

PHENOTYPIC FLEXIBILITY AND DIET-RELATED HEALTH (PHENFLEX)



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INTRODUCTION

A major need in today's nutrition and health research is the ability to demonstrate health improvement in dietary intervention studies with apparently healthy consumers. Such demonstrations would be in the interest of health-conscious consumers and would help food industry to build convincing health-claim dossiers. TNO, together with industrial and academic partners, is developing innovative concepts to address this need. In 2012, TNO initiated the 'PhenFlex' project, a pre-competitive collaborative project co-financed by 5 industrial partners. The project is a public-private partnership with the collective mission to bring nutritional intervention studies to a higher level in the interest of science, business and the consumer. PhenFlex is aimed at developing and assessing objective approaches for quantification of optimal health and substantiating health

benefits of diet. A board of three international key scientists and opinion leaders act as advisors to PhenFlex. Simultaneously, the FP7 project 'Nutritech', also coordinated by TNO, was launched. PhenFlex and Nutritech cross-fertilize through their scientific boards, joint meetings and by adherence and support of the International Life Sciences Institute (ILSI) to both projects.

ASSESSING OPTIMAL HEALTH

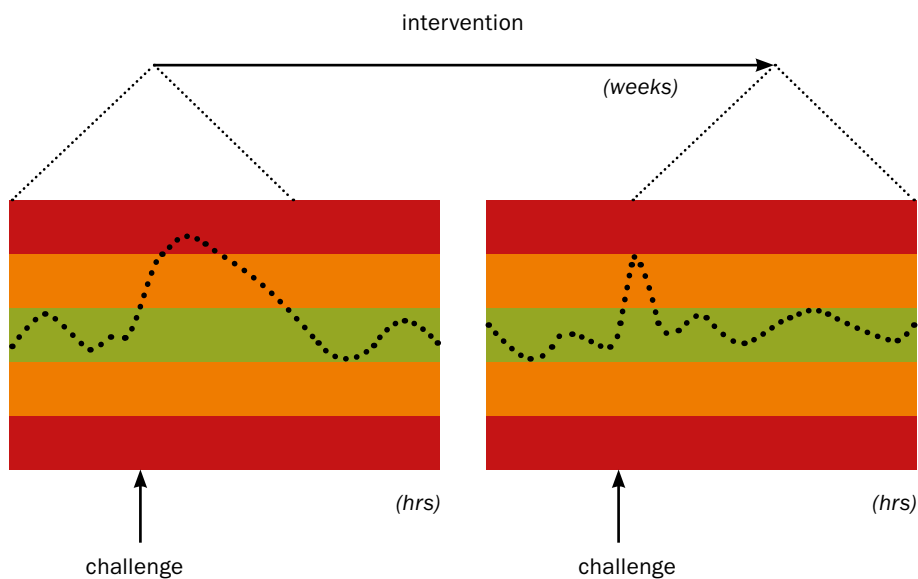
Optimal health, also defined as 'optimal resilience' or 'flexibility', is explicitly chosen as target to make a clear statement on one of the roles of nutrition: maintaining physiological functions (*Phenotypic flexibility as key factor in the human nutrition and health relationship*. van Ommen B, van der Greef J, Ordovas JM, Daniel H. *Genes Nutr.* 2014 Sep; 9(5): 423. doi: 10.1007/s12263-014-0423-5). Optimal health may also be rephrased as

the ability to cope with daily stressors. In this view, the kinetics of the response of physiology to a short-term stress situation is a measure for health. In both the PhenFlex and Nutritech projects, the application of a short-term perturbation of homeostasis, followed by quantifying the response profiles of a range of markers, is elementary. This so-called PhenFlex Challenge consists of a high-caloric macronutrient-rich drink.

CURRENT STATUS

The aim of phase 1 of the PhenFlex project was to develop and introduce novel methodology to determine optimal (metabolic) health. To this end, focus has been directed at three aspects:

- a. Measuring health as a dynamic response to a challenge ('measuring resilience'). The PhenFlex Challenge was developed and evaluated in a



Improved response profile of a challenged biomarker upon dietary intervention

series of tests with different population subgroups. These tests showed that healthy groups could be distinguished from type 2 diabetics and that there is loss of flexibility in physiological responses with increasing age and fat percentage. The PhenFlex Challenge has meanwhile been adopted in studies and consortia of other international groups.

- b. Finding new biomarkers to quantify Phenotypic Flexibility: by conducting a systematic literature review and using the outcomes of the human tests with the PhenFlex Challenge a list of candidate biomarkers is composed that could be used in a nutritional intervention study.
- c. Disseminate the PhenFlex concept regarding quantifying health and its results to stimulate embracement of this approach and acceptance of experts in various domains and to leverage the project outcomes with current and future nutritional health claim demands. A symposium on 'Phenotypic Flexibility' was organized in Madrid (February 2013) and 'Phenotypic flexibility as a new measure of health' was discussed with a selected group of experts in a workshop in Brussels (May 2014). Also an introductory animation is made. Publications are currently being prepared.

PHASE 2 OBJECTIVE

In the second phase of the PhenFlex project, the aim is to provide proof of concept that new biomarkers of health (as identified in phase 1, based on quantification of resilience) can be used to substantiate beneficial health effects in a nutritional intervention study. The proposed intervention will consist of an 'optimal diet' according to dietary recommendations, both in qualitative (macro- and micronutrients) and in quantitative (kcal) aspects. Effects of the intervention will be assessed by measuring and comparing responses of new and known biomarkers to the PhenFlex challenge at baseline and at the end of the intervention.

Focus on a limited number of health domains, such as vascular function, glucose metabolism and lipid handling by adipose tissue and liver is subject to further discussion. Since a relatively long intervention period is foreseen, intermediate (weekly, monthly) measurements in an 'at-home setting' by using Do-It-Yourself tools (i.e. without visiting the intervention study facility) will be part of the study. Aspects of the study, such as target population, size, duration are subject to further discussion and agreement between project members.

INVITATION TO JOIN PHENFLEX

In phase 1, 75% of the budget (2 M€) was provided by Dutch government through TNO.

New industrial partners are invited and welcome to join and contribute to the PhenFlex project in phase 2. In phase 2, 40% of the budget will come through TNO.

Phase 2 is projected to start early 2015. If you are interested to join the PhenFlex core group or would like to receive more information, please contact us.

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TNO HEALTHY LIVING

TNO initiates technological and societal innovation for healthy living and a dynamic society.

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