The Ability of N-Glycan Inhibitors to Suppress Pancreatic Cancer Growth

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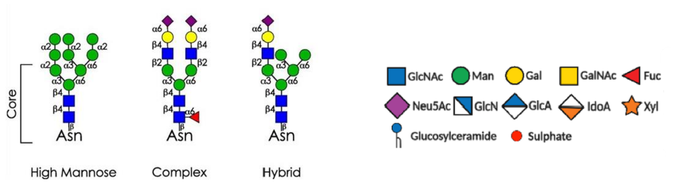
Abstract

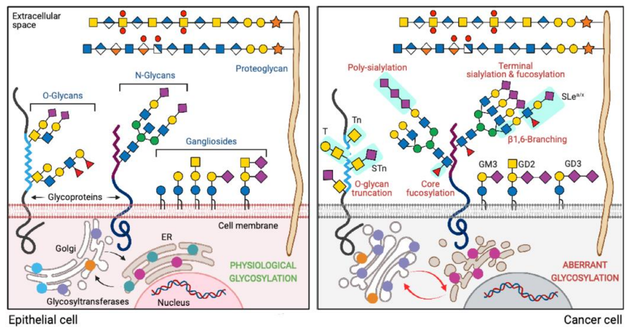
N-glycan inhibitors are potent drugs for suppressing pancreatic cancer. Their ability to block the pathway of the production of complex type N-glycans allows the N-glycosylation distribution in pancreatic cancer cells to alter in a way that is unfavorable for cancer growth. Our research focuses on the effects N-glycan inhibitors have on the viability and sphere formation of pancreatic cancer cell lines. Our experiments demonstrate that N-glycan inhibitors can reduce cell viability of cancer cells, although they will also reduce cell viability of fibroblasts and normal pancreatic cells. However, N-glycan inhibitors are effective in suppressing sphere formation of cancer cells. This result establishes altering N-glycosylation distribution as a promising treatment for pancreatic cancer.

Introduction

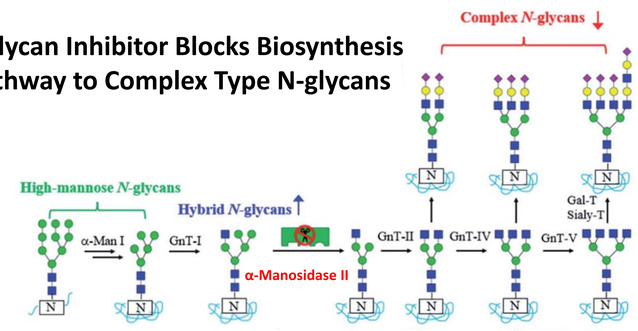
Types of N-Glycosylation



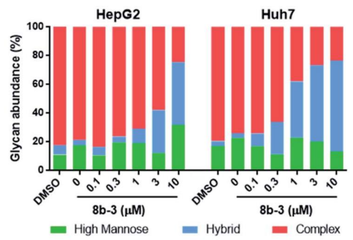
Glycosylation Alteration during Cancer Transformation



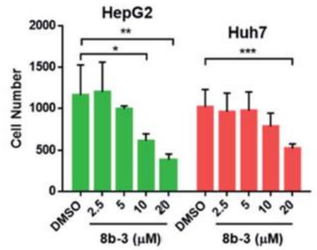
N-Glycan Inhibitor Blocks Biosynthesis Pathway to Complex Type N-glycans



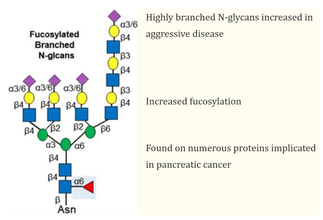
N-Glycan Inhibitor Alters N-Glycosylation Distribution



N-Glycan Inhibitor Suppresses Liver Cancer Cell Growth



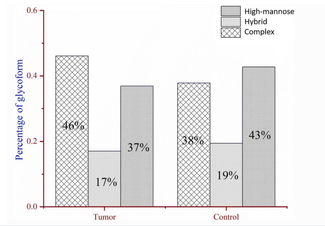
High Abundance of Complex Type N-glycans in Pancreatic Cancer



