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Investigation of proteomic signatures related to gender, age and body mass index

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Proteomics has played an important role in advancing nutrition research in recent years[(1)]. The area has strong potential to contribute towards the identification of new biomarkers in nutrition research, however understanding the impact of phenotypic and biochemical variables on the proteomic signature is key to doing this. The primary objectives of this research are to 1) examine the impact of phenotypic parameters on the proteomic signature and 2) uncover pathways enriched by the significant proteins.

This research focuses on data obtained from the Metabolic Challenge (MECHE) study. Healthy participants aged 18–60 years were recruited, and baseline samples from those who completed an OGTT and had complete proteomic data, were selected (n = 100). The MECHE dataset contains information on 1129 proteins measured using the SOMAscan assay from SomaLogic. The impact of gender, age and body mass index (BMI) on the proteomic signature was assessed using principal component analysis (PCA) and partial least squares discriminant analysis (PLS-DA). Pathway analysis was performed using PathVisio[(2)]. This study was performed according to the Declaration of Helsinki.

PLS-DA models demonstrated that gender, age and BMI all had an effect on the proteomic profile of the 100 healthy individuals. Based on the PLS-DA models, males and females were discriminated with an R^2 of 0·870, and a Q^2 of 0·550. Age categories were discriminated with an R^2 of 0·741 and a Q^2 of 0·159, while BMI categories were discriminated with an R^2 of 0·614 and a Q^2 of 0·314. When variable importance of projection values ≥ 2 were taken from the PLS-DA models, 40 proteins were associated with gender, 36 with ageing and 28 with BMI. Associated molecular functions and biological processes were extracted from the UniProt database and representative pie charts were created. Pathway analysis revealed altered pathways for gender, age and BMI. Bone metabolism pathways such as osteoblast signalling were significantly altered by age related proteins, along with complement pathways and micronutrient pathways (see table below).

Pathway (WikiPathway Identifier)	# Proteins/total	Z Score	*P*-value	% of proteins measured by assay
Complement Activation (WP545)	8/17	5·57	0·001	77·3
Complement and Coagulation Cascades (WP558)	12/38	5·00	0·001	64·4
Osteoblast Signalling (WP322)	3/8	2·85	0·031	57·1
Vitamin B12 Metabolism (WP1533)	6/25	2·68	0·011	49·0
Overview of nanoparticle effects (WP3287)	3/9	2·58	0·026	47·4
Allograft Rejection (WP2328)	7/36	2·26	0·027	46·2
Folate Metabolism (WP176)	6/27	2·46	0·019	40·9
Selenium Micronutrient Network (WP15)	6/28	2·36	0·020	33·7
Osteoclast Signalling (WP12)	2/6	2·10	0·035	37·5

Pathway statistics in PathVisio revealed significantly altered pathways by age related proteins (Z-score > 1·96, *P*-value < 0·05). The number of proteins (#proteins/total) represent the number of differentially expressed proteins in the pathway compared to the total number of measured proteins by SOMAscan assay in the pathway.

To our knowledge, this is the first study to give an overview of proteins related to each of the phenotypic parameters gender, age and BMI in a healthy cohort. Future work will investigate the overlap of significant proteins for these phenotypic parameters and the potential links between proteins and health status.

1. de Roos B, McArdle HJ (2008) *Br J Nutr*. **99**(3): S66–71.
2. Kutmon M, van Iersel MP, Bohler A *et al.* (2015) *PLoS Comput Biol*. **11**(2): e1004085.