

平成23年度

ライフサイエンスイノベーション推進機構セミナー 第371回 学内セミナー(大学院セミナー)

日時：平成24年2月3日(金)18:00~19:30

会場：研究棟3階会議室(松岡キャンパス)

演者：Prof. Hisataka Sabe

Dept. Molecular Biology, Hokkaido University Graduate School of Medicine

演題：「p53 mutation and TGF β signaling culminate in cancer
invasiveness via GEP100-Arf6-AMAP1 pathway」

Contrary to the long believed hypothesis, it is now evident that breast cancer cells can disseminate from the early phases of the oncogenesis; and that such early disseminated cells sometimes survive at the sites of dissemination and may outgrow after a long latency of years and decades. For cancer cells to leave their origin, they must at least transiently loosen their adhesion with adjacent epithelial cells and stroma, and become motile while avoiding anoikis. Such processes resemble epithelial-mesenchymal transdifferentiation (EMT), which normally takes place in situations such as embryogenesis and wound healing. TGF β 1 is produced mostly upon inflammation and wounding. Interestingly, the occurrence of an EMT-like process in breast cancer cells has been implicated in the generation of cancer stem-like cells, in which TGF β 1 signaling often plays core roles.

On the other hand, mutation of p53 tumor suppressor protein is very frequent in cancer, and often gains oncogenic activities, rather than simply abrogating its tumor suppressive functions. Identification of genes whose expression is altered as a result of p53 mutation and hence elicit tumor malignancy is another major goal of current cancer research.

A series of our studies have shown that GEP100-Arf6-AMAP1 signaling pathway is frequently upregulated in many breast cancers and contributes to invasiveness and cancerous EMT, by promoting the recycling of β 1 integrins, such as α 3 β 1, and the downregulation of E-cadherin. Here, we show that TGF β 1 signaling activates this GEP100-Arf6-AMAP1 pathway to evoke cancerous EMT, and provide lines of evidence that mutant p53s, like R280K, are essential for activation of the Arf6 pathway. Our clinical study moreover suggest that high levels of the expression of components of this pathway correlates with the statistical significance with recurrence of breast tumors after physical resection and the consecutive radiotherapy. We would hence discuss possible involvement of the Arf6 pathway in dissemination of breast cancer cells at early phases of their oncogenesis.

本学内セミナーは大学院セミナーも兼ねていますので、大学院1・2年生は是非出席して下さい。
(必修科目「医学研究総論」「医科学特論」「先端応用医学概論」の出席回数にカウントされます)。
また、学内の研究者間の交流をはかることも目的としていますので、多数の御来聴をお願い致します。



主催：福井大学ライフサイエンスイノベーション推進機構

(生命科学複合研究教育センター・トランスレーショナルリサーチ推進センター・ライフサイエンス支援センター)

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担当者：総合戦略部門研究推進課学内共同教育研究施設等 田口、中川(内線2059)