Electronic Supplementary Material (ESI) for RSC Advances.
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Supporting Information

Materials:

Fmoc-amino acids were purchased from GL Biochem (Shanghai). Taxol was obtained from Tianfeng (Shenyang, China); Chemical reagents were obtained from Alfa. Alkali phosphatase (30 U/μL) was purchased from Takara Bio. (Dalian, P. R. China); 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) was purchased from Invitrogen (Grand Island, NY); Dulbecco's Modified Eagle's Medium (DMEM)/F12 (GIBCO) and fetal bovine serum (FBS, GIBCO) was purchased from GIBCO (shanghai, P. R. China); Anti-beta Tubulinantibody was purchased from Abcam and Alexa Fluor® 488 Goat Anti-Mouse IgG (H+L) was purchased from Life technologies。

General methods:

ESI-MS spectrometric analyses were tested at the Thermo Finnigan LCQAD System. LCMS-20AD (Shimadzu) and LUMTECH HPLC (Germany) system using a C 18 RP column was used to characterize and purify the compounds. Rheology was performed on an AR 2000ex (TA instrument) system. TEM was done on a Tecnai G2 F20 system. Bio-RAD iMark TM Microplate Reader (Bio-Rad, America) was used for the MTT assay. CLSM image of the HeLa cells were performed on Leica TCS SP8(Germany).

Peptide synthesis:

Standard Fmoc- solid phase peptide synthesis (SPPS) was applied to prepare the peptide. 2-chlorotrityl chloride resin was activated in DCM for 10 minutes and the corresponding N-Fmoc protected amino acids Fmoc-Tyr(H_2PO_3)-OH (1 equivalent to the resin) with side chains carrying phosphoric acid group was added and with DIEPA (4 equivalents). The reaction mixture was stirred at room temperature for 1h. Fmoc group de-protection were performed by 20% of piperidine in N,N 0 -dimethylformamide (DMF). The second amino acid Fmoc-Phe-OH was coupled to the free amino group using O-(Benzotriazol-1-yl)-N,N,N ' ,N' -tetramethyluronium Hexafluorophosphate (HBTU) as the coupling reagent. 95% of trifluoroacetic acid (TFA) with 2.5% of TIS and 2.5% of H_2O was

used to cleave the peptides from the resin for 30 minutes. The solvent was evaporated under reduced pressure and the residue was dissolved in DMF and purified by HPLC. The D-dipeptide was synthesized with the similar procedure.

