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# Small molecules with antiproliferative activity against pancreatic cancer cells

Small molecules that show antiproliferative activity against the pancreatic cancer cell line MiaPaca-2.

Technology No. 20160388

**IP Status:** US Patent Issued

## Applications

- Pancreatic cancer treatment
- Autophagy modulator

## Key Benefits & Differentiators

- **Targets tumor cells:** Small molecules potentially able to selectively target poorly vascularized solid tumor cells under metabolic stress and hypoxia
- **Increased cell killing:** Compared to known autophagy and tyrosine kinase inhibitors these small molecules were more potent and active in killing pancreatic cancer cells

## Pancreatic Ductal Adenocarcinoma Treatment

Pancreatic ductal adenocarcinoma (PDAC), one of the most lethal forms of cancer in the US, is commonly diagnosed in late stages and is often resistant to standard of care chemotherapies. Autophagy, activated by mTORC1 inhibition, behaves as a tumor suppressor in normal cells. However, in cancer cells, increasing evidence shows that autophagy is a cytoprotective mechanism often exploited to promote chemotherapy resistance. In PDAC tumors autophagy is activated and is associated with poor patient outcomes. Therefore, autophagy inhibitors, used alone or in combination with other cancer therapeutics, have been proposed as a promising strategy to combat PDAC.

Researchers at the University of Minnesota have developed newly-designed small molecules that show high antiproliferative activity against the pancreatic cancer cell line MiaPaca-2. These small molecules reduce mTORC1 activity and increase basal autophagy. However, under starvation and starvation/refeed conditions, they reduce mTORC1 reactivation and impair

autophagic flux. No other compounds with such differential activities on autophagy have been previously reported. Therefore, these small molecules might represent a new class of autophagy modulators that possess remarkable anticancer activity. These small molecules have submicromolar activity and good metabolic stability in both plasma and liver microsomes. Compared to known autophagy and tyrosine kinase inhibitors, these small molecules were more potent and active in killing pancreatic cancer cells. These small molecules are expected to be advantageous over conventional autophagy inhibitors that unselectively suppress autophagy in normal and cancerous cells.

## Phase of Development

**TRL: 3-4**
Compounds designed and synthesized; in vitro antiproliferative data; in vitro metabolic stability in both plasma and liver microsomes.

### Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

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### Researchers

- **Liqiang Chen, PhD** Associate Professor, Center for Drug Design

## References

Teng Ai, Rose Willett, Jessica Williams, Rui Ding, Daniel J. Wilson, Jiashu Xie, Do-Hyung Kim, Rosa Puertollano, and Liqiang Chen(2017), https://pubs.acs.org/doi/10.1021/acsmedchemlett.6b00392, https://pubs.acs.org/journal/amclct, 8, 90–95

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