G6-53 unfolds at ~250 pN. Using their characteristic unfolding forces as a reporter, we were able to directly quantify the partitioning of G6-53 between the apo and N22- bound states at different N22- concentration and measure the binding affinity of N22- to G6-53. The distinct unfolding forces of apo and holo forms of G6-53 also allow us to discriminate different species in the process of folding and N22- binding and measure their kinetic evolution. We unfolded G6-53 by force and waited to allow it to fold and bind with N22-. We found that the unfolded G6-53 folds to apo form before incorporating N22-. The folding rate of G6-53 is independent of N22- concentration, while the binding rate of N22- to apo form of G6-53 is directly proportional to the N22- concentration. Our kinetic data can be fully described using a “folding before binding” model. We anticipate that this novel assay will find unique applications in the study of various protein-ligand interactions.

215-Pos Binding of Antimicrobial Lactoferricin Peptides to Targets in the Angiogenesis Pathway
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Peptides derived from lactoferricin B (LfB25, FKKRRQRRTRMKKGLAP-SITCVYRARF-38), a 25-residue cationic innate immunity peptide released from bovine lactoferrin, exhibit broad spectrum antimicrobial and anti-angiogenic properties. An increase in drug-resistant bacteria and the role of angiogenesis in promoting tumor growth make LfB peptides attractive candidates for future drug development. An important principle for the design of peptide drugs is to reduce the number of amino acids and the sequence complexity, while obtaining maximal activity and minimal toxicity. LfB25 is proposed to inhibit angiogenesis, the formation of new blood vessels, by competing with fibroblast growth factor (FGF) for binding to negatively charged heparin.

218-Pos Urea Destabilization of DNA and RNA Double Helices: Preferential Interactions with Nucleobase Conjugated Pi-Pi-Systems
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Thermal denaturation transition temperatures of AT (adenine-thymine)- and AU (adenine-uracil)- rich double helices are discussed. The work presented here seeks to identify the chemical functional groups urea preferentially interacts with to account for the greater destabilization of AT- and AU-rich double helices. Vapor pressure osmometry was used to determine the preferential interaction coefficients of urea with nucleoside 5'-monophosphates (5'-NMPs) to quantify the accumulation of urea near the 5'-NMP solvent accessible surface areas. Additionally, molecular dynamics (MD) simulations of the 5'-NMPs in explicit water and 1 molal urea predict urea preferential interactions above and below the nucleobase plane through pi-pi interactions. These MD simulation results are supported by the strong correlation between the fraction of accessible surface area devoted to the base conjugated pi-system and the preferential interaction coefficients determined from vapor pressure osmometry.

219-Pos The Effect of Site-Specific Modifications of DNA on Thermodynamic Stability, Ion Binding and Hydration
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Cations, which associate with DNA in both the major and minor grooves, play a significant role in determining DNA conformation. In the major groove, cations are associated with the N7/O6 edge of guanines, while in the minor groove they are found at A-T pairs. Both G-C and A-T have potential cation binding sites that when modified should result in the reorganization of salts and water, which in turn would affect local conformation and stability. We report herein the biophysical characterization of DNA duplexes in which we altered the N7 position in the major groove of purines (7-deazaguanine, 7-aminoethyl-7-deazaguanine, 7-hydroxymethyl-7-deazaguanine and 7-deaza-adenine) and at N-3 position of adenine in the minor groove (3-deazaadenine and 3-methyl-3-deazaadenine). These modifications alter the electronic properties of the heterocyclic bases and specifically eliminate DNA cation binding sites in the different grooves, or in the case of 7-aminoethyl-7-deazaguanine between SKobs and number of ion pairs, but we found that SKobs is better correlated with the Coulombic interaction energies between molecules of the complex.