

The effect of Diabetes-associated genetic variation in *TCF7L2* on Pulsatile Insulin Secretion in nondiabetic subjects

Marcello C. Laurenti ¹, Chiara Dalla Man PhD ², Ron T. Varghese MBBS ¹, James C. Andrews MD ³, Robert A. Rizza MD ¹, Aleksey Matveyenko PhD ^{1,4}, Giuseppe De Nicolao PhD ⁵, Claudio Cobelli PhD ², Adrian Vella MD ^{1*}.

¹Division of Endocrinology, Diabetes & Metabolism, Mayo Clinic, Rochester, MN, USA

²Department of Information Engineering, University of Padova, Padova, Italy

³Vascular and Interventional Radiology, Mayo Clinic, Rochester, MN, USA

⁴Physiology and Biomedical Engineering, Mayo Clinic, Rochester, MN, USA

⁵Department of Computer Engineering and Systems Science, University of Pavia, Pavia, Italy

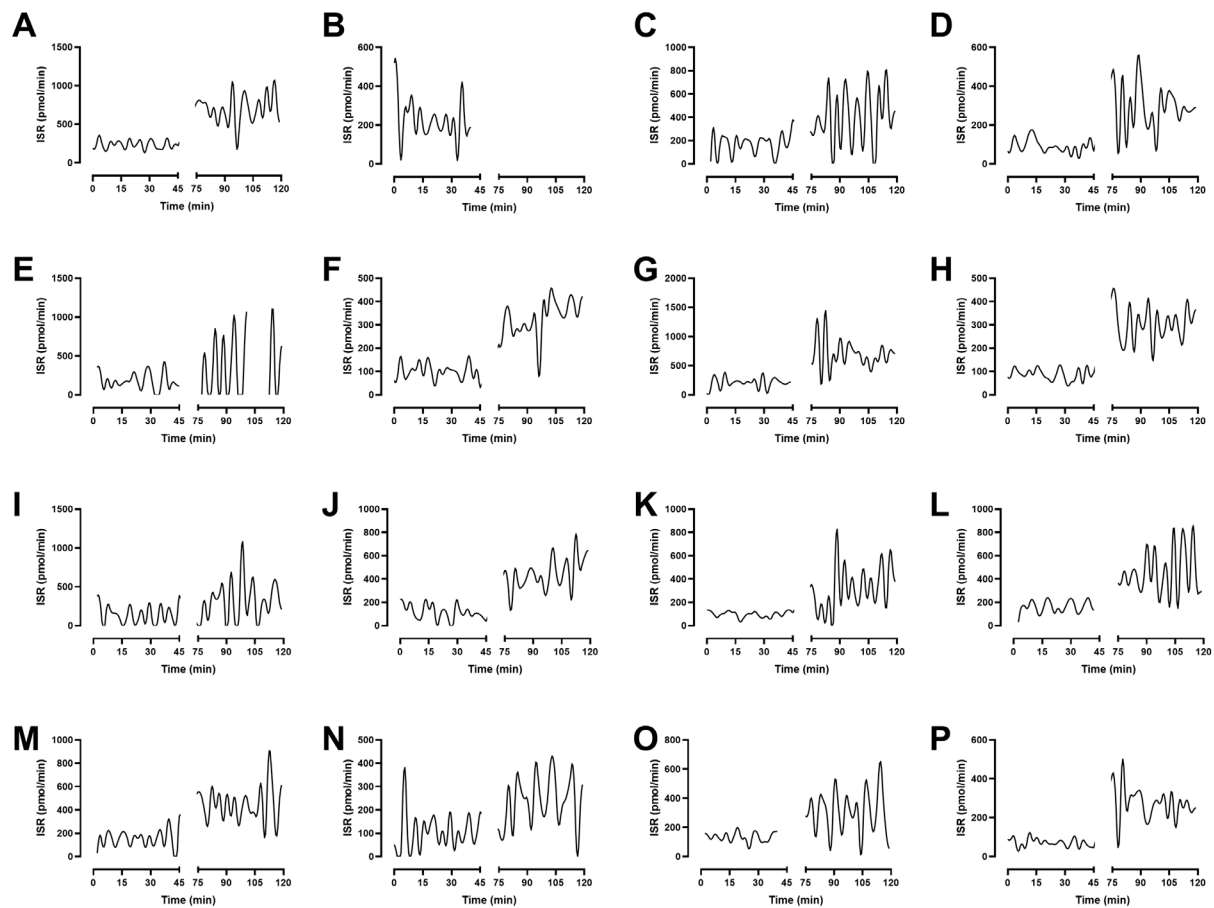
Running title: Effect of *TCF7L2* on insulin pulsatility

Key-words: insulin pulses, C-peptide kinetics, hepatic extraction, *TCF7L2*, Approximate Entropy.

