HelmholtzZentrum münchen
German Research Center for Environmental Health

Scientific Highlight   October 2016

☐ co-ordinated with the Director of the Institute / Research Unit

Research Unit Protein Science

PSP-Element:
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Title of the highlight:
Proteins in plasma can be used to detect prediabetes

Keywords:
Prediabetes, Targeted Proteomic, T2D, cross-sectional

Central statement of the highlight in one sentence:
Targeted proteomic analysis identified associations between four proteins and so-called pre-diabetes, which had hitherto not been described.

Text of the highlight:
Patients progress towards overt type 2 diabetes through lengthy preliminary stages, during which initial metabolic alterations occur. A team of researchers led by Dr. Stefanie Hauck and Dr. Barbara Thorand, the respective heads of the Research Unit Protein Science and the Diabetes Epidemiology working group at the Helmholtz Zentrum München, has now succeeded in identifying specific proteins which serve as biomarkers for these processes, and which may also cause them.

For the purposes of analysis, the scientists examined 439 randomly selected blood plasma samples obtained from men and women between the ages of 47 and 76 as part of the population-based KORA (Cooperative Health Research in the Region of Augsburg) study. In this instance, the scientists were able to refer to data from Augsburg residents who had undergone oral glucose tolerance testing between 2006 and 2008 in cooperation with the German Diabetes Center (DDZ) in Düsseldorf in order to identify previously undiscovered type 2 diabetes and its pre-stages.

The samples were analysed using targeted mass spectrometry. Using Selected Reaction Monitoring (SRM-MS), 23 proteins relatively quantified in a multiplexed fashion. "We were able to identify associations between four proteins and so-called pre-diabetes, which had hitherto not been described," explain Dr. Christine von Toerne and Dr. Cornelia Huth, the two first authors of the study.

According to the authors, this is the largest-ever proteomic study of type 2 diabetes based on mass spectrometry to be described. However, how exactly the proteins contribute to diabetes remains unclear, and this is a question that the authors plan to address in future studies. To enable longitudinal analyses, an additional 750 samples from Augsburg residents obtained within the framework of the KORA study were measured and are currently analysed.

The scientists are confident that their observations will not just be of theoretical interest and have already applied for the respective patent. "In the long term, we plan to channel our results into the development of a kit for the early diagnosis of type 2 diabetes," says research team leader Dr. Stefanie Hauck.

**Taking account of the HMGU mission:**
This study translates findings in the context of type 2 diabetes from a mouse model into the human situation. Identifying markers for prediabetes might help to understand disease development towards overt type 2 diabetes and to establish prevention programs for patients.

