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Sodium/potassium ATPase and oxidative damage: A new paradigm for development of anti-cancer drugs?

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The Na^+-K^+ pump is a membrane protein that catalyses bi-directional ATP dependent transport of sodium and serves a significant role in cell growth, differentiation and cell death. We have developed a protein-based therapeutic approach to target the pump in cancer cells centered on a novel molecular mechanism for regulation of the pump activity. The mammary tumor protein 8 (or "Mat8") is well recognized and overexpressed in cancers such as prostate, breast and pancreas. Mat8 is recognized for its close association with the Na^+-K^+ pump and its ability to modulate the pump's functional characteristics. We have demonstrated that glutathionylation, a specific oxidative modification of the β1 Na^+-K^+ pump subunit is induced by oxidative stimuli and results in pump inhibition. Reversal of glutathionylation depends on the specific cysteine residues of Mat-8 proteins. We hypothesize that Mat8 proteins protect pump function against inhibition due to the high levels of oxidative stress that cancer cells typically encounter. Preliminary results indicate that overexpression of Mat8 in breast cancer cells protect against treatment-induced oxidative stress. A cysteine-mutated Mat8 "loss-of-function" derivative (Cysless Mat8) can displace wild type within the membrane of Na^+-K^+ pumps and abolish its role in reversing oxidative inhibition of the pump. Results also suggest that silencing wild type Mat8 protein with a loss-of-function derivative may greatly strengthen the efficacy of treatments that increase oxidative stress within tumors. This ongoing study endeavors to develop amalgamated novel treatments for cancer patients while alleviating side effects associated with traditional therapy and improve overall patient well-being.

Biography

Chia-Chi Liu is a Research Fellow at the University of Sydney. She completed her PhD in Chemistry and Bio-molecular Science from Macquarie University. Her core research focus is investigating the relationship between oxidative stress and the sodium pump function. Her research interests include the development of new diagnostic methods for oxidative damage of the pump; the discovery of new drugs for heart disease; and the design of novel therapeutic proteins for cancer treatment. Since 2009, she published more than 20 high impact factor publications with peer-reviewed journals and is the inventor for an innovative patent in diagnostic technology.

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