

August 28th 2023


Subject: Citation (summary) of outstanding research work of **Dr Prabhat Ranjan Mishra** for SUN Pharma Research Award-2023 nomination in Pharmaceutical Sciences

Dr Mishra has made an outstanding contribution to developing bio-functionalized nano-biomaterials for therapeutics & diagnostic applications and elucidating the mechanistic aspect of its cellular translocation to achieve a higher therapeutic index with the low toxicity of drugs. His contributions signify a major role in establishing specific delivery of drugs through innovative nano-therapeutics thereby bypassing the otherwise established biological barriers.

Knowledge generation and development: In brief, he elucidated Aggregation Induced Emission (AIE) mechanism demonstrating image-guided chemotherapy through anisamide anchored nano-liquid crystals with enhanced antitumor efficacy (*ACS Appl. Mater. Interfaces* 2018; I.F. 10.38) while modulation of tumor microenvironment using endogenous stimuli-responsive lyotropic nano-liquid crystals to achieve advanced comprehensive cancer nano-theranostics (*Acta Biomaterialia* 2020 I.F. 10.63). He also demonstrated that lipid bilayer-camouflaged mesoporous silica nanoparticles ensue synchronized translocation of topotecan and metformin to promote apoptosis via mitochondrial membrane depolarization and cell cycle arrest to achieve 100-fold higher drug concentration in tumor (*Adv. Healthcare Mater* 2018 I.F. 11.12) while establishing proton sponge effect escaping lysosomal degradation by pyridoxine tethered nanoparticles facilitating intracellular localization resulting in fifteen-fold reduction in therapeutic dose of doxorubicin with enhanced antitumor efficacy (*ACS Appl. Mater. Interfaces* 2016; I.F. 10.38). He discovered that hyaluronic acid anchored nanocrystals expedites CD44 receptor-mediated endocytosis to exhibit reduced lung metastasis and toxicity of paclitaxel while enhancing oral bioavailability through reversible P-gp modulation with a significant reduction in tumor growth ensuing patient-friendly "chemotherapy at home" (*Acta Biomater.* 2015; I.F. 10.63). He established the potential role of putrescine in targeting glypican-1 receptor spatially and also elucidated that redox-sensitive micellar system bearing epalrestat and doxorubicin gets disrupted in tumor redox environment through VTC receptor-mediated uptake to promote synergistic tumor suppression ensuing receptor-mediated endocytosis (*Biomater. Sci* 2019, 2020, I.F. 7.59).

Translational contribution and commercialization: He successfully developed layer-by-layer (LBL) and SMEDDS technology that impacted product development in the area of bone-related disorders. He has been instrumental in patenting 25 technologies, out of which **FIVE have been licensed** to Industries while **TWO are commercialized** as **Joint Fresh™** and **Reunion™** [(Granted **US patent** 8,496,964; **AU Patent**; 2010217238A; **EP patent** 2400957 B1) Other products for the treatment of osteoarthritis and bone loss are also developed (Granted **US Patent** 10,596,115; **AU Patent** 2014291615; **US patent** 10265297)]. In addition, he has been actively involved in developing Umifenovir and its formulation under repurposing for COVID patients whose **Phase III clinical trial** has been completed.

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