



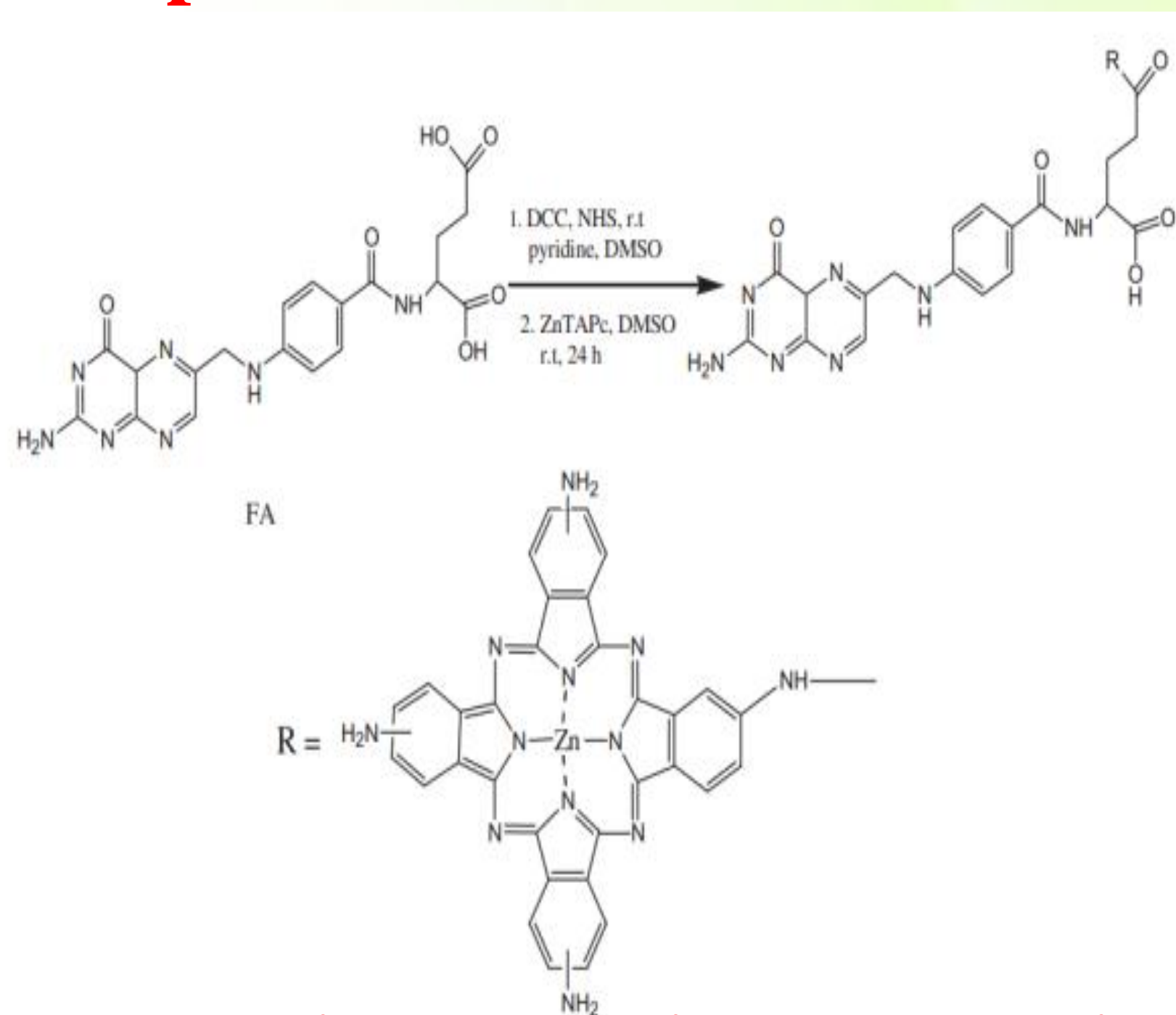
The application of a new conjugate zinc tetraaminophthalocyanine of folic acid in photodynamic therapy

