_b.png _b.bb _b.png height

Contribution ID: **38** Type: **Poster**

High-resolution structure of a modified G-quadruplex: implications for conformational preferences of 2'-F-riboguanosine and V-loop flanking residues

Among the various alternative DNA structures, G-quadruplexes exhibit a remarkable variety of topologies. In this study, two adjacent guanosine residues adopting *syn* glycosidic bond conformations in a G-quadruplex of (3+1)-hybrid type were substituted by *anti*-favoring 2'-F-riboguanosine nucleosides (FrG). Residue-specific 15N labeling along with 2D NOE, 1H-13C HSQC and HMBC spectra allowed for the complete resonance assignment of the FrG-modified sequence. Strikingly, it adopts an unusual quadruplex fold with G1 as part of the central tetrad and a zero-nucleotide V-shaped loop connecting the two FrG residues. While some identical or similar topologies with V-loops have been reported in the past years, it is remarkable that this particular modification provokes a fold with one of the incorporated FrG residues forced into the unfavoured *syn* conformation.

In an attempt to better understand the driving force for this rearrangement, conformations of the two FrG residues flanking the V-loop were analyzed in detail based on 2D NOE and DQF-COSY spectra as well as on F2'-H3' and F2'-H1' heteronuclear scalar couplings extracted from selectively 1H-decoupled 19F spectra. In contrast to S-puckered unmodified residues, both FrGs adopt a sugar pucker in the favoured *north* domain. The C3'-*endo* pucker of the FrG residue at the 3'-end of the V-loop seems essential for the following sharp turn of the phosphate backbone, as seen in the high-resolution structure calculated from NOE-derived distance restraints. The NMR-structure also demonstrates, that even the *syn* glycosidic torsion angle of the FrG residue at the V-loop 5'-end is compatible with an N-type sugar pucker. Apparently, the preference of FrG analogs for a C3'-*endo* conformation outweighs its propensity for an *anti* glycosidic torsion angle, allowing for the unexpected refolding to the V-loop topology. Finally, stabilization of this fold by *north*-favouring FrG residues points to a general importance of the C3'-*endo* conformation for V-loop formation.

Primary authors: HAASE, Linn (Universität Greifswald); WEISZ, Klaus (Universität Greifswald)

Presenter: HAASE, Linn (Universität Greifswald)

Session Classification: Posters