

September 27, 2019

Christopher Lynch, PhD  
National Institute of Diabetes, Digestive and Kidney Diseases  
National Institutes of Health  
Bethesda, MD 20892

Dear Dr. Lynch,

The Endocrine Society appreciates the opportunity to comment on precision nutrition tools for continuous monitoring of nutrients and metabolites in humans. Founded in 1916, the Endocrine Society is the world's oldest, largest, and most active organization devoted to research on hormones and the clinical practice of endocrinology. Our membership of over 18,000 includes clinical, translational, and basic scientists studying metabolic disorders and endocrine disease. We are encouraged that NIDDK is pursuing innovative research programs to better understand the links between dietary exposures and the development of disease. In our response, we highlight some emerging technologies for continuous sensing of nutrients or metabolites, recommend some nutrients or metabolites for NIDDK to prioritize in order to better understand the links between nutrition and endocrine disease, and identify challenges that need to be overcome to advance the use of these and other continuous sensors.

#### **Sensors currently in development**

Our members are aware of exciting technologies that are enabling the continuous monitoring of various biological systems and analytes. While these may not necessarily have immediate application for nutrition research, they may help inform the development of sensors that are more uniquely tailored to the research topics included in the RFI.

- Microfluidic devices that can sample interstitial fluid can be used to collect information on nutrients and hormonal status.
- Patch-based electrochemical sensors that sample sweat could be used to measure analytes such as calcium, glucose, and sodium<sup>12</sup>. Patch-based sensors are also demonstrating potential utility in clinical settings, e.g., to monitor for sepsis<sup>3</sup> and other biomarkers of disease.
- In the field of sleep disorders, researchers are working to further develop sensors to monitor oxygen and CO<sub>2</sub> more simply, safely, and effectively<sup>4</sup>.

#### **Priority metabolites for continuous measurement**

In general, continuous biosensors for hormone levels would be of immense benefit to researchers studying the mechanistic links between hormone levels and a variety of clinical endpoints. Studying these links can be fundamentally challenging due to natural hormone level changes e.g., due to diurnal cycles. Continuous monitoring systems would also enable more detailed studies of pulsatile secretion of hormones. In addition to the ability to measure hormone levels, we suggest that NIDDK consider the following metabolites for prioritization in the context of this RFI.

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<sup>1</sup> Payne M.E., et al., *Nature Scientific Reports*. (2019) 9:13720 | <https://doi.org/10.1038/s41598-019-49689-7>

<sup>2</sup> Gao W., et al., *Nature*. 2016 Jan 28;529(7587):509-514. doi: 10.1038/nature16521.

<sup>3</sup> <https://www.technologynetworks.com/diagnostics/news/needle-shaped-sensors-can-detect-multiple-sepsis-indicators-315590>

<sup>4</sup> Amaddeo A., and Fauroux, B., *Paediatr Respir Rev*. 2016 Sep;20:42-44. doi: 10.1016/j.prrv.2015.11.009. Epub 2015 Dec 4.

- Lactate – for studies involving inborn errors of metabolism and other disorders of carbohydrate metabolism more broadly, since there is growing recognition regarding the important role of lactate in energy and carbon flux<sup>5</sup>.
- Sodium – For the assessment of hydration status but also for individuals with water balance disorders such as diabetes insipidus it will be helpful for families to have accurate measurements of Na status.

### **Challenges to the development of novel sensors**

The scope of challenges that NIDDK will face as it develops research programs around novel biosensors will depend in part on whether monitoring systems will involve sample collection in addition to monitoring, data fidelity and reproducibility. In general, researchers supported by FOAs for the development of sensors will need to thoughtfully consider how other substances or dietary components might interfere with the measurement of the target analyte. It will be important to consider how different tissues might require different sampling methodologies. NIDDK may want to prioritize those tissues where researchers are already using intermittent sampling but would benefit from the development of sensors for continuous sampling, such as continuous monitoring of beta-hydroxybutyrate in the context of ketogenic diets or for assessment of ketone metabolism in the context of SGLT2 inhibitors used in diabetes.

Another issue that NIDDK should be prepared to address are the data challenges that may emerge from continuous monitoring. Continuous data streams, in either a clinical or research setting, will be expected to generate a large amount of highly-sensitive data necessitating secure long-term storage and data processing solutions. Appropriate standards and reference ranges will also need to be developed to ensure that data is reliable, comparable across different sites, and can be related to common healthy reference populations. We therefore recommend that NIDDK explicitly support the development of resources to address these data challenges through FOAs on the development of nutrient/metabolite sensors.

As a final point, we urge NIDDK to be sensitive to accessibility issues that may arise in the future as sensors move out of the research setting and into clinical practice or the commercial space. For example, a highly-technical but extremely expensive monitoring device could exacerbate existing health disparities. NIDDK should consider the practicalities of proposals (e.g., how large is the device, how invasive) and whether they are interoperable with other companion technologies.

### **In Summary**

We appreciate NIDDK's thoughtful approach to the development of novel sensors as tools to further research on nutrition, metabolism and disease. We believe that these sensors will also have utility for other important endocrine-related research areas and look forward to learning more about NIDDK's priorities. Thank you for considering the Endocrine Society's comments. If we can be of any further assistance, please contact Joe Laakso, Director of Science Policy at [jlakso@endocrine.org](mailto:jlakso@endocrine.org).

Sincerely,



E. Dale Abel MB.BS, D.Phil. (MD PhD)  
President Endocrine Society

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<sup>5</sup> Hui, S. et al., *Nature*. 2017 Nov 2;551(7678):115-118. doi: 10.1038/nature24057. Epub 2017 Oct 18.