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1. Project Number : 5395
2. Title of the Project: ROLE OF CONNEXINS IN CARDIAC FIBROBLAST PHENOTYPE TRANSFORMATION AND EXTRACELLULAR MATRIX SYNTHESIS IN CARDIAC DISEASES
3. Funding Agency Name: ICMR
4. Project Reference Number provided by the Funding Agency: 2019-0776-CMB/adhoc/BMS
5. Principal Investigator (Name & Address): Dr. Neethu Mohan, Scientist E, Division of Cellular and Molecular Cardiology, Department of Pathology, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum, India-695011. Email: neethum@sctimst.ac.in
6. Co-Investigators (Name & Address): Dr. Deepti A N, Associate Professor, Department of Pathology, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum, India-695011. Email: akkihebbal@sctimst.ac.in
7. Implementing Institution: SCTIMST
8. Collaborating Institutions: None
9. Date of Commencement: 28-8-2019 as per award letter, Actual initiation of work on 23-07-2020 on receipt of first-year fund
10. Duration: 2 years
11. Date of Completion: 27-8-2022
12. Objectives as approved: (a) Is Connexin43 under the regulatory control of the collagen receptors (b) Does Connexin43 regulate phenotypic transformation of cardiac fibroblasts into myofibroblasts (c) Corroboration of the findings in an in vivo model (d) Does Connexin43 have a role in regulating the expression of microRNAs that control cardiac fibroblast differentiation
13. Deviation made from original objectives if any, while implementing the project and reasons thereof: None
14. Field/Experimental work giving full details of summary of methods adopted, data collected supported by necessary tables, charts, diagrams and photographs :

Detailed results can be submitted only after the publication of the data
15. Detailed analysis of results: Detailed results can be submitted only after publication of data
16. Summary sheet of not more than 2 pages under following heads :

ROLE OF CONNEXINS IN CARDIAC FIBROBLAST PHENOTYPE TRANSFORMATION AND EXTRACELLULAR MATRIX SYNTHESIS IN CARDIAC DISEASES

Cardiac fibroblasts play an important role in repair and remodeling of the heart after myocardial infarction. Cardiac fibroblasts are activated in response to Angiotensin II/TGF β , in the injured myocardium. They proliferate, transform into myofibroblasts, deposit collagen, and avoid cardiac wall rupture. However, excessive collagen deposition by myofibroblasts during adverse cardiac remodelling leads to myocardial fibrosis that can compromise cardiac function. CX43 expression is impaired after cardiac injury which leads to conduction abnormalities. Cardiac diseases such as atrial fibrillation, hypertrophy, abnormal impulse propagation, arrhythmia and heart failure is associated with alterations in the distribution of Cx43. However, how connexins are regulated in cardiac fibroblasts are not investigated. Hence this study aims to investigate

whether connexins are under the regulatory control of collagen receptors and to correlate the findings invitro in an invivo model. Cardiac fibroblasts were isolated, characterized, and activated to myofibroblasts. The regulatory relationship between collagen receptor and Cx43 was established through silencing & over-expression studies. The molecular mechanisms were elucidated. This data was correlated in wild and knock-out models of mouse heart tissue sections. Invitro findings were further correlated in an invivo model.

17. Contributions made towards increasing the state of knowledge in the subject :

18. Conclusions summarising the achievements and indication of scope for future work :

19. Science and Technology benefits accrued :

- a. List of research publications with complete details :
 1. Sruthi Radhakrishnan, Neethu Mohan, DDR2 mediated regulation of CX43: Implications for conduction abnormalities in cardiac fibrosis, Heart Failure Conflux, 5- 6 February, 2021 organized by Heart Failure Association of India, SCTIMST, IACS & ICMR.
 2. Neethu Mohan, Therapeutic targets for Cardiac Fibrosis. Indo-US Conference on Recent biochemical approaches in therapeutics, February 1-3, 2023, University of Kerala, Trivandrum.
 3. Publications to be communicated
- b. Manpower trained on the project :
 - i. Research Scientists or Research Fellows: One
 - ii. No. of PhD's produced: One PhD is ongoing as part of this work
 - iii. Other Technical Personnel trained: 3 project fellows
- c. Patents taken, if any: Nil
- d. Products developed, if any: Nil

20. Abstract: (In 300 words for possible publication in Bulletin)

Methodology & results can be submitted only after the publication of the data

21. Procurement/Usage of Equipment: Nil

a. Details of Equipment:

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No.	Name of Equipment	Make/ Model	Cost
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(Rs.)	Date of Installation	Utilisation	Remarks regarding maintenance breakdow
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c. Suggestions for disposal of equipment(s):