第35回プロテオーム医療創薬研究会

【実施日】　2011年12月12日(月)　18:00～19:00

【会　場】　横浜市立大学医学部 福浦キャンパス B441教室

【来場者】　30名

【内　容】

演題：How do cells collectively shape organs in development and disease?

The mammary epithelium is a bilayered tube, with luminal and myoepithelial cells. However, during morphogenesis the mammary epithelium reorganizes to a low polarity, multilayered architecture, with mixed localization of E-cadherin (E-cad), scribble, and aPKC-ξ in the interior. In our real-time imaging, we observe: (1) vertical division of luminal cells to create an interior luminal population, (2) restraint of interior cell migration by myoepithelial cells, and (3) restoration of polarized simple epithelial organization in interior cells as ducts cease elongating. Given the critical role of E-cad in luminal adhesion, we hypothesized that its deletion would be sufficient for dissemination of interior cells. However, in Matrigel, E-cad deletion resulted in epithelial disorganization and single-file invasion, but not dissemination. In contrast, in collagen I, E-cad deletion resulted in robust dissemination. Our data suggest that reduction in luminal cell-cell adhesion is only sufficient to induce dissemination in some matrix environments. Myoepithelial cells actively restrain the dissemination of E-cad- luminal cells in our real-time movies. We hypothesize that this restraint requires P-cadherin dependent myoepithelial adhesion. In Matrigel, P-cad deletion induced hyperplasia, while in collagen I, P-cad deletion induced myoepithelial dissemination. We are now testing whether P-cadmyoepithelial cells can still limit the dissemination of E-cad- luminal cells in Matrigel and in vivo. Our data suggest that adhesion mutations can accumulate with modest morphologic consequences, but produce rapid dissemination as the tumor microenvironment changes during cancer progression.