

# HUPO INITIATIVES

## Mouse Models of Disease

Mouse/Rat Quantitative Organellar Proteomics Initiative

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Through quantitative organellar proteomics we produce complete molecular maps of the major organelles of both adipose and hepatic tissue and model cell lines from lean and obese rats and mice. This includes the mitochondria, the secretory pathway (the ER and the Golgi apparatus), the endocytic pathway, lipid droplets, peroxisomes, autophagosomes and the nucleus.

Proteins and protein complexes of interest are then analyzed for functionality using high end cell biology techniques including correlative microscopy, EM-tomography, knockdown experiments, live cell imaging and high content and high throughput screening. This is followed by an in-depth study in humans where the identified proteins of interest are correlated at the human level drawing on cohorts from existing and past genomics studies in both Canada and Italy to identify and map genetic backgrounds for obesity. Through high-content screening and high throughput screening, we also identify genes and low molecular compounds, respectively that serve as regulatory in energy expenditure with a focus on eliciting facultative thermogenesis, a unique feature of brown adipose tissue whereby energy is converted into heat. Previously thought to be restricted to infants, recent evidence conclusively demonstrates the presence of brown adipose tissue in adult humans opening up for the distinct possibility of enhancing energy expenditure through elicited facultative thermogenesis as a new non-invasive treatment strategy to prevent or combat obesity. We estimate that approximately 5kg of fat can be converted into heat through this process alone/per year.

A Canada-Italy constellation consists of 13 group participants distributed evenly between the two countries (7 in Canada, 6 in Italy) is in place.

The proteomics (and other genomics technologies) will from the start feed into the outstanding and internationally leading cell biology community of Italy .

The cell biology of the secretory pathway through Negri Sud and Milan is also complemented by infrastructure for high throughput screening as well as high endmicroscopy platforms for high content screening (Negri Sud). Experts on obesity and diabetes are included on both sides of the Atlantic.

Key collaborators ensure access to and support for genomics, transgenic mice strains and high-end bioinformatics. By bringing together the genomics and cell biology of Canada and Italy, respectively, we generate a high impact constellation that neither country can muster alone. The scientific merits of the combined groups alone outnumbers, by far, most current and past research constellations with an average citation index of 4849 per team and an average Hirsch-index of 35. GE3LS are included through Dr.Knoppers, Montreal, a highly distinguished specialist in legal and ethical issues pertaining to genomic studies in humans.