

MASTER PROJECT OFFER:

Molecular Mechanisms Regulating Ethanol-Induced Changes in Apolipoprotein Expression

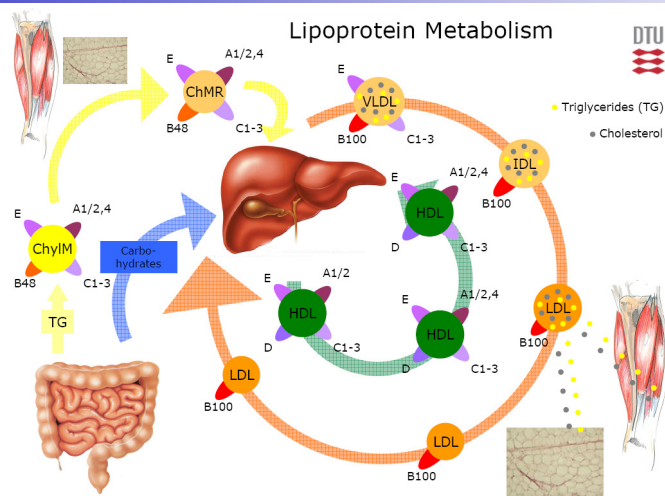


Fig. 1:
A complex of lipoproteins regulates exogenous (orange) and endogenous (green) transport and distribution of lipids such as cholesterol. Ethanol was proven to reduce mortality and incidence of coronary vascular disease by enhancing transport of cholesterol from periphery back to the liver and to reduce hereby atherogenesis.

What we know:

1. Moderate alcohol consumption enhances the concentration of apolipoproteins that are produced in the liver (Fig. 2).
2. This increase is associated with an reduced risk of CVD.

=> How does ethanol regulate the expression of apolipoproteins?

Methods:

1. Cell culture
2. Isolation/purification/reverse transcription of mRNA.
3. Semi-quantitative cDNA-chip microarray technology
4. Quantitative real-time-PCR
5. Statistical evaluation/ontology annotation of chip array data

What we have to support this thesis:

1. Cells isolated from the liver of mice (C57/BL6)
2. A transcriptomics platform capable of dealing with microchip arrays for the mouse genome
3. An animal facility
4. Cell culture facility suitable for human hepatocyte cell lines.

Background:

- Coronary vascular disease (CVD) is the most common cause of death in industrialized countries.
- Moderate (!) alcohol consumption reduces both CVD and over-all mortality (appr. 50 000 deaths/year in USA).
- This effect is mediated by enhanced transport of cholesterol from the periphery to the liver (Fig. 1).
- The molecular mechanism for this effect is unknown.

Nutrient Intake <-> DV, $P < 10^{-4}$

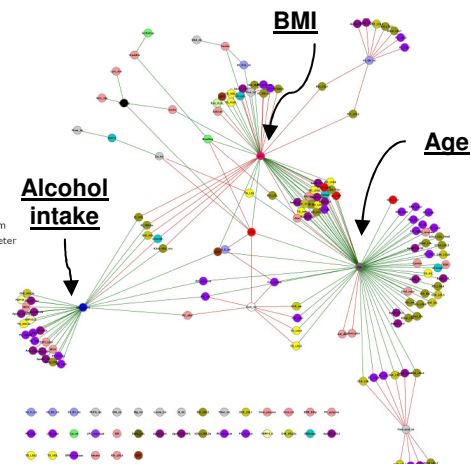


Fig. 2:
Positive (green) and negative (red) correlations between independent variables (life style factors, nutrient intake, age, body-mass-index - BMI) and dependent variables (e.g. (phospho-)lipids, apolipoproteins). Age, BMI, and alcohol intake dominate the majority of plasma concentrations of (phospho-)lipids, apolipoproteins, and other clinical-chemical parameters. Only correlations with a significance level $P < 0.0001$ are regarded.

Aim: To identify key factors of ethanol-induced changes in the apolipoprotein production profile of hepatocytes.

The project will be supervised by: Alexandr Parlesak, associate professor at DTU, Nutritional Immunology Group (NIG), Center for Biological Sequence Analysis (CBS) and is kindly supported by Laurent Gautier/Chris Workman, CBS and Lisbeth Buus Rosholm/Pernille W. Gullich, Nutritional Immunology Group (NIG)
Contact: A. Parlesak, phone ++4525 2783, e-mail: alpa@bio.dtu.dk; DTU campus, Bldg. 224, room 014.