UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002.

Final Project Completion Report of the work done on the Major Research Project.

Project reference no. **F. No. 43-61/2014 (SR)**

Project Title: ***Asporin function in aortic endothelial cell mineralization and calcification***

Project duration: **01.07.2015 to 30.06.2018**

Principal Investigator: **Dr. Santanu Chakraborty**

University: **Presidency University, Kolkata**

Annexure- VIII

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Annual/Final Report of the work done on the Major Research Project.
(Report to be submitted within 6 weeks after completion of each year)

1. Project report No. 1st /2nd /3rd/Final **Final**

2. UGC Reference No.F. **No. 43-61/2014(SR)**

3. Period of report: from **01.07.2015** to **30.06.2018**

4. Title of research project **"Asporin function in aortic endothelial cell mineralization and calcification"**

5. (a) Name of the Principal Investigator **Dr. Santanu Chakraborty**

   (b) Deptt. **Life Sciences**

   (c) University/College where work has progressed **Presidency University**

6. Effective date of starting of the project **01/07/2015**

7. Grant approved and expenditure incurred during the period of the report:

   a. Total amount approved Rs. **17,24,535**

   b. Total expenditure Rs. **15,83,461**

c. Report of the work done: (Please attach a separate sheet)

i. Brief objective of the project: **To determine Asporin function in aortic valve mineralization and calcification disease process using avian model system**

ii. Work done so far and results achieved and publications, if any, resulting from the work (Give details of the papers and names of the journals in which it has been published or accepted for publication: **As hypothesized, all the generated data (please see the attached final report) have been compiled into one manuscript and submitted in the journal of Cell biology International in December, 2018.**

iii. Has the progress been according to original plan of work and towards achieving the objective. if not, state reasons. **Yes, the progress is in accordance with all overall plans of the proposed**

research/experimental works and towards achieving the prime objective.

iv. Please indicate the difficulties, if any, experienced in implementing the project. **No such difficulties were experienced in implementation of the project.**

v. If project has not been completed, please indicate the approximate time by which it is likely to be completed. A summary of the work done for the period (Annual basis) may please be sent to the Commission on a separate sheet. **Yes, the project is completed and the resulting manuscript is submitted in the journal of Cell Biology International in December 2018.**

vi. If the project has been completed, please enclose a summary of the findings of the study. One bound copy of the final report of work done may also be sent to University Grants Commission. **Please find the attached a summary of the findings.**

vii. Any other information, which would help in evaluation of work done on the project. At the completion of the project, the first report should indicate the output, such as (a) Manpower trained (b) Ph. D. awarded (c) Publication of results (d) other impact, if any

a) Manpower trained: **Ms. Anisha Polley**
b) Ph.D. awarded: **Ms. Anisha Polley is working on this proposal and this is a major part of her ongoing PhD program. She is successfully defended her 5000 words pre-synopsis towards her PhD thesis in November, 2018.**
c) Publication of results: **Manuscript is submitted in the journal of *Cell Biology International* in December 2018.**

(PRINCIPAL INVESTIGATOR)

Dr. Santanu Chakraborty
Assistant Professor(Life Sciences)
PRESIDENCY UNIVERSITY, KOLKATA

08/02/2019

(REGISTRAR/PRINCIPAL)

Registrar
Presidency University
Kolkata

(Seal)

(CO-INVESTIGATOR)

Annexure – IX

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PROFORMA FOR SUBMISSION OF INFORMATION AT THE TIME OF SENDING THE FINAL REPORT OF THE WORK DONE ON THE PROJECT

1. Title of the Project: **Asporin function in aortic endothelial cell mineralization and calcification**

2. NAME AND ADDRESS OF THE PRINCIPAL INVESTIGATOR: **Dr. Santanu Chakraborty, PhD, Assistant Professor of Zoology, Heart development & diseases laboratory, Department of Life Sciences, Presidency University (Baker Building, 2nd floor), 86/1-college street, Kolkata-73**

