Reprogramming of Steroid Metabolism in Natural Killer Cell Activation via Lipids

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Agenda

- Background
- Objectives
- Results
- Conclusions
- Future Directions
Background

- Pancreatic ductal adenocarcinoma (PDAC) is a type of pancreatic cancer that is extremely lethal and essentially untreatable
  - Accounts for 90% of all pancreatic cancer cases [1]
- 5 year survival rate of only 6% [2]
Background

- Natural Killer (NK) cells are an important part of the innate immune system
  - Innately monitor and kill cancer cells
- Understanding metabolic requirements can help them become more effective at fighting PDAC
Background

- NK cells use a reprogrammed metabolism based on SREBP2
  - SREBP2: master regulator of sterol and fatty acid synthesis
- Statins lower cholesterol levels in the body
- Steroids are synthesized via the mevalonate pathway
  - Building block: acetyl-CoA from glucose
  - Protein prenylation
Objectives

1. Determine the metabolic requirements of NK cells for mevalonate pathway

2. Understand how protein prenylation regulates NK cell activity

3. Investigate how peroxisomes, which metabolize unsaturated fatty acids, relate to cholesterol metabolism
Glucose metabolism is altered by statin treatment in NK cells
NK cells are dependent upon prenylation substrates for cytotoxicity
NK cell surface markers are downregulated by statin treatment and rescued by prenylation substrates.
Statin treatment displaces vital trafficking proteins, affecting NK cell function
Lipids can regulate peroxisome and cholesterol metabolism genes
Conclusions

- Protein prenylation is vital for NK cell function
- NK cell function is determined by lipid metabolism
- GGPP treatment
Future Directions

- Investigate how peroxisomes connect NK lipid metabolism to cholesterol metabolism in the tumor microenvironment
Thank you for listening!
FAQ

How did you get involved in this project?

What inspired you?

How do you hope to use what you learned from this project in your future career?
References


