DiaComp Pilot & Feasibility Program - 2014

There is strong evidence that diabetic complications are linked via dysregulation of common pathways. The Diabetic Complications Consortium (DiaComp) promotes communication and collaboration between research communities investigating similar pathologic mechanisms in different organs by organizing and annual scientific meeting and funding new basic and translational research activities.

The DiaComp P&F program solicits proposals that advance the mission of DiaComp and welcomes applications that are either general in nature or that target specific areas of interest.

Applicant: CHAUDHURY, ARUN

Project Title: Defects in transcytosis may cause multiorgan diabetic complications

INDIVIDUAL CRITERIA SCORES

Please provide individual scores for the following 5 review criteria. Scores should range from 1-9 with 1 being outstanding.

- 1) Significance 3
- 2) Investigator(s) 4
- 3) Innovation 6
- 4) Approach 5
- 5) Environment 6

WRITTEN COMMENTS - please address the following points:

•Does the proposal have high scientific merit

Will the proposal further the mission of the DiaComp

·Will the proposal significantly advance/impact the field in the complication(s) being addressed

Our knowledge of the pathogenesis of multiorgan diabetic complications remains very limited. Therefore, innovative research targeting the potential pathomechanism to help to understand the nature of many severe complications would allow the development of possible better, targeted therapeutic interventions, and represents a significant, urgent and unmet clinical need.

Thorough testing of transcytosis defects in multiorgan diabetic complications, is going to have a quite significant approach to pathogenesis of this debilitating disease. Hence, it is anticipated that current grant could bring such meaningful answers, but some clarifications and adjustments are necessary to be considered before its implementation.

Based on Dr. Chaudhury's record of publications and grants, investigator is suitable to conduct this study. A research environment where PI is employed seems to have an acceptable support securing successful implementation of all research aims and objectives listed in this study protocol.

On the other hand, it is very unusual to be "a solo investigator" on any of the research projects. Unfortunately, it is not clear to me, if other collaborates are expected to play some roles in this investigation. There is a disproportional difference between cost of chemical and purchase of animals, versus other budgetary request.

This study is of some innovative nature, as it is going to test the role of myosin Va protein and its specific transcription factor "Snail" expression as well as membrane localized nNOS in myenteric motor neurons, pancreatic tissue and skeletal muscles in diabetic mice.

However, employed methodology may not have adequate sophistication in detection of changes at the subcellular level.

These tests conducted in mice model of diabetes have still to be discussed in terms of their translational capacity to human scenario based on other results published and obtained from studies that were explored both in animal model and in clinical scenario.

Mentioned above potential challenge may significantly hamper an approach within this study protocol, therefore requires clarification and potential further adjustments at the bench.

OVERALL IMPACT SCORE

Please provide an overall 'impact' score for the proposal (1-9). Feel free to weight the 5 individual scores as you

see fit. It does NOT have to be the average of the 5 scores.

OVERALL IMPACT SCORE 5