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Blockade of the renin-angiotensin system by the angiotensin-converting enzyme inhibitor ramipril alters gene expression in skeletal muscle in healthy subjects

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Background

Angiotensin-converting enzyme (ACE) inhibitors were reported to increase skeletal muscle insulin sensitivity by a yet unknown molecular mechanism. We therefore investigated differential gene expression profiles in skeletal muscle biopsies obtained from healthy subjects before and after administration of ramipril.

Methods

Nine subjects were randomly allocated to either receiving 10 mg ramipril (n = 6) or placebo (n = 3) as a single oral dose. Muscle biopsies were obtained from the quadriceps femoris muscle before (baseline) and 9 h after ramipril administration (post treatment). Total RNA samples isolated from biopsies were subjected to whole-genome expression profiling using an Affymetrix Human Gene 1.0 ST GeneChip array, which interrogates the expression level of more than 28,000 well-annotated genes and additionally allows performing exon-level analyses.

Results

We could identify a small set of genes with either increased or decreased expression in subjects receiving ramipril but not placebo. Analysis of these genes revealed diverse functional annotations, such as cell signaling, regulation of apoptosis, transcriptional regulation, and ubiquitin-dependent protein catabolism. Focusing on metabolic processes, we successfully identified candidate ramipril-responsive genes involved in carbohydrate, amino acid, lipid, steroid, and prostaglandin metabolism. Notably, we also identified two genes encoding growth factors involved in regulating angiogenesis.

Conclusions

Changes in skeletal muscle gene expression induced by ramipril might help not only to explain previously described effects of ACE inhibition on glucose metabolism but also to identify novel cellular functions that are affected by RAS blockade.