Shedding new light on dark DNA

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The observation of infrared (IR) spectral differences between normal and cancerous human cells and tissue has been reported in the literature. These differences are manifested, among other changes, in the intensity of the phosphodiester vibrations (*ca.* 1080 and 1235 cm^{-1}) of DNA; however, these vibrational modes may be partially masked by vibrations of phospholipids and RNA.[1] It has been established *via* digestion studies and spatially resolved IR microspectroscopy that the infrared absorption intensities of DNA vary with the state of metabolic and proliferative activity of the cell or tissue.[2-3] Particularly intriguing is the absence of the DNA signature in pyknotic nuclei of metabolically inactive cells.[3] It has been suggested that pyknotic nuclei, the very high local concentration of DNA leads to opaqueness of the chromatin and, consequently, the absence of DNA signals in the IR spectra of very small nuclei.[4]

Recently we performed synchrotron FTIR measurements on live nucleated chicken erythrocytes at the Australian Synchrotron. The spectra were recorded in a purpose built IR cell in isotonic saline with a 6 μm spacer. Spectra were recorded over an 8 hour period as the cell dehydrated. We found that the degree of hydration is a critical factor in accounting for the intensity of the symmetric phosphodiester band at 1080 cm^{-1} and the base pairing vibration at 1710 cm^{-1} from DNA. In the fully hydrated state these bands are clearly visible; however, after osmotic shock induced by high salt concentration the bands disappear. We hypothesise that the intensity of specific DNA vibrations in the nucleus of the cell is primarily dependent on the supramolecular structure of the DNA in the nucleus. The supramolecular structure of the nucleus, which includes the histones as well as the DNA, collapses upon osmotic shock denaturing the histones and breaking electrostatic bonds between DNA base pairs and in the process altering the tertiary structure of the phosphodiester backbone. These results have important implications in understanding the contribution DNA makes to the spectrum of a single cell and thus sheds some new light on an old puzzle.

References:

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