

मनोज कुमार भट, पीएच डी
निदेशक

Manoj Kumar Bhat, PhD
Director

Justification Letter for sponsoring nomination to the

Sun Pharma Research Award (Basic Science) 2021

TO WHOMSOEVER IT MAY CONCERN

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 as 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 include—

- Identification of a definitive association of EMT transcriptional factors (TFs) Snail and Slug with the aggressiveness of ovarian cancer metastases.
- Elucidation of the mechanistic role of Snail and Slug with post-therapy CSC enrichment through acquisition of self-renewal capabilities and resistance to p53-mediated apoptosis to assign a 'stem-like' cell state.
- Resolution of discrete molecular sub-types associated with specific biological functions in high-grade serous ovarian cancer that assign relevance to clinical disease. A defining feature of one sub-types was Slug-driven EMT, while another presented with a strong epithelial identity that resisted EMT.
- Mechanistic understanding of regulation of Slug expression (auto-regulation vs. transcriptional repression by TCF21).
- Clinical validation of predicted EMT sub-type of HGSC.
- Identification of different modes of cell migration (active / passive cooperative cell migration – aCCM/pCCM vs. EMT) through Live cell imaging.
- Mapping of a gradient of cellular phenotypes regulated by the TFs Slug and TCF21 in HGSC positing phenotypic plasticity and differential capabilities of migration and metastases.
- Development of a monoclonal antibody (mAb150) that is indicated to be useful in treatment of the EMT subtype.

These findings are published in well-recognized journals in cancer biology and are highly cited, which indicates the high degree of excellence and original, 'out of the box' thinking that Dr. Sharmila Bapat has striven for over the last two decades at NCCS.

Most importantly, these provide a strong justification for me to nominate her for the Sun Pharma Research Award (Basic Science) 2021 in Medical and Pharmaceutical Sciences.

Manoj Kumar Bhat

20/09/2021

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