

Supplementary Methods S1

Creating cervical cancer specific hypoxia gene sets:

2902 probes had a >2-fold change in expression after hypoxia treatment (0.2% O₂ for 24h) compared with control (normoxia) in at least one of the HeLa, SiHa and CaSki cell lines, corresponding to 2497 unique gene IDs. A number of other studies have been published where hypoxia regulated genes are reported (1-15), and 469 of the 2497 genes that were hypoxia regulated in our cervical cancer cell lines were also described to be hypoxia regulated in one or more of these published articles. Out of these, 286 genes were up-regulated in the cervical cell lines and were included in the gene set “Hypoxia cervical up & literature”. The remaining 183 were down- regulated and constituted the gene set “Hypoxia cervical down & literature”. Additionally, two other hypoxia gene sets were made from genes which were up- or down- regulated, respectively, by >2-fold in all three cervical cancer cell lines, but not necessarily known hypoxia regulated genes from the literature. These were named “Hypoxia cervical up x3” and “Hypoxia cervical down x3”, and included 79 and 10 genes, respectively. The four created hypoxia gene sets together with fold-change of individual genes after hypoxia treatment, are listed in **Supplementary Methods S2**.

The up- and down -listed gene signatures were based on the direction of regulation by hypoxia in the cell lines. If a gene was >2x up-regulated in one cell line, and >2x down-regulated in another, or the contrary, it was excluded from the lists.

Reference List

- (1) Denko NC, Fontana LA, Hudson KM, Sutphin PD, Raychaudhuri S, Altman R, et al. Investigating hypoxic tumor physiology through gene expression patterns. *Oncogene* 2003;22:5907-14.
- (2) Harris AL. Hypoxia--a key regulatory factor in tumour growth. *Nat Rev Cancer* 2002;2:38-47.
- (3) Lal A, Peters H, St CB, Haroon ZA, Dewhirst MW, Strausberg RL, et al. Transcriptional response to hypoxia in human tumors. *J Natl Cancer Inst* 2001;93:1337-43.
- (4) Mense SM, Sengupta A, Zhou M, Lan C, Bentsman G, Volsky DJ, et al. Gene expression profiling reveals the profound upregulation of hypoxia-responsive genes in primary human astrocytes. *Physiol Genomics* 2006;25:435-49.

- (5) Ning W, Chu TJ, Li CJ, Choi AM, Peters DG. Genome-wide analysis of the endothelial transcriptome under short-term chronic hypoxia. *Physiol Genomics* 2004;18:70-8.
- (6) Sung FL, Hui EP, Tao Q, Li H, Tsui NB, nis Lo YM, et al. Genome-wide expression analysis using microarray identified complex signaling pathways modulated by hypoxia in nasopharyngeal carcinoma. *Cancer Lett* 2007;253:74-88.
- (7) Weinmann M, Belka C, Guner D, Goecke B, Muller I, Bamberg M, et al. Array-based comparative gene expression analysis of tumor cells with increased apoptosis resistance after hypoxic selection. *Oncogene* 2005;24:5914-22.
- (8) Winter SC, Buffa FM, Silva P, Miller C, Valentine HR, Turley H, et al. Relation of a hypoxia metagene derived from head and neck cancer to prognosis of multiple cancers. *Cancer Res* 2007;67:3441-9.
- (9) Jiang Y, Zhang W, Kondo K, Klco JM, St Martin TB, Dufault MR, et al. Gene expression profiling in a renal cell carcinoma cell line: dissecting VHL and hypoxia-dependent pathways. *Mol Cancer Res* 2003;1:453-62.
- (10) Leonard MO, Cottell DC, Godson C, Brady HR, Taylor CT. The role of HIF-1 alpha in transcriptional regulation of the proximal tubular epithelial cell response to hypoxia. *J Biol Chem* 2003;278:40296-304.
- (11) Mizukami Y, Jo WS, Duerr EM, Gala M, Li J, Zhang X, et al. Induction of interleukin-8 preserves the angiogenic response in HIF-1alpha-deficient colon cancer cells. *Nat Med* 2005;11:992-7.
- (12) Manalo DJ, Rowan A, Lavoie T, Natarajan L, Kelly BD, Ye SQ, et al. Transcriptional regulation of vascular endothelial cell responses to hypoxia by HIF-1. *Blood* 2005;105:659-69.
- (13) Elvidge GP, Glenny L, Appelhoff RJ, Ratcliffe PJ, Ragoussis J, Gleadle JM. Concordant regulation of gene expression by hypoxia and 2-oxoglutarate-dependent dioxygenase inhibition: the role of HIF-1alpha, HIF-2alpha, and other pathways. *J Biol Chem* 2006;281:15215-26.
- (14) Le QT, Denko NC, Giaccia AJ. Hypoxic gene expression and metastasis. *Cancer Metastasis Rev* 2004;23:293-310.
- (15) Papandreou I, Powell A, Lim AL, Denko N. Cellular reaction to hypoxia: sensing and responding to an adverse environment. *Mutat Res* 2005;569:87-100.