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Comment

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Reply to "Comment on 'Label-Free Single Exosome Detection Using Frequency-Locked Microtoroid Optical Resonators'"

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We thank Smith et al.,[1] for their positive comments regarding our work[2] on label-free single exosome detection and their comment highlighting that our study involved a xenograft of human tumor cells inside a mouse. Our paper represents just a single step on the path toward both clinical applications and further fundamental biological applications. The intent was to show that small and rare signals could be detected. As noted by Smith et al.,[1] effective use of such a sensor in the clinic requires tumor-specific capture agents that will bind to tumor-specific biomarkers. We hope that our work will help to further motivate the discovery of such markers.

With regard to the statement that no such tumor-specific biomarkers or capture agents have been discovered to date, we would like to point out that both tumor cells and the exosomes generated by those tumor cells have unique surface proteins. Furthermore, cancer detection via antibody capture of exosomes targeting those unique proteins has already been reported in the literature[3−8] for a variety of cancer types, including pancreatic,[3] breast,[3] lung,[6,7] ovarian,[5] colorectal,[4] and metastatic melanoma.[8] These studies do not rely on xenograft models. Antibodies from these studies, combined with our sensor, may allow for the identification of tumors from human patients with extremely high sensitivity. As a specific example, one future step could involve conjugating anti-Glypican-1 (which has been shown to bind pancreatic cancer-specific exosomes)[3] to the surface of the toroid and seeing if it is possible to distinguish between patients with pancreatic cancer and those that are cancer-free.

The more sensitive the sensor, the earlier a diagnosis can be made. Out of the studies cited above, the minimum number of exosomes that could be sensed was ∼3000.[5] FLOWER is capable of sensing single exosomes. We believe that FLOWER's high sensitivity[9,10] will positively impact clinical studies for a variety of diseases for which markers exist or are being sought. That said, we of course recognize that "the proof is in the pudding" and, as with all sensing technologies, will come from characterization of control and patient samples in the clinic.

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Notes

The authors declare no competing financial interest.

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