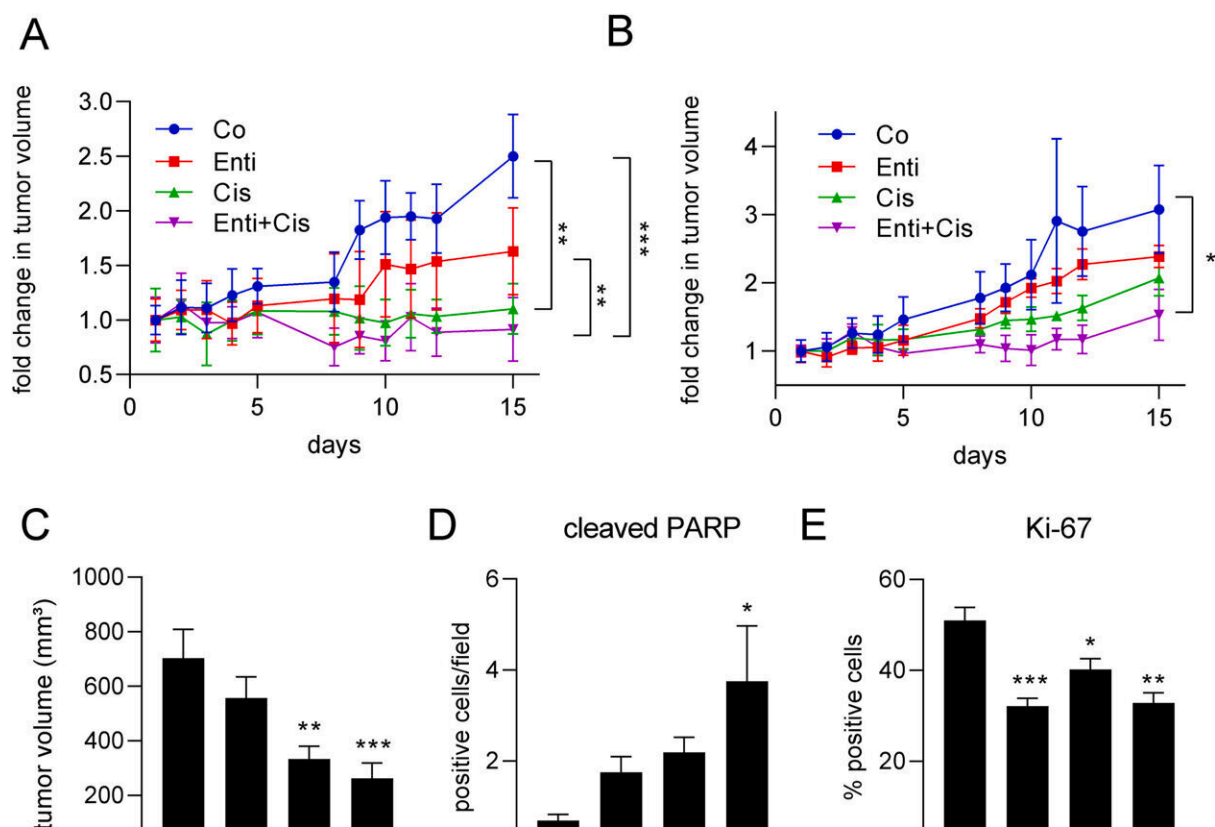


# Pleural mesothelioma: New therapeutic approach enhances sensitivity to chemo- and radiotherapy

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Entinostat enhances cisplatin-induced tumor growth inhibition and cell death induction in vivo. Tumor growth of MSTO-211H cells injected subcutaneously into (A) female and (B) male SCID mice treated with 25 mg/kg entinostat (Enti), 3 mg/kg cisplatin (Cis), a combination of both (Enti + Cis) or respective vehicles (Co, 5% DMSO in corn oil for entinostat, 0.9% NaCl for cisplatin). Data is shown as mean  $\pm$  SEM of the fold change in tumor volume after treatment start.

N = 4 mice per group/sex. ANOVA and Kruskal-Wallis test for multiple comparisons. (C) Volumes of the tumors on day 15 from both sexes combined. Quantification of positively stained cells per high magnification image in the male group was done for (D) cleaved PARP and (E) Ki-67, determined by immunohistochemistry. For each tumor (N = 4 per group), 3–4 representative pictures were evaluated. Data is shown as mean  $\pm$  SEM. ANOVA and Dunnett's multiple comparisons test vs. Co in C, D and E. \*p Cancer Letters (2023). DOI: 10.1016/j.canlet.2023.216395

Pleural mesothelioma (PM) is mainly caused by asbestos exposure and characterized by poor prognosis and limited therapeutic options. A recent research study led by Karin Schelch and Michael Grusch from MedUni Vienna identified the oncoprotein YB-1 as an attractive therapeutic target in PM and demonstrates that indirect targeting of YB-1 is a promising approach to enhance sensitivity to chemo- and radiotherapy. The study results were published in the journal [Cancer Letters](#).

The study follows [findings published earlier this year](#) by the research group led by Michael Grusch (Center for Cancer Research at MedUni Vienna and Comprehensive Cancer Center at MedUni Vienna and University Hospital Vienna), according to which the oncoprotein YB-1 is involved in regulating multiple traits of [pleural mesothelioma](#) (PM) such as [cell growth](#), [cell death](#) and migration.

The current study proves its relevance in drug response. Accordingly, YB-1 knockdown via siRNA resulted in significantly reduced [tumor growth](#) and furthermore enhanced the sensitivity to cisplatin and radiation.

## Reaching the target

Histone deacetylase inhibitors (HDACi) have already been shown in trials to be effective in fighting tumor cells of different types. Since there are no pharmaceutical YB-1 inhibitors available, indirect targeting of YB-1 was achieved by the HDACi entinostat, which also inhibits YB-1 deacetylation, thereby modifying its function.

"Our findings provide the basis for the development of novel, clinically feasible therapy approaches," says principal investigator Michael Grusch from the Center of Cancer Research and Comprehensive Cancer Center, highlighting the study's high clinical relevance.

## **Combination instead of single therapy**

Entinostat proved to be very effective against PM cells and showed strong synergistic interactions with cisplatin chemotherapy, which was linked to significantly increased cellular platinum uptake. In a [mouse model](#), the combination of cisplatin and entinostat also resulted in stronger growth inhibition than each treatment alone.

"These data go hand in hand with another study performed in parallel in Small Cell Lung Cancer where we showed similar synergistic effects between these two drugs," says Karin Schelch also from MedUni Vienna's Center for Cancer Research, Comprehensive Cancer Center and Department of Thoracic Surgery at MedUni Vienna and University Hospital Vienna, first author of the present and last author of the [parallel study](#) recently published in *Clinical Cancer Research*.

Taken together, these studies highlight YB-1 as an attractive target in PM and demonstrates that targeting YB-1 via entinostat is an urgently needed novel treatment approach for PM.

**More information:** Karin Schelch et al, Targeting YB-1 via entinostat enhances cisplatin sensitivity of pleural mesothelioma in vitro and in

vivo, *Cancer Letters* (2023). [DOI: 10.1016/j.canlet.2023.216395](https://doi.org/10.1016/j.canlet.2023.216395)

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