## Shri Ramniklal J. Kinarivala Cancer Research Award- 2023

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## Two Decades of Ovarian Cancer Research - Knowledge Generated, Resources Developed and Hope Ahead

Ovarian Cancer is a highly dreaded disease. Until the turn of this century, there was hardly any fundamental research of this disease at a cellular or molecular level, while globally it was recognized as a "Silent Killer" and associated with high mortality in patients. My group was first in India to initiate research on high-grade serous ovarian cancer (HGSC), which is its most aggressive pathological subtype, that is recognized to be challenging for basic and clinical research. Over the years, we focused on understanding HGSC at the molecular, cellular and disease levels with the long-term aim of identifying novel targets for effective cancer therapy. Towards the development of resources for the Indian research community, we established several cell lines from Indian patients and protocols for xenograft and orthotropic mouse models including patient derived xenograft (PDX) models. The earliest work in our lab provided the first global evidence of the involvement of stem/progenitor cells in human ovarian tumors. We further followed this with studying their evolution, quiescence, recruitment of primitive endothelial stem cells for neovascularization and generation of tumor heterogeneity that links with tumor dormancy, aneuploidy and minimal residual disease. Another important identification was the role of epithelial to mesenchymal transition that not only led to the understanding of metastases, but culminated in the resolution of discrete molecular classes and specific biological functions in HGSC that with further validation in clinical samples through establishment of a biomarker panel and development of standard immunohistochemistry-based operating protocols and collaboration with clinical pathologists assigned relevance to the heterogeneity of the disease. Together, the approaches developed in our lab have and continue to generate new knowledge and opportunities towards personalized cancer therapy in ovarian cancer.