Emerald BioStructures announces discovery of small molecule modulators of PDE4

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Emerald BioStructures (formerly deCODE biostructures) announced a publication in the December 27, 2009 advance online issue of *Nature Biotechnology*, detailing the application of structure-based drug design (SBDD) to engineer new allosteric small molecule modulators of the enzyme phosphodiesterase-4 (PDE4), with reduced side effects. According to the paper, the researchers established the structural basis of PDE4 regulation through crystal structures of the PDE4 regulatory domain in contact with small molecules.

"This paper demonstrates Emerald's ability to address key challenges in drug discovery through our world-class X-ray crystallography and structure-based design capabilities," said Lance Stewart, Chief Executive Officer of Emerald BioStructures. "Our approach allows us to deliver valuable, 'game-changing' information in active areas of drug discovery and development, including intracellular protein-protein interactions, as shown in this case. I believe this expertise establishes Emerald BioStructures as a valuable partner to companies that need help solving their important problems in drug discovery, such as reaching historically undruggable targets."

PDE4 is an important therapeutic target, due to its involvement in an array of inflammatory diseases including asthma, psoriasis and COPD, and central nervous system disorders including schizophrenia, Alzheimer's disease, and other cognitive impairments. However, previously developed PDE4 inhibitors have been associated with side effects that have severely limited their potential as potential therapies,

and no PDE4 inhibitor has been FDA-approved.

Dr. Alex Burgin, Chief Operating Officer of the Company and one of the corresponding authors on the paper, said, "Establishing novel PDE4 regulatory domain crystal structures enabled our research team to develop small molecules that interact with those regulatory domains and only partially inhibit enzyme activity. As a result, these newly reported modulators do not have the side effects of traditional PDE4 inhibitors, but have maintained therapeutic activity and efficacy in preclinical models of cognition. This is a strong demonstration of Emerald's ability to use its structural-based insights to rationally design enhanced and selective drug candidates."

More information: "Design of phosphodiesterase 4D (PDE4D) allosteric modulators for enhancing cognition with improved safety," was authored by Alex B. Burgin, Olafur T. Magnusson, Jasbir Singh, Pam Witte, Bart L. Staker, Jon M. Bjornsson, Margret Thorsteinsdottir, Sigrun Hrafnsdottir, Timothy Hagen, Alex S. Kiselyov, Lance J. Stewart and Mark E. Gurney.

Source MacDougall Biomedical Communications