INHIBITION OF PROLINE CATABOLISM TO TREAT CANCER

TECHNOLOGY DESCRIPTION

Buck investigators discovered that the p53-inducible gene and mitochondrial enzyme, proline dehydrogenase (PRODH), supports breast cancer cell survival by supplying much needed energy and carbon nutrients, especially under nutritional and hypoxic stress conditions. Their study of MDM2-inhibiting anticancer agents that restore wildtype p53 expression indicated that p53 transcriptional induction of PRODH supports breast cancer survival and, by implication, survival of other cancers.

Furthermore, data shows that PRODH knockdown not only impairs breast cancer growth by itself, but when combined with either a p53 restoring drug (e.g., MI-63 or nutlin-3a) or a clinical GLS1 inhibitor (e.g. CB-839) produces a "synthetic lethal" and synergistic anticancer response against malignant but not normal breast epithelial cells.

APPLICATIONS

- Methods for treating cancer via inhibition of PRODH/proline catabolism.
- Combination therapy for cancer which includes inhibition of PRODH and restoration of p53 function.

PATENT STATUS

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