# Webinar Q&A Report:
# Fine Tuning Nutrient Intake Timing for Cardiac Health

1. **How does the data translate clinically, should lipids and protein be consumed all as the first meal?**

   On caveat of our research is that the studies utilized rodent models. However, epidemiologic and (limited) translational studies do suggest that specific aspects of our findings (particularly for cardiometabolic parameters) are likely to translate to humans. So much so, that the American Heart Association recommends eating a great number of calories earlier in the day (to reduce diabetes and heart disease risk). With regards to your specific question, I am unaware of a controlled human study that has directly investigated whether limiting lipid and protein only to first meal of the day is beneficial.

2. **Have you looked over the inflammatory factors (cytokines) in your diet paradigms?**

   Great question. This is an active area of research in the lab. Undoubtedly, immune cell function is regulated by circadian clocks. We are now trying to understand the interaction of meal timing, immune cell clocks, inflammation, and cardiometabolic disease.

3. **Since the circadian clock is temperature compensated, we surmise that the effects of diet are temperature independent, however is this so? Can you reset the heart clock?**

   Certainly, the heart clock is very sensitive to environmental factors. These include cortisol, norepinephrine, and the timing of food intake; in the latter case, the precise mechanisms by which the timing of food intake effects of the heart clock are currently unknown.

4. **Any recommendations on the timing of aerobic and anaerobic (strength training) exercise to maximize its protective effects on cardiometabolic health?**

   Another great question. Some information is available in the kinesiology field. It appears that in healthy individuals, aerobic capacity is higher in the morning, while muscle strength is higher in the afternoon. Recent animal-based studies do indeed suggest that the time of day at which exercise is performed impacts metabolic parameters (https://www.sciencedirect.com/science/article/pii/S1550413121006355)

5. **Would you expect to see weight loss in combination with a reversal of heart remodelling with a stricter intermittent fasting feeding pattern? Like 4 hours HF breakfast, 4 hours LF dinner, 16 hours fast?**

   Thank you for the question. Yes, a longer fasting period does have the potential to increase likelihood of weight loss in our mouse studies. The protocol you describe is similar to the studies that we published in

2010. Since that time, we have tried to avoid overly long periods of fasting in mice; most recently we have tried our best to limit fasting to only the 12 hour light (inactive period, when food intake in naturally low in rodents), or for two 4 hour periods of fasting (between which the mice will have access to food). The reason for this is due to the higher metabolic rate of mice relative to humans (approx. 5-8 times higher).

6. **Does the myosin ATPase have the same role in cardiomyocytes and skeletal muscle?**

   In general, yes. Myosin is involved in cross-bridge cycling, which underlies contraction. However, it should be noted that abundance of distinct isoforms of contractile proteins can differ between cardiac and skeletal muscle.

7. **How do you think disturbing protein intake throughout the day would impact cardio health?**

   Interesting question. When mice are provided diets freely (i.e., not time of day restricted), then protein intake will be proportional to food intake. However, mice exhibit 24hr patterns in food intake, so protein intake will also have a 24hour rhythm. I do recall studies that have provided small frequent and evenly distributed meals to rodents across the 24hr period, in an attempt to maintain calories fairly constant and evenly distributed. However, I do not recall whether any of these studies investigated effects on the heart, or if protein levels were manipulated within the diets.

8. **Is there any circadian effect in other micronutrients such as sodium, zinc, magnesium?**

   Great question. Certainly, micronutrients that you mention are known to impact circadian related processes (including clocks themselves, as well as sleep). Moreover, sodium intake can impact 24hr rhythms in blood pressure. In our studies, we ensured that the distinct diets utilized were equal in micronutrient content.

9. **Will the other amino acids carry the same effect as BCAA?**

   This is certainly something that we wish to investigate. We started with BCAAs due to their links with cardiometabolic and cardiovascular disease, the relative ease of measuring established outcomes (mTOR signaling, cardiac growth), and that these are essential amino acids (meaning dietary manipulation leads to reciprocal changes in circulating levels that cannot be compensated by de novo synthesis). However, the NHANES epidemiologic data I mentioned towards the end of my talk focused more on total protein intake, which would include intake of all amino acids.

10. **In view of potential adverse effects of fat and protein, especially in people with cardiovascular disease or risk what should we recommend for dinner, only carbs, skip dinner and how long before going to sleep should eating be discontinued?**

    I always try to be cautious went extrapolating our rodent based studies to recommendations in humans (particular in at risk populations, such as individuals with heart disease). Certainly, the American Heart Association has recommended eating a greater share of calories towards to the beginning of the day. Moreover, benefits from intermittent fasting (e.g., 8 hour window of feeding plus 16 hour window of fasting) are seen for multiple cardiometabolic and cardiovascular disease parameters. Combining these two concepts, it is possible that when performing intermittent fasting, benefit may be best if calories (including calories from lipid and protein) are consumed towards the beginning of the day (which would result in avoiding meals before going to bed).

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## Columbus Instruments

950 North Hague Avenue, Columbus, Ohio, United States, 43204
http://www.colinst.com/
Phone: +1 614 276-0861
Email: sales@colinst.com