Using Tunable Resistive Pulse Sensing to Identify and Quantify Extracellular Vesicles

by Jessica E. Molina | Dr. Joshua D. Hutcheson

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Calcification, the leading predictor of and direct contributor to cardiovascular disease, begins with the release of small, ~100 nm sized extracellular vesicles (EVs) by cells in response to pathological conditions such as plaque formation in arteries. Studies have shown that calcifying EVs released in bone possess a negative charge, which plays a vital role in the calcification process. These calcifying EVs exist within larger populations of vesicles released during normal cellular processes. One of the biggest challenges in studying EVs comes from their heterogeneity and small size. There are no methods that currently exist to separately assess and quantify calcifying EVs from the total EV population. Tunable resistive pulse sensing (TRPS) allows for EV-by-EV analysis and simultaneously captures both the unique size and charge of each particle, while also calculating EV concentration. TPRS uses an electrical current across a nanometer-sized pore to measure specific EV properties. When an EV travels through the pore, the current is disrupted. The magnitude of the disruption is proportional to EV size, while the duration of the disruption elicits EV charge properties. EV release from human vascular smooth muscle cells under different mechanical and chemical stimuli can be measured using this TRPS methodology. The use of TRPS can aid in the differentiation of unique EV properties that contribute to disease and potentially lead to better treatment options through the development of vesicle-specific therapies.