34. Recommendations of the Director of the Lab/Institute:

a) Comments of the Director on the information given above by the applicant.

Dr. Sonia Verma has submitted a comprehensive and well-structured application titled "NANOFERROBLOCK: DNA Origami Nanostructures Equipped with ssDNA Aptamers as DMT1 and ACSL4 Inhibitors for Combating Ferroptosis during Neuroinflammation," for the Raman Research Fellowship for the year 2024-2025. This is a highly innovative proposal with high translational potential. It is well thought out and systematic. Developing aptamers that can limit neuroinflammation could lead to novel therapeutic interventions that are specific, effective, and safe.

b) Remarks of the Director on the potential and credentials of the applicant.

Dr. Sonia Verma is working as a Scientist at the division of "Neuroscience & Ageing Biology" in CSIR-Central Drug Research Institute since June, 2021. Her major research focuses on delineating the role of novel targets in neurodegeneration and neuroinflammation. In a short span of time, Dr. Verma has developed primary/secondary assays for screening and identifying molecules targeting mitochondrial biogenesis leading to neuroinflammation and neurodegeneration. I am confident that her work will contribute immensely to new knowledge generation and also have a meaningful impact on the development of therapeutics for neuroinflammation and neurodegenration. One of the most striking aspects of Dr. Verma's work is her interdisciplinary approach. She is well suited for this unique opportunity and I am fully confident that her work will yield some interesting new avenues of exploration for the future. I strongly recommend her to this program.

c) Field of proposed study and its relation to the Lab's priorities, particularly with regard to the priority Themes/Projects/Programmes of CSIR

The proposed study aligns well with the priorities of CSIR-CDRI. This research is pertinent to the institute's focus on developing innovative therapeutic strategies for neurodegenerative diseases. Neurodegenerative diseases, such as Alzheimer's and Parkinson's represent major public health challenges due to their increasing prevalence and the lack of effective treatments. The research also fits well with CDRI's interest in understanding the role of inflammation in neurodegeneration.

Further, the research aligns with CSIR-CDRI's mission to foster technological innovation and translational research. The development of such advanced therapeutic strategies not only enhances the institute's research capabilities but also positions it at the forefront of neurodegenerative disease research globally. The project's interdisciplinary approach, integrating biology, chemistry, and nanotechnology, exemplifies the kind of translational research that CSIR-CDRI prioritizes.

d) Remarks on chosen place of work, special features of the concerned Lab.

The selection of Dr. Xing Wang's lab at the University of Illinois Urbana-Champaign (UIUC) is well-justified due to its state-of-the-art facilities and expertise in DNA nanotechnology and aptamer development. Dr. Wang's lab is renowned for its pioneering work in nucleic acids and protein engineering, making it an ideal environment for advancing the proposed research. The lab's cutting-edge infrastructure includes advanced tools and technologies essential for DNA nanostructure design, SELEX pipeline, surface plasmon resonance, and NGS facilities. These resources are critical for the successful execution of Dr. Verma's research project.

Furthermore, Dr. Wang's lab has a proven track record of innovative research in DNA nanotechnology, particularly in creating and customizing designer DNA nanostructures for various bioengineering applications. This includes the development of DNA origami structures that can be utilized to enhance the delivery and efficacy of therapeutic aptamers. The opportunity to work with such advanced DNA nanostructures will provide Dr. Verma with hands-on experience in cutting-edge nanotechnology, significantly enhancing her research capabilities and expertise.

e) Scientific and economic implication of the proposed work during the Fellowship (both on Indian as well as global scene).

The proposed research aims to develop novel therapeutic strategies that can inhibit ferroptosis, thereby potentially halting or reversing the damage caused by chronic neuroinflammation. This innovative approach not only offers a deeper insight into the mechanisms driving neurodegenerative diseases but also paves the way for the creation of highly specific and effective treatments.

The development of new aptamer-based therapies represents a breakthrough in precision medicine. Aptamers, which are single-stranded DNA or RNA molecules, can be designed to bind with high specificity and affinity to target proteins involved in neuroinflammation and ferroptosis. This specificity reduces the likelihood of off-target effects and increases the therapeutic efficacy, making aptamers a promising alternative to traditional small molecule drugs and antibodies.

Moreover, the commercialization prospects of these novel therapies are substantial. Successful development and validation of these aptamer-based treatments can attract interest from pharmaceutical companies looking for innovative solutions to tackle not only neurodegenerative diseases but other conditions where ferroptosis is involved. This creates opportunities for CSIR to license these technologies and collaborate with industry partners, facilitating the translation of research findings into clinical applications. Such collaborations can lead to the development of new diagnostic tools and therapeutic products, generating revenue for CSIR through licensing agreements and fostering the growth of biotechnology sectors within India.

f) Nature of expected output from the proposed study.

The expected outputs include:

1. Development of DNA origami nanostructures loaded with ssDNA aptamers targeting DMT1 and ACSL4.
2. Detailed characterization of these aptamers and their efficacy in inhibiting ferroptosis and neuroinflammation.
3. High-impact scientific publications and potential patents.
4. Enhanced capacity in the field of DNA nanotechnology and aptamer development.

g) Commercialisation prospect and likely users of the proposed research in the industrial sectors.

The goal of the current research is to establish proof-of-concept using DNA Origami Nanostructures Equipped with ssDNA Aptamers for combating Ferroptosis during Neuroinflammation. The results of the project could provide leads for drug discovery and diagnostics. There would be potentially applications in multiple disease areas and commercial interest would be very likely from the Pharma and Biotech industry.

h) List of scientific peers, who can appreciate and comment on the scientific approach and overall utility of the proposed work.

Dr Arjun Ramakrishnan, IIT Kanpur

Dr Subhas Biswas, IICB Kolkata

Dr Jayanta Chatterjee, IISc Bengaluru

Signature of the Director with Stamp and Date.

निदेशक
Director
केन्द्रीय औषधि अनुसंधान संस्थान
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25 JUL 2024