

Nu.Q® Capture- Mass spectrometry is a novel proteomics approach to epigenetic profiling of circulating nucleosomes



Volition

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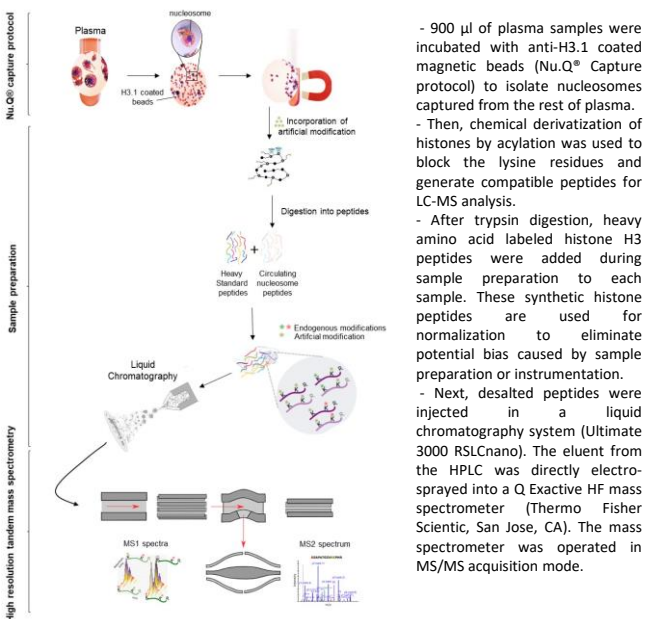
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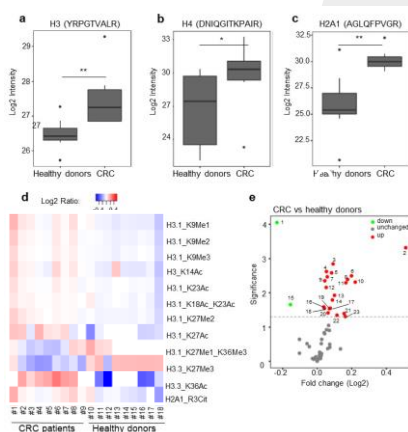
Summary

Alteration of epigenetic modifications plays an important role in human cancer. Notably, the dysregulation of histone post-translational modifications (PTMs) has been associated with several cancers including colorectal cancer (CRC). However, the signature of histone PTMs on circulating nucleosomes is still not well described. We have developed a fast and robust enrichment method to isolate circulating nucleosomes from plasma for further downstream proteomic analysis (Nu.Q®-MS). This method enabled us to quantify the global alterations of histone PTMs from 9 CRC patients and 9 healthy donors. Among 54 histone proteoforms identified and quantified in plasma samples, 13 histone PTMs were distinctive in CRC. Notably, methylation of histone H3K9 and H3K27, acetylation of histone H3 and citrullination of histone H2A1R3 were upregulated in plasma of CRC patients. A comparative analysis of paired samples identified 3 common histone PTMs in plasma and tumor tissue including the methylation and acetylation state of lysine 27 of histone H3. Moreover, we highlight for the first time that histone H2A1R3 citrulline is a modification upregulated in CRC patients. This new method presented herein allows the detection and quantification of histone variants and histone PTMs from circulating nucleosomes in plasma samples and could be used for biomarker discovery of cancer.

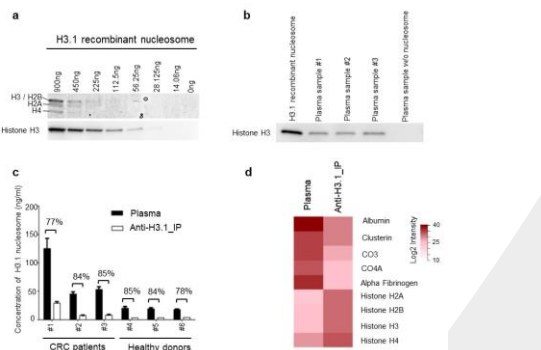
1) Nu.Q® Capture—Mass spectrometry



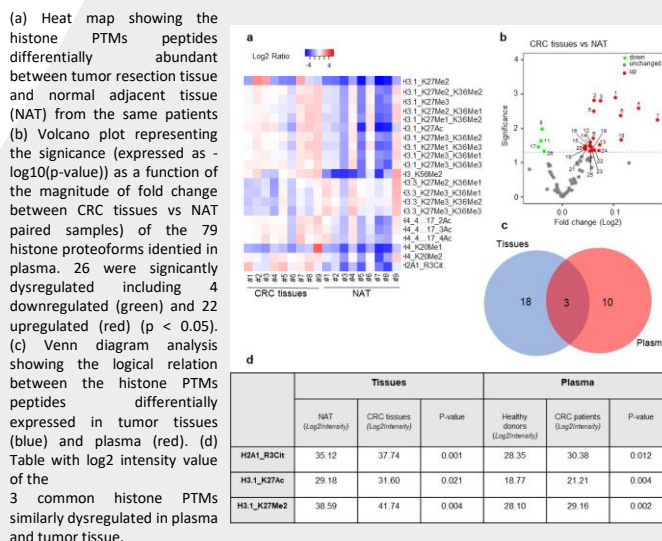
3) Quantitative analysis of histone PTMs from circulating nucleosomes by LC-MS/MS



2) Enrichment of nucleosomes from plasma



4) Histone PTMs on circulating nucleosomes reflect the epigenetic signature of the tumor



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