

1. **Faculty Name: S.M.Periyasamy**
2. **Academic Rank: Associate Professor**
3. **Department: Medicine**
5. **Name(s), Academic Rank, and Department(s) of any Co-Investigators: Joseph Shapiro, Professor, Medicine.**
6. **Project Title: Signaling Pathways for Cell Cycle regulation by Marinobufagenin (MBG)**
7. **Brief Summary/Description of Project: (Limit this section to one page. Include a well-defined Specific Aim for the student's project and related methodology. DO NOT append a copy of your grant application.)**

Marinobufagenin (MBG), a cardiotoxic steroid found in the skin of toads, is also present in humans and rats. It earned the name "endogenous digitalis like substance" because it meets all the criteria for being a digitalis like substance. One of the properties of digitalis like substances is cardiovascular remodeling upon interaction with the Na/K-ATPase. Here, we investigated whether the MBG also produces cardiac remodeling. In rats with experimentally induced chronic renal failure (via 5/6th nephrectomy), we measured plasma MBG levels, and evaluated cardiac function. We found that plasma levels of MBG were elevated significantly in response to partial nephrectomy. The experimentally induced chronic renal failure also produced cardiac fibrosis and impairment of left ventricular function in these rats. Moreover, immunization of rats against MBG attenuated the MBG-induced cardiac fibrosis and improved left ventricular function. In view of these findings, we suggest that MBG plays a role in cardiac dysfunction seen in the animal model of chronic renal failure. Collectively, our findings suggest that MBG, an endogenous digitalis like substance, could play a role in cardiovascular remodeling that occurs in various cardiovascular diseases. Although the effect of MBG on cardiac remodeling has been studied, the role of MBG on the remodeling of vascular system has not been studied. A recent study has shown that MBG in very low concentration by interacting with sodium-pump, produced proliferation of smooth muscle cells derived from the vascular tissue. This suggests that MBG could play a role in cell cycle regulation. However, the molecular mechanisms involved in cell cycle regulation have not been examined.

It is well established that in several cell types including vascular smooth muscles, PI3-kinase and AKT is a key mediator of cell proliferation. Therefore, the aim of the present study is to examine the potential role and mechanisms of MBG signaling through PI3-kinase/AKT pathway in cell cycle regulation using rat vascular smooth cell line, A7r5.

8. Describe Student's Role and Responsibilities.

- 1) The student's role in this project is to grow the cells to sub-confluence to confluence and prepare cell lysate and determine the protein content of cell lysate.
- 2) Separate the proteins of the cell lysate by gel electrophoresis and transfer the proteins to a membrane.
- 3) Detect the protein(s) of interest (PI3-kinase and AKT-kinase) on the membrane using a specific antibody for that protein.
- 4) Interpret the data with the help of advisor

9. Special Qualifications Required (NAME OF STUDENT, IF IDENTIFIED). None