Synthesis and Structural Evaluation of Macrocyclic Peptides Binding Heterodimer NF-YB/NF-YC
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Abstract

Aberrant activity of the sequence-specific transcription factor NF-Y is implicated in numerous diseases, such as autoimmune diseases and cancer. Owing to the ubiquitous role of NF-Y with other transcription factors in cell proliferation, apoptosis and DNA damage response it is considered a therapeutic target. The progression of these diseases can be prevented by using inhibitors that modulate the activity of the NF-Y-DNA complex by intervening the interaction between NF-YA and the heterodimer NF-YB/NF-YC. For modulation of these protein-protein interactions, stapled peptides have proven useful. Removing the methyl groups from the alpha,alpha-disubstituted amino acids in these peptides has shown a strong influence on the affinity of the peptide to the dimer. The objective of this thesis was to gain more insight on the effect of demethylation at different positions (in the primary structure) on the binding affinity of the peptides to the heterodimer.