According to recent research, circadian disruption alters the consistence of the gut microbiota, disrupts host immunity, and increases the risk of inflammation and metabolic complications. Moreover, abnormal clock function interferes with mitochondrial function and reactive oxygen species production. Consequently, circadian disruptions have been linked to insulin resistance and metabolic syndrome.

Recent evidence also indicates that increased plasma trimethylamine N-oxide (TMAO) is closely correlated with the prevalence of diabetes. Since TMAO is mainly produced by trimethylamine (TMA) oxidation, it has been postulated that the consumption of TMA precursors, phosphatidylcholine/choline or L-carnitine (LC), may be promoting pathogenesis. On the other hand, LC supplementation has been recommended as a promising adjuvant in the treatment or prevention of insulin resistance and its complications.

The precise mechanism is not known, but involvement of mitochondrial function, oxidative stress, and inflammation have been suggested. LC represents a direct antioxidant, and anti-inflammatory activity. On the contrary, TMAO induces oxidative stress and promotes cellular inflammation.

Because LC supplementation elevates plasma TMAO, we hypothesize that 1) insulin sensitivity is modified depending on circulating metabolite levels – TMA, TMAO; or free, total, and acyl-L-carnitines profile; 2) decrease in insulin sensitivity induced by simulated night-shift work is enhanced by TMAO, or attenuated by carnitine ester profile modification; 3) observed changes in insulin sensitivity are associated with mitochondrial function, oxidative stress or inflammatory markers

This project assumes to investigate the unknown effect of gut microbiota metabolites (TMA and TMAO), modified by LC supplementation, on insulin sensitivity.

To establish, whether TMAO is responsible for the development and progression of insulin resistance, the project is composed of two complementary tasks aimed:
1) to evaluate the potential effect of TMA and TMAO on insulin sensitivity, using LC supplementation for modulation of gut microbiota metabolites;
2) to use simulated night-shift work intervention as a stress factor to explore the effect of circulating metabolite levels on insulin sensitivity.

Moreover, the results of night shift work model study improve the knowledge about metabolic changes in persons subjected to circadian disruptions such as medical staff, firefighters, and security officers.