Research Theme
Infection and Immunity

Research Project Title
An Immune Suppression Model for Early Diagnosis of Overtraining Syndrome: A Community Health Challenge with an Increasingly Active Population

Principal Investigator
Associate Professor Fabian Lim, LKCMedicine

Co-supervisor
Associate Professor Eric Yap, LKCMedicine

Project Description
Aims and Hypotheses
Thousands of students, civilians and athletes are exposed unknowingly to the health risks of prolonged intense training (a.k.a. overtraining, OT) without being aware of the consequences involved. A consensus on the diagnosis and prevention of overtraining syndrome (OTS) is also lacking presently. This study aims to investigate the impact of prolonged exposure to high training load on the health, physiology and mood of individuals to support the following research aims:

- To develop an evidence-based definition of OTS that can be used as a diagnostic tool for OTS e.g., identifying the roles of primary and secondary symptoms
- To determine the variants in OTS expressions, if any e.g., based on clustering of phenotypes, duration of exposure to OT, specific population and sport.
- To develop capability for early identification of risks and onset of OTS that can support early intervention and prevention.

We hypothesise that OTS can be diagnosed objectively by combining performance degradation, immune parameters (e.g., Leukocyte and lymphocyte subsets, IgA, inflammatory cytokines) and incidence of upper respiratory tract infection (URTI) as the primary symptoms with biomarkers for tissue damage (e.g., myoglobin and creatine kinase) and Profile of Mood Scale (POMS) scores as the secondary symptoms. We also hypothesise that the same primary and secondary symptoms can be used effectively to calibrate training load for an optimal balance between performance and health outcomes.

Organisation of Study
This proposal constitutes the first 3 years of a 6-year study plan, with half the number of intended subjects and surveys to be investigated over the first cycle. The aim and hypotheses of the study will be investigated...
in two phases, to be conducted non-sequentially:

**Phase I** will investigate the monthly incidence of upper respiratory tract infection in the three months leading up to a major endurance race and two weeks after the race. Survey forms will be sent out to participants in major endurance race events to obtain this data. The survey will provide information on training load / pattern, endurance performance status and the incidence and severity of URTI symptoms experienced by the participant.

In addition, laboratory investigations will be conducted on a sub-sample to provide more insights into the status of the immune system, POMS mood score, and physiological indicators of stress and soft tissue damage in the same sampling period.

The laboratory investigations will include the following parameters:

- Aerobic capacity and body composition
- Pulse wave velocity, brachial and central blood pressures, and flow-mediated dilation
- Immune markers (e.g., leukocyte and lymphocyte subsets)
- Myoglobin and creatine kinase to indicate soft-tissue damage
- Pro- and anti-inflammatory cytokines, C-reactive proteins as biomarkers for the inflammatory pathway
- Cortisol, epinephrine, norepinephrine, dopamine and serotonin. Cortisol, epinephrine and norepinephrine are central stress biomarkers, serotonin is positively associated with fatigue, and dopamine promotes exercise performance.
- Biological antioxidant potential (BAP) as an indicator of antioxidant capacity.

**Phase II** will conduct the same laboratory tests as Phase I in another group of athletes, twice annually, over 3 years. Athletes who are exposed to prolonged intense training will be tested every 6 monthly to track their health and performance in relation to the training load. Additional tests will be conducted in the 3 months before and 2 weeks after major races, and when the athletes start to show symptoms of OTS e.g., unexplained degradation in performance, frequent URTI and decrease in mood. Conducting the same laboratory measurements in Phase II is an important feature of the study design to link and build upon both phases of investigation.

Phase I will attempt to detect pre-OTS and early-OTS symptoms in a single event among athletes preparing for an endurance race. This phase can help to identify immune, physiological and psychological signatures that are associated with the development of OTS during the intense period of race preparation. These results will be verified in Phase II, which will assess the same interaction between training load /stress and immune, physiological and psychological parameters on a longer term basis. Long term assessment provides...
a more robust assessment of the trends and interaction between training-load stress, lifestyle factors, and appearance of OTS symptoms. Taken together, these two phases will provides a comprehensive understanding of the various biological signatures that are associated with training load stress over time, which can be used for risk identification and early detection of OTS. These capabilities to identify risks and detect OTS early are important bases for developing intervention strategies against OTS to protect the health of athletes.

The extent of laboratory investigation will depend on the outcome of ongoing grant application for this project.

Contact Us

If you have questions regarding this project, please email the Principal Investigator.

Associate Professor Fabian Lim

fabianlim@ntu.edu.sg