Novel Stapled Peptide as a Therapeutic Agent Against Integrin-Related Diseases

(FCCC Ref. 541-JW)

Background

Integrin hyperactivation and the overexpression of talin, a major cytoplasmic activator of integrins, have been linked to thrombotic disorders, impaired immune function, cardiovascular diseases, and cancer. Current anti-integrin therapeutic reagents, targeting the extracellular ligand-binding sites of integrins, cause severe adverse effects associated with the complete loss of integrin activity, and show little effect for treating cancer. Instead, intracellular disruption of talin-integrin interaction has been shown to reduce adverse effects in mice. Thus, blocking the talin-dependent integrin activation may achieve optimal potency and greater selectivity, and also inhibit the ligand-independent integrin activity.

Summary of the Invention

Researcher from Fox Chase Cancer Center designed a stapled peptide that has the potential to effectively inhibit integrin activity by suppressing talin translocation and occluding the integrin-binding site. The crystal structure of the peptide sequence bound to talin was determined. Data show that the stapled peptide stabilized its helical configuration, possesses outstanding membrane permeability, and is able to inhibit integrin activation. Thus, the peptide and its optimized derivatives are projected highly effective therapeutic agents against integrin-related diseases such as thrombotic disorders, auto-immune diseases, CVD, and cancers.

Reference:
https://pubmed.ncbi.nlm.nih.gov/25465129/

Advantages

- First peptide-mimetic agent that targets integrin function by interacting with the cytoplasmic activator talin.
- Able to hit the target protein at multiple sites, resulting in enhanced effect.
- Possesses high cell permeability, strong binding affinity, and significant biological effect.

IP Status

Patent application has been filed.

For Partnering/Licensing information, please contact:

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