McNair Scholars Journal

Volume 21 | Issue 1 Article 9

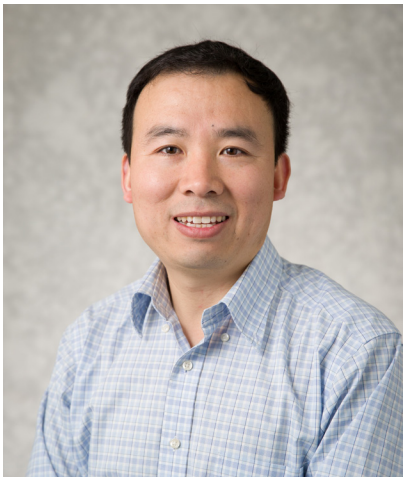
2017

Characterizing the Cellular Function of Protein Phosphatase 1 Isoforms

Christian Miller
Grand Valley State University

Characterizing the Cellular Function of Protein Phosphatase 1 Isoforms*

Christian Miller
McNair Scholar



Ruijie Liu
Faculty Mentor

A protein phosphatase is an enzyme that removes a phosphate group from a specific amino acid residue on a target protein substrate. This protein phosphatase-regulated dephosphorylation is an important mechanism for many different processes and regulations inside mammalian cells (Rebleo, 2015). One of the major classes of protein phosphatases is the Ser/Thr-specific family. These phosphatases target the amino acids serine and threonine. There are many different members of the Ser/Thr-specific family, but the phosphatase that this study focuses on is called protein phosphatase 1 (PP1). PP1 has three different isoforms: alpha, beta, and gamma. These isoforms share roughly 90% of their amino acid composition (Liu, 2015). The main distinguishing factor between the isoforms are the unique sequences that each has at the C and N termini (Liu, 2015). Previous studies of neural cells have shown that PP1 may play a role in regulating and inactivating the nuclear transcription factor, cAMP regulatory element binding (CREB) (Bernhard, 2001). Other studies have indicated that PP1 may have an indirect function in the inactivation histone deacetylase, a group of enzymes that help regulate genes by removing an acetyl group from DNA histones (Gao, 2009). It is not yet known which of the PP1 isoforms is the main agent for dephosphorylation in these cases. Other studies have also shown that PP1 may affect heart failure and that inhibition of PP1 beta appears to benefit the performance of cardiac contractility and relaxation in the short-term (Liu, 2015).

The primary purpose of this study is to investigate whether the alpha and beta isoforms of protein phosphatase 1 exhibit specific localization in either the nucleus or the cytoplasm of cells. Furthermore, we wanted to examine the role that protein phosphatase 1 plays in terms of gene regulation and expression in the nucleus, as well as investigate other possible substrate targets. From this study, we have evidence that the beta isoform of PP1 is localized to the nucleus and that the alpha isoform is localized to the cytoplasm. Additionally, we also found that PP1 beta is the isoform that is primarily responsible for the regulation of histone deacetylase 7 in the nucleus. We also considered the effect that the overexpression of the isoforms would have on the enzyme phospholamban (PLB), which is an enzyme that plays a regulatory role in cardiac myocytes (Koss 1996). We found that the overexpression of PP1 alpha decreased the overall phosphorylation level of PLB, whereas PP1 beta had no effect.

Possible implications of this study include providing a better idea of the mechanisms of PP1, which grants us a clearer understanding of the functions that PP1 may have in cardiac cells. Moreover, this study may provide the baseline of knowledge necessary for future potential therapeutic interventions to treat heart disease. For example, if PP1 isoforms are also demonstrated to be localized in the nucleus to influence gene expression for cardiac disease, we can inhibit its activity by disrupting its binding with regulatory proteins while their cytosolic activities are still intact.

*This scholar and faculty mentor have requested that only an abstract be published.