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LIST ALL AUTHORS and AFFILIATIONS – underline presenting author
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TITLE:
Identifying important residues for anti-cancer activity of CJ-15,208 isomers

HYPOTHESIS:
We expect that alanine analogs of the L- and D-Trp isomers of CJ-15,208 will exhibit differences in anti-proliferative activity and provide information on what residues are important for this activity.

BACKGROUND/AIMS:
c-Myc is an important transcription factor that regulates various cellular functions such as cell growth and apoptosis. The regulation of c-Myc expression is important to maintain normal cellular function, and deregulation of c-Myc protein levels in cells is often associated with cancer. Overexpression of c-Myc has been found in prostate cancer. Our group has demonstrated that two isomers of a macrocyclic tetrapeptide based on the natural product CJ-15,208 down regulate the levels of c-Myc protein and inhibit proliferation in the PC-3 prostate cancer cell line. The aim of this research is to perform alanine scans of our lead compound to guide structure optimization.

METHODS:
Alanine substitutions were made to both L- and D-Trp isomers of CJ-15,208, and the anti-proliferative activity of each analog was quantified by the WST-1 assay following treatment of the cells with varying concentrations of peptide for 48 hours.

RESULTS & CONCLUSIONS
Preliminary results suggest that as expected alanine substitution at different positions has different effects on the activity of the peptides, depending on the position. The results from this research will allow us to determine possible types of modifications that can be examined at each residue of the lead compound to improve activity. We hope to identify a promising therapeutic lead for the treatment of prostate cancer.