

**Technology:** [Isoform-selective inhibitors and activators of PDE3 cyclic nucleotide phosphodiesterases](#)

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**Inventor:** Matthew A Movsesian

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**Contact:** [kaplana.reddy@va.gov](mailto:kaplana.reddy@va.gov)

**Abstract:** The present invention concerns methods and compositions related to type 3 phosphodiesterases (PDE3). Certain embodiments concern isolated peptides corresponding to various PDE3A isoforms and/or site-specific mutants of PDE3A isoforms, along with expression vectors encoding such isoforms or mutants. In specific embodiments, methods for identifying isoform-selective inhibitors or activators of PDE3 are provided, along with methods of use of such inhibitors or activators in the treatment of dilated cardiomyopathy, pulmonary hypertension and/or other medical conditions related to PDE3 effects on cAMP levels in different intracellular compartments. In particular, techniques are disclosed herein relating to the identification of a test compound that binds to an isolated polypeptide such as PDE3A2 and assaying the test compound for its ability to exhibit superior ability to interfere with binding of the isolated polypeptide when compared with at least a second isolated polypeptide such as of PDE3A1 and methods of treatment of cardiomyopathy, pulmonary hypertension involving the resulting test compound.