7. In the mating factor signaling pathway Ste7, another serine/threonine kinase is the substrate for Ste11. When the mating factor signaling pathway is activated, Ste7, Ste11, and the other relevant kinases in the cascade form a complex with the scaffold protein Ste5. Binding to Ste5 ensures that Ste7 is the only substrate to which Ste11 has access.

8. Maximal activation of protein kinase B requires 1) release of inhibition by its own PH domain, which is achieved when PI 3-phosphate binds the PH domain; 2) phosphorylation of a serine in the activation lip of protein kinase B by PDK1, which occurs when both protein kinase B and PDK1 are recruited to the cytosolic surface of the plasma membrane by binding PI 3-phosphates; and 3) phosphorylation of an additional serine residue located outside the activation lip. In muscle cells, insulin-stimulated activation of protein kinase B causes fusion of intracellular vesicles containing the GLUT4 glucose transporter with the plasma membrane, resulting in increased influx of glucose. Insulin-stimulated activation of protein kinase B also promotes glycogen synthesis because protein kinase B phosphorylates and inhibits glycogen synthase kinase 3 (GSK3), an inhibitor of glycogen synthase.

9. PTEN phosphatase removes the 3-phosphate from PI 3,4,5-triphosphate, thus reversing the reaction catalyzed by PI-3 kinase and rendering the PI phosphate unable to bind protein kinase B and PDK1. Loss-of-function mutations are cancer promoting because constitutive activation of protein kinase B results in constitutive phosphorylation and inactivation of proapoptotic proteins such as Bad and Forkhead-1. Cancers are typically characterized by cells that are resistant to apoptosis. A gain-of-function mutation in PTEN phosphatase would promote cell death by causing the apoptotic pathway to be active even in the presence of survival factors that signal through protein kinase B.

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10. In multiple cell types, TGFb activates a conserved signaling pathway that results in translocation of Smad2 or Smad3 to the nucleus in complexes with co-Smad4. Once in the nucleus, the Smads interact with other transcription factors to regulate the expression of target genes. The complement of these other transcription factors is cell-type specific, and thus the TGFb signaling pathway will induce the transcription of different genes in different cell types.

11. TGFb binds to its type II receptor either directly or when presented by the type III receptor. The type II receptor is a constitutively active serine/threonine kinase. When the type II receptor binds TGFb, it forms a tetrameric complex consisting of two molecules of the type II receptor and two molecules of the type I receptor. The type II receptor then phosphorylates the type I receptor, activating the type I receptor as a serine/threonine kinase. The type I receptor then phosphorylates R-Smad2 or R-Smad3, inducing a conformational change that exposes a nuclear localization signal on the R-Smad. The R-Smad then forms a complex consisting of two molecules of R-Smad and one molecule each of co-Smad4 and importin-b. This complex translocates to the nucleus, where it interacts with other transcription factors to elicit changes in gene expression. A nuclear phosphatase continuously dephosphorylates and inactivates Smads in the nucleus.