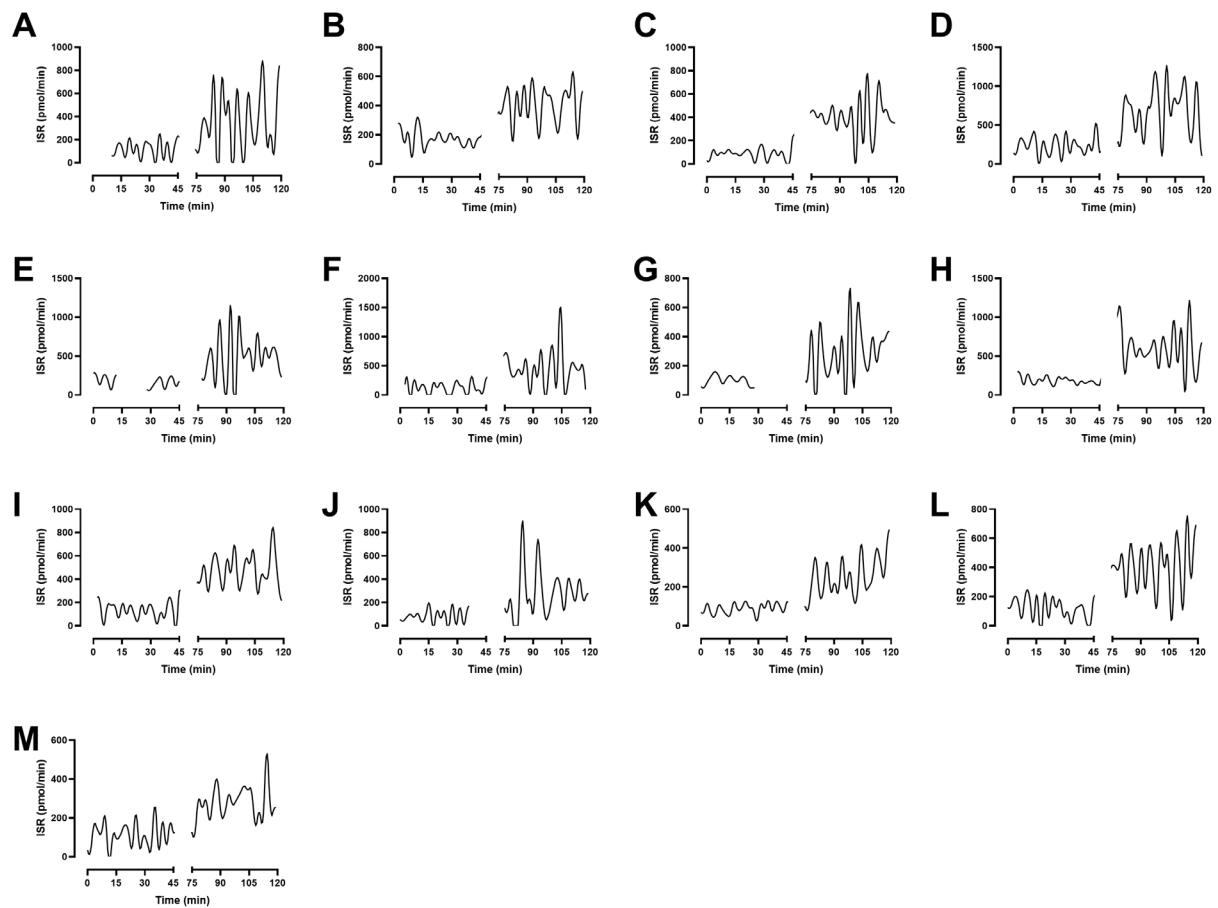
*Address for Correspondence: Adrian Vella MD
Endocrine Research Unit
Mayo Clinic College of Medicine
200 First ST SW, 5-194 Joseph
Rochester, MN 55905
(T) 507-255-6515
(F) 507-255-4828
Email: vella.adrian@mayo.edu

