MitoNEET: A New Approach for Designing Diabetes Drugs

Tech ID: 19440 / UC Case 2008-040-0

BACKGROUND

MitoNEET is an outer mitochondrial membrane protein that binds pioglitzaone (ActosTM), an insulin-sensitizing drug of the thiazolidinedione class used in the treatment of Type II diabetes. This protein has a unique dimeric structure where the two components interact to form a new fold not previously seen in any Fe-S protein structures or in any know protein. This new fold forms a binding domain between two acid labile 2Fe-2S clusters.

Defects in the ability of the mitoNEET protein to control assembly and transfer of Fe-S clusters typically result in mitochondrial dysfunction such as that found in Type II diabetes.

TECHNOLOGY DESCRIPTION

The overall structure is described as a beta rich domain with a strand swap from opposite ends of the primary structure that forms a ‘beta cap’ domain. Crystallographic analysis was performed on isolated and truncated mitoNEET protein (AA33-108) to determine the precise structure of the novel fold. The Fe-S clusters are 16A from each other, oriented close to the outer mitochondrial membrane.

Pioglitzaone, a member of the thiazolidinedione class of insulin-sensitizing drugs has always been thought to work thru the nuclear receptor PPAR-gamma by effecting lipid metabolism and oxidative capacity. Investigators at UC San Diego have demonstrated that it also binds to the 2FE-2S binding site of mitoNEET.

ADVANTAGES

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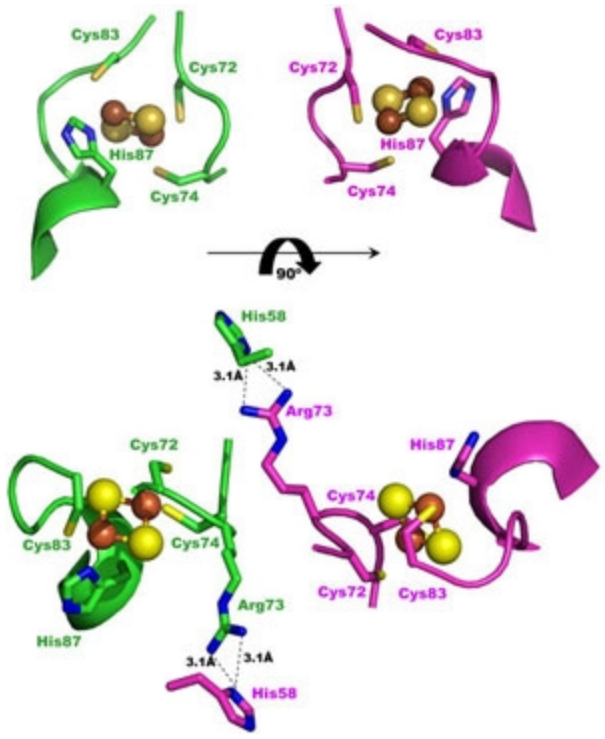
OTHER INFORMATION

CATEGORIZED AS

- **Medical**
  - Disease: Metabolic/Endocrinology

RELATED CASES

2008-040-0



RELATED MATERIALS

► J. Biol. Chem. 2007 Aug. 17 282(33)::23745-9. The outer mitochondrial membrane protein mitoNEET contains a novel redox-active 2FE-2S cluster. Wiley SE, Paddock ML, Abresch EC, Gross L, van der Geer P, Nechushtai R, Murphy AN, Jennings PA, Dixon JE.

► Proc Natl Acad Sci U S A. 2007 Sep 4;104(36):14342-7. MitoNEET is a uniquely folded 2Fe 2S outer mitochondrial membrane protein stabilized by pioglitazone. Paddock ML, Wiley SE, Axelrod HL, Cohen AE, Roy M, Abresch EC, Capraro D, Murphy AN, Nechushtai R, Dixon JE, Jennings PA

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	8,350,007	01/08/2013	2008-040

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