SAMIR K MAJI

10 best publications (with discoveries and contribution):

1. Ray, S., Singh, N., Kumar, R., Patel, K., Pandey, S., Datta, D, Mahato, J., Panigrahi R., Navalkar, A., Mehra, S., Gadhe, L., Chatterjee, D., Sawner AS., Maiti, S., Bhatia, S., Gerez, J., Chowdhury, A., Kumar, A., Padinhateeri, R., Riek, R., Krishnamoorthy, G and **Maji, S. K** (2020) α-Synuclein aggregation nucleates through liquid-liquid phase separation, **Nature Chemistry**, 12, 705–716

   Discovery: The study demonstrates that the natively unstructured protein α-Synuclein (α-Syn), undergoes liquid-liquid phase separation (LLPS) in crowded cellular milleu. The high local concentration inside the droplet promotes liquid-to-solid transition into amyloid hydrogel consisting of oligomers and fibrillar species. Factors such as low pH, familial Parkinson's disease mutations aggravate LLPS and subsequent maturation. Furthermore, the study demonstrates formation of α-Syn liquid droplets in cells. The cellular α-Syn liquid droplets eventually transform into aggresome, a cryoprotective mechanism against protein aggregates.

   Contributions: Prof. Maji conceived the idea. The study was designed, directed and coordinated by Prof. Maji as Principal Investigator. He provided the infrastructure and funding for conducting all the experiments. He provided conceptual and technical guidance throughout the project. Most of the experiments (~90 %) were performed in Prof. Maji's lab. NMR study was done in Prof. Ashutosh Kumar's lab and single droplet imaging and spectroscopy was done in Prof. Arindam Chowdhury's lab (IIT Bombay). Time resolved fluorescence studies were done in consultation with Prof. G.Krishnamoorthy. Prof. Ranjith Padinhateeri provided helped in analyzing kinetics data (IIT Bombay). Prof. Roland Riek provided C4-α-Syn cell line (ETH Zurich).

2. Sawner, AS., Ray, S., Yadav, P., Mukherjee, S., Panigrahi, R., Poudyal, M., Patel, K., Ghosh, D., Kummerant, E., Kumar, A., Riek, R. and **Maji, S. K** (2021) Modulating α-Synuclein Liquid-Liquid Phase Separation. **Biochemistry**, 60(48):3676–96

   Discovery: The study demonstrates how the environmental and experimental parameters regulate α-Syn LLPS. The factors known to regulate α-Syn aggregation such as pH, N-terminal acetylation, salt/counterion, etc. can modulate the kinetics of α-Syn LLPS. Presence of salt leads to charge neutralization at both terminus of the unstructured protein promoting hydrophobic interaction supportive for LLPS of α-Syn. Furthermore, different purification techniques have been adopted which causes either spontaneous or delayed LLPS.

Contributions: Prof. Maji conceived the idea. The study was designed, directed and coordinated by Prof. Maji as Principal Investigator. He provided the infrastructure and funding for conducting all the experiments. He provided conceptual and technical guidance throughout the project. The NMR study was performed in Prof. Ashutosh Kumar's lab (IIT Bombay). Prof. Roland Riek provided expertise in explaining NMR observations (ETH Zurich). Prof. Maji and team analysed the data, interpreted the results and contributed in drafting the manuscript and critical revision.

3. Chatterjee, D., Jacob, R.S., Ray, S., Navalkar, A., Singh, N., Sengupta, S., Gadhe, L., Kadu, P., Datta, D., Paul, A., Mehra, S., Pindi, C., Kumar, S., Singru, P.S., Senapati, S.K. and **Maji, S. K**., (2022) Co-aggregation and secondary nucleation in the life cycle of human prolactin/galanin functional amyloids, **eLife** 11: e73835

   Discovery: The major discovery of the work involves the synergistic co-aggregation and cross-seeding of two different protein/peptides in amyloid formation. The study demonstrates co-storage of human Prolactin and neuropeptide Galanin as functional amyloids in secretory granules of rat. The study mainly focuses that the two hormones facilitate the synergistic aggregation to amyloid fibrils, irrespective of the difference in sequence and structure. Further, each of the hormone posses homotypic seeding ability. The study also shows that the unidirectional cross-seeding of GAL aggregation by PRL seeds and inability of cross-seeding by mixed fibrils mediates tight regulation of functional amyloid formation by the two hormones and their storage in stress granules. This study also puts forward a novel mechanism of heterogenous amyloid formation in functional amyloid of stress granules. Moreover, the faster release of functional monomers from mixed fibrils in comparison to the individual hormone amyloid, depicts the effective and novel mechanism which is crucial in balancing the hormone homeostasis in
   the living body.

   Contributions: Prof. Maji conceived the idea. The study was designed, directed and coordinated by Prof. Maji as Principal Investigator. He provided conceptual and technical guidance throughout the project. Rat pituitary tissue sectioning was performed under the guidance of Prof. Praful Singru in NISER, Bhubaneshwar, India. Molecular dynamics simulations study was performed at IIT Madras by Prof. Sanjib Senapati.

