

TITLE:	Circulating Histone Proteins as Biomarkers of Disease – ChIP-BiD
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PROJECT MANAGER:	Manlio Vinciguerra PhD
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Summary: Nucleosomes, composed of histones and DNA, are the basic repeating units of chromatin. They govern cellular responses, translating into changes in gene expression, during health and in pathological settings. Nucleosomes, histone complexes and DNA fragments are released from cells undergoing apoptosis into the bloodstream, for instance, in cancer patients. Chromatin specimens freely circulating in the blood are innovative “liquid biopsies”, a non-invasive technology used in tailored medicine. A current major limitation of liquid biopsies, such as cell-free DNA fragments, is the need for genetic differences in order to discern between tissues of origin. Pathologies such as cardio-metabolic conditions and sepsis also correlate with augmented cell-free chromatin fragments. While this is potentially due to tissue damage, the phenomenon is hard to detect because they are “self”. Our main goal is to dissect how physiologically finely tuned release of histone complexes and intact nucleosomes into the bloodstream may mirror health or frequent diseases. We propose to the community to change the current concept from a “DNA-centric” to a “histone-centric” methodology. We will develop here an innovative imaging technology based on a multispectral / imaging flowcytometer coupled to high-resolution microscopy, to assess circulating histone complexes in the bloodstream. This innovative methodology, together with a deep biological understanding of the assembly and turnover of nucleosomes, will allow deciphering human cell-free nucleosome or histone complexes composition in health, in common cardiovascular risks and disease, and in selected cancer types with severe prognosis (brain and liver). Our objectives consist in: 1) Probing the combinations of histone complexes, or nucleosome composition, in conferring detection specificity for the proposed medical conditions versus the healthy state; 2) Elucidating the tissue of origin of circulating intact nucleosomes, or histone complexes.

<https://www.mu-varna.bg/BG/AboutUs/Pages/nauchna-programa-vihren.aspx>



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