Figures: 7

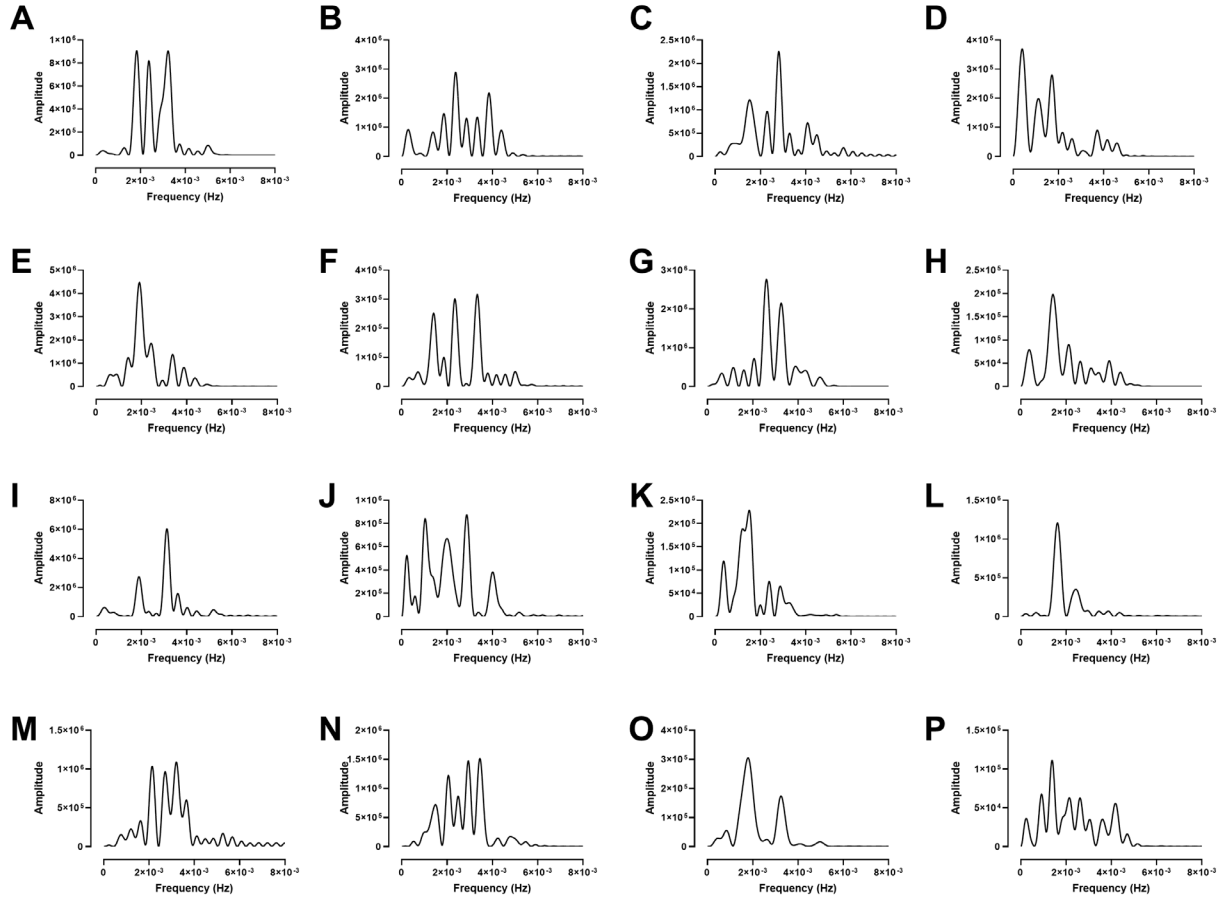
Conflict of Interest: The authors have declared that no conflict of interest exists.



