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Significance of PELP1/HDAC2/microRNA-200 regulatory network in EMT and metastasis of breast cancer

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Tumor metastasis remains a significant clinical problem and is the leading cause of death among breast cancer patients. ER-coregulators play an essential role in cancer progression and metastatic tumors express increased levels of coregulators. PELP1 is an ER coregulator, its expression is upregulated during breast cancer progression to metastasis and is an independent prognostic predictor of shorter survival of breast cancer patients. MicroRNA mediated regulation of tumorigenesis is emerging as a new paradigm in cancer biology and widespread misexpression of microRNAs has been reported in breast cancer. The objective of this study is to examine the mechanism and therapeutic significance of PELP1 regulation of miRs leading to breast cancer metastasis. We have used both ER+ve and ER-ve models that either stably overexpress PELP1 or PELP1shRNA. Boyden chamber assays demonstrated that PELP1 down regulation significantly affect migration of both ER+ve and ER-ve cells. EMT and whole genome microRNA array analysis revealed that PELP1 modulate expression of EMT genes and miR200a and miR141. ChIP analysis elucidated PELP1 down regulated expression of miR200a and miR141 by promoting repressive chromatin modifications via HDAC2. IVIS imaging of nude mice based assays of GFP-Luc labeled cells demonstrated therapeutic efficacy of miRIDIAN shMIMIC of miR200a and miR141 on PELP1 driven *in vivo* metastasis. Collectively, these novel findings demonstrate for the first time a previously unknown role for PELP1 in epigenetically controlling the functions of tumor metastasis suppressor miR-200a and miR141. These results suggest that PELP1-miR axis may be crucial stimulus for promoting EMT and breast cancer metastasis

Biography

Sudipa Sasha Roy has completed her Ph.D in 2009 from Jadavpur University, India and she is currently a post-doctoral fellow at the UTHSCSA, San Antonio. At present, she is in the T-32 NRSA fellowship program. Her research work has resulted in 7 publications in reputed journals, 8 oral presentations and 24 abstracts in prestigious conferences. She has also received several prestigious awards in breast cancer research field

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