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Authors' Response

Sir,

Thank you for the opportunity to respond to the concerns of Drs. Melton and Isenberg regarding our research in identifying the manufacturers of improvised explosive devices (IEDs). We appreciate their input in our research, and as always, would welcome the chance to involve them directly if they find our work of interest. As an academic laboratory we always appreciate opportunities to collaborate with private and government laboratories, as we have done with the FBI in the past.

Having worked on a great variety of mitochondrial DNAs (mtDNAs) for well over 20 years (e.g., [1]), I am very aware of its strengths and weaknesses, thus I am happy to address Drs. Melton and Isenberg's concerns. For the sake of brevity, I will cover some of these in short order:

- Positive, negative, and reagent blank controls were used, the latter two of which did not produce product after nested PCR. We should have been more explicit about this.
- The 28% of bombs that could not be assigned were because the sequence obtained was not informative (had no diagnostic polymorphisms). These were not errors of some type, simply lack of resolution with mtDNA analysis.
- Comparing our work with Grzybowski et al.'s (their reference [1]) is apples and oranges; we made no claims about heteroplasmy, which was the sole point of that manuscript. Everyone agrees (including the original authors, in their reference [2]) that those heteroplasmy results were somewhat ''fantastic''; however, that does not take away from the utility of mtDNA analysis in forensics.
- We are very aware that forensic mtDNA analysis is most useful for exclusions, but certainly neither Drs. Melton's nor Isenberg's laboratories limit their reports solely to those who are excluded; they take into account inclusions as well (usually as a statistical statement).
- Multiple factors will influence the ability to obtain DNA data from compromised materials. mtDNA copy number is one of these, as is the mitochondrion itself (2). These, along with DNA degradation levels, are key in obtaining results from things like deflagrated IEDs, so I think we are all on the same page here.

More important than these lesser points is taking a look at the actual *goal and context* of the work we presented. Nowhere in the JFS manuscript did we introduce these methods as a crime laboratory standard operating procedure. This was a *research* study, and was conducted and presented as such. Michigan State University's research on DNA from IEDs goes back many years, and has been evolving ever since. Original trials using standard short tandem repeat (STR) testing (3) largely failed to identify the handlers of IEDs. In the research just published in JFS we had moved on to more sensitive mtDNA, which, as hoped, had a higher success rate. We believe Dr. Melton or Isenberg or both attended the last two AAFS annual meetings, and thus should be aware of our subsequent IED testing using mini-STRs, including those originally supplied to us by NIST, and then the commercially available variety. Again, the research continues to evolve.

But none of that should really subtract from our published research using mtDNA, and the greatly enhanced ability to identify the handlers of deflagrated IEDs that we have shown. The nature of research is that new methods will be tested, and that some (or even most) will be different from the standard ones presently in use, otherwise it is not research, it is simply duplication. Being willing to ''push the envelope'' is not bad science, it is part of exploration; had we not done so here, we would have learned little or nothing from the mtDNA/IED experiments. A researcher's job is to conduct the work very carefully, and present the findings to the scientific community. This may include both good news and bad news, and we did not shy away from presenting weaknesses in our findings; indeed ''caveats'' were a substantial portion of our Discussion section. Given this, our mtDNA/IED-based research on bomb assignments, conducted blindly through generation of a haplotype and comparison with a (closed) population of donors, was very successful. Our ''identification'' rate was *c.* 2 in 3, with a misassignment of just a single bomb. This is a huge increase in the accurate assignment for this type of highly compromised evidence, it is worthy of publication, and it has led some agencies to change the way they process post-blast IED material in the lab.

References

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