

# GENOME-WIDE ANALYSIS OF TRANSLATIONAL-REGULATED GEGE in Hypoxic Alveolar Epithelial Cells

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**Introduction:** Hypoxia poses a major stress in many diseases including cystic fibrosis and chronic obstructive pulmonary disease. The hypoxic response of alveolar epithelial cells (AEC) is important for homeostasis. We investigated the effect of acute hypoxia on the transcriptional and translational landscape in adult rat AEC and sought to identify translationally regulated transcripts and the putative miRNAs controlling them.

**Methods:** MP48 adult rat AEC at 75% confluence were exposed to normoxia or hypoxia (1% O<sub>2</sub>) for 24 h. Polyribosome fractions were prepared and the heavy fractions (actively translated mRNA) were pooled. RNA was extracted from the total RNA and heavy polyribosome fractions and mRNA expression was evaluated genome-wide with Affymetrix microarray technology. The modified PERL package GO::TermFinder was used to analyze the enrichment of miRNA targets and known RNA elements in the translationally regulated transcripts

**Results:** With hypoxia the heavy polyribosome fraction decreased compared to the normoxic heavy fraction, indicating decreased global translation. There were 768 genes showing significant changes in translation during hypoxia ( $P < 0.05$ ). After correction for changes in transcription and using a 1.5 fold change cutoff, 190 genes had significant changes in translation. Of these 190, 78 genes were more actively translated and 112 genes were less actively translated. Several miRNA targets (miRNA-190, miRNA-224, miRNA-96/1271, miRNA-133, miRNA-182, miRNA-124/506, miRNA-1/206, and miRNA-376/376ab/376b-3p) and one known mRNA element (cytoplasmic polyadenylation) were enriched in the translationally regulated transcripts.

**Conclusions:** Hypoxia significantly alters translation and transcription of the adult rat AEC genes in complex patterns. Further studies are needed to test which of the putative miRNA actually mediate regulation of mRNA translation with hypoxic stress.

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