



टाटा स्मारक केंद्र  
TATA MEMORIAL CENTRE

कैंसर उपचार, अनुसंधान एवं शिक्षा का प्रगत केंद्र  
ADVANCED CENTRE FOR TREATMENT RESEARCH  
& EDUCATION IN CANCER

- CANCER RESEARCH INSTITUTE
- CLINICAL RESEARCH CENTRE

**A Grant-in-Aid Institution of the Department of Atomic Energy, Govt. of India**

18<sup>th</sup> September, 2021

### Summary of the research of Nazia Choudhary

Our previously published work demonstrated that loss of the desmosomal plaque protein, plakophilin3 (PKP3), led to an increase in tumor progression and metastasis in multiple cell types, particularly in cell lines derived from the colon (1). Nazia contributed to work that showed that PKP3 loss leads to an increase in the expression of LCN2, which was required for the increase in invasion and tumor progression observed upon PKP3 loss (2). Nazia went on to demonstrate that the increase in LCN2 expression is required for resistance to 5 fluorouracil (5FU) (3) and  $\gamma$ -radiation. The resistance is dependent on the ability of LCN2 to bind to and sequester iron and to modulate the levels of ferrous and ferric iron in cells. LCN2 inhibits ferroptosis by stimulating the expression of the transcription factor Ets1, which drives xCT expression. Our collaborators at MSMF and Beyond antibody have generated a monoclonal antibody that can inhibit LCN2 function. Nazia demonstrated that this antibody which sensitizes cells to therapy, promotes ferroptosis and inhibits tumor growth in xenograft mouse models (3). Her preliminary data indicate that LCN2 stimulates autophagy, which is required for both therapy resistance in response to 5FU and  $\gamma$ -radiation in vitro and in vivo and this manuscript is currently under preparation.

Sincerely,

Sorab N. Dalal  
Principal Investigator and S. O. 'H' ACTREC  
Professor HBNI  
[sdalal@actrec.gov.in](mailto:sdalal@actrec.gov.in)

### References.

1. Kundu, S. T., Gosavi, P., Khapare, N., Patel, R., Hosing, A. S., Maru, G. B., Ingle, A., Decaprio, J. A., and Dalal, S. N. (2008) Plakophilin3 downregulation leads to a decrease in cell adhesion and promotes metastasis. *Int J Cancer* **123**, 2303-2314
2. Basu, S., Chaudhary, N., Shah, S., Braggs, C., Sawant, A., Vaz, S., Thorat, R., Gupta, S., and Dalal, S. N. (2018) Plakophilin3 loss leads to an increase in lipocalin2 expression, which is required for tumour formation. *Exp Cell Res* **369**, 251-265
3. Chaudhary, N., Choudhary, B. S., Shah, S. G., Khapare, N., Dwivedi, N., Gaikwad, A., Joshi, N., Raichanna, J., Basu, S., Gurjar, M., Smitha, P. K., Saklani, A., Gera, P., Ramadwar, M., Patil, P., Thorat, R., Gota, V., Dhar, S. K., Gupta, S., Das, M., and Dalal, S. N. (2021) Lipocalin 2 expression

promotes tumor progression and therapy resistance by inhibiting ferroptosis in colorectal cancer. *Int J Cancer*