P031 Nucleosomics™: Searching beyond the Histone Code to diagnose early stage cancer

Jake V Micallef, Marielle Herzog, Muriel Chapelier, Katty Scoubeau, Gaelle Cuvelier and Mark E Eccleston

VolitionRx, Namur, Belgium

Nucleosomes, 147 base pairs of DNA wrapped around an octamer of pairs of histone proteins, are the fundamental unit of chromatin. This dynamic structure, responsible for packaging and storage of DNA in cells, helps control gene expression of the associated DNA through epigenetic signalling mechanisms. Specific epigenetic regulation of gene expression varies with cell type, stage of development and differentiation and is modified in disease states. Epigenetic alterations are becoming increasingly recognized in the pathogenesis of diseases with disruption of this epigenetic control of gene expression cited a hallmark of cancer and one of the earliest events in the development of cancer.

For these reasons nucleosome structure is considered a key diagnostic opportunity in cancer.

Nucleosomics™ is based on quantification and profiling of histone variants, post translational histone modifications and DNA modifications in intact nucleosomes as well as adducts between nucleosomes and other proteins (including the estrogen receptor, progesterone receptor and HMGB1) in blood (serum and plasma) and urine.

Attempts to correlate general blood nucleosome levels with cancer have been confounded for a decade by poor clinical sensitivity and lack of specificity. Indeed, raised nucleosomes occur in various conditions including stroke, trauma, sepsis, autoimmune diseases and endometriosis. Volition’s simple, robust, Nu-Q™ ELISAs have overcome both problems by mapping histone variants and modifications alongside DNA modifications to identify cancer-derived nucleosomes in blood. This approach is validated with our early clinical data.