Oxide nanowires for urinary extracellular vesicle analysis

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Abstract

Extracellular vesicles (EVs) of 40-5000 nm in diameter have shown promising features as biomarkers for early cancer and other disease diagnoses. EV-encapsulated microRNAs (miRNAs) and EV membrane proteins have been found in various body fluids of both healthy subjects and cancer patients. The difference in the EV-encapsulated miRNAs and EV membrane proteins between the two groups of people may represent a warning sign for various disease scenarios. To take advantage of their full potential as biomarkers, methodologies that investigate the correlation between various disease scenarios and profiled miRNAs or profiled EV membrane proteins are strongly required. Conventionally, three major methodologies have been used for EV collection: ultracentrifugation or differential centrifugation, immunoaffinity-based capture, and size exclusion chromatography. Some emerging methodologies have been reported as promising alternatives, including polymer precipitation, microfluidic-based platforms, and size-based filtration. However, none of the existing methodologies for collecting EV-encapsulated miRNAs have satisfied the requirements for non-invasive urine-based early cancer diagnoses due to the low concentration of EVs in urine.

Here we propose an oxide nanowire-based methodology via charge-based isolation for collecting urine EV-encapsulated miRNAs that unveils over 1000 species of urinary miRNAs of different sequences [1] and elucidates the correlation between the surface charge and membrane proteins of EVs. Since the surface charge is determined by molecular compositions of EV surface consisting of lipid bilayers, membrane proteins, and proteoglycans, and therefore, reflects donor cell information, the surface charge should have a stronger relationship to miRNAs inside EVs and expressed membrane proteins on EVs than conventional classification items of density, size and immunoaffinity.

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