HDAC Inhibitors for Treatment of Toxin-Mediated Bacterial Infections

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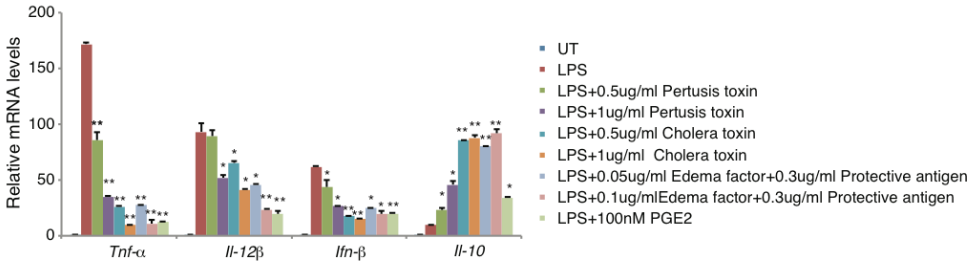
Some bacteria evade immune destruction or suppress the immune response of their host by producing toxins that stimulate cAMP production in macrophages. Dr. Montminy and colleagues at the Salk Institute have shown that this increase in cAMP activates histone deacetylase HDAC4. Increased HADC4 activity in macrophages suppresses the pro-inflammatory immune response and activates the anti-inflammatory immune response, resulting in an overall impaired host immune response to the bacterial infection.

We propose a novel strategy for the treatment of toxin-mediated bacterial infections that stimulate cAMP production and suppress the immune response. By targeting and preventing activation of HDAC4, macrophages will be able to restore and mount a pro-inflammatory response to the infection. Several HDAC inhibitors have been approved or are in clinical development, and we are currently carrying out pre-clinical validation of these drugs to treat tuberculosis (TB) and anthrax infections. HDAC class II inhibitors may represent an alternative or complementary treatment for deadly human infections such as TB and anthrax, which have developed strains resistant to existing anti-bacterial treatment



Secreted bacterial toxins, such as anthrax, pertussis and cholera increase the host intracellular levels of cAMP, which in turn affects macrophage function. The cAMP activation of HDAC4 in macrophages suppresses the production of pro-inflammatory cytokines such as TNF-α and IL-12β, and increases the production of anti-inflammatory cytokines, such as IL-10.

Luan et al., Leptin-Mediated Increases in Catecholamine Signaling Reduce Adipose Tissue Inflammation via Activation of Macrophage HDAC4, Cell Metabolism (2014), http://dx.doi.org/10.1016/j.cmet.2014.03.024

PCT/US15/25072 and US14/682,263 CLASS IIA HDAC INHIBITORS FOR THE TREATMENT OF INFECTION

HDAC inhibitors have a long clinical history of use in various psychiatric and neurological indications including use as anti-epileptics and mood stabilizers. HDAC inhibitors are currently in clinical development for other indications such as cancer and inflammatory diseases.

Our research demonstrates that Class IIa HDAC inhibitors are excellent candidates to treat tuberculosis, anthrax, pertussis and cholera.

We are seeking partners to license our patents and help develop these novel therapeutic strategies.

Clayton Biotechnologies commercializes technologies that are developed and owned by the Clayton Foundation for Research and its supporting entities through research programs at leading research hospitals and institutions in the US and Switzerland.

To date, our research programs have lead to the creation of several successful companies and the launch of 8 products ranging from therapeutic products, medical devices to diagnostics.

Clayton Biotechnologies Inc.
One Riverway, Suite 1520
Houston, TX 77056
+41-76-342-7147
arichardson@claytonbiotech.com

www.claytonbiotech.com