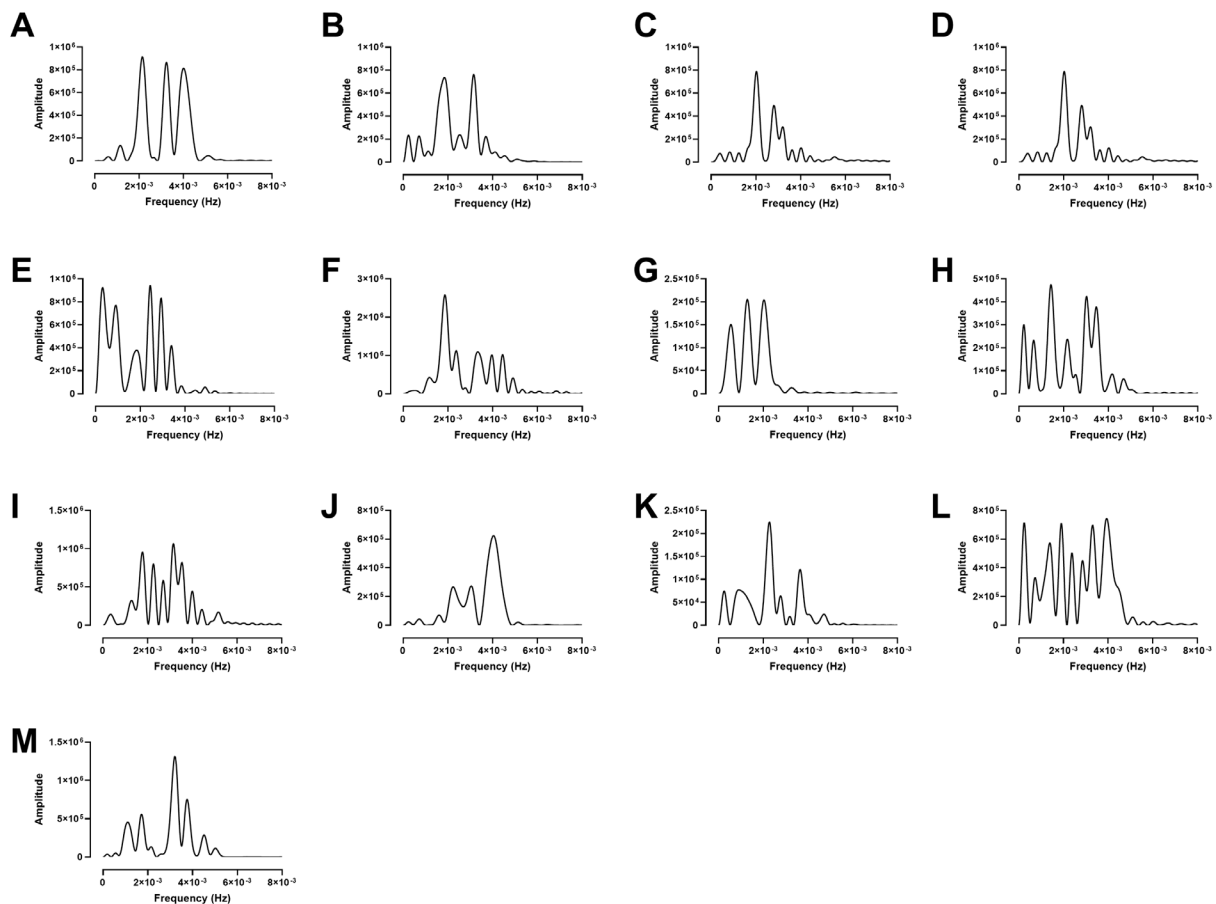
Supplementary Figure 1: The Insulin secretion rate in each individual with the CC genotype at rs7903146 during the fasting (0-45 minutes) and hyperglycemic (75-120 minutes) phases of the experiment.



