Statement of research achievements, if any, on which any award has already been received by the applicant. Please also upload brief citation(s) on the research work(s) for which the applicant has already received the award(s) (not to exceed 2000 words)

Prof. Maji's work impacts basic as well as applied areas of amyloid biology. He has made significant contributions and published in top-tier journals with high citations during his entire career. On the basic science front, his team has provided an understanding of the early development of Parkinson's disease (PD) and studied the aggregation of α-synuclein as well as discovered novel intermediates of protein aggregation that would facilitate the development of drug targets. From the application perspective, they have developed unique amyloid-based hydrogels which is a major breakthrough capable of solving two pressing challenges in the field of stem cell transplantation i.e. cell survival and ectopic migration post-transplantation (***Das et al, NPG Asia Mater, 2016)***. Prof. Maji conceived the novel idea of using amyloid hydrogel as a bio-mimetic extracellular matrix for the development of a three-dimensional tumor spheroid model (***Singh et al., bioRχiv, 2020 (under revision in Biomaterials***). These hydrogels can also be used as a depot for the sustained delivery of various proteins, peptides and drugs (Indian Patent file No: 201921000523, PCT application No: PCT/IB2020/050026, US Application No: 17/263,278).

Prof. Maji has received three awards based on the development of smart biomaterials derived from amyloidogenic sequences for various nanotechnology and tissue engineering applications.

National Bioscience award for career development, 2016

Tissue engineering applications largely depend on the potentiality of biomaterial capable of mimicking extracellular matrix. In such a regard, hydrogel serves as a potential candidate. Hydrogels derived from animals such as Matrigel or collagen can introduce complexity in terms of immunogenicity and toxicity, hence limiting their *in vivo* applications. The research work related to this award involves the development of structurally robust hydrogel derived from functional non-toxic amyloidogenic proteins present in humans. The study resulted in extensive morphological and biophysical characterization of the designed hydrogels. The toxicity of the hydrogels was also investigated, which demonstrated that the gels were non-toxic and biocompatible in nature. Once the suitability of the hydrogel as a scaffold was established, human mesenchymal stem cells (hMSCs) were cultured *in vitro* using both 2D and 3D cell culture models. The early differentiation of hMSCs towards neuronal lineage was also evaluated by immunostaining and monitoring gene expression levels of the early neuronal markers. Therefore, this study from Prof. Maji's group significantly contributed to exploring the potential of the designed amyloid hydrogels in the field of neuronal tissue engineering and also provided promising leads for the present ongoing projects.

NASI-Reliance platinum jubilee award, 2019

Prof. Maji was awarded the NASI-Reliance platinum jubilee award based on his scientific contributions which reflect application-oriented innovations. Parkinson's disease (PD) is characterized by the degeneration of dopaminergic neurons in the substantia nigra. Stem cell-based therapy helps regenerate the lost neurons using scaffolding techniques, hence providing a true reversal of the disease. Although having a huge potential in curing PD, such a form of therapy is associated with a low cell survival rate and ectopic migration upon transplantation, largely reducing its success rate. Biomaterials can be used as a suitable substrate for stem cell differentiation as well as transplantation of the differentiated cells in a PD patient's brain. A previous study from Prof. Maji's lab suggests that irrespective of sequence and absence of integrin recognition motif, amyloid fibrils can mimic the extracellular matrix and can be used as a potential biomaterial (***Jacob et al, J. Biol. Chem, 2017***). Using such an interdisciplinary approach, smart hydrogels based on amyloidogenic sequences were designed for stem cell-based therapy. These hydrogels possess a thixotropic feature that enables the easy encapsulation of stem cells as well as various small molecules/growth factors. The soft nature and unique topography promote the differentiation of stem cells to neuronal lineage *in vitro* (***Jacob et al, Biomaterials, 2015 and Das et al, NPG Asia Mater, 2016***). The fine-tuning of porosity of the designed hydrogels regulates the release of encapsulated growth factors, hence controlling the diffusion rate ***(Das et al, Adv Healthcare Mater, 2017).*** Additionally, hydrogels being biodegradable get metabolized in the brain once the purpose is served. These classes of amyloid hydrogels do not elicit an immune response (***Das et al, NPG Asia Mater, 2016***). They have also successfully transplanted stem cells encapsulated within the designed hydrogel, into a PD animal model and assessed the fate of those transplanted cells. Their scaffolding technology with amyloid-inspired hydrogels has led to at least three times better cell survival rate as well as prevention of ectopic cell migration after stem cell transplantation. The key advantage of such hydrogel is that it can be delivered to the brain with minimal invasive surgery (***Das et al, NPG Asia Mater, 2016***).

This work has resulted in 5 publications in top-notch peer-reviewed journals and three patents. Two patents (Patent File No.3712/MUM/2015; Patent File No. 20172107280) are licensed to Convalescence Inc. San Francisco, USA.

TATA Innovation fellowship, 2020:

A previous study from Prof. Maji's group demonstrated that amyloid hydrogels can potentially initiate differentiation of human mesenchymal stem cells (hMSCs) towards neuronal lineage. The observations obtained from this study directed the proposal for the TATA Innovation award. In this study, Prof. Maji and his group aim to establish the differentiation of hMSCs to functional dopaminergic neurons using various growth factor cocktails. It is expected that as a smart biomaterial, which mimics the extracellular matrix, it will modulate the differentiation of

encapsulated stem cells via the concomitant presentation of both biochemical and mechanical cues. The objectives of the study involve culturing of hMSCs using designed amyloid hydrogels derived from functional amyloids. Secondly, optimization of the growth factors cocktail for achieving neuronal differentiation in 3D cell culture, as various supplementations of soluble molecules and growth factors govern the terminal differentiation of hMSCs into dopaminergic neurons. Thirdly, investigation of the functionality of differentiated neurons by assessing the release capability of the neurotransmitter *in vitro.* The final aim involves the implantation of the hMSCs with the optimized scaffold growth factor concoction in caudate putamen of the PD mouse model and accessing the fate as well as the functionality of the differentiated dopaminergic neurons. This study is expected to significantly contribute to engineering 3D scaffolds for the differentiation of hMSCs to dopaminergic neurons. This would be extremely beneficial for modeling PD. Additionally, patient-specific stem cells could be harvested and differentiated into dopaminergic neurons to study the disease and delineate drug efficacies. If functional dopaminergic neurons are successfully developed by the end of this study, then cell replacement therapy for PD patients via stem cell transplantation would be possible.

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