METTL3 contributes to osimertinib resistance in non-small cell lung cancer cell lines by regulating CDC25A and AURKB mRNA stability

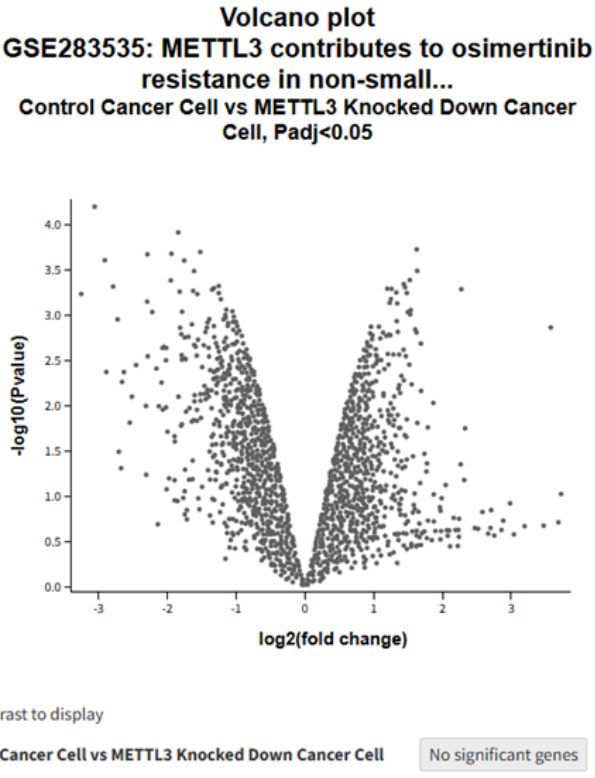
Background:

The dataset looked for the possibility of METTL3 as a contributor to Osimertinib resistance. Osimertinib is commonly used to treat non-small cell lung cancer (NSLC).

Method:

The possibility was examined by comparing METTL3 knocked down cancer cells and control cancer cells from GSE283535 dataset on GEO and was analyzed using GEO2R. Significant genes were determined by adjusted p-value of <0.05.

Result:



Based on analysis on GEO2R, there is no significant gene that is differentially expressed identified. But, this is suspected due to the small number of samples available (4). The results itself still shows genes with log2FC values that would be considered significant. However, a

study that had used the same set of data suggested that METTL3 indeed has a role in inhibiting CDC25A and AURKB mRNA stability and hence, their expression which contribute to osimertinib resistance. METTL3 down regulation was then shown to attenuate said resistance.[1]

Transcriptome analysis of the effects of sorafenib and osimertinib in PC9 cells

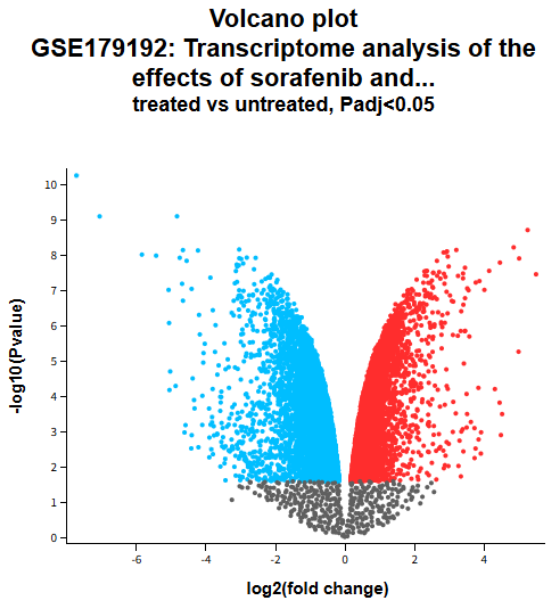
Background:

The dataset looked for gene expression profiles between untreated and treated P9 cells with sorafenib, osimertinib, and both.

Method:

The possibility expressions were examined by comparing untreated cells and treated cells with both sorafenib and osimertinib from GSE179192 dataset on GEO and were analyzed using GEO2R. Significant genes were determined by adjusted p-value of <0.05.