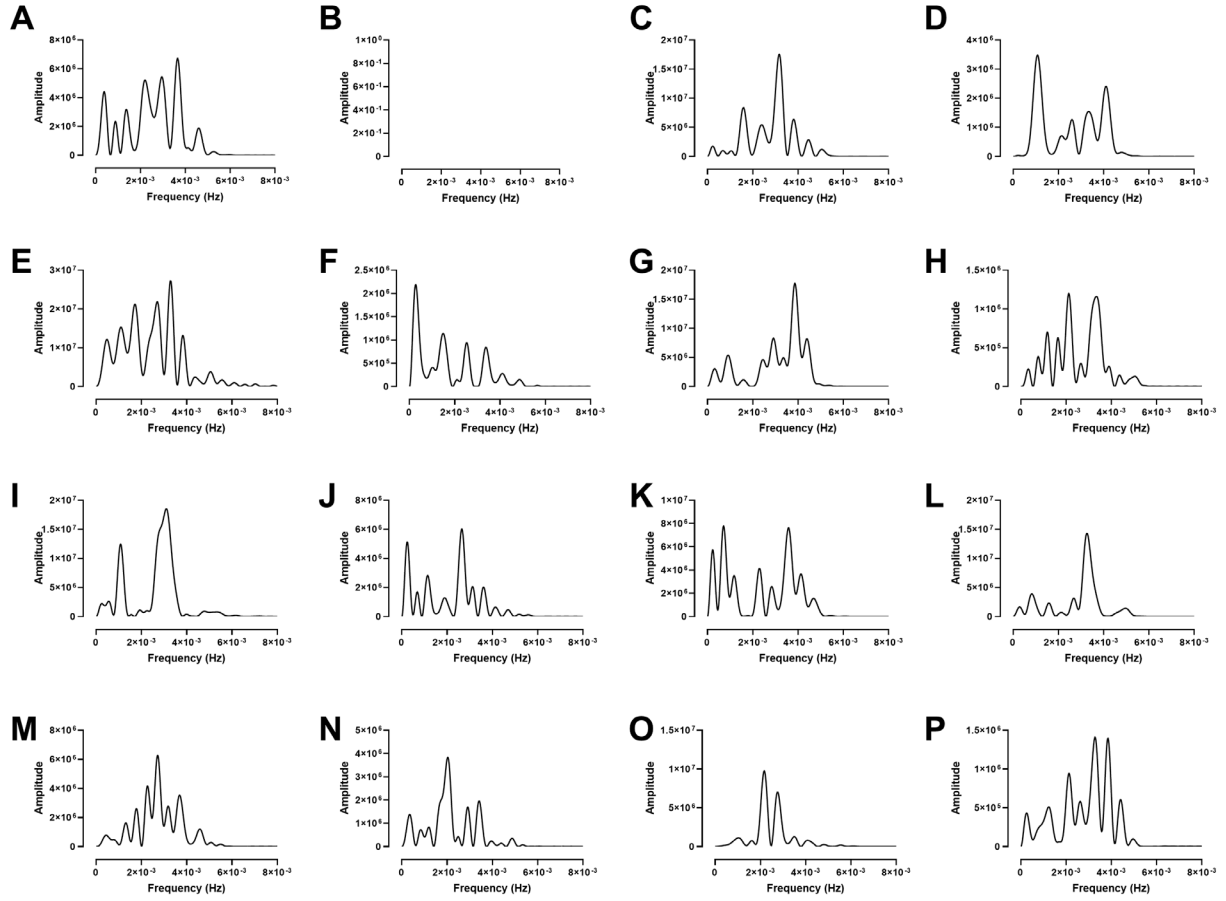
Supplementary Figure 2: The Insulin secretion rate in each individual with the TT genotype at rs7903146 during the fasting (0-45 minutes) and hyperglycemic (75-120 minutes) phases of the experiment.



