Regulation of HIF1α function by FBP1 and FBP2

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In cancer cells, hypoxia-inducible factor 1α (HIF1α), a master regulator of the transcriptional response to hypoxic conditions, can be affected in a non-enzymatic manner by fructose 1,6-bisphosphatase (FBP). Both isozymes of FBP, namely liver (FBP1) and muscle (FBP2) forms, can interact with HIF1α. In this poster, we present quantitative data on the interaction of FBP1 and FBP2 with HIF1α in vitro, in the presence and absence of natural and synthetic allosteric effectors of FBP. We also demonstrate the effectors-induced changes in the formation of the FBP-HIF1α complex in lung cancer cells, under normoxic and hypoxic conditions. Our results reveal that the amount of the FBP1-HIF1α complex depends only on the titer of FBP1, while the FBP2-HIF1α association is regulated by AMP, an allosteric FBP inhibitor whose concentration is a function of the metabolic state of the cell. In the short term, the interaction between FBP and HIF1α leads to the degradation of the former and reduced expression of HIF1α-dependent genes. The dynamic regulation of FBP2-HIF1α complex formation is strong evidence that this isozyme has a bigger role in maintaining HIF1α levels in cells than FBP1. This difference is probably caused by distinct conformational changes in FBP oligomers in response to the allosteric effectors.