1. **What is the medically relevant insight from the article?**

The medically relevant insight from the article "Reconstruction of Insulin Signal Flow from Phosphoproteome and Metabolome Data" is the identification of the signal flow of insulin and its role in regulating cellular homeostasis. By analyzing time-course phosphoproteome and metabolome data, the study reveals the influence of insulin signaling on metabolic homeostasis. Insights from the conducted study also provide more comprehensive understanding of insulin signaling and could potentially be exploited for development of more effective treatments for metabolic disorders such as diabetes. Apart from medically relevant insight, researchers also provide computational workflow that can be further applied with any signaling network at the cellular and in vivo levels.

1. **Which genomics technology/ technologies were used?**

The main -omic technologies this study is based upon include phosphoproteomics and metabolomics. Here, phosphoproteomics was used for detection and quantification of phosphorylated proteins involved in insulin signaling. Metabolomics, on the other hand, focuses on the quantitative measurement of low molecular weight molecules, also known as metabolites, that are present in a cell, tissue, or an organism. In this study, metabolomics was used to capture changes in metabolite levels associated with insulin signaling. Using information from phosphoproteome, metabolome and various databases researchers reconstructed detailed insulin signaling involving 13 protein kinases, 26 phosphorylated enzymes, numerous allosteric effectors, and metabolites.

1. **List and explain at least three questions/ hypotheses you can think of that extend the analysis presented in the paper**

Three questions/hypotheses that extend the analysis presented in the paper could be: a. How does insulin signaling differ in different cell types? Exploring the variations in insulin signal flow across cell types can provide deeper insights into tissue-specific metabolic regulation. b. How does insulin signaling interact with other signaling pathways? Investigating the crosstalk between insulin signaling and other signaling pathways can elucidate the complex interplay between different cellular processes. c. How does signal flow change in response to perturbations? By subjecting cells to different experimental conditions or stimuli, we can track the changes in signal flow and identify the dynamic responses of cellular networks. This can help uncover how cells adapt and maintain homeostasis.

1. **Devise a computational analysis strategy for (some of) the listed in previous question**

A computational analysis strategy for the listed questions could involve: a. Integration of transcriptomics data: Analyzing gene expression profiles in conjunction with phosphoproteome and metabolome data can provide a more comprehensive understanding of insulin signaling and its downstream effects. b. Machine learning-based prediction: Utilizing machine learning algorithms to predict novel insulin targets or identify potential crosstalk between insulin signaling and other pathways, based on the available data and existing knowledge in the field. c. Apply computational methods to analyze the flow of signals through the network. This could involve techniques such as flux balance analysis, pathway analysis, or dynamical modeling. The aim is to identify the paths and dynamics of signal flow within the network.