

The role for alcohol-induced Golgi fragmentation in progression of prostate cancer

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There is accumulating evidence that chronic alcohol abuse is considered as a risk factor for prostate cancer (PCa), however, neither the precise mechanism of carcinogenesis nor the effect of alcohol on PCa progression have been analyzed. To address these uncertainties, we hypothesized that alcohol intake may alter organization of Golgi apparatus, thus facilitating formation of tumor-associated antigens and activation of the anti-apoptotic pathway mediated by PI3K/Akt. Here, we have found that EtOH metabolite induces Golgi fragmentation in normal and PCa cells both *in vitro* and *in vivo*. Further, EtOH treatment enhances degradation of the largest Golgi matrix protein giantin, which is responsible for the formation of Golgi intercisternal connections and its compact structure. Intriguingly, data indicate that EtOH-induced Golgi fragmentation is accompanied by the reduced level of androgen receptor (AR) and mistargeting of Golgi residential enzymes, which normally compete with pathways leading to formation of cancer-specific glycosyl epitopes. It results in appearance of sialyl-T and sialylLewis^x antigens, one of the characteristics of advanced PCa. Importantly, Golgi fragmentation increases Golgi targeting for both PI3K and P-Akt-1 and depletion of AR accelerates EtOH-induced Golgi fragmentation, but, conversely, cells lacking Akt-1 are less susceptible to this effect of EtOH. We anticipate that alcohol-induced Golgi fragmentation is responsible for activation of PI3K/Akt pathway in the Golgi followed by down-regulation of AR and reciprocal reinforcement of Golgi remodeling, which results in formation of cancer-specific glycosyl epitopes and PI3K/Akt/mTOR-mediated pathways that has been linked to both tumorigenesis and resistance to therapy in PCa. Thus, EtOH-induced Golgi fragmentation may open the door for the cascade of pathways which may result in initiation or progression of PCa.

Biography

Armen Petrosyan has completed his PhD in 2008 from M. Gorky Donetsk National Medical University, (Donetsk, Ukraine) and Postdoctoral studies from University of Nebraska Medical Center (UNMC) in 2014. Currently he is an Assistant Professor at the UNMC. He is the main contributing author of more than 25 papers in peer-reviewed journals.

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