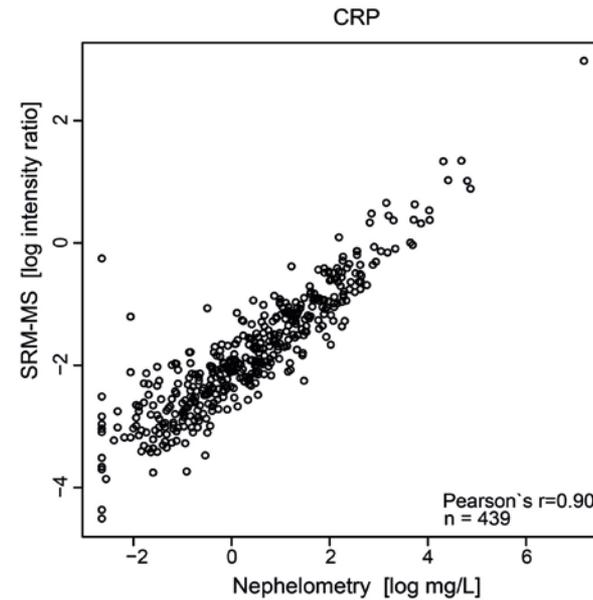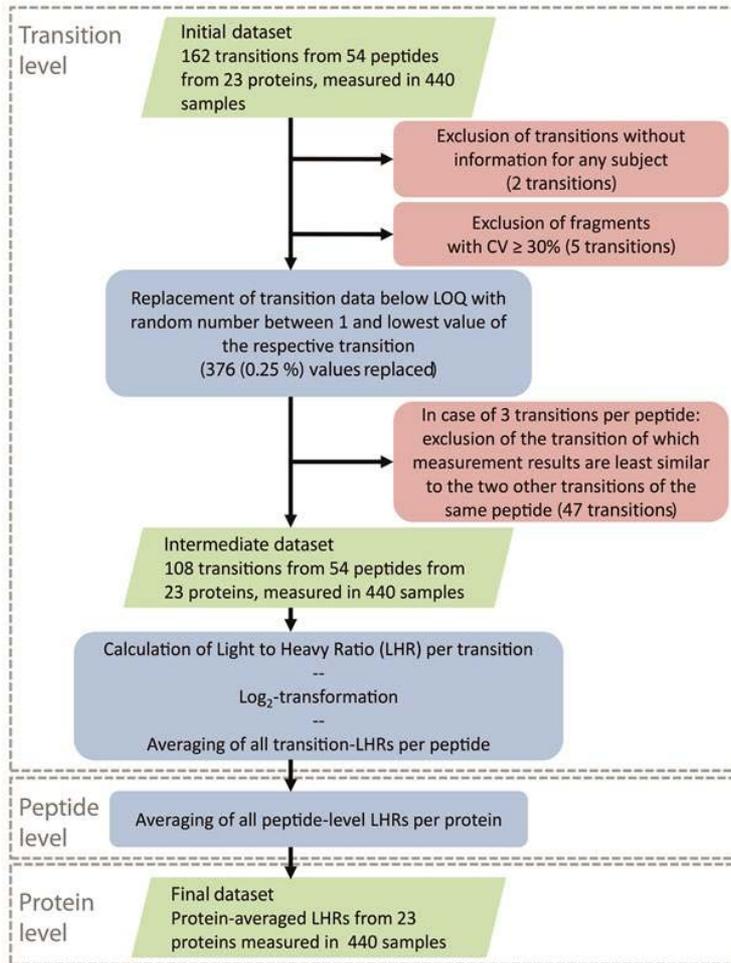**The internal HMGU co-operation partners with whom the highlight was compiled, if appropriate:**
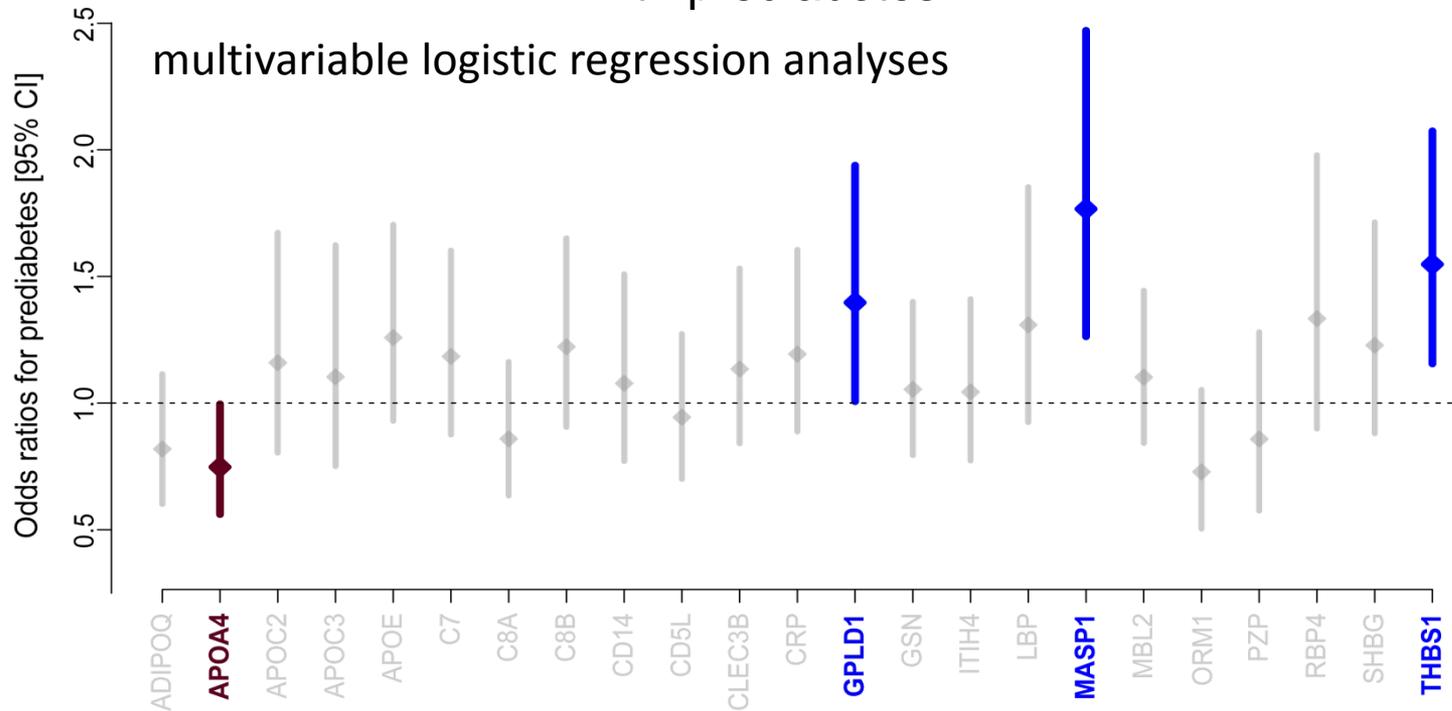Institute of Epidemiology II, EPI II; G-504000-002
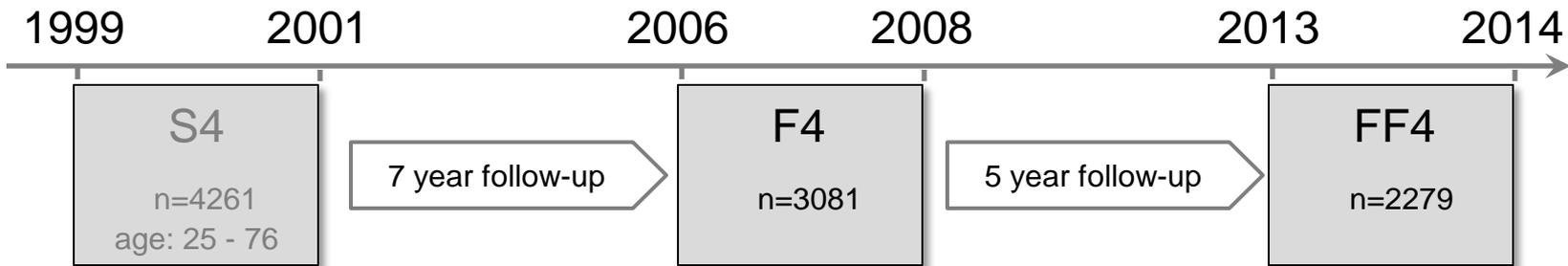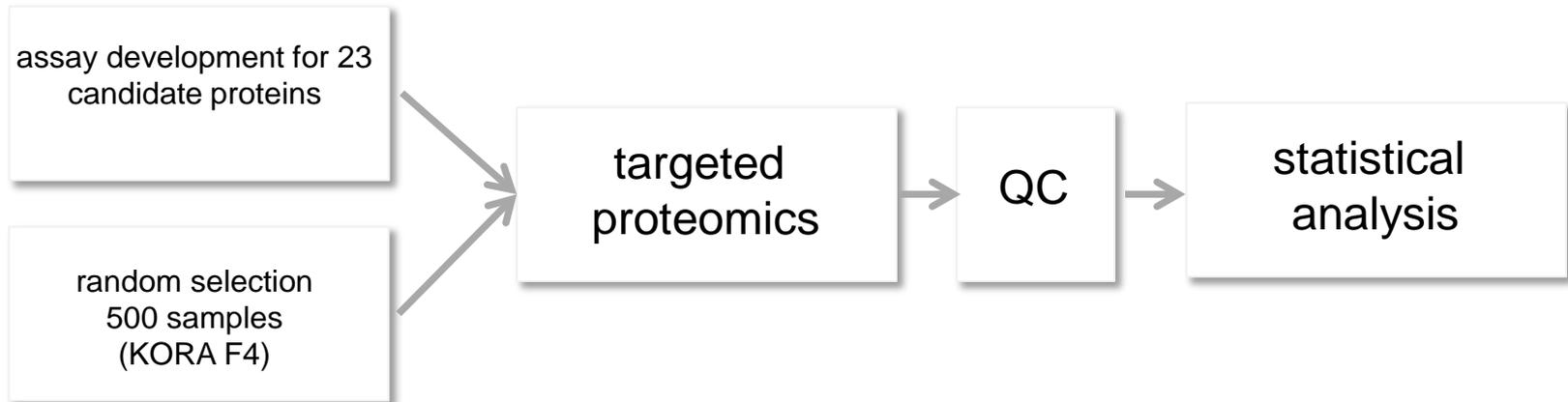
281 NGM – normal glucose metabolism