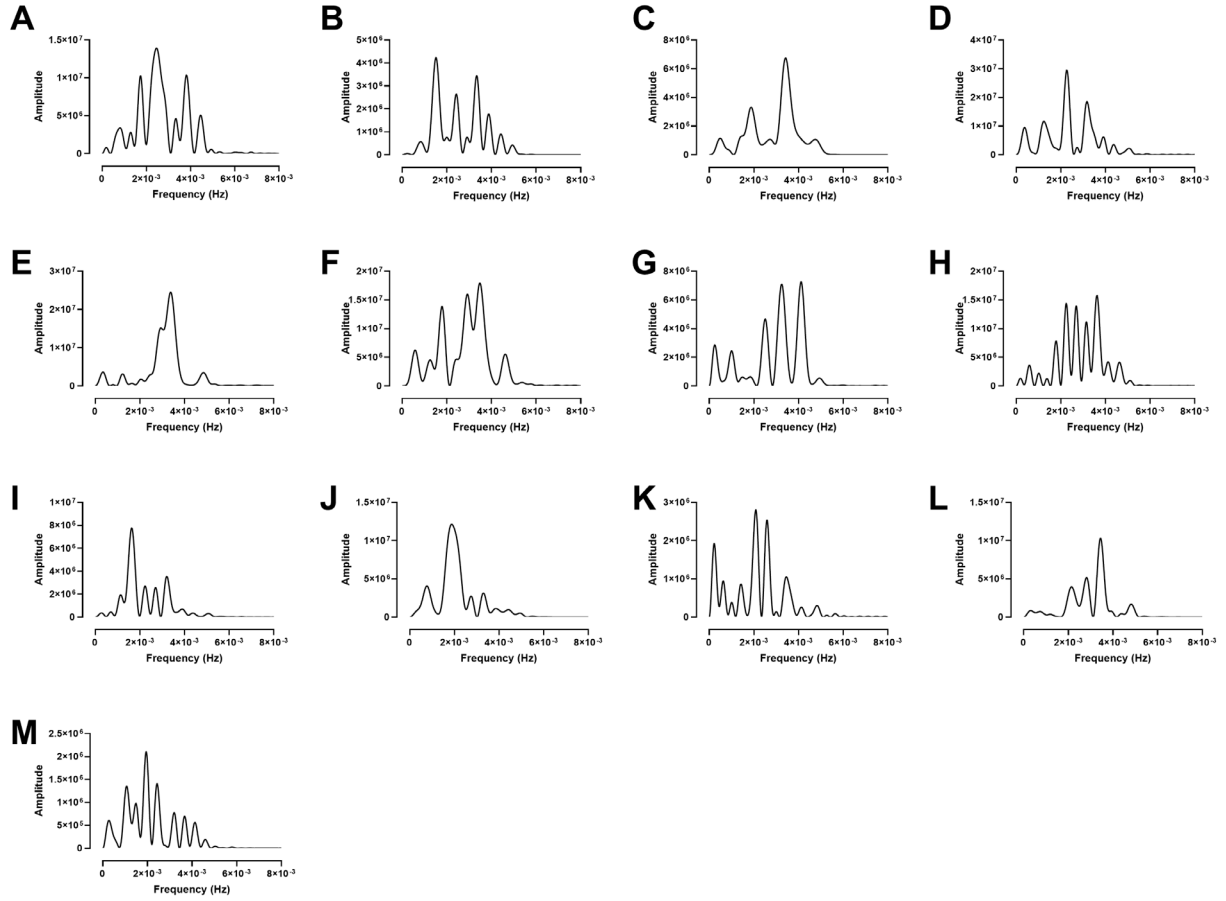
Supplementary Figure 3: The Periodogram obtained from the insulin secretion rate over time for each individual with the CC genotype at rs7903146 during the fasting phase of the experiment.



