



4D Biomedical Advisory Board
Annual Review of Biomedicine
25 September 2008

4D Biomedical Advisory Board – Annual Review of Biomedicine



Welcome!

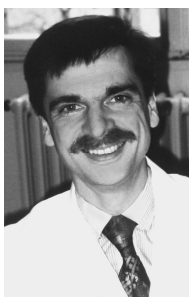
Agenda

- 15:00 Tea and coffee, arrival of Advisory Board
- 15:30 Advisory Board Meeting
- 4D Report on Workflow
 - General Review of Trends/Deals
- 17:50 Close of Advisory Board meeting
- 18:00 Drinks reception, arrival of guests, networking
- 18:30 Foresight Discussion with Guests round a topical theme
- 19:30 Buffet Supper on the Lawn
- 21:00 Close

4D Biomedical are delighted to announce the following new appointments to the 4D team:

ADVISORY BOARD

- Professor Martin Wehling MD



CONSULTANTS

- Andrew Williams
- Chris Rumball
- Hakim Yadi

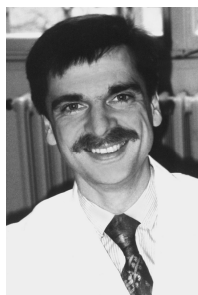


RESEARCH TEAM

- Rob Morgan
- Kumi Kumathasan



Professor Martin Wehling MD



Formerly Director of Discovery Medicine at Astra Zeneca's cardiovascular site in Mölndal, Professor Wehling is full Professor of clinical pharmacology at the University of Heidelberg. He has longstanding experiences in translating basic science into human studies. His specialist field is in bridging gaps between preclinical and clinical development, assembling, developing and profiling of biomarkers with particular assessment of their predictive value and translational medicine planning from early discovery/human stages to clinical trials, smart early human trial design and developmental decision trees (stop/go algorithms).

