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(54) **DECREASING LACTATE LEVEL AND INCREASING POLYPEPTIDE PRODUCTION BY DOWNREGULATING THE EXPRESSION OF LACTATE DEHYDROGENASE AND PYRUVATE DEHYDROGENASE KINASE**

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See application file for complete search history.

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(57) **ABSTRACT**

The present invention provides methods and compositions for reducing lactate production and increasing polypeptide production in cultured cells. In one aspect, the invention provides a method comprising culturing cells expressing a) a small interfering RNA (siRNA) specific for a lactate dehydrogenase (LDH) and b) an siRNA specific for a pyruvate dehydrogenase kinase (PDHK). In another aspect, the invention provides cultured cells or vectors comprising an siRNA specific for a LDH and an siRNA specific for a PDHK.

12 Claims, 12 Drawing Sheets