**Effects of prolyl hydroxylase inhibitors on tumor blood vessels in tumor mouse model.**

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Tumor blood vessel structure is different from normal blood vessel features in terms of short lumen diameter, serpentine course, irregular sprouting and poor tight junction formation. These phenomena lead to form leaky tumor vessels with low blood flow. These tumor microenvironments (TME) lead to hypoxia. The TME polarizes tumor-infiltrating macrophages towards tumor supportive phenotype. Macrophage-abundant tumors are highly malignant and are the cause of poor prognosis and therapeutic resistance.

In this study, we have used Lewis lung carcinoma (LLC) syngeneic tumor mouse models, which existed abundant macrophages in tumor tissues. These cells were subcutaneously transplanted into the right flank of mice. Mice were treated with prolyl hydroxylase (PHD) inhibitors intraperitoneally at day10 after tumor transplantation. Once every other day, tumors were measured in two dimensions and the tumor tissue volume was calculated. Tumor tissues were collected at day16 and analyzed tumor vessels and immune cells by immunofluorescence staining.

PHD inhibitors treatment induced tumor blood vessel reconstitution and normalization in tumor tissues, these results led to increase perfusion and oxygenation. macrophages contributed to blood vessel normalization. In this study, we characterized macrophage function and subsets which can be altered phenotype after PHD inhibitors treatment. Our results imply that the PHD inhibitors could promote the anti-tumor potential of macrophages to improve malignant cancer therapy.