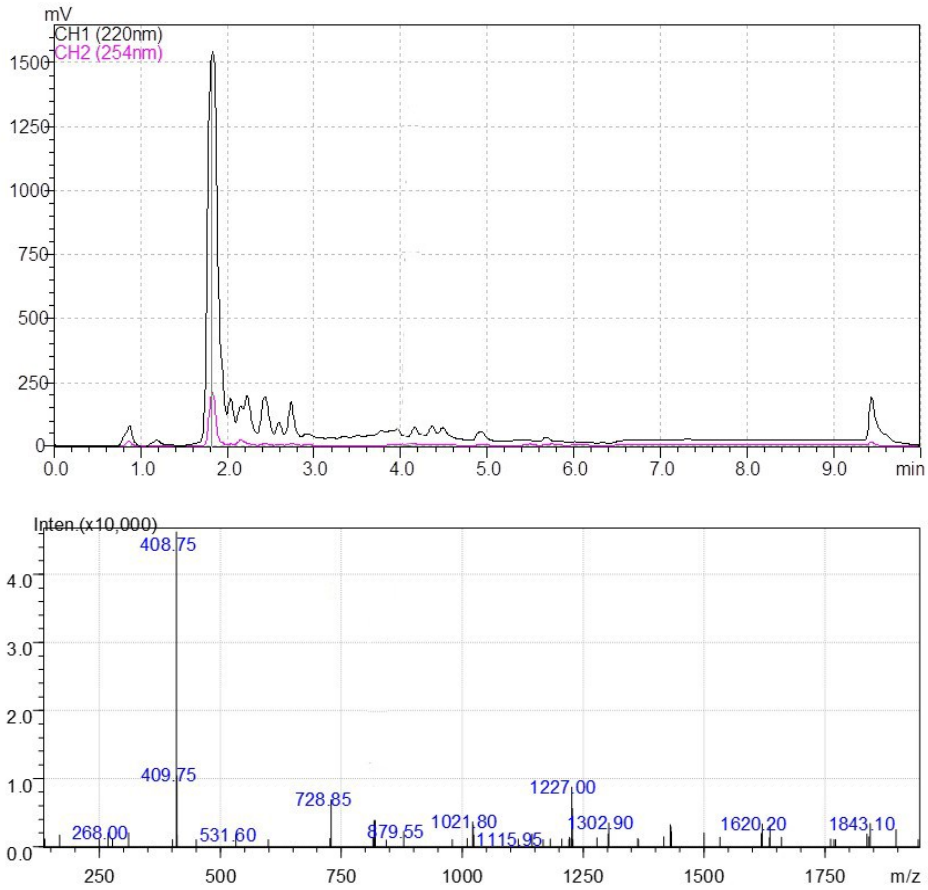
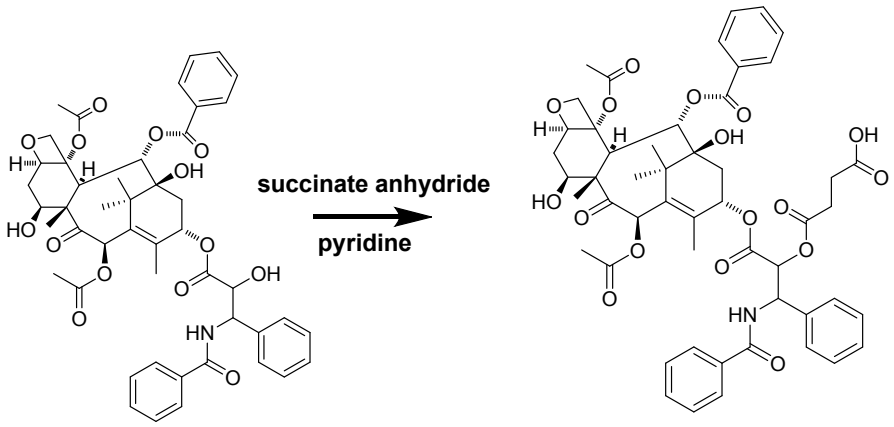


Fig. S-1. LC-MS traces of FpY

Preparation of Taxol-SA:

1 equivalent of Taxol and 1.1 equivalents of succinic anhydride were dissolved in 10 mL of pyridine with stirring at room temperature for 3hs. The solvent was evaporated under reduced pressure and 20 mL of water was added to the residue with stirring for 20 minutes. The dispersion was filtered through a filter paper. The obtained solid was dissolved in Acetone, and water was then added to the solution slowly to form crystals, the dispersion was stored at 4 ℃ overnight, and the crystals were collected by filtration.