4. Navalkar, A., Paul, A., Skunthala, A., Pandey, S., Dey, A.K., Saha, S., Sahoo, S., Jolly, M.K., Maiti, T.K., **Maji, S. K**., (2022), Oncogenic gain of function due to p53 amyloids occurs through aberrant alteration of cell cycle and proliferation, **Journal of Cell Science** 135 (15): jcs260459

   Discovery: p53 aggregation and amyloid formation has been predicted to be involved in the loss-of function of p53. This study demonstrates the mechanism of loss of p53 tumor-suppressive

function with concomitant oncogenic gain-of functions. Genomic and proteomic profiling of cells suggests that p53 amyloid formation dysregulates the genes associated with cell cycle, proliferation, apoptosis, senescence along with major signaling pathways. Hence, the wild-type p53 amyloid formation can be a potential target for therapeutic intervention against cancer.

Contributions: Prof. Maji conceived the idea. The study was designed, directed and coordinated by Prof. Maji as Principal Investigator. Prof. Mohit K. Jolly supervised in the data analysis of gene expression for mutational data at IISc Bangalore, India. The proteomics analysis was carried out under the guidance of Prof. Tushar K. Maiti at Regional Center for Biotechnology, Faridabad, India.

5. Navalkar, A., Pandey, S., Singh, N., Patel, K., Mohanty, B., Jadhav, S., Chaudhari, P. and **Maji S. K.,** (2021) Direct evidence of cellular transformation by prion-like p53 amyloid infection, **Journal of Cell Science,** 134(11)

Discovery: p53 aggregation and amyloid formation has been predicted to be involved in the loss-of function of p53. This study provides evidence for the presence of p53 amyloid fibrils (in human and animal cancer tissues); along with their isolation from human cancer tissues and the biophysical characterization of these tissue-derived fibrils. It is demonstrated that wild-type p53 amyloid formation imparts oncogenic properties to non-cancerous cells. The p53 amyloids can be transferred through cell generations, contributing to enhanced survival, apoptotic resistance with increased proliferation and migration. Cells with p53 amyloids show the establishment of tumors in a mouse xenograft model. p53 disaggregation rescues the cellular transformation and inhibits tumor development in mice.

Contribution: Prof. Maji conceived the idea. The study was designed, directed and coordinated by Prof. Maji as Principal Investigator. Animal study was performed at Agharkar Research Institute, Pune with the help of Dr. S. Jadhav. PET and CT experiments were done at Advanced Centre for Treatment, Research and Education in Cancer, Mumbai with the help of Dr. Pradip Chaudhari. Prof. Maji's group analyzed the data, interpreted the results and contributed in drafting the manuscript and critical revision.

6. Mehra, S., Ahlawat, S., Kumar, H., Datta, D., Navalkar, A., Singh, N., Gadhe, L., Kumar, R., Jha, N. N., Sakunthala, A., Sawner, A.S., Padinhateeri, R., Udgaonkar, J.B., Agarwal, V., Maji, S. K., (2022), α-Synuclein aggregation intermediates form fibril polymorphs with distinct prion-like properties, **Journal of Molecular Biology**, 434(19), 167761

Discovery: The study investigates the structure-function relationship of pre-matured fibrils and helix-matured fibrils. Interestingly, the two polymorphs display structural differences as evident through solid solid-state NMR and mass spectrometry studies. Moreover, the polymorphs possess

diverse cellular activities such as seeding, cell-to cell transfer of aggregates and internalization. The helix matured fibrils exhibit low seeding potential but it easily internalises while the pre-matured fibrils induces α-Syn pathology and triggers the aggresome formation in cells but lacks the transcellular transfer ability.

Contribution: Prof. Maji conceived the idea. The study was designed, directed and coordinated by Prof. Maji as Principal Investigator. He provided the infrastructure and funding for conducting all the experiments. He provided conceptual and technical guidance throughout the project. His group analyzed the data, interpreted the results and contributed in drafting the manuscript and critical revision. Solid-state NMR was performed by Prof. Vipin Agarwal at TIFR Hyderabad. HDX-MS study was carried out under the guidance of Prof. Jayant B. Udgaonkar at IISER, Pune.

7. Ghosh, S., Salot, S., Sengupta, S., Navalkar, A., Ghosh, D., Jacob, R., Das, S., Kumar, R., Jha, N.N., Sahay, S., Mehra, S., Mohite G.M., Ghosh S.K., Kombrabail M., Krishnamoorthy G., Chaudhari P. and **Maji S.K** (2017) p53 amyloid formation leading to its loss of function: implications in cancer pathogenesis, **Cell death and differentiation,** 24(10), 1784-1798

   Discovery: p53 aggregation and amyloid formation has been predicted to be involved in the loss-of-function of p53. This study provides evidence for the presence of p53 amyloid fibrils (in human and animal cancer tissues); along with their isolation from human cancer tissues and the biophysical characterization of these tissue-derived fibrils. Moreover, mutation in p53 can accelerate p53 aggregation kinetics. Using seeds of p53 derived peptide p53(250-257), the amyloid formation of endogenous p53 was induced in the cells. Further, the prion-like cell-to-cell transmission of p53 amyloid species was also established.

