

## Supplemental Figure S7: Temperature-dependence of HPI-wt and HPI

Spectra of (**A**) HPI-wt and (**B**) HPI were recorded in 50 mM sodium phosphate buffer at pH 6.2, containing 90/10 H<sub>2</sub>O/D<sub>2</sub>O. The resonances corresponding to G69-H1, G70-H1, G73-H1 and G74-H1 are broadened, which is characteristic of a fast exchange with the solvent, indicating a short life-time for these base-pairs. At 308 K, the imino protons of G69 and G70 could not be detected any more. G73-H1 and G74-H1 broaden upon increasing temperature, indicating a destabilization of these two base-pairs. The cross-peaks observable for these residues, in NOESY experiments, progressively broadened upon increased temperature.