



INTERNATIONAL CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY

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TO WHOM IT MAY CONCERN

I nominate, Prof Ruchi Anand for consideration for the Sun Pharma Science Foundation Research Award **Pharmaceutical Sciences** for 2023 for her significant research contributions in arenas of **new therapies to combat drug resistance towards design and development of new drugs**. Prof. Anand's research focus is twofold in this area; first towards understanding origins of antibiotic resistance and in development of drug candidates to combat it. Second towards targeting essential enzymes as new drug targets. Multidrug resistant (MDR) bacteria such as *staphylococcus aureus* harbor methyltransferases that methylate ribosomes and make macrolide lincomamide and streptogramin class of antibiotics more than 50 in number ineffective. With the aim of designing specific drug targets for these methyltransferases she embarked on unraveling the specificity determinants (**JACS 2019**). Her studies lead her to discover a unique allosteric pocket, present in this class of enzymes, that enable their specific function (**JBC 2022, ACS Chem Bio. 2022**). Currently, their group has discovered selective compounds that selectively inhibit this enzyme and impart renewed sensitivity to the MDRs enabling sensitivity to the existing antibiotics thereby, "**reversing resistance**". In an era where discovering new antibiotics is a very daunting task her strategy has paved the way towards logical reversing the resistance problem. To further her efforts, she has been awarded the **Senior DBT-Welcome Trust India Alliance Fellowship**. On a similar vein she is also studying mechanism that are involved in efflux of antibiotics present in several MDRs. Here the aim is again to develop tetracycline receptor (TetR) like inhibitors. Her structural biology efforts on these regulators (**NAR 2014 JPC 2014, JBC 2017**) uncovered the allosteric relay between the antibiotic and DNA binding sites, providing important insights toward design of efflux pump inhibitors.

Towards unraveling new drug targets, she has been working with nucleobase deaminases and has discovered a new enzyme that imparts innate resistance to *M. Tuberculosis* towards aza-scaffold drugs (**JAC 2017, Biochemistry 2013, JSB 2017**). Notably, she has meticulously deciphered the mechanics of **allosteric communication and molecular tunnel formation** within an essential purine biosynthetic enzyme, contrasting evolutionary variations between humans and bacteria (**Sci Adv 2020, ACS Catal. 2022, Curr. Opin. Chem. Biol. 2023**).

Sincerely,

Dr. Amit Sharma

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