Highly branched N-glycans increased in aggressive disease

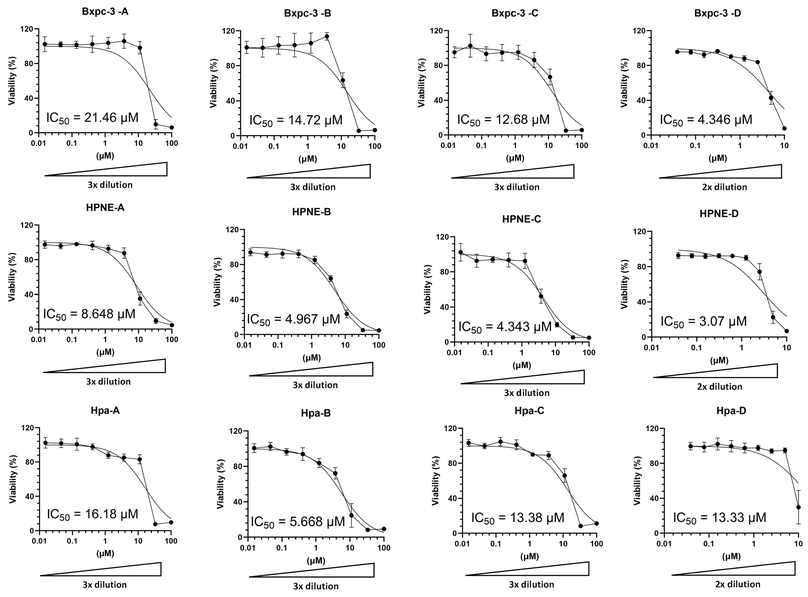
Increased fucosylation

Found on numerous proteins implicated in pancreatic cancer



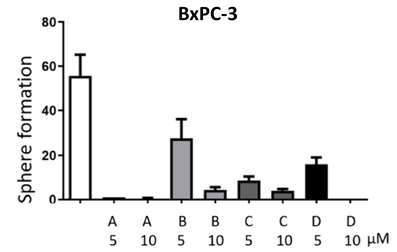
Results

N-Glycan Inhibitors Suppress Sphere Formation and Viability of Pancreatic Cancer Cells



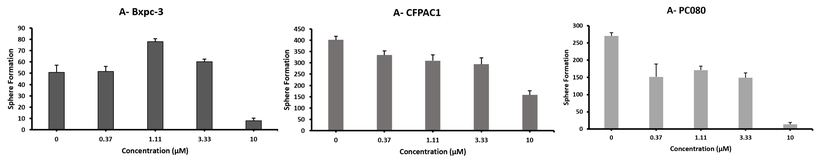
Result: N-glycan inhibitor A is the least effective in killing pancreatic cancer cells

BxPC-3



Result: N-glycan inhibitor A is the most effective in suppressing sphere formation of pancreatic cancer cells

N-Glycan Inhibitor A Suppresses Sphere Formation in Pancreatic Cancer Cells



Result: N-glycan inhibitor A can suppress sphere formation of pancreatic cancer cells in three different cell lines

Conclusion

All the N-glycan inhibitors can suppress sphere formation and viability of pancreatic cancer cells. N-glycan inhibitor A has the highest IC_{50} for both normal and cancer cells, suggesting that it has the lowest level of toxicity compared to the other inhibitors. It is also the most effective in inhibiting cancer stemness.

Discussion

Previous research has shown that N-glycan inhibitors can suppress liver cancer growth. In our study, we successfully demonstrated that N-glycan inhibitors can also inhibit cancer development in pancreatic cancer. However, what effects the decreased amount of complex type N-glycans have on the expression of proteins and how that leads to killing cancer cells require further study. Future research will focus on finding out the proteins affected by the inhibitors and developing new drugs that only target the specific proteins that need to have their N-glycosylation distribution altered to suppress cancer development.

References

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