Title
In vivo imaging of cell-cycle phase of individual cancer cells throughout growing tumors in live mice

Authors
Yano, S
Tome, Y
Digman, MA
et al.

Publication Date
2013

34

In vivo imaging of cell-cycle phase of individual cancer cells throughout growing tumors in live mice. S. Yano[1], Y. Tome[1], M.A. Digman[2], M. Momiyama[1], A. Suetsugu[1], H. Kishimoto[3], H. Tazawa[4], T. Fujiwara[3], E. Gratton[2], R.M. Hoffman[1]; [1]AntiCancer Inc., San Diego, CA, [2]Department of Biomedical Engineering, Physics, and College of Medicine, University of California, Irvine, CA, [3]Department of Gastroenterological Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharma Sci, Okayama, Japan, [4]Center for Innovative Clinical Medicine, Okayama University Hospital, Okayama, Japan

The phase of the cell cycle can determine whether a cancer cell can respond to a given drug. This report presents imaging methodology to obtain real-time cell cycle information on cancer cells throughout tumors in live mice using a fluorescence ubiquitination cell cycle indicator (FUCCI). In nascent tumors in nude mice, approximately 30% of the cells in the center of the tumor were in G_0/G_1 and 70% in $S/G_2/M$. In contrast, approximately 90% of cancer cells in the center of an established tumor were in G_0/G_1 phase. Similarly, approximately 75% of cancer cells far from (>100 μm) tumor vessels were in G_0/G_1. Although 60–70% of cancer cells near the surface in an established tumor (< 100 μm) or near blood vessels were in $S/G_2/M$, these cells are a small minority of an established tumor. Moreover, static tumors in mice consisted of mostly G_0/G_1 cells, suggesting they are dormant. Real-time imaging of the cancer cell cycle has profound implications for cancer therapy, since most drugs currently in use target cells in $S/G_2/M$, which are a minor fraction in an established tumor. With the imaging method developments reported here, drugs that target non-dividing cancer cells can be readily identified.