Title: Identifying New G Protein Coupled Receptor Kinase 6 Substrates among Proteins Closely Linked to Prognoses of Pancreatic Cancer

Primary Author: Christine Taing

Other Authors: Jelena Jovanovic, Nicole Khalil, and Christopher So

Purpose

G protein coupled receptor kinases (GRKs), in addition to playing important roles in controlling the activity of drug receptors, may also modulate the activity of non-receptor proteins involved in cancer development. The identification of these protein-protein interactions may provide important clues as to how these associations may lead to the development of cancers and, therefore, how best to treat them. In this study, we sought to identify if GRK6 can interact with various proteins associated with negative or positive prognosis of pancreatic cancer and, if there are connections, what this may mean in terms of their effect on biological and molecular activities.

Methods

In this study, the phosphorylation site predictors Phosphonet and GPS (versions 3.0 and 5.0) were utilized to determine if GRK6 is predicted to phosphorylate the top 20 proteins found to be most associated with negative or positive prognosis according to proteinatlas.org. For the top 6 proteins identified to be the most likely proteins phosphorylated by GRK6 by these sites, their biological and molecular functions from their gene ontology terminologies were collected and word clouds generated to determine common trends associated with these top 6 proteins.

Results

In this study, we found that several proteins from the negative or positive prognosis lists were predicted to more likely be GRK6 substrates compared to others, suggesting a potential specificity for GRK6- protein interactions among proteins most likely to be linked to cancer prognosis. Biologically, the top 6 proteins associated with negative prognosis and GRK6 were more associated with cell signaling events whereas, for positive prognosis and GRK6, more were associated with DNA transcription. Molecularly, the top 6 proteins associated with GRK6 and negative prognosis were more associated with proteins whereas, for positive prognosis and GRK6, more were associated with DNA.

Conclusion

This study identified potential GRK6 substrates among the list of proteins most likely associated with either negative or positive prognosis of pancreatic cancer. This study showed that the proteins associated with negative prognosis and GRK6 the best were affiliated more with cell signaling whereas those best associated with positive prognosis and GRK6 were linked to DNA transcription. Overall, these results show that GRK6, if involved in the development of pancreatic cancer, could play different roles depending on if the pancreatic cancer has a positive or a negative prognosis. This may suggest that GRK6 could potentially be a key biological marker to determine the appropriate pancreatic cancer therapy.