Sumita Sengupta, J Cancer Sci Ther, 3:7
doi: http://dx.doi.org/10.4172/1948-5956.S1.10

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Microtubule: A target for withaferin-a induced cell death

Sumita Sengupta[1], Kamalini Ghosh[1], Amlan Das[2], Ansuman Lahiri[1] and Gopal Chakrabarti[2]

[1]Department of Biophysics, University of Calcutta, India
[2]Department of Biotechnology University of Calcutta, India

Background: Withaferin-A effectively induces cell cycle arrest and apoptosis by targeting multiple proteins in variety of carcinomas. WA limits migratory and invasive capabilities of cancer cells by interfering with actin cytoskeleton and intermediate filament protein vimentin, but, heretofore, no evidence has been reported whether it can binds to tubulin directly resulting in inhibiting microtubule assembly.

Methods: MTT assay was done to get the IC-50 value of WA for cancer cells, cell cycle arrest was determined by FACS, apoptosis was found by AnnexinV/ PI staining, immune-cytochemistry was performed to check microtubular network within cells, cellular migratory activity was monitored by wound healing assay. *In vitro* tubulin polymerization was studied by light scattering technique, kinetics of WA-tubulin interaction was monitored by fluorometric assays and probable WA-tubulin interaction site was proposed by molecular modeling method.

Results: WA inhibited proliferation of cancer cells, caused S and G2-M arrest as well as apoptosis, caused significant disruption of interphase and spindle microtubules, inhibited microtubule polymerization of purified tubulin *in vitro*. Direct binding of WA to tubulin altered fluorescence of tubulin tryptophan residues, ANS-tubulin complex. Competition assays showed no binding of WA to colchicine binding site of tubulin. Molecular docking simulations indicated preferential binding site of WA to tubulin which is different from colchicine or vinblastin binding sites.

Conclusion: These findings provide strong evidence that WA suppresses microtubule dynamics within cells by directly binding to tubulin, thereby perturbs cancer progression.