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Methionine Gamma Lyase 2-AminoButyrate Deaminase (MEGL-2ABD) as a global gene therapeutic agent for cancers

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Methionine is a key nutrient that is required for many metabolic processes/pathways. Particularly methionine serves as the precursor for s-adenosylmethionine (SAM). In addition methionine is the first amino acid residue that is incorporated into many proteins during synthesis. In bacteria methionine is cleaved into methanethiol and 2-aminobutyrate which is deaminated into ∝-ketobutyrate and ammonia by methionine γ-lyase 2-aminobutyrate deaminase (MEGL-2ABD). MEGL-2ABD is absent in mammals. We have molecularly cloned MEGL-2ABD gene into pEGFP-C3 mammalian expression vector and have transfected the construct into various cancer cell lines such as Hela, HEK-AD293-T, BHK-21, methionine dependent prostate PC-3, and independent DU-145 cancer cell lines. Confocal microscopy evinced two interesting observations that occur under methionine deprivation due to *in vivo* MEGL-2ABD. 1. Severe cell aggregation due to quiescence process. 2. Cell death perhaps due to apoptotic signaling. Both of these processes are reversed by propargylglycine an inhibitor of MEGL-2ABD. When MEGL-2ABD gene therapeutic agent was compared to existing anticancer drugs such as methotrexate, MEGL-2ABD had equal or slightly higher cell death effect assessed by MTT assay. Combination of MEGL-2ABD, along with methotrexate, AraC and vesicular stomatitis virus (VSV) had much higher cell death in most cell lines that was tested. Thus, cytoplasmic localization of MEGL-2ABD is a great gene therapeutic agent to control cancer cell division. We are on our way to localize MEGL-2ABD into nucleus and we hypothesize that the effects would be even severe since methionine depletion would affect the fundamentally important primordial process of methionine/SAM dependent mRNA (7methylG) capping.

Biography

K.V. Venkatachalam earned his Ph.D. degree from Texas A&M University and postdoctoral studies from Baylor College of Medicine, Houston, Texas. He was then an IRTA fellow and Scientist for several years at National Institutes of Health, NICHD, Bethesda, MD. He then moved to Florida in 1999 as Associate Professor of Biochemistry and since 2005 he has been Professor of Biochemistry at Nova Southeastern University, Ft. Lauderdale, Florida.

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