A SERS-active plasmonic nanosensor-chemometrics platform reveals a biphasic zinc switch that controls breast-cancer metastasis

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Labile Zn^{2+} is emerging as a quantitative driver, not just a biomarker, of metastasis, yet rapid, second-resolved intracellular measurement remains elusive. Here we engineer terpyridine-functionalised, hollow Au@SiO_2 nanocapsules (NCs@TPY) and couple their SERS signal to cell-specific partial-least-squares (PLS) chemometrics, yielding an 8-log dynamic range (10^{-12} – 10^{-4} M), a low-nanomolar detection limit and ≤4.5 % cross-validated error while rejecting Ca^{2+} / Mg^{2+} interference. Applying this platform to four breast-cancer lines reveals that basal cytosolic Zn^{2+} forms a "ladder" paralleling metastatic aggressiveness (MCF-7 25 pM < MDA 430 pM < LM2 4.7 nM < BrM2 51 nM). Manipulating extracellular zinc uncovers a biphasic switch: migration, invasion and proliferation all peak when intracellular Zn^{2+} rises into the nanomolar band (~ 10 – 560 nM) and collapse once it exceeds ~5–70 µM (line-specific). Primary-tumour-derived MDA cells are hypersensitive, reaching maximal metastatic traits at ~0.6 µM Zn^{2+}, whereas lung- and brain-tropic variants show partial resistance, indicating micro-environmental adaptation. The NCs@TPY-PLS assay thus provides the first tool to track intracellular zinc across eight orders of magnitude *in situ* and demonstrates that tightly regulated Zn^{2+} dyshomeostasis controls metastatic behaviour. Because the Raman ligand is exchangeable, the capsule architecture is readily extendable to multiplex ion or redox sensing, and the identified "functional window" positions zinc transporters as actionable targets for anti-metastatic therapy.

References

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Figures

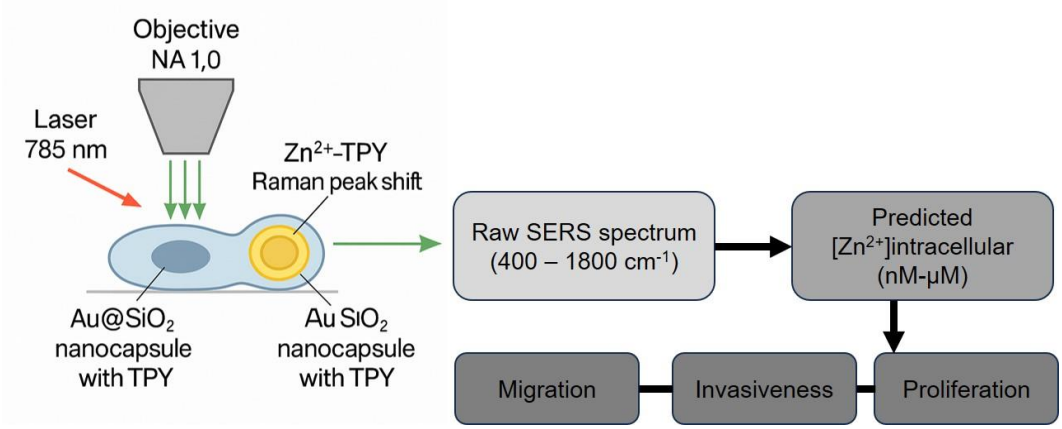

Figure 1: Data analysis pipeline for intracellular Zn^{2+} quantification.