Scheme S-1. Synthesis and chemical structure of Taxol-SA

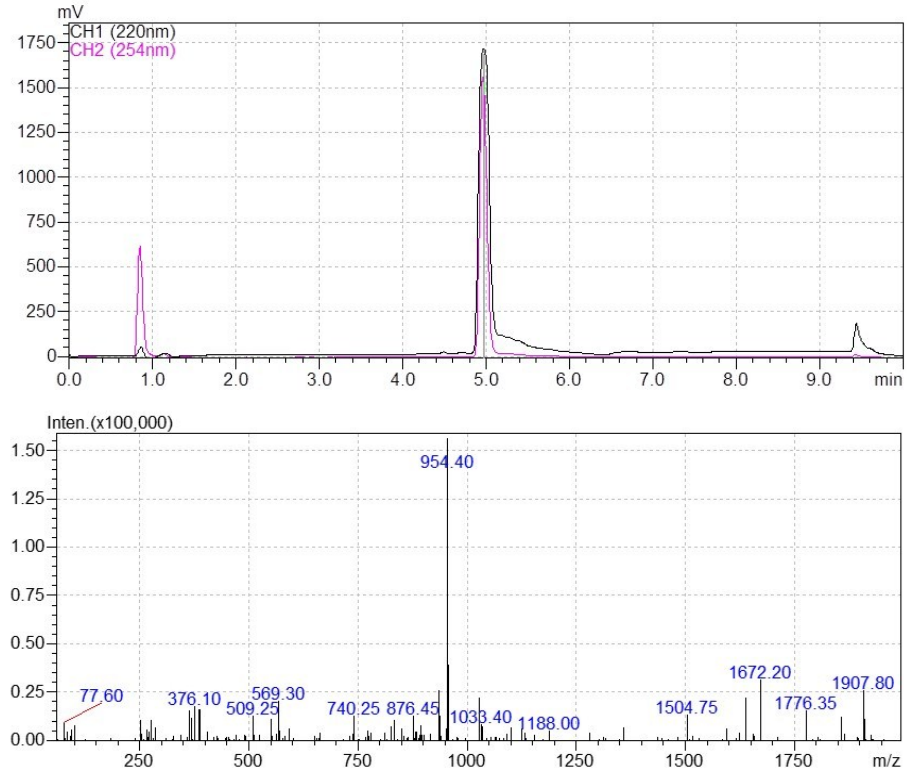
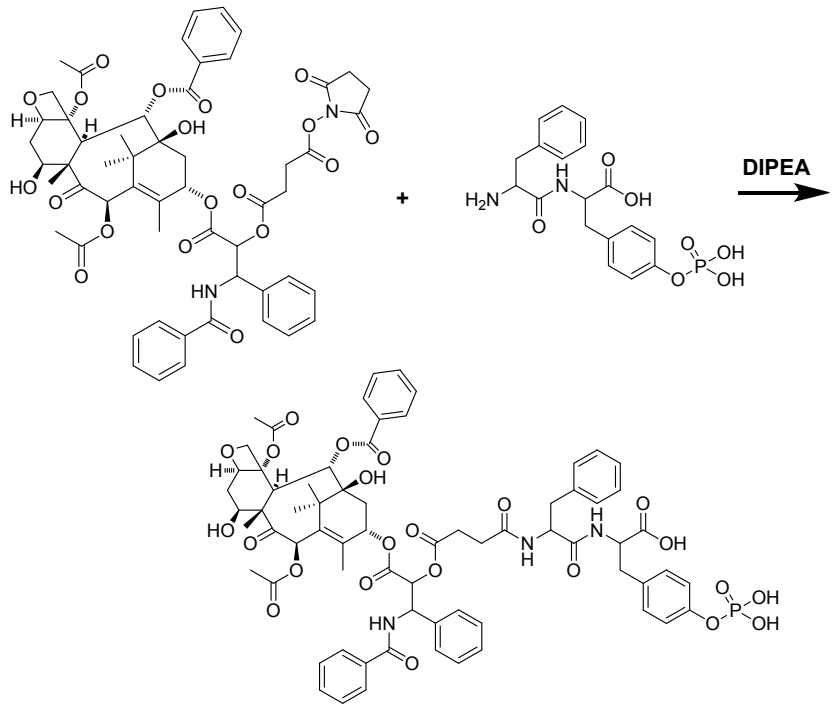


Fig. S-2. LC-MS traces of Taxol-SA

Taxol-SA-FpY synthesis:

1 equivalent of Taxol-SA and 1.1 equivalents of N-hydroxysuccinimide was dissolved in 20 mL of CH_2Cl_2, with adding 2 equivalent of dicyclohexylcarbodiimide stirring at room temperature in dark for 3hs, the reaction mixture was evaporated to dryness in vacuo. 1.5 equivalents of peptide was added to the residue with 5mL of DMF as solvent. The mixture was regulated the pH to 8 with DIEPA then was stirred at room temperature overnight. The reaction mixture was subjected to HPLC purification.



Scheme S-2. Chemical structure of and synthetic route for the L-precursor: Taxol-FpY

