During the past decade it has become evident that histone post-translational modifications are key regulators of all nuclear processes whose substrate is DNA. Whilst the effects of, for instance, histone post-translational modification on transcription are well-documented, there is no mechanistic understanding of how such modification regulate chromatin condensation directly, or indirectly. Such an understanding is dependent on knowledge of the three-dimensional structure of chromatin. Although the structure of the first level of DNA folding, the nucleosome core, is known at atomic resolution, the structure of the second level of folding, whereby a string of nucleosomes folds into a fibre with an approximate diameter of 30 nm - the “30 nm” chromatin fibre, remains undetermined. I will describe our studies on chromatin structure with three primary aims:
1) Determination of the structure of the “30 nm” chromatin fibre to provide an understanding of fibre topology.
2) Biophysical characterization of the effects of the linker histone and histone modifications on the compaction of chromatin higher order structure.
3) Histone mark read-out by the ADD domain of ATRX.