improving tumor oxygenation to enhance delivery of cytotoxic agents to the tumor mass [1]. Selective plane illumination microscopy (SPIM) is a powerful tool to study large 3D samples for long term [2]. We cocultured human umbilical vein endothelial cells (HUVECs) with hepatocellular carcinoma cells as cellular spheroids (diameter > 100 µm) in a microfluidic device [3] and studied the distributions and modification of these HUVECs by using SPIM for more than 72 hours. In our experiments, HUVECs migrated outwards to the edge of the spheroids in normal culture conditions within 48 hours [Fig. 1(A)]. This outward migration was hindered when the spheroid was treated with 100 ng/ml VEGF and 100 ng/ml β-FGF. Moreover, some of the HUVECs formed hollow vascular cross section within 72 hours under such a treatment [Fig.1 (B)].

Figure 1. (A) SPIM image of a coculture cellular spheroid after 48 hours. The HUVECs migrate outward the spheroid. (B) Surface plot image of HUVECs with the treatment of VEGF and β-FGF. The outward migration is stopped, and some HUVECs form hallow vascular cross section structure. Scale bar: 20 µm.

REFERENCES