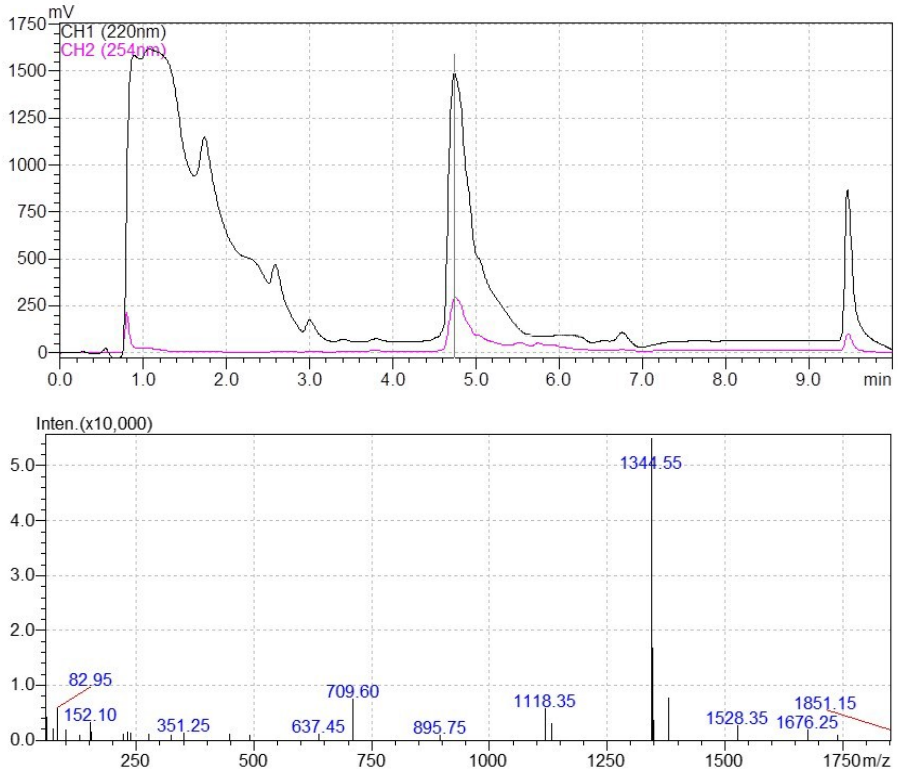


Fig. S-3. LC-MS traces of Taxol-FpY

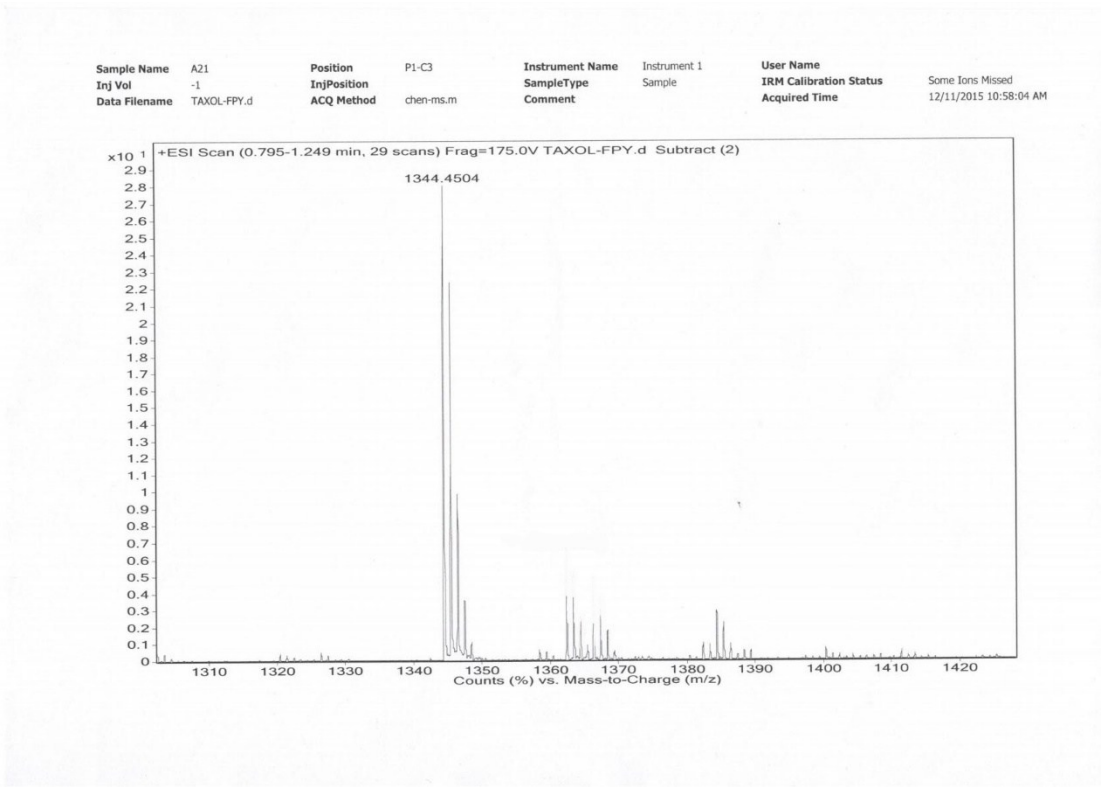


Fig. S-4. HR-MS spectrum of Taxol-FpY

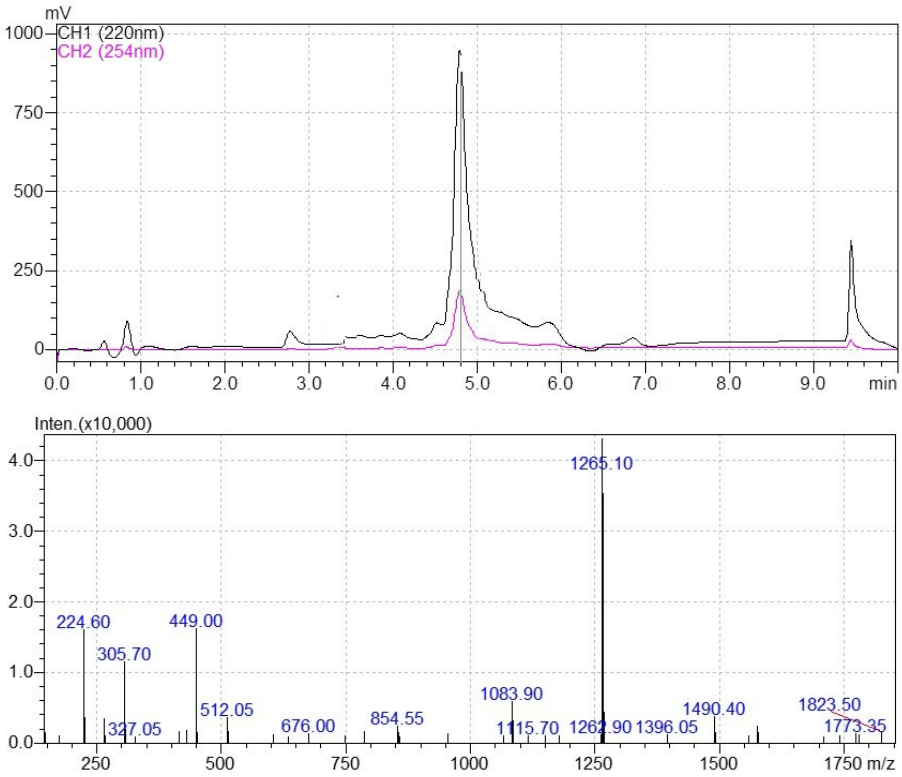


Fig. S-5. LC-MS traces of the L-gelator Taxol-FY

Rheology:

AR 2000ex (TA instrument) system was used for rheology test with 25 mm parallel plates and setting the gap of 300 μm during the experiment. Before the dynamic time sweep, the rheometer was heating for obtaining the physiological temperature 37℃ with the sample. The frequency was set to be 1 rad/s and the strain was 0.1% for the dynamic time sweep. The dynamic strain sweep was