TITLE: Serum histones as new 'liquid biopsies' in human malignancies	
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GRANT AGREEMENT:	KP-06-H53/6 of 11.11.2021
PROJECT MANAGER:	Manlio Vinciguera, PhD
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Summary: This project proposal focuses on nucleosomes, the main repeating units of chromatin that orchestrate the cellular response to gene-inducing signals in health and disease. Cell-free intact nucleosomes, single histones and DNA fragments are released from dying cells into the bloodstream and are elevated in patients with neoplastic diseases. Extracellular chromatin fragments represent promising 'liquid biopsies', a major non-invasive tool for personalised medicine. Despite this progress, a significant limitation of 'liquid biopsies' (in particular, DNA fragments released by cells) is the requirement for genetic differences to make a diagnosis about the underlying tissue, e.g., a foetus compared to a mother or a tumour compared to a normal tissue. Conditions such as heart-metabolic disease and sepsis are also associated with an increase in extracellular chromatin fragments, possibly due to tissue damage, but cannot be specifically observed as they emanate from one's organism. Our ambitious goal is to decipher how the physiologically well-organised release of histone complexes and intact nucleosomes into the bloodstream can faithfully reflect the severity and progression of malignancies such as haematological malignancies, breast cancer, lung cancer and colorectal cancer. Our vision is to change the current standard for 'liquid biopsies' from a single 'DNA-centric' to a 'histonocentric' approach. We propose to develop an innovative imaging methodology based on a multispectral flow cytometric approach to detect circulating histone complexes in the blood. This new approach, combined with a deep biological understanding of the nucleosome cycle, will enable the deciphering of the composition of human cell-free nucleosomes or histone complexes in health and in common cancers, including colorectal, lung, and leukaemias.

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