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### Statement from Applicant

I, Ruchi Anand, Professor in the Department of Chemistry, IIT Bombay have been using my structural biology skills as a versatile tool to study problems with societal implications. For the last few years, we have made significant contributions in the field of structural biochemistry, where we have worked towards understanding and devising strategies to combat antibiotic resistance. It is projected that by 2050 if nothing is done to combat drug resistance more than 300 million people will suffer. Therefore, the problem that we are addressing in our research group is to find new therapies as well as **reversing resistance**. Our work on efflux pump regulators aims at understanding the regulation of antibiotic levels in the cell (*NAR 2014, JSB 2017, JBC 2017*). Developing efflux pump blockers can help reverse resistance and re-sensitize the pathogens towards existing antibiotics. Alternatively finding novel pathways that can be utilized as drug targets have led us to find innate resistance mechanisms present in *M. Tuberculosis*. We have discovered enzymes that impart natural resistance to these organisms towards aza group of compounds (*JACS 2017*). Thus, blocking this newly discovered pathway can sensitize these organisms to the existing drugs. Our recent work on deciphering the mechanism of targeting in ribosomal methyltransferases has unraveled a unique pocket that can now be used to design new selective drugs (*JACS 2019*). Parallely, we have also deciphered the mechanism of specific RNA targeting by ribosomal methyltransferases through cryo-electron microscopy (*ACS Chem. Biol. 2022*). This work was done in collaboration with Prof. Vinothkumar from NCBS, Bangalore. We have also identified allosteric hotspots regulating the binding of antibiotic resistance-conferring methyltransferases to its cognate substrate in collaboration with Prof. Yves Mély affiliated to the University of Strasbourg, France. Our lab also has significant contributions to the understanding of conformational allostery and long-distance cross-talks in large macromolecules (*Science Advances 2020, ACS Catalysis 2022*). I have been awarded with the Wellcome Trust Fellowship 2019 and have also received a grant (5 million US dollars) from SERB, India as a principal investigator to setup the state-of-the-art cryo-electron-microscopy center at IIT Bombay and take the field of structural biology further ahead. I have been honored with the Impactful Research Award 2020 from IIT Bombay for my research work. I wish to declare here that the research work under reference has not been awarded before.

Sincerely,

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