characterized in the strain region of 0.1-10 % at the frequency of 1 rad/s. The dynamic frequency sweep in the frequency region of 0.1-100 rad/s and at the strain of 0.1% was used to test the resulting gel formed after the addition of enzyme at 4h time point.

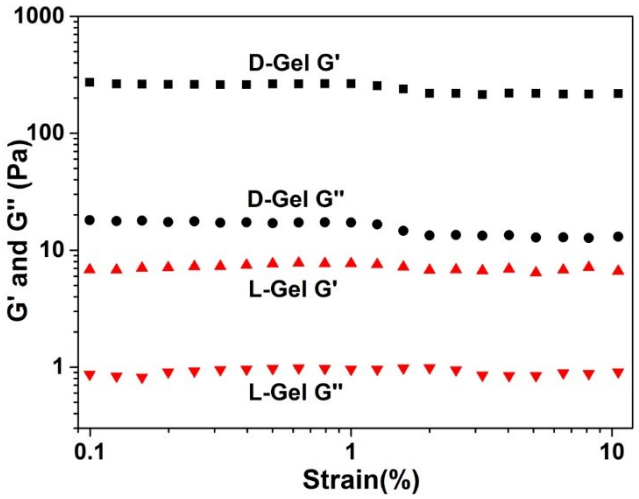


Fig. S-6. Dynamic strain sweep of both gels: L-Gel and D-Gel.

Formation of hydrogels:

2.5 mg of L-precursor or D-precursor was dissolved in PBS buffer (total volume was 500 μL, the pH was adjusted to be 7.4 with Na_2CO_3 solution (50 mg/ml)), 1μL of Phosphatase (1U/ μL) was then added. The mixture was incubated at 37℃ for 10 minutes to form a gel.

