PDE4 inhibition promising tx for metabolic disorders

April 12 2016

(HealthDay)—Inhibition of phosphodiesterase-4 (PDE4), which

hydrolyses cyclic adenosine monophosphate (cAMP), may be useful for treating metabolic disorders, according to research published in the May issue of *Obesity Reviews*.

Noting that PDE4 activity is tightly controlled by post-translational regulation, structure-based auto-regulation, and locus specific compartmentalization with its interactive proteins (signalsomes) in order to regulate cAMP levels and signaling, Chaoneng Wu, M.D., and Sanjay Rajagopalan, M.B.B.S., from the University of Maryland School of Medicine in Baltimore, discuss the role of PDE4 inhibition as a therapeutic strategy for metabolic disorders.

The researchers found that derangement of the PDE4-cAMP signaling represents a pathophysiologically relevant pathway in metabolic disorders, with a critical role seen in inflammation, disordered glucose and lipid metabolism, hepatic steatosis, abnormal lipolysis, suppressed thermogenic function, and deranged neuroendocrine functions. PDE4 inhibitors are currently being evaluated for treatment of disorders such as type 2 diabetes and non-alcoholic steatohepatitis.

"The discovery of novel PDE4 allosteric inhibitors and signalsome-based strategies targeting individual PDE4 variants may allow PDE4 isoform selective inhibition, which may offer safer strategies for chronic treatment of metabolic disorders," the authors write.

More information: Abstract
Full Text (subscription or payment may be required)