

Department of Biotechnology Ministry of Science and Technology Government of India

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Classroom for Advanced & Frontier Education





Series - 32

Date and Time: October 29, 2018 (3:30 JST) Venue: Central 5-41 2F (Meeting Room #1)

Speaker: Shama Prasada Affiliation: MAHE, Manipal, India E-mail: spbhat81@gmail.com



Title: Regulation of Double C2 Like Domain Beta and its Biological Function in Human Cervical Cancer

Double C2 like domain containing protein Beta (DOC2B), ubiquitously expressed isoform of DOC2, is involved in calcium-dependent release of neurotransmitter, trafficking of intracellular vesicles and exocytosis. Herein, we showed that DOC2B is downregulated in cervical cancer via promoter hyper-methylation and acts as tumor growth regulator. The overexpression of DOC2B gene in SiHa cells when compared to controls, showed significantly reduced colony formation, cell proliferation, induced cell cycle arrest and repressed cell migration and invasion (P<0.05). Ectopic expression of DOC2B resulted in anoikis mediated cell death and repressed tumor growth in a nude mice xenograft model (P<0.05). By RT-PCR, western blotting and confocal microscopy, we showed upregulation of CDH1 and downregulation of CTNNB1, CDH2, VIM, TWIST1, TWIST2, CLDN1, SNAI2 and ZEB1 upon ectopic expression of DOC2B. Further, DOC2B, CTNNB1, and CDH1 were also found to be co-localized in the plasma membrane in SiHa-DOC2B as opposed to SiHa-Control. DOC2B expressing cells showed a significant increase in intracellular calcium level (P<0.05), impaired AKT 1 and ERK1/2 signaling and induced actin cytoskeleton remodeling. DOC2B expression induces senescence by induction of CDKN1A and CDKN1B. SA-B gal staining showed significant increase in the percentage of senescent positive cells in DOC2B expressing SiHa cells. Western blot analysis revealed the higher expression of CDKN2A and CDKN1B upon ectopic expression of DOC2B. Our result show that promoter hypermethylation and silencing of DOC2B gene is an early and frequent event during cervical carcinogenesis and whose reduced expression due to DNA promoter methylation may lead to selective cervical tumor growth



SERIES - 32

Thanks for participation!

Dr. Prasad

Speaker: Dr. Shama Prasada K

Topic: Regulation of double C: like domain beta and its biological function in human cervical cancer

Date: 29h October 2018 (1530-

1630 hours JST)

Host: Manipal University, India



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