A new pH- sensitive chloride channel in hepatocyte rough endoplasmic reticulum as a specific drug target in hepatocellular carcinoma treatment

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Introduction and Aim: pH gradient in cancer cells is differing from normal cells. It is because of production of lactic acid and hydrolysis of ATP in tumor hypoxic environment. Accommodation with this more acidic situation is crucial for cancer cells viability also metastatic potential. For this reason pH-regulating factors importance is obvious. Our study indicates a new chloride channel in hepatocyte rough endoplasmic reticulum (RER) that was pH-sensitive.

Methods: L-*a*-lecithin was extracted from fresh egg yolk and then utilized to form artificial bilayer lipid membrane in a 150 µ m diameter hole. Rough microsomes derived from RER of rat homogenized liver tissue and Fusion of the vesicles was initiated by gently touching the bilayer. After record in normal pH, record was repeated in acidic pH throe adding HCl, in cis and Trans environments. Statistical analysis was performed based on Markov noise free single channel analysis.

Results: Our results demonstrated that the channel conductance was approximately 304 pS in 200 mM KCl cis/50 mM KCl Trans. The channel open probability (Po) appeared voltage-dependent at -50 to +50 mV and has lower amounts in more

negative and positive voltages. The I-V curve of this channel was linear. This channel was involved in pH regulation in both luminal and cytoplasmic face of ER.

Conclusion: Our results suggest that this new chloride channel may be involved in many physiological functions of ER and could be one of important drug targets in hepatocellular cancer treatment.

Key word: Electrophysiology, Rough endoplasmic reticulum, Chloride channel, Hepatocellular carcinoma.