95 IGM – impaired glucose metabolism
„prediabetics"

63 T2D – type 2 diabetics

APOA4, GPLD1, MASP1, THBS1 – novel biomarkers associated with prediabetes

multivariable logistic regression analyses

APOA4 apolipoprotein A-IV
GPLD1 glycosylphosphatidylinositol specific phospholipase D1
MASP1 mannan-binding lectin serine peptidase 1
THBS1 thrombospondin 1

von Toerne et al., *Diabtologia, 2016*

Proteomic signatures for T2D

APOA4, GPLD1, MASP1, THBS1 – novel biomarkers associated with prediabetes

Protein	Prediabetes vs NGM (n=95 vs 281)			T2D vs NGM (n=63 vs 281)		
	OR	95% CI	Stat	OR	95% CI	Stat
APOA4	0.75	[0.56; 1.00]	*	1.53	[1.01; 2.33]	*
GPLD1	1.40	[1.01; 1.94]	*	2.33	[1.42; 3.82]	***
MASP1	1.77	[1.26; 2.47]	***	1.61	[0.95; 2.72]	
THBS1	1.55	[1.16; 2.07]	**	1.05	[0.70; 1.56]	

NGM: Normal glucose metabolism,
OR: odds ratio,
95%CI: 95% confidence interval
*P<0.05; **P<0.01; ***P<0.001.

adjusted for:
age,
sex,
BMI,
smoking status,
alcohol intake,
physical inactivity,
actual hypertension,
triacylglycerides,
total/HDL cholesterol ratio,
hsCRP

von Toerne et al., Diabetologia, 2016

Currently evaluated: additional 600 samples for longitudinal analysis
→ can prediabetes be predicted?