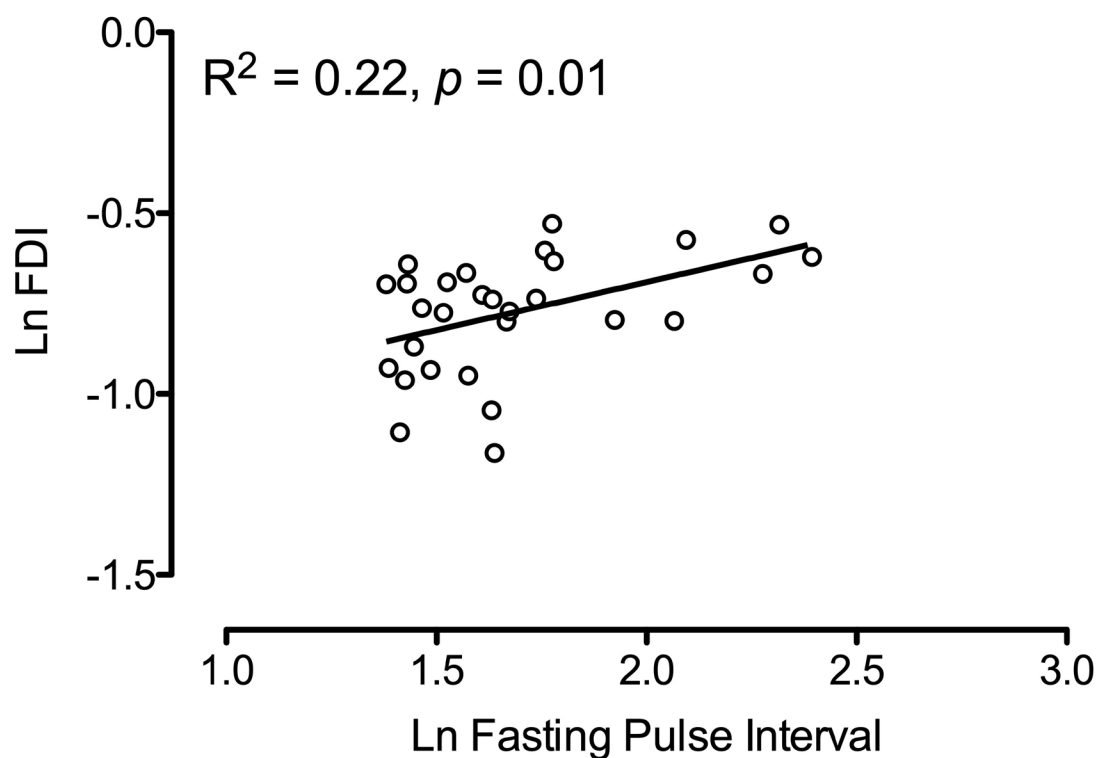
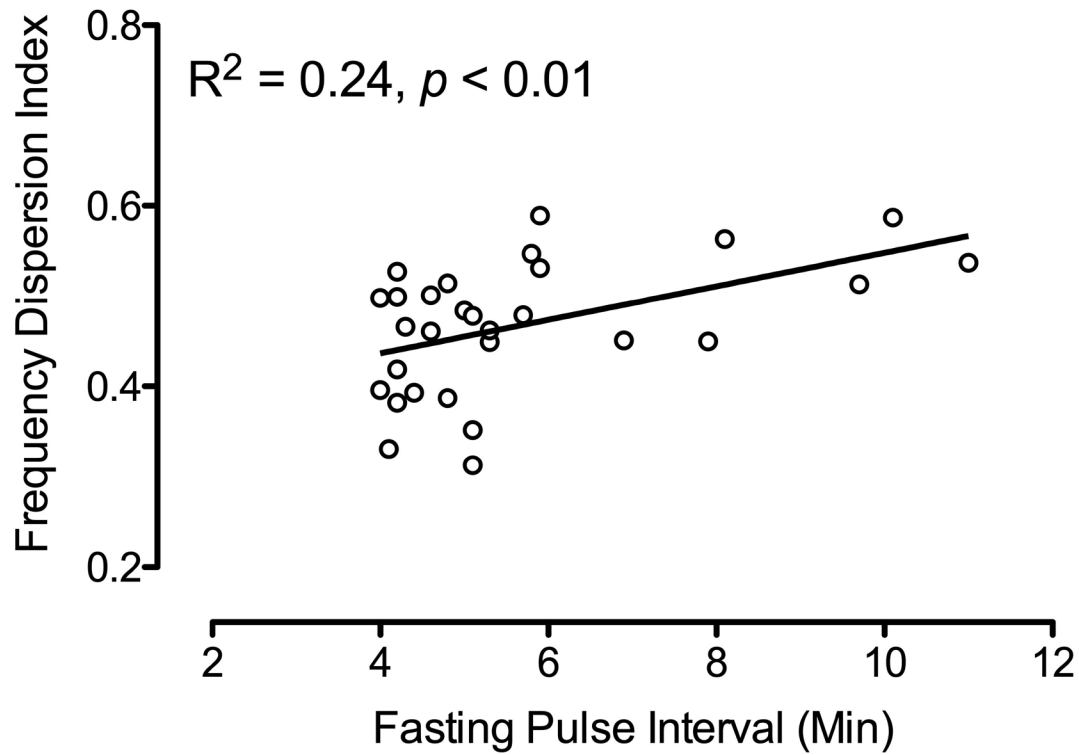
Supplementary Figure 4: The Periodogram obtained from the insulin secretion rate over time for each individual with the TT genotype at rs7903146 during the fasting phase of the experiment.



Supplementary Figure 5: The Periodogram obtained from the insulin secretion rate over time for each individual with the CC genotype at rs7903146 during the hyperglycemic phase of the experiment.



Supplementary Figure 6: The Periodogram obtained from the insulin secretion rate over time for each individual with the TT genotype at rs7903146 during the hyperglycemic phase of the experiment.



Supplementary Figure 7: Relationship of the Frequency Dispersion Index (Panel A) and of Log_e-transformed data (Panel B) with pulse interval during the fasting phase of the experiment for all subjects.