Nanotechnology meets Oncology: Interrogating the Personalized Nanoparticle-Protein Corona for Early Cancer Detection

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The exploitation of nanotechnology in biomedical applications has made significant strides in the research for new cancer diagnostic technologies. Recently, the arena of bio-nano interactions has provided new prospects for cancer detection. Early studies in this field showed that nanoparticles (NPs) immersed in biological fluids are coated with a protein-enriched layer called the "protein corona" (PC)[1]. Looking back over the past 15 years, it has been clarified that the PC is the result of a complex interplay between the NPs features, the source of proteins (e.g., blood, saliva, gastric fluids, interstitial fluids), and environmental factors (e.g., exposure time, temperature, and shear stress). Notably, it was found the PC is not simply a reflection of the human proteome but is instead personalized, i.e., unique for each individual and human condition[2]. This opened a new avenue to isolate low-abundant proteins, undetectable by standard blood tests, in a biospecimen *ex vivo* and thus increased the possibility to detect cancer biomarkers through downstream analytical workflows. Over the last ten years, our research group has been working on the design, development, and validation of new technologies for early cancer detection based on the characterization of the personalized PC. These studies gave impetus to more serious work in the field setting the principle of novel nanoparticle-enabled blood (NEB) tests for cancer detection[3, 4], i.e., tests based on the differences between the PCs formed on different NPs after exposure to cancer and non-cancer plasma samples (as shown in **Figure 1**). Here, we present a version of the NEB test for pancreatic ductal adenocarcinoma (PDAC) and discuss the main challenges to transforming the NEB test into a reliable diagnostic tool for early diagnosis, follow-up, and management of cancer patients.

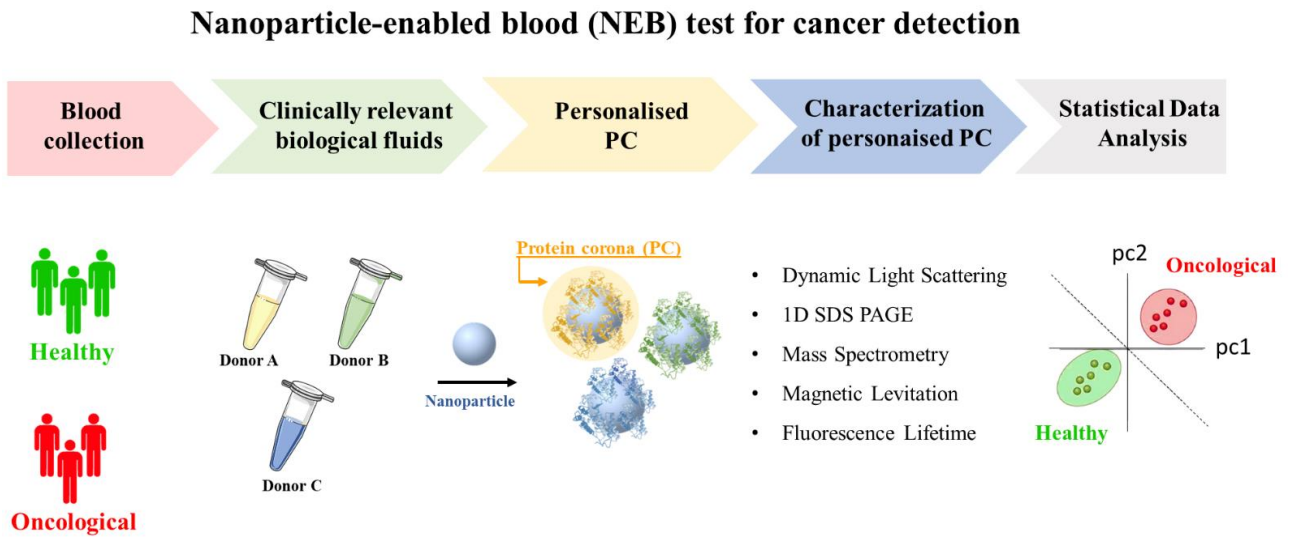

Figure 1. Nanoparticle-enabled blood test for cancer detection. Biological fluids (e.g., human plasma) are collected from healthy and oncological donors and incubated with nanoparticles to generate personalised protein coronas (PCs). The personalised PCs are further characterized through different analytical techniques (e.g., SDS PAGE). Finally, the data are processed through statistical analysis (e.g., principal component analysis (PCA)) to distinguish healthy from oncological donors.