"NEW TARGET AND METHOD OF INHIBITING TBK-1 KINASE" VCU #12-109

Applications

- Breast, prostate cancer
- Potentially other solid tumor cancers
- Obesity

Advantages

- Potential for development small molecule inhibitors
- Possible non-peptidomimetic drug development
- High binding affinity and increased efficiency

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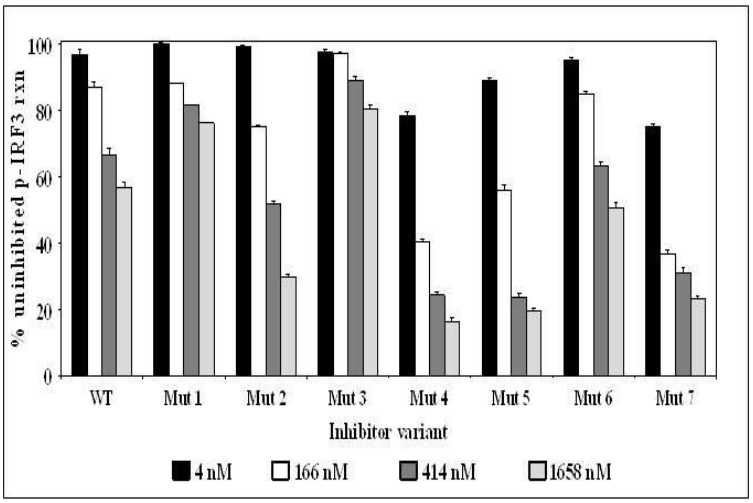
Market Need

The non-canonical Inhibitor of κB kinases (IKK), TANK-binding kinase 1 (TBK-1) and IKKε are serine/threonine protein kinases that play an essential role in activating an inflammatory response to foreign agents. TBK-1/IKKε activation also promotes oncogenic transformation of human cells by restricting initiation of apoptotic programs and their increased activation was reported in breast and prostate cancer, as well as, liver adipocytes and adipose tissue associated macrophages. Inhibition of these kinases can provide a potential treatment for above-mentioned conditions.

Technology Summary

This is a new method of inhibiting TBK-1 and a potential new target for treatment for cancer, and other diseases. Suppressor of IKKepsilon (SIKE) binds to TBK-1 and acts as its endogenous inhibitor. Dr. Bell and colleagues have identified several post-translational modifications of SIKE that affect its inhibitory activity (as shown on the figure). Using site-directed mutagenesis researchers have identified a short sequence within SIKE that mediates a high affinity interaction with TBK-1 and could be potentially exploited to develop small molecule, high affinity inhibitors of TBK-1.



Inhibition of TBK-1 mediated phosphorylation of IRF3 by SIKE and SIKE mutants. Mutants that examined truncated forms of SIKE (Mut 1, 2) or point mutations to alter post-translational modification sites (Mut 3-7) modulated SIKE's inhibitory effect on TBK1 activity.

Technology Status

In vitro and human cell-based data available.

Patent pending: U.S. and foreign rights available.

This technology is available for licensing to industry for further development and commercialization.