

Title: Saliva as a non-invasive diagnostic tool for inflammation and insulin-resistance

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We thank the reviewers for the constructive review of the submitted manuscript. Reviewer 2 had no comments for revision. We have now included all suggestions/comments raised by the reviewer #1 in the revised manuscript. Shown below is a point by point response to the reviewer's comments.

1. Reviewer 1 has suggested that the manuscript could be improved by adding authors own views. This has been incorporated throughout the manuscript, as shown below
  - a. Core tip has been revised to better reflect authors' own views
  - b. Sections on glucose in saliva, insulin in saliva, cortisol in saliva, adipokines in saliva, inflammatory markers in saliva, and conclusions and future directions have been revised to include author's views
2. Reviewer 1 has suggested that a critical review of literature findings would be beneficial for future research. This has been included for most every section, and also the section on future directions have been revised.
3. Reviewer 1 has indicated that much of studies use techniques currently not popular due to the availability of more sensitive techniques
  - a. Changes have been made to the manuscript in several sections to document newer analytical techniques used.
  - b. Abstract: Line 2: is revised as follows: Currently, saliva testing is used for clinical assessment of hormonal perturbations, detection of HIV antibodies, DNA analysis, alcohol screening, and drug testing.
  - c. Salivary glucose: Revised, by including this sentence: Ongoing research is focused on the development of nanotechnology-based biochip sensors for salivary glucose measurements. Such a novel biochemical sensor that provides a compact, high-throughput device for real-time glucose measurements may have implications in point-of-care clinical settings
  - d. Salivary cortisol: Added ECL technique as comparison to ELISA technique for quantitation.
  - e. Adipokines: The need for research into saliva processing techniques for better outcomes related to saliva and serum correlations, has now been added.
  - f. CRP: Lab-on-a-chip salivary assay for CRP measurement is now included
  - g. Salivary transcriptome analyses: Using microarray analysis and qPCR for biomarker detection in saliva is now included
  - h. Oral fluid nanosensor test – for cytokine analyses in saliva is now included