See corresponding article on page 1028.

Postprandial metabolism and inflammation—a comprehensive model to advance Precision Nutrition? Lessons learned from the Personalised REsponses to DIetary Composition Trial (PREDICT study)

Helen M Roche[1,2]

[1]UCD Conway Institute and UCD Institute of Food and Health, School of Public Health, Physiotherapy and Sport Science, University College Dublin (UCD), Dublin, Ireland; and [2]Institute for Global Food Security, Queen's University Belfast, Belfast, United Kingdom

The PREDICT study (Personalised REsponses to DIetary Composition Trial) profiled the postprandial metabolic-inflammatory state in some 1002 generally healthy subjects with a view to determining if/how abnormal postprandial metabolic responses may contribute to inflammation (1). In this case inflammation was characterized by "traditional" (IL-6) and "emerging" [glycoprotein acetylation (GlycA)] biomarkers. In the postprandial state, GlycA showed greater variation wherein the authors suggest that postprandial GlycA concentrations may provide better discrimination of an individual's inflammatory tolerance. Interestingly, machine learning approaches revealed that postprandial triacylglycerol (TAG) metabolism, as opposed to postprandial glucose profiles, was a stronger predictor of the postprandial GlycA response. Thus, the authors proposed that diet, lifestyle, and/or pharmacological interventions to control TAG metabolism may be the key to modulating successive chronic inflammatory excursions after meal intake.

Notwithstanding the great value and knowledge accrued from this very large postprandial study, it would be interesting to understand why the PREDICT study specifically prioritized just 2 inflammatory markers. Presumably, many more were potentially determined using the NMR and inflammatory platforms. Given the complex interrelations between inflammatory pathways, which reflect biological synergies, elements of redundancy, and antagonistic counter-regulatory interactions, going forward we need to go beyond 2 inflammatory biomarkers. In terms of maximal knowledge acquisition, it is important to know which inflammatory markers were significantly modulated in the postprandial state, or not, as the case may be.

Such large postprandial study approaches are highly relevant, because depending on meal frequency humans can spend a large majority of their time in an almost constant postprandial state. Indeed, the highly anticipated NIH Precision Nutrition initiative has a large emphasis on understanding the nature of interindividual postprandial responses. To this end, there are several outstanding questions that need to be addressed in future studies. In doing so, it is important that prior learnings are well reflected within future study design. For example, it is not only the composition of the meal that affects a subsequent postprandial metabolic response. Several factors affect postprandial lipid metabolism and de novo lipogenesis, including habitual dietary fat intake, other macronutrients including alcohol, the composition of the meal before the postprandial challenge, age, gender, BMI, and presumably ethnicity, to mention but a few (2–5). It should of course be acknowledged that several of the earlier studies were light in terms of accurately characterizing the nature of the inflammatory response. Going forward, simply measuring plasma cytokine concentrations is perhaps too simple an approach. Given the heterogeneous nature of immune cell biology, more cell-specific profiles would be informative.

Data from the immunology field, for example, should be "road tested" within the context of postprandial responses to food intake. For example, it has been demonstrated that the metabolic configuration of immune cells determines the subsequent proinflammatory or resolving immuno-phenotype based upon the preponderance of glycolysis relative to oxidative phosphorylation cellular energy metabolism (6). Because diet is an important source of exogenous metabolites and substrates for many endogenous metabolites, we need to define if/how this paradigm is also relevant to chronic diet-related inflammatory responses. Innate immune training is another key space; traditionally the innate immune system was presumed not to have memory. Nevertheless, preclinical research suggests that high fat dietary exposure can prime and train myeloid cells affecting the innate immune response (7). Again, the relevance of this within the context of human nutrition and health needs clarity. There is a paucity of information in relation to the temporal cell-specific immuno-phenotypes associated with postprandial dietary exposures. This cellular perspective is very much needed to progress understanding in relation to mechanisms underpinning diet-induced postprandial inflammation. To do this, we may need to develop more clinically relevant experimental models to characterize the diet-induced inflammatory response. Exploring the utility of experimental agonists beyond LPS and understanding the impact of diet-related metabolic agonists such

The author reported no funding received for this study.

Address correspondence to HMR (e-mail: helen.roche@ucd.ie).

First published online June 18, 2021; doi: https://doi.org/10.1093/ajcn/nqab200.

Am J Clin Nutr 2021;114:841–842. Printed in USA.

as palmitate relative to other fatty acids, glucose, ATP, etc. to better mimic both basal and metabolic-induced inflammatory responses are important future steps.

A final key challenge in the realm of metabolic inflammation is the resolution of inflammation. Is this a malleable process, and is there a metabolic-inflammatory threshold beyond which dietary interventions cannot revert or resolve? Indeed, recent insights in relation to the role of cellular metabolism in determining the nature of the immune response would suggest that anti-inflammatory strategies may be somewhat naïve and perhaps ineffective. Rather, should we focus on diet-mediated metabolic reconfiguration to adjust postprandial inflammatory excursions? To that end, the findings of the PREDICT study are important in terms of beginning to better define the large interindividual variables that predict postprandial metabolism from the genetic, physiological, and metabolic perspectives, in order to design more effective means to attenuate chronic inflammation.

The sole author was responsible for all aspects of this manuscript. The author reports no conflicts of interest.

References

1. Mazidi M, Valdes AM, Ordovas JM, Hall WL, Pujol JC, Wolf J, Hadjigeorgiou G, Segata N, Sattar N, Koivula R, et al. Meal-induced inflammation: postprandial insights from the Personalised REsponses to DIetary Composition Trial (PREDICT) study in 1000 participants. Am J Clin Nutr 2021;114(3):1028–38.
2. Cruz-Teno C, Pérez-Martínez P, Delgado-Lista J, Yubero-Serrano EM, García-Ríos A, Marín C, Gómez P, Jiménez-Gómez Y, Camargo A, Rodríguez-Cantalejo F, et al. Dietary fat modifies the postprandial inflammatory state in subjects with the metabolic syndrome: the LIPGENE study. Mol Nutr Food Res 2012;56(6):854–65.
3. Jackson KG, Zampelas A, Knapper JM, Roche HM, Gibney MJ, Kafatos A, Gould BJ, Wright JW, Williams CM. Differences in glucose-dependent insulinotropic polypeptide hormone and hepatic lipase in subjects of southern and northern Europe: implications for postprandial lipemia. Am J Clin Nutr 2000;71(1):13–20.
4. Syed-Abdul MM, Jacome-Sosa M, Hu Q, Gaballah AH, Winn NC, Lee NT, Mucinski JM, Manrique-Acevedo C, Lastra G, Anderson JM, et al. The Tailgate Study: differing metabolic effects of a bout of excessive eating and drinking. Alcohol 2021;90:45–55.
5. Ryan MF, O'Grada CM, Morris C, Segurado R, Walsh MC, Gibney ER, Brennan L, Roche HM, Gibney MJ. Within-person variation within the postprandial lipaemic response of healthy adults. Am J Clin Nutr 2013;97(2):261–7.
6. Jha AK, Huang SC-C, Sergushichev A, Lampropoulou V, Ivanova Y, Loginicheva E, Chmielewski K, Stewart KM, Ashall J, Everts B, et al. Network integration of parallel metabolic and transcriptional data reveals metabolic modules that regulate macrophage polarization. Immunity 2015;42(3):419–30.
7. Charles-Messance H, Mitchelson KAJ, De Marco Castro E, Sheedy FJ, Roche HM. Regulating metabolic inflammation by nutritional modulation. J Allergy Clin Immunol 2020;146(4):706–20.