Song Wang and Ji-Yao Chen

State Key Laboratory of Surface Physics, Fudan University, Shanghai 200433, PRC

Abstract: Zinc tetraaminophthalocyanine (Zntapc) were selected to conjugate with folic acid(FA), forming Zntapc-FA. This study aims to examine the selectivity of Zntapc-FA to the cell lines in which folate acceptor(FR) is overexpressed, such as KB cell—FR-positive human nasopharyngeal carcinoma cells. The enhancement of cellular uptake in KB cells are found by confocal fluorescence microscopy under single-photon and two-photon excitation. However, the uptake enhancement was suppressed when KB cells had been pretreated by excess FA, reflecting that the enhancement was mediated by the association of FR at cell membranes with Zntapc-FA. When human lung cancer cells A549(FR-negative cells) and KB cells, respectively, were incubated with Zntapc-FA(1uM) for 30mins, the Zntapc-FA uptake by A549 was much weaker than that by KB cells, demonstrating that Zntapc-FA could undergo preferential binding on FR-positive cancer cells.

The structure of Zntapc and Zntapc-Fa

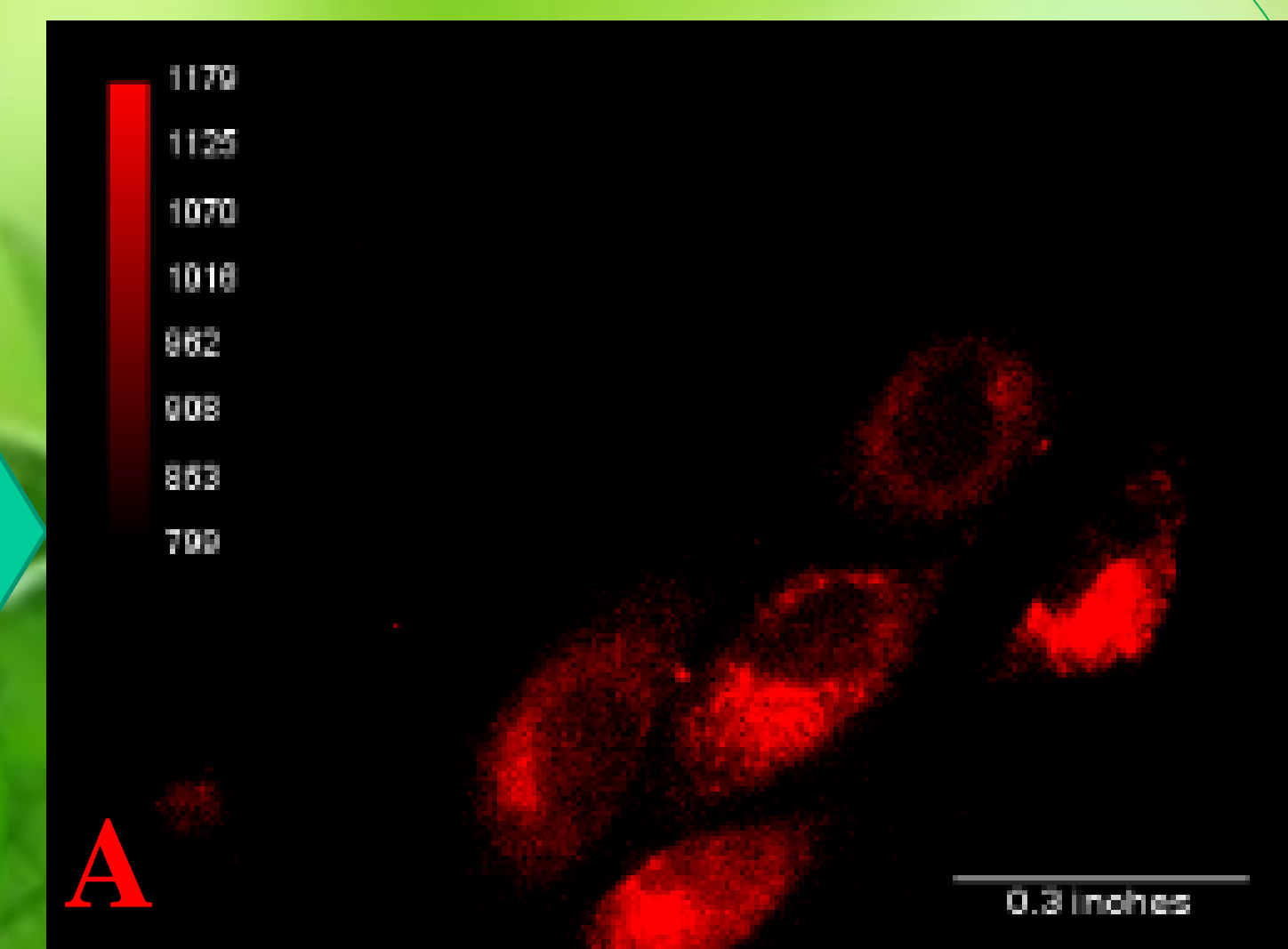


Fa conjugated with zntapc via the γ -carboxyl group

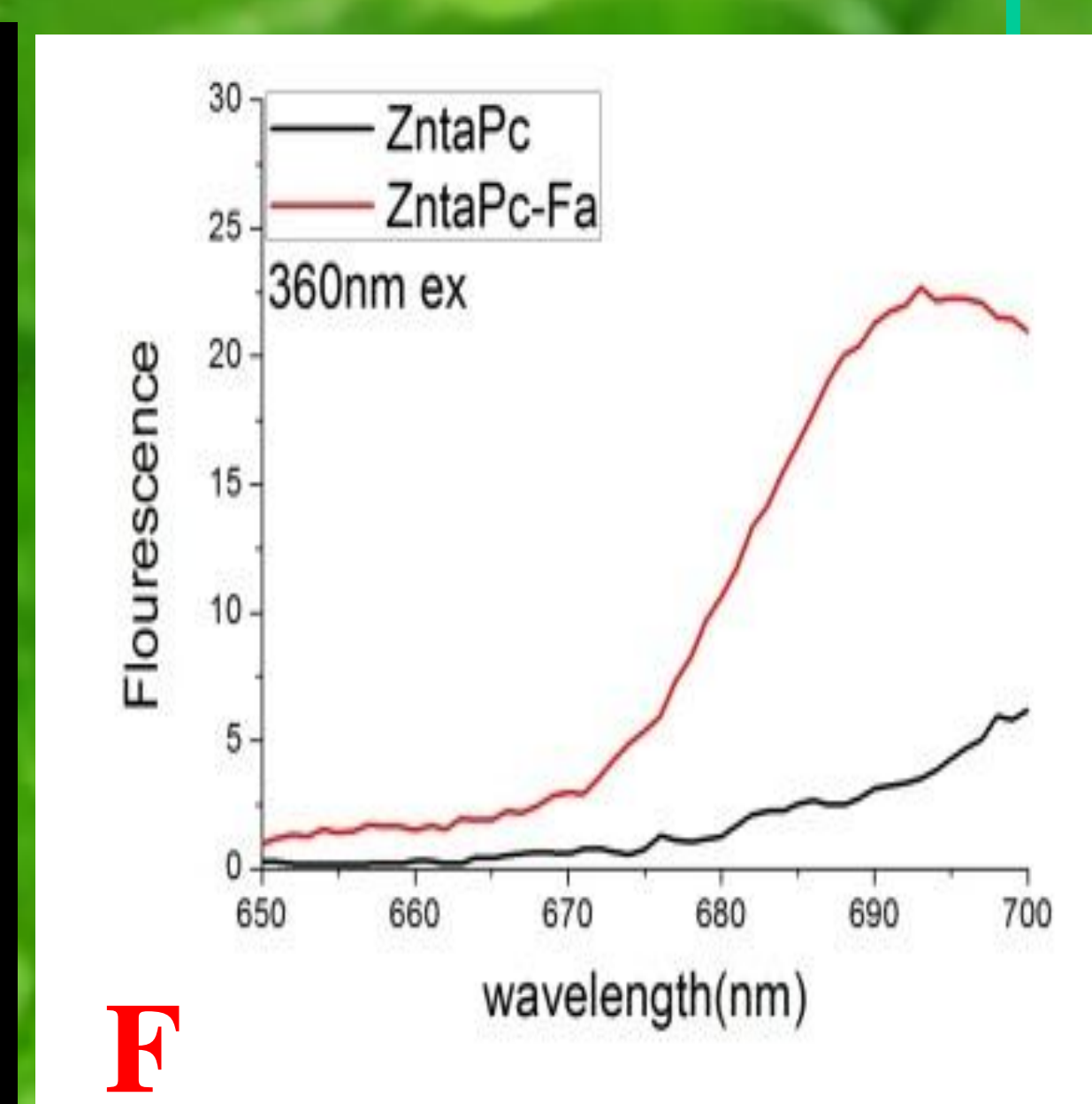
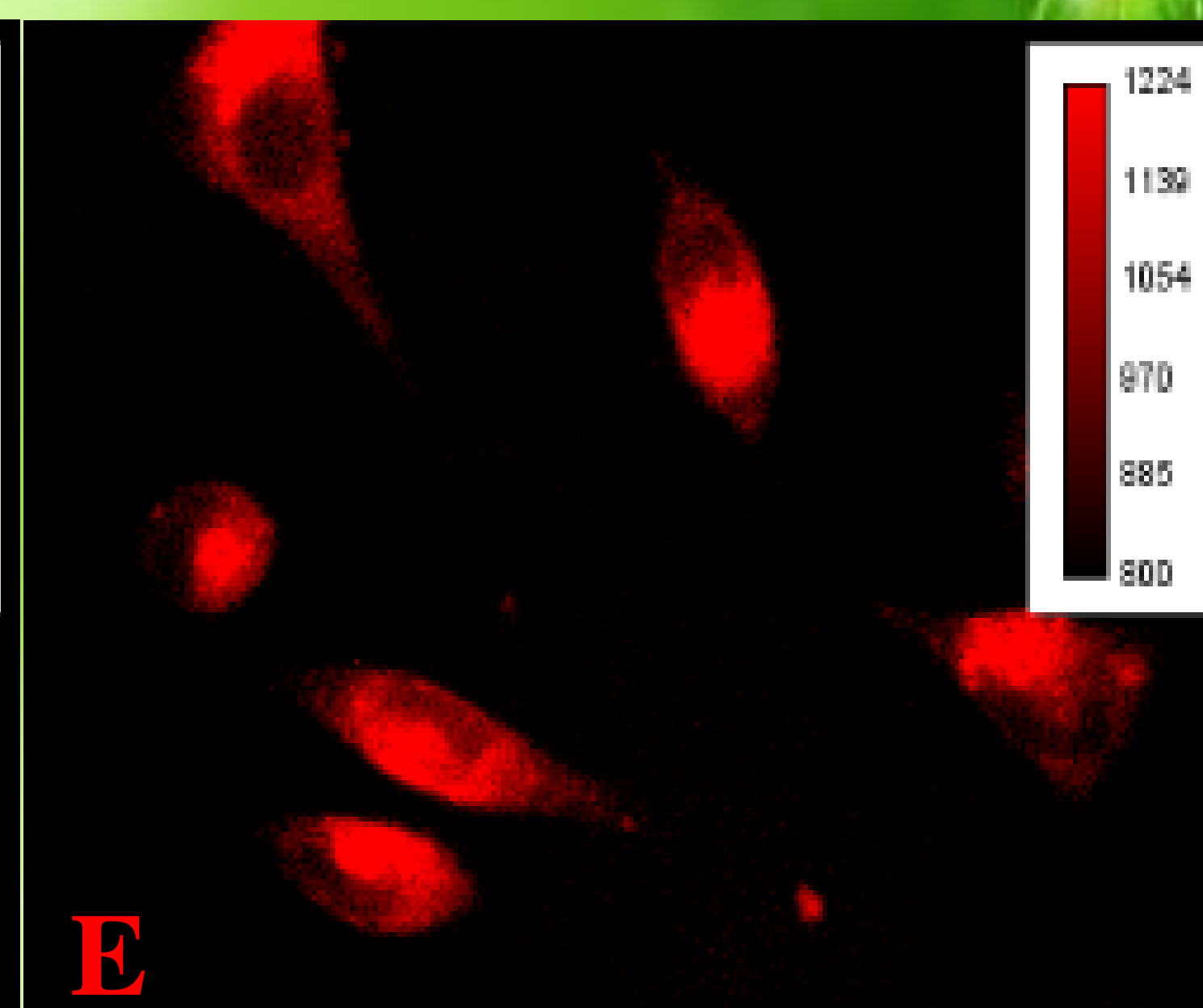
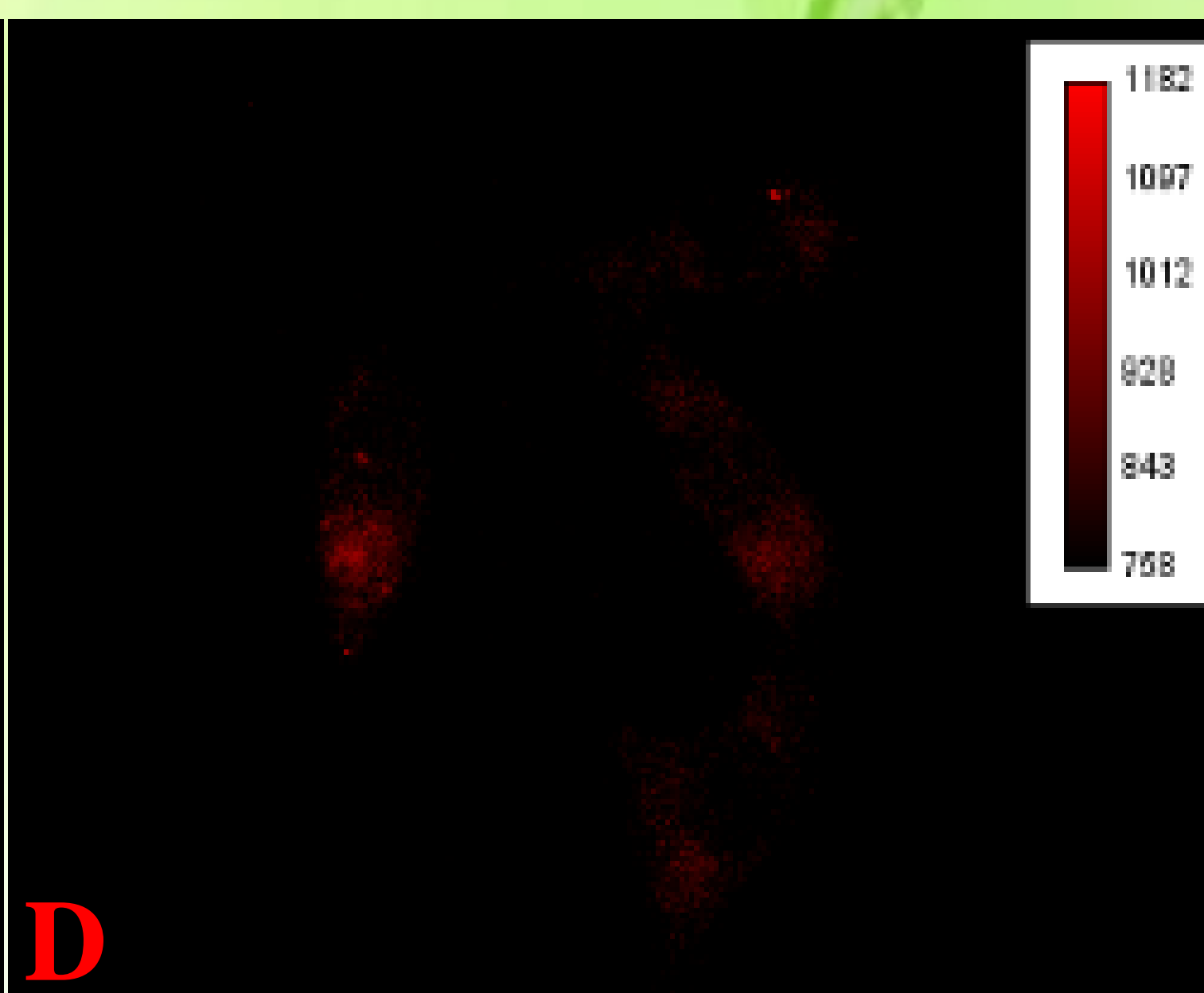
