

Measuring functional PI3K pathway activity in cancer tissue using FOXO target gene expression in a diagnostic computational model

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Summary

- The PI3K pathway is commonly hyper-activated in various types of cancer, but reliable predictive diagnostics for PI3K inhibitors is lacking.
- The PI3K pathway negatively regulates tumor suppressive FOXO transcription factors.
- We developed a computational model to assess functional activity of the PI3K-FOXO pathway in individual samples, using tissue mRNA expression data of FOXO target genes.
- Our model has been biologically validated on various cell lines with FOXO induction and PI3K inhibition, and tested on a large cohort of breast cancer patient samples.
- FOXO activity may be high while PI3K is active in case of oxidative stress, which we measure by SOD2 expression. This occurs most frequently in more aggressive breast cancer subtypes.
- Our functional PI3K pathway assessment may be highly relevant for PI3K therapy prediction.

