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## Core-Shell Hydrogel Particles Harvest, Concentrate and Preserve Labile Low Abundance Biomarkers.

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The blood proteome is thought to represent a rich source of biomarkers for early stage disease detection. Nevertheless, three major challenges have hindered biomarker discovery: a) candidate biomarkers exist at extremely low concentrations in blood; b) high abundance resident proteins such as albumin mask the rare biomarkers; c) biomarkers are rapidly degraded by endogenous and exogenous proteinases. *N*-isopropylacrylamide based core (599nm)-shell (177 nm) hydrogel nanoparticles functionalized with a charged based bait (acrylic acid) were studied as a technology for addressing all these problems, in one step, in solution. The particles are designed to simultaneously conduct size exclusion and affinity chromatography in solution. Platelet derived growth factor (PDGF), a clinically relevant, highly labile, and very low abundance biomarker, was chosen as a model. PDGF was completely sequestered from carrier albumin, concentrated, and fully preserved, within minutes, when spiked in human serum. Particle sequestered PDGF was fully protected from exogenously added tryptic degradation. When the nanoparticles were added to a 1mL dilute solution of PDGF at non detectable levels (less than 20 picograms per mL) the particles sequestered all the PDGF into an elution volume of 100 uL concentrating the PDGF and bringing it into the detection range of ELISA and mass spectrometry. We envision the application of harvesting core-shell nanoparticles to whole blood for concentration and immediate preservation of low abundance and labile analytes at the time of venipuncture.

