



SDI FINAL EVALUATION FORM 1.1

PART 1:

Journal Name:	Journal of Advances in Medical and Pharmaceutical Sciences
Manuscript Number:	Ms_JAMPS_29407
Title of the Manuscript:	Effect of hypoxia-inducible factor-1 and 2 on tumor growth
New title:	Effect of hypoxia inducible factor on hypoxia inducible gene expression and glycolysis
Type of Article:	Original Research Article

PART 2:

FINAL EVALUATOR'S comments on revised paper (if any)	Authors' response to final evaluator's comments
The result and discussion sections are exemplary. One sincerely appreciates the effort which the authors took. Need to just check few very minor grammatical errors such missing 'is' and 'are', more so in the introduction section.	The following has been corrected with green colour: ABSTRACT Aim: The effect of both HIF-1 and HIF-2 drastically affect hypoxia responses. Because the relative contributions to hypoxic gene induction and transcriptions are unknown; we aim to evaluate HIF2 target genes, and discuss the secondary gene activations and RNA expression transcripts. Place and Duration of Study: This study was carried out in the Department of Biochemistry, Faculty of Science, Center of Innovation in Personalized Medicine, King Fahd Center for Medical Research, King Abdulaziz University, Jeddah, Saudi Arabia, in the year 2015. Methodology: Both HIF-1α and HIF-2α have been implicated in hypoxia responses. However, till now, their relative contributions to hypoxic gene induction and transcriptions is unknown. Here in this study we evaluate HIF2α target genes, and discuss the secondary gene activations and RNA expression transcripts, specifically glycolytic genes and we believe such information can translate into further hypothesis generating studies that could result in oncology and drug discoveries. Results: This study showed that, HIF1α stimulates glycolytic GE in both types of cells clearly showing for the HIF1α and HIF2α (or HIF1 and HIF2) have singular aims; however, growing proof distinguishes between both molecules in terms of transcriptional targets and effect on different physiological pathways and tumorigenesis. Moreover, more interest has been paid in order to understand the real effect of HIF2α in order to control/regulate different sides of digestive-tumors; including angiogenesis, proliferation and apoptosis, metastasis, metabolism and resistance to chemotherapy. Conclusions: The study shows that HIF2α plays an essential and crucial role as regulator of the malignant phenotype. In the present study, one shows the importance role played by both HIF1 and 2 through tumor growth. Keywords: HIF1α and HIF2α, tumor growth, malignant phenotype, regulated resistance, 1. INTRODUCTION The hypoxia-inducible factor is complex-protein containing the well-known three proteins HIF1α (HIF1), HIF2α (HIF2). The amino-acid sequence of HIF 2α is compatible with HIF1 to about 48% [1-8]. In particular, HIF1 is a nitrogenous organic compound that consists of huge molecules of amino acids and it is a vital portion of all living cells. It constitutes an important part in the physiology of human responses to deficiencies of oxygen. HIF-1 is among the fundamental genes implicated in the metabolic mechanisms which keep the body functions in its normal and steady state; for example normal temperature, common fluid composition, average blood sugar, gas concentrations, blood pressure, etc. HIF-1 is also important for vital process such as defense against invading materials including virus, antigen or even bacteria/fungus. In addition, it fabricates defender materials (for example antibodies) against these overrun materials. The legend of figure 1 has been changed: Figure 1 (a): Schematic illustration shows in full line hypoxia-direct and in dotted line hypoxia-indirect: The reverse effect of HIF-1α which up adjusts P53 activity while HIF-2α down adjusts P53 activity; Figure 1 (b) Schematic illustration shows HIF-1α and HIF-2α adjust in peculiar manner c-Myc reaction with its reproduction cofactors. HIF-1α reduces the assembly with MAX and SP1, and then reduces MYC action, while HIF-2α joins with MAX and SP1 complex, that way rising MYC action.