

## THE CHRONOMICS STUDY: DESIGN & PROTOCOL.

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The rationale of this study is based on the Tsim Tsoum concept of 'a return to natural foods' enjoyed some centuries ago when ingestion of  $\omega$ -3 and  $\omega$ -6 were roughly equal unlike today in most Western societies. Evidence suggests that these high w-6/w-3 ratios have an increased impact on endothelial dysfunction (Singh et al. (2008). In: Wild Type Foods in Health Promotion and Disease Prevention (De Meester F & Watson RR, eds), Humana Press, pp. 263-284) and that this will be reflected in the early detection of preHypertension as indicated by Vascular Variability Disorders (Halberg F, et al. (2007) Am J Med 2007;120:e19-e20) or indeed, similarly, preMetabolic Syndrome. Understanding the role of psychological and oxidative stresses upon, inter alia, chronic generative diseases (cardio- and cerebro-vascular diseases such as blood pressure and ischaemia, etc.) through adverse mechanical and oxidative 'stresses'.

The Chronomics Project is a 2-treatment, 4y, double-blind randomized prospective cohort dietary intervention study based on w-3 oral administration (and placebo) with diet as usual (DAU) each treatment administered at fixed time intervals (3h) along a circadian timespan (stages: AW=time of awakening – AW+12h inclusive). However the study is stratified for 3 mixed-gender age groups (Poles living in southern Poland: adolescent, active adults and the retired-elderly). The main objective is to monitor Mind/Body interaction and to identify/confirm potential new MESOR-biomarkers of the pre-metabolic syndrome (pMS) that may eventually be transformed into chronic degenerative diseases in the absence of tissue self-healing barriers (Columbus Concept, i.e. Omega-6 Status = 25% in blood total lipids). Thus the effect of circadian-time-staged dietary intake of  $\omega$ -3 fatty acid that results in plasma-monitored % $\omega$ 6 HUFA (highly unsaturated fatty acids/ blood lipids), is to be monitored. The effect of % $\omega$ 6 HUFA upon vascular variability disorders and 'Mind' variables such as mood/vigour and emotion/ ambivert characteristics/scores have been assessed. The hypotheses are a) Primary:- Is a low Omega-6 Status ( $\Omega$ 6S~25) in total blood lipids correlated with acceptable circadian heart rhythms in adolescents, active adults, and retired adults of southern Poland? b) Secondary:-Is 'evolutionary' blood lipid composition an effective barrier against pre-Metabolic Syndrome (pMS)? Tertiary:- Is  $\Omega$ 6S~75 a threat to developing MS? High % $\omega$ 6 HUFA may lead to tissue desensitvity and overproduction of reactive oxygen species, persistent inflammation and thence cell proliferation and the advent of possible future atherogenesis, cancer, and brain dysfunction.

This project was subject to formal literature (published and grey) review (e.g. Medline, EMBASE, PsycINFO, Web of Knowledge) using indexed and free-text terms from 1980 to 2010 and references collated and the  $\omega$ -3 FA chronobiological dietary trial design formulated, *vide supra*, the sample size may be adjusted when pilot information is obtained. The sampling schedules for blood pressure measurements (parameters will be calculated separately for systolic and diastolic blood pressure from ambulatory blood pressure monitoring equipment) and those for FAME (fatty acid methyl esters) profiles and sub-groups and ratios (*varia*) data. 'Mind' variables have been developed and will be presented by other talks on the Chronomics study. Standard Operating Procedures for implementing this project in the field, and quality assurance of all laboratory-based methods have been/are important features of this study.

Project management tools for conducting the trial have been used for external assessment and an audit trail for external assessors is on-going. This also includes all aspects of data management, statistical analysis and reporting. All members of the trial team will agree on intended publications and presentations.

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