

演題:Switching phenotypes, a new model for cancer progression

演者: Dr. Keith Hoek

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日時:2008年5月13日(火) 6:10-7:00

会場:Room 311, Sogo-kenkyu (Building D)

要旨: Genome-wide expression analyses of melanoma cell line libraries have

identified two transcription signatures which are predicted to correspond with proliferation and invasion. Cell lines with proliferative or invasive signatures were injected into the flanks of immuno-compromised mice and allowed to form tumors. Tumor growth rates were monitored and immunohistochemistry was used to follow signature switching and in vivo proliferation, respectively. We found that tumors grew faster from cells with a proliferative signature than those with an invasive signature. Critically, all tumors displayed immunohistochemical evidence for both proliferative and invasive signatures, in specific intralesional regions, regardless of which line was used for seeding. Staining of human cutaneous metastases showed similar region-specific staining patterns, indicating that invasive or proliferative states are determined by intralesional location. Finally, we used siRNA to knock down a factor critical to the proliferative signature and show that these cells subsequently take on a phenotype typical of invasive signature cells. These data indicate that melanoma cells undergo transcriptional signature switching in vivo which is likely regulated by local microenvironmental conditions.

Dr. Keith Hoek's research is concerned with the molecular biology of melanoma cells using microarray experiments. His research description can be found at the following web address. <u>http://www.haskell.org:80/keith/work.html</u>

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