NCCS

राष्ट्रीय कोशिका विज्ञान केन्द्र

National Centre For Cell Science

जैवप्रौद्योगिकी विभाग, भारत सरकार का स्वायत्त संस्थान

(An Autonomous Institution of the Department of Biotechnology, Government of India)

Justification Letter for sponsoring nomination to the

Sun Pharma Research Award (Basic Science) 2023

Dr. Bapat was the first in India to initiate research on high-grade serous ovarian cancer (HGSC), recognized as an aggressive, challenging disease for basic and clinical research. Her work has focused on understanding the disease at molecular and cellular levels with a long-term aim of identifying novel targets for personalized medicine. Though considered a pioneer in the area of cancer stem cells (CSCs), Dr. Bapat also was one of the first researchers in India to recognize the contribution of **Epithelial to Mesenchymal Transition (EMT) in cancer** and has generated new knowledge and opportunities in dissecting out its mechanistic and regulatory implications in varying cellular contexts to develop applications in personalized HGSC therapy. Her achievements in the field of EMT include–

- Identification of association of EMT-transcriptional factors (EMT-TFs) Snail and Slug with ovarian cancer and understanding their mechanistic contribution to metastases.
- Elucidation of the orchestration of global transcription mediated by Snail and Slug leading to enrichment of CSCs following therapy through acquisition of self-renewal capabilities and resistance to p53-mediated apoptosis.
- Resolution of discrete molecular sub-classes and specific biological functions in high-grade serous ovarian cancer that assign relevance to clinical disease. A striking difference was that the defining feature of one sub-class was Slug-driven EMT, while another presented with a strong epithelial identity that resisted EMT.
- Identification of an 'EMT-module' in pan-cancer expression datasets with PRRX1, AIF1 and Slug being suggested to be master regulators.
- Mechanistic understanding of regulation of *SNAI2* expression (auto-regulation *vs.* transcriptional repression by TCF21)
- Clinical identification of the predicted molecular classes in human HGSC tumors leading to clinical validation of the EMT sub-type
- Mapping of associations between phenotypic plasticity as a gradient of cellular phenotypes regulated by the TFs Slug and TCF21 in HGSC positing differential capabilities of migration and metastases
- Identification of different modes of cell migration (active / passive cooperative cell migration – aCCM/pCCM *vs.* EMT) through Live cell imaging.
- Development of a monoclonal antibody (mAb150) that is indicated to be useful in treatment of the mesenchymal subtype of tumors

These findings are published in well-recognized journals in cancer biology and are highly citied, which indicates the high degree of excellence and original, 'out of the box' thinking and multidisciplinary approaches that Dr. Sharmila Bapat has striven to incorporate in our understanding of cancer biology since the last two decades at NCCS.

These strengths in her research provide a strong justification for me to nominate her for the Sun Pharma Research Award (Basic Science) 2022 in Medical and Pharmaceutical Sciences.

Place: Pune
Date: 29th August, 2022

Prof. Mohan R Wani
Director, NCCS

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