   Contribution: Prof. Maji conceived the idea. The study was designed, directed and coordinated by Prof. Maji as Principal Investigator. He provided the infrastructure and funding for conducting all the experiments. He provided conceptual and technical guidance throughout the project. His group analyzed the data, interpreted the results and contributed in drafting the manuscript and critical revision. Most of the experiments (~90 %) were performed in Prof. Maji's lab and remaining study was performed in collaboration with different institutes. Time-resolved fluorescence Intensity decay kinetics data were acquired in Prof. G Krishnamoorthy's lab (TIFR, Mumbai) and he was instrumental to analyze time resolved fluorescence data.

8. Kumar, R., Das, S., Mohite, G.M., Rout, S.K., Halder, S., Jha, N.N., Ray, S., Mehra, S., Agarwal, V., **Maji, S.K** (2018) Cytotoxic oligomers and fibrils trapped in a gel-like state of α-synuclein assemblies, **Angewandte Chemie International Edition**, 57(19): 5262-5266

   Discovery: The study shows that α-Syn monomers transitions into gel like state from a solution state upon incubation at high concentrations. The detailed characterization of gel shows the

presence of monomers, oligomers as well as short fibrils. The cytotoxicity assay of gel demonstrates that the gel formed is highly cytotoxic to human neuroblastoma cells. Moreover, the gel comprises of heterogenous population of α-helical and β-sheet rich oligomers and fibrils with cross-β motif.

Contribution: Prof. Maji conceived the idea. The study was designed, directed and coordinated by Prof. Maji as Principal Investigator. He provided the infrastructure and funding for conducting all the experiments. His group analyzed the data, interpreted the results and contributed in drafting the manuscript and critical revision. The NMR study was performed in Dr. Vipin Agrawal's lab (TIFR, Hyderabad) and he also helped in analyzing the NMR spectra.

9. Jacob, R.S., Ghosh, D., Singh, P.K., Basu, S.K., Jha, N.N., Das, S., Sukul, P.K., Patil, S., Sathaye, S., Kumar, A., Chowdhury, A., Malik S., Sen S., and **Maji S.K** (2015) Self-healing hydrogels composed of amyloid nano fibrils for cell culture and stem cell differentiation**, Biomaterials**, 54, 97-105

   Discovery: Amyloids are the ordered protein/peptide aggregates associated either with human diseases or native function. This study hypothesizes that the highly ordered amyloid could be used as a potential biomaterial for tissue engineering applications. A series of Fmoc protected peptides isolated from the aggregation prone C-terminus region of Aβ42 associated with Alzheimer's disease, self-assembles into β-sheet rich fibrils forming hydrogel. The designed hydrogels are non-toxic, thermo-reversible and thixotropic. Further, the study demonstrates the use of hydrogel in supporting cell attachment. Interestingly, the stiffness of hydrogel can be modulated by tuning the peptide concentration as well as salt concentration. Moreover, the smart hydrogels can be used as scaffold for the differentiation of mesenchymal stem cells.

   Contribution: Prof. Maji conceived the idea. The study was designed, directed and coordinated by Prof. Maji as Principal Investigator. He provided the infrastructure and funding for conducting all the experiments. His group analyzed the data, interpreted the results and contributed in drafting the manuscript and critical revision. Amyloid fibril imaging with Nile red was done in Prof. Arindam Chowdhury's lab (IIT Bombay). Shamik Sen (IIT Bombay) helped for analysis of selected data.

10. Das, S., Zhou, K., Ghosh, D., Jha, N. N., Singh, P. K., Jacob, R. S., Bernard C.C., Finkelstein D.I., Forsythe J.S., and **Maji, S. K** (2016) Implantable amyloid hydrogels for promoting stem cell differentiation to neurons, **NPG Asia Materials,** 8(9), e304

    Discovery: The major discovery of this study involves development of a series of hydrogels based on the self-recognition motif of α-Syn. The hydrogels were tested for neural tissue engineering applications *in vitro* as well as *in vivo.* The study demonstrates that the designed hydrogel promotes

differentiation of mesenchymal stem cells into neuronal lineage. Moreover, the human mesenchymal stem cells when implanted with the hydrogel into (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) MPTP mice, improved the survival rate as well as cells were contained at the transplanted site.

Contribution: Prof. Maji provided conceptual and technical guidance throughout the project. Majority of experiments were conducted in Prof Maji's lab. He provided the infrastructure and funding for conducting all the experiments. Animal study comprising of stem cell implantation in mouse model was performed in Prof. John S. Forsythe's lab (Monash University, Australia)