

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

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## **Purpose**

G protein coupled receptor kinases (GRKs), best known to phosphorylate activated G protein coupled receptors, can also interact with many non-receptor proteins. These interactions may play important roles in the development of a variety of diseases, such as cancer. Therefore, the identification of GRK interactors, and the signaling cascades they may modulate, could be important to determine how various diseases develop and how they can be successfully treated. In this study, GRK6 interactions with various proteins associated with negative or positive prognosis of liver cancer were explored and the additional protein networks associated with these connections were determined.

## **Methods**

In this study, the phosphorylation site predictors phosphonet and GPS (versions 3.0 and 5.0) were used to determine if GRK6 can 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, connections with other proteins were then determined by STRING and connections with other top proteins were determined to figure out if these top proteins connect through a single protein.

## **Results**

In this study, we found that a number of proteins linked to negative or positive prognosis of liver cancer were predicted to be GRK6 substrates far more than others. Some of these proteins shared a connection through another protein, suggesting a close relationship in terms of their cellular activities. However, other proteins did not have these kinds of connections, implying a less close association of their activities.

## **Conclusion**

This study found potential proteins that were phosphorylated by GRK6 among proteins most likely associated with either negative or positive prognosis of liver cancer. Some of these proteins may have closer connections of activity over others, as they can interact through a single protein. Overall, this shows that GRK6, if involved in the development of liver cancer, could be modulating activities among proteins most likely to lead to negative or positive prognosis of this cancer. These proteins may be forming novel signaling cascades that could be explored for drug development purposes.