



Summary of intermolecular interactions in the human arginase I – N-hydroxy-L-arginine complex. From Di Costanzo et al, 2010.

New designs of arginase inhibitors as therapeutic and diagnostic agents

Brief Description

Arginase inhibitor compositions and methods of use

INVENTORS

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STATE OF DEVELOPMENT

Proof-of-concept

INTELLECTUAL PROPERTY

US, AU, CN, EU, HK, JP
pending ([WO2010085797 A3](#))

USSN [6,387,890](#)

USSN [6,723,710](#)

REFERENCE MEDIA

Di Costanzo et al. [Archives of Biochem and Biophys](#), 2010, 496(2), p. 101-108.

Di Costanzo et al. [PNAS](#), 2009, 102(37), p. 13058-13063.

Kim et al. [J. of Applied Physiology](#), 2009, 107(4), p. 1249-1257.

Christianson et al. [Accounts of Chem Research](#), 2005, 38(3), p. 191-201.

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Technology Overview

Researchers in the Christianson lab have designed arginase inhibitors that bind to arginase I and II and conducted structural analyses of several three-dimensional crystal structures with arginase-inhibitor complexes. Inhibiting arginase enhances nitric oxide-dependent smooth muscle relaxation, including gastrointestinal, airway, and genital smooth muscle. Therefore, arginase inhibitors can be used to treat allergen-induced asthma, chronic obstructive pulmonary disease (COPD) pulmonary hypertension, erectile dysfunction, and premature labor. Additionally, inhibiting arginase can enhance the nitric oxide-dependent tumor-killing properties of white blood cells. Thus, arginase inhibitors can be used in cancer immunotherapy. These new structures developed by the Christianson lab provide enhanced flexibility, stability, and solubility compared to existing parent compounds (e.g. ABH, BEC, nor-NOHA) that inhibit arginase.

Advantages

- R group of inhibitor can be highly varied to include polar and nonpolar substituents, halogens
- Aliphatic or aromatic linkages with peptides, peptidomimetics, or carbohydrates
- Compounds bind with higher affinity than parent molecules
- Alter pharmaceutically relevant properties, including crystal phase stability, water solubility, and lipophilicity

Applications

- Arginase inhibitors can be used for treatment of asthma/COPD, diabetes, hypertension, and sexual dysfunction
- Spectroscopic probe when attached to fluorescent molecule or NMR/MRI probe
- Diagnostic tool for determination of arginase overexpression as associated with asthma, cancer, or bacterial infections (*H. pylori*)