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Monitoring the Temporal Distribution of Taxol® in a Living Tumor Cell Using Raman Imaging Microscopy

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Direct Raman imaging techniques are being developed to study drug distribution in living cells. The advantage of Raman imaging over the fluorescent imaging is that no external markers are required, which makes sample preparation much simpler for experiments. At the same time, the mechanism of action of the drug is minimally disturbed during imaging. In this study, Raman imaging was used to monitor the change of Taxol® (paclitaxel) distribution in cultured human breast tumor cells.

Approximately 10^5 MDA-435 breast tumor cells were cultured on gold-coated Petri dishes and allowed to stabilize for 24 hours in a RPMI-1640 medium supplemented with fetal bovine serum. Before imaging, the RPMI nutrition medium was exchanged with a phosphate buffered salt (PBS) solution. Control images were first obtained while the cells were in the PBS solution. Cells were then treated with Taxol (0.3 mg/ml or 350 μM) for one hour. After drug treatment, the Taxol solution was washed out and the cells were put back into the PBS solution. Images of the same cell were acquired before, during and after the Taxol treatment. Each measurement is composed of three images of the cell: a conventional white-light image and two Raman images acquired at the 1000 cm^{-1} and 1080 cm^{-1} Raman bands, respectively. The white-light image is used to record the cell structure and any changes that might occur to it. The Raman image acquired at the 1000 cm^{-1} records Taxol distribution in the cell as well as background fluorescence from the cell. Using the Raman image acquired at 1080 cm^{-1}, the contribution of background fluorescence present in the 1000 cm^{-1} image can be eliminated, thereby leaving behind only Taxol-related information.

The superimposition of the Raman and white-light images illustrate how the distribution of Taxol changes with time in live tumor cells. It was found that Taxol does not enter the cell nucleus under these conditions, but is more concentrated around the cell centrosome and near the cell membrane. This result is well explained by the accepted binding characteristics of Taxol and its molecular target – the microtubules.

In conclusion, this work demonstrated the feasibility of using direct Raman imaging to study the distribution of anticancer agents in single living cells. Based on this study, direct Raman imaging can be further extended to study drug mechanisms, cellular uptake, resistance, and intracellular pharmacokinetics.