# 令和元年　第 1 回分子生体膜研究所セミナー

(7 月 19 日（金）16:00-17:00; 中央棟 2F 20 講義室)

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**演 題 ： Targeting PI3K/Akt pathway for cancer therapy**

**抄録：**Phosphatidylinositol 3-kinase (PI3K)/Akt pathway is frequently activated in human cancers. Class I PI3Ks are lipid kinases that phosphorylate phosphatidylinositol 4, 5-bisphosphate (PIP2) at the 3-OH of the inositol ring to generate phosphatidylinositol 3, 4, 5-trisphosphate (PIP3), which in turn activates Akt and the downstream effectors like mammalian target of rapamycin (mTOR) to play key roles in carcinogenesis. Since frequent overactivation of the upstream RTK (receptor tyrosine kinase), gain-of-function mutations of PI3Ks and loss-of-function mutations of PTEN are found in human cancers, inhibitors targeting PI3K/Akt pathway have been expected as promising anticancer drug candidates. Some PI3K inhibitors like Idelalisib and mTOR inhibitors like Everolimus have been approved, many more inhibitors targeting this pathway are in clinical trials. ZSTK474 is a pan class I PI3K inhibitor we identified. Favorable in vitro and in vivo antitumor efficacy of ZSTK474 led to its proceeding to clinical trial. Stellettin B (STELB) is a triterpene we isolated from marine sponge. Potent antiproliferative activities of STELB were shown on various tumor cell lines while no obvious cytotoxicity was indicated on several normal cell lines. Inhibition of PI3K/Akt pathway by STELB was demonstrated. Potent in vitro and in vivo anti-glioblastoma actitivities of STELB alone or in combination with Temozolomide were shown. In this presentation, the discovery of ZSTK474 and STELB as well as their pharmacological study will be reported after a brief introduction of PI3K/Akt pathway.

**略歴：**孔教授は、2005 年大阪大学薬学部博士課程修了、2005-2006 年香港中文大学研究員、2006-2010 年日本がん研究会研究員を経て、2011 年―現在至る天津医科大学薬学部教授、2012 年天津市特別招聘教授となっている。

**主催：**分子生体膜研究所 細胞制御学 (内線：4509)