MTT assay:

We used the MTT assay to test the IC_{50} values of Taxol, the precursors and gelators. The HeLa, HepG2 or NIH 3T3 cells were seeded in 96-well plates at a density of 7,000 cells per-well and incubated for 24 hours. Then the solutions (100 μL/well) containing a serial of concentrations of the compounds were added into each well replacing the previous medium, and the cells were incubated for another 48 hours. 100 μL of total fresh medium supplemented with MTT reagent (the final

concentration was 0.5 mg/mL) was added to each well to exchange the old medium. After incubating for 4 hours, 100 μL of DMSO was added to each well when the previous medium was removed. The microplate reader (Bio-RAD iMark TM, America) was applied to test the optical density of the solution at 490 nm. The same procedure was repeated for 3 times. The formula: The cell viability percent (%) = OD sample /OD control *100% was used to record the cell viability percent and 50% of that will represent the IC_{50} values of each compound.

Table S-1. IC_{50} values (μM) of each compound for two kinds of cancer cells.

	HeLa		HepG2	
IC_{50} (μM)	mean	SD	mean	SD
Taxol	0.1012	0.0061	0.0713	0.0021
L-Pro	0.1221	0.0149	0.1309	0.0014
L-Gel	0.2023	0.0087	0.1889	0.0105
D-Pro	0.0962	0.0003	0.0646	0.0129
D-Gel	0.2970	0.0123	0.2422	0.0074

Table S-2. IC_{50} values (μM) of each compound for NIH 3T3 cells.

IC_{50} (μM)	**mean**	**SD**
Taxol	40	2.8
L-Pro	60	2.5
L-Gel	109	3.4
D-Pro	50	1.8
D-Gel	85	2.2

Cellular uptake test

The HeLa cells were seeded in 6-well plates at the density of 2×10^5 /well for 24 hours. After the old medium was removed, the fresh medium with 50 μM/L of D-precursor or the gel was added to each well incubating for another 4h. The old medium was removed and cells was washed by PBS buffer for 3 times, 1mL of DMSO was added to the cells with ultrasonic for 30 minutes to dissolve compounds. The cell lysate was collected and centrifuged at 10000r.p. for 5minutes. The supernatant was collected and was subjected to LCMS to test the concentration of taxol in these samples.

Table S-3. Cellular uptake concentrations (μM) of D-Pro and D-Gel at 4h for the HeLa cells.

	4h	
Concentrations (μM)	mean	SD
D-precursor	69.01	1.96
D-gelator	14.73	1.34

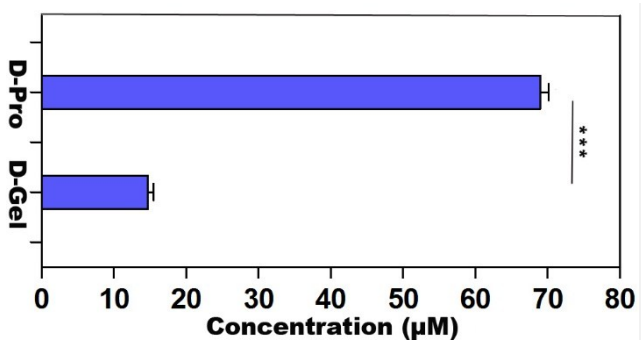


Fig. S-7. Cellular uptake of D-precursor Taxol-FpY and the gel by HeLa cells at 4h time point. (***：$p<0.001$)

Cell Imaging

The HeLa cells (2×10^4 /well) were seeded in 24-well plates with the glass slide and incubated for 24 hours. The medium was then exchanged for 1 mL of fresh complete medium with precursor or Taxol-FpY (200 nM) incubating for different times (0h, 6h, 12h, 24h, 48h). At each time point, the glass slides were collected and were washed with PBS buffer for 3 times and the cells were fixed by PBS with 4% of paraformaldehyde for 20minutes. After washing with PBS 3 times, the first antibody was added which was diluted to the concentration 1% previously and was incubated at r.t. for 2.5hs. The same procedure was done to the second antibody (the final concentration was 0.5%). The nuclei were stained by 4', 6-diamidino-2-phenylindole (DAPI) at r.t. for 3 minutes. The glass slides were scanned under the confocal laser scanning microscopy with excitation at 488 nm and signal collection above 490 nm for FITC and with excitation at 405 nm and signal collection above 410 nm for DAPI.