3. NAME AND ADDRESS OF THE INSTITUTION: **Presidency University, 86/1 College Street, Kolkata-700073**

4. UGC APPROVAL LETTER NO. AND DATE: **F. No. 43-61/2014(SR) dated 12/08/2015**

5. DATE OF IMPLEMENTATION: **01/07/2015**

6. TENURE OF THE PROJECT: **3 years**

7. TOTAL GRANT ALLOCATED: Rs. **17,24,535**

8. TOTAL GRANT RECEIVED: Rs. **16,05,141**

9. FINAL EXPENDITURE: Rs. **15,83,461**

10. TITLE OF THE PROJECT: **Asporin function in aortic endothelial cell mineralization and calcification**

11. OBJECTIVES OF THE PROJECT: **Aim1: Identify if aortic endothelial cells overexpressing Asporin is protected against calcification upon induction of osteogenesis in culture. Aim 2: Determine the effected signaling pathway downstream of Asporin to inhibit mineralization and calcification**

12. WHETHER OBJECTIVES WERE ACHIEVED: **Yes, both the objectives were achieved. For proposed aim 1, we have successfully established adult aortic valve interstitial cell culture system with indicated Asporin expression. Next, Osteogenic induction was induced for mineralizarion and calcification process in cultured cells. As hypothesized, direct addition of human recombinant Asporin protein inhibits the mineralization process. In addition, for proposed aim 2 and to better understand the effected signaling pathways, we have shown that Wnt/β-catenin signaling promotes mineratization process in cultured aortic valve cells, but addition of Asporin inhibits such disease process in vitro. In addition, our generated data also implicated that Asporin might acts upstream of multiple osteogenic promoting pathways to inhibit mineralization and calcification. (Please refer to the attached final report for details)**

13. ACHIEVEMENTS FROM THE PROJECT: **The major achievements are follows: 1. Establishment of adult aortic valvular cell culture system; 2. Establishment of osteogenic induction in cultured aortic valve cells; 3. Identification of Asporin as a natural anti-calcific molecule in the context of adult heart valve calcification process.; 4. Identification of Asporin as a negative regulator of multiple calcification promoting pathways including Wnt/β-catenin and Bmp-Smad1/5/8 signaling; 5. The use of Asporin as an anti calcific molecule might be an attractive therspeutiv approach in adult heart valve calcification process in clinical settings.**

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14. SUMMARY OF THE FINDINGS: **Worldwide, calcific aortic valve disease is one of the leading causes of morbidity and mortality among patients with cardiac abnormalities. Aortic valve mineralization and calcification are the key events of adult calcific aortic valve disease manifestation and functional insufficiency. Due to heavy mineralization and calcification, adult aortic valvular cusps show disorganized and dispersed stratification concomitant with deposition of calcific nodules with severely compromised adult valve function. Interestingly, shared gene regulatory pathways are identified between bone forming cells and heart valve cells during development. *Asporin*, a small leucine rich proteoglycan, acts to inhibit mineralization in periodontal ligament cells and is also detected in normal murine adult aortic valve leaflets with unknown function. Therefore, to understand the Asporin function in aortic cusp mineralization and calcification, adult avian aortic valvular interstitial cell culture system is established and osteogenesis has been induced in these cells successfully. Upon induction of osteogenesis, reduced expression of *Asporin* mRNA and increased expression of bone and osteogenesis markers are detected compared to cells maintained without osteogenic induction.**

15. CONTRIBUTION TO THE SOCIETY: **Importantly, treatment with human recombinant Asporin protein reduces the mineralization level in osteogenic media induced aortic valvular interstitial cells with the concomitant decreased level of Wnt/β-catenin signaling. Overall, all these data are highly indicative that *Asporin* might be a novel bio-molecular target to treat patients of calcific aortic valve disease over current cusp replacement surgery.**

16. WHETHER ANY PH.D. ENROLLED/PRODUCED OUT OF THE PROJECT: **Yes. Ms Anisha Polley (enrolled with Registration Number: R-14RS18210033 and suceessfully defended her 5000 words pre-thesis synopsis)**

17. NO. OF PUBLICATIONS OUT OF THE PROJECT :

- **Polley A, Khanam R, Sengupta A and Chakraborty S. Asporin inhibits adult aortic valve interstitial cell mineralization induced by osteogenic media and Wnt signaling activation in vitro. Submitted in *Cell Biology Interntional (Under review)***

(PRINCIPAL INVESTIGATOR)

Dr. Santanu Chakraborty
Assistant Professor(Life Sciences)
PRESIDENCY UNIVERSITY, KOLKATA

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