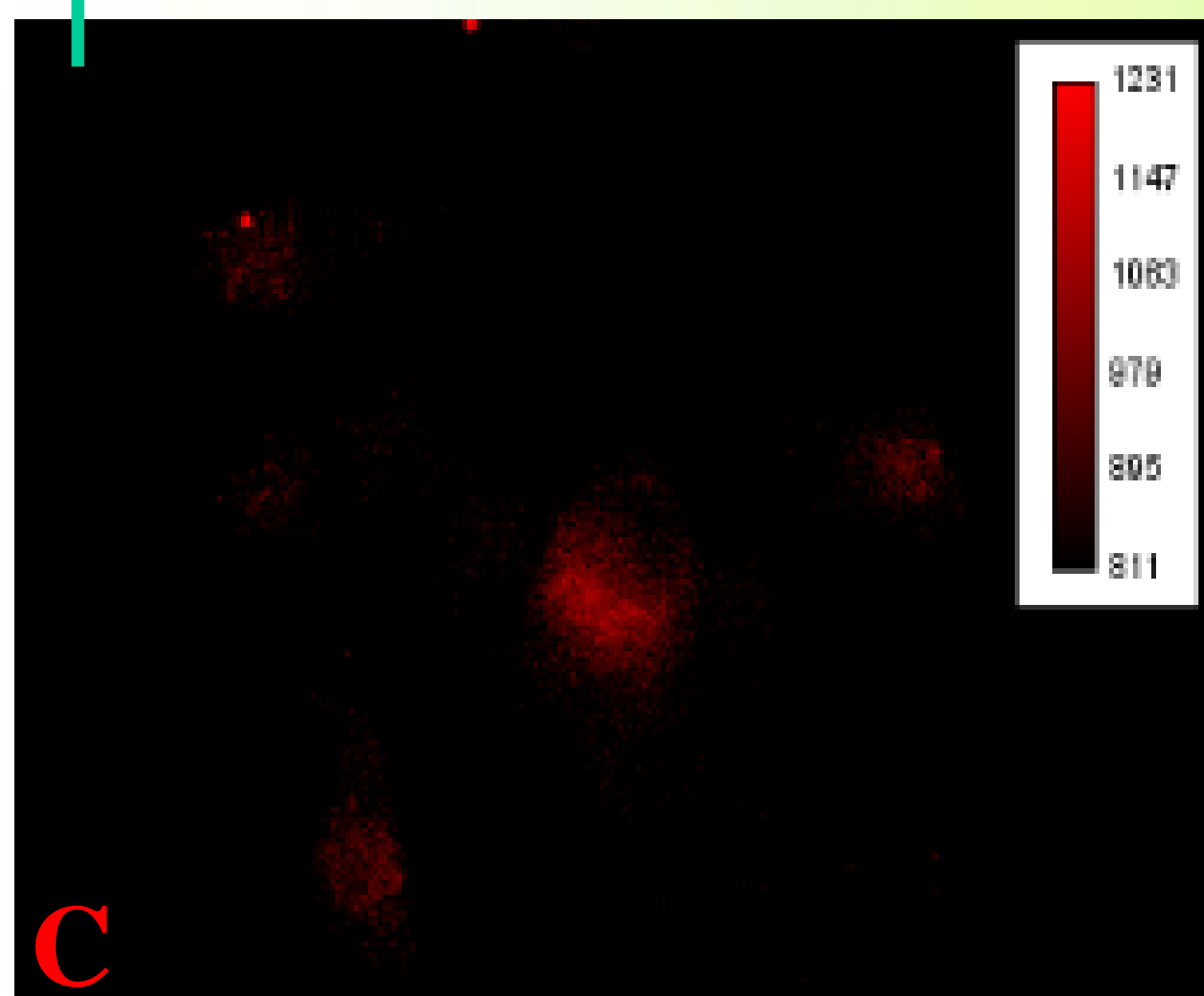
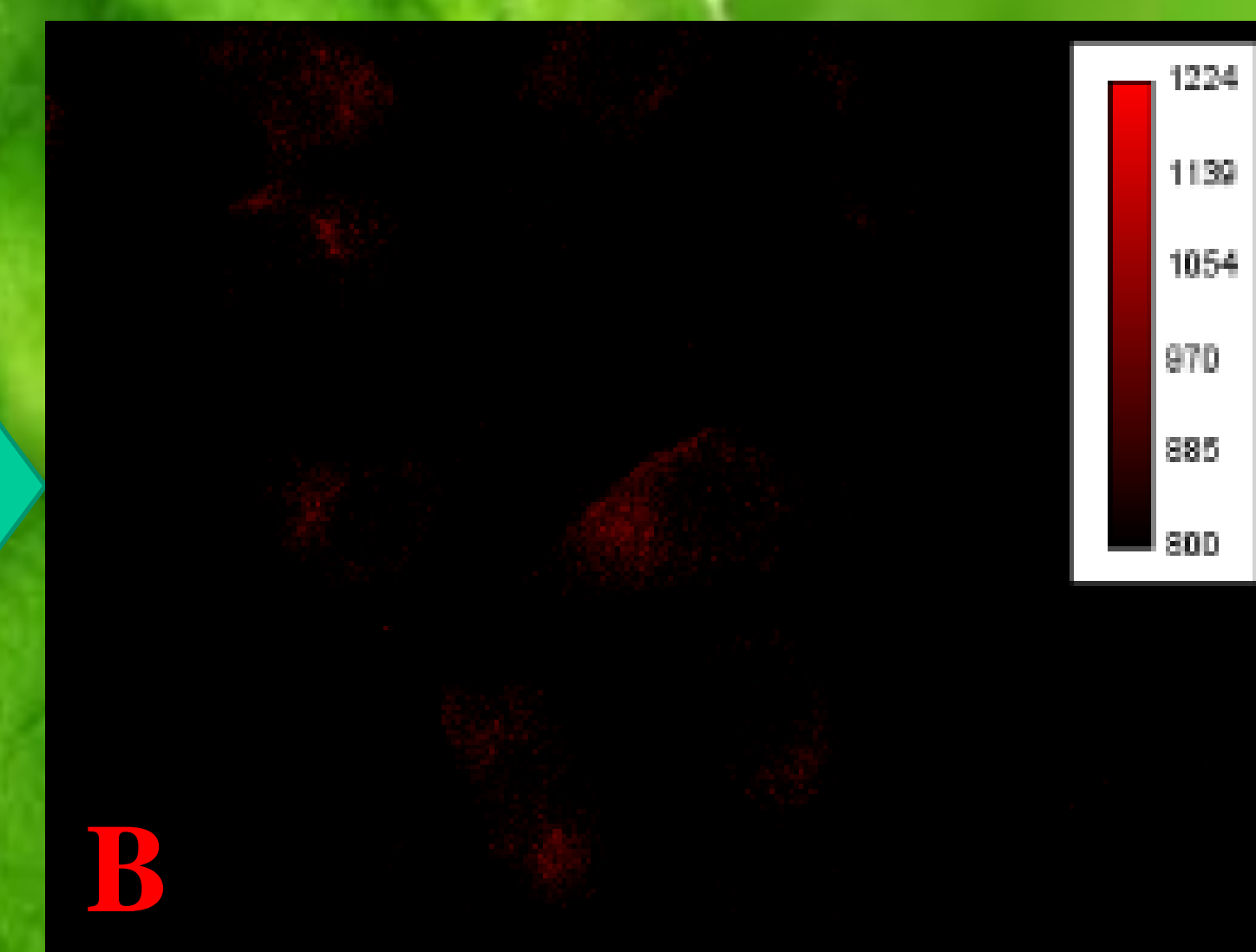
Experiments of Zntapc

Experiments of Zntapc-fa

KB cells were incubated with Zntapc-FA(1uM) for 50min



KB cells were treated with excess fa and then incubated with Zntapc-FA(1uM) for 50min



A549 cells were incubated with Zntapc-FA(1uM) for 50min

KB cells were incubated with Zntapc(1uM) for 50min

A549 cells were incubated with Zntapc(1uM) for 50min

Fluorescence spectrum of Zntapc-fa(5uM) and Zntapc(5uM),excited by 360nm

- Conclusion:**
- 1.A shows clearly that a large quantity of Zntapc-FA had penetrated into the cytoplasm of KB cells .
 - 2.Bshowed that when we pretreated KB cells with excess free folic acid, the cellular uptake of Zntapc-FA by KB cells had cut down.This result indicated that the association of folate with FR mediated the cellular-uptake.
 - 3.F displays that the fluorecence quantum yield of Zntapc-FA is two times of Zntapc.
 - 4.C、 D、 E、 F together reveals that Zntapc-FA could specifically associate with FR—positive cells(KB cells).

Reference:(1) Langer R. Drug delivery and targeting. Nature 1998;392:5-10.

(2) Antony AC. 1992. The biological chemistry offolate receptors. Blood 79:2807–2820

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