Results:



[1] Suzuki, R., Terashima, M., Ishimura, A., Meguro-Horike, M., Horike, S., Wanna-Udom, S., Takino, T., & Suzuki, T. (2025). METTL3 contributes to osimertinib resistance in non-small cell lung cancer cell lines by regulating CDC25A and AURKB mRNA stability. *Cellular Signalling*, *136*, 112156. https://doi.org/10.1016/j.cellsig.2025.112156

Based on GEO2R analysis, there are more than 250 significant genes that are differentially expressed between untreated and treated P9 cells with the most differentially expressed gene marked A_23_P214080 having log2FC value of -7.73, meaning that the gene is heavily down regulated in treated samples. A study cited on the dataset page suggests that treatment with sorafenib to be highly effective and treatment with both sorafenib and osimertinib are still effective in treating osimertinib resistant cells.[2]

Gene expression of KP4 and A549 cells regulated by matrix stiffness and ATF5

Background:

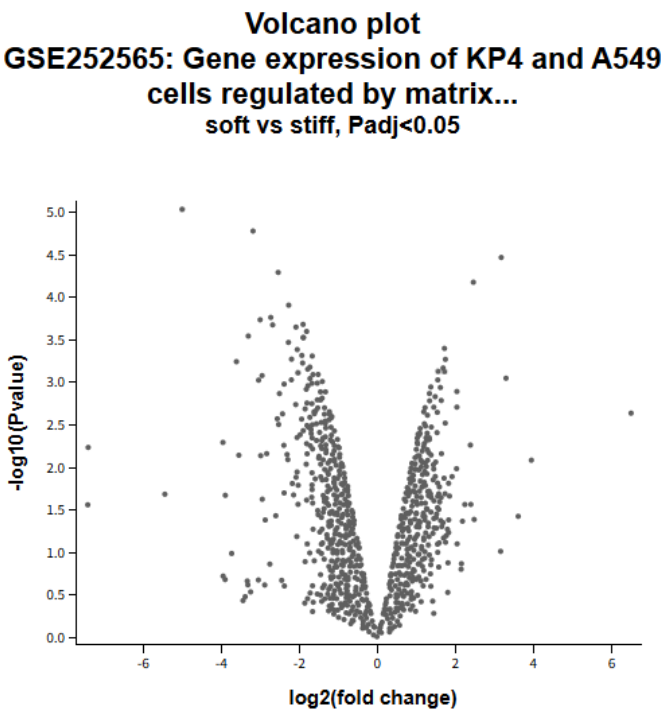
The dataset looked for gene expression differences between KP4 (pancreatic cancer cells) and A549 (lung cancer cells) cultured on stiff and stiff media. Additionally the dataset also compared it to ones with negative control RNA, siATF5-1, and siATF5-2 on stiff media.

Method:

The possibility was examined by comparing lung cancer cells cultured on soft media with stiff media, including with siATF5s from GSE252565 dataset on GEO and was analyzed using GEO2R. Significant genes were determined by adjusted p-value of <0.05.

Result:

[2] Brunet, L., Alexandre, D., Lee, J., Del Mar Blanquer-Rosselló, M., Bracquemond, D., Guernet, A., Chhouri, H., Goupil, M., Kherrouche, Z., Arabo, A., Mancini, M., Cartier, D., Yao, S., Godefroy, D., Dehedin, J., Li, J., Duparc, C., Jamme, P., Vinchent, A., . . . Grumolato, L. (2025). Prolonging lung cancer response to EGFR inhibition by targeting the selective advantage of resistant cells. *Nature Communications*, *16*(1), 7853. https://doi.org/10.1038/s41467-025-61788-w



GEO2R analysis showed no significant genes that are differentially expressed between the two groups compared, albeit there still are genes that show significant log2FC values. The study cited on the dataset page suggests that ATF5 activation and cancer proliferation are caused by the stiffening of the extracellular matrix (ECM) of cancerous cells. It happens because ECM stiffening triggers a pathway that activates ATF5.[3]

[3] Ishihara, S., Enomoto, A., Sakai, A., Iida, T., Tange, S., Kioka, N., Nukuda, A., Nagasato, A. I., Yasuda, M., Tokino, T., & Haga, H. (2025). Stiff extracellular matrix activates the transcription factor ATF5 to promote the proliferation of cancer cells. *iScience*, *28*(3), 112057. https://doi.org/10.1016/j.isci.2025.112057