昆虫バイオメディカル研究セミナー

日時：2017 年 5 月 26 日（金）　　午後 4 時 30 分～5 時 30 分
場所：2 号館 4 階 441 号室　　（応用生物学専攻　大学院演習室）
講演者：

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講演要旨

Exosome mediated premetastatic niche formation in breast cancer

Tumor-derived exosomes are emerging mediators of tumorigenesis and tissue-specific metastasis. Proteomic profiling has identified Annexin A2 as one of the most highly expressed proteins in the exosomes; however, studies focused on the biological role of exosomal-AnnexinA2 (exo-AnxA2) are still lacking. We have characterized exo-AnxA2 and determined its function in angiogenesis and breast cancer metastasis. We used multiple *in vitro* and *in vivo* techniques to study the role of exo-AnxA2 in angiogenesis. Using atomic force microscopy and Western blotting, we characterized exo-AnxA2 expression in normal and breast cancer cells. In addition, using organ specific metastatic breast cancer cells and animal models we studied the role exo-AnxA2 in breast cancer metastasis. Results showed that exo-AnxA2 expression is significantly higher in malignant cells than normal and pre-metastatic breast cancer cells. In vitro and in vivo studies showed that exo-AnxA2 promotes tPA-dependent angiogenesis. *In vivo* studies showed that metastatic exosomes create a favorable microenvironment for metastasis and exo-AnxA2 plays an important role in this process, since priming with AnxA2-depleted exosomes reduces brain (~4-fold) and lung (~2-fold) metastasis. Upon delineating the mechanism we discovered that exo-AnxA2 causes macrophage-mediated activation of the p38MAPK, NF-κB, and STAT3 pathways and increased secretion of IL-6 and TNF-alpha. These data demonstrate an important role for exo-AnxA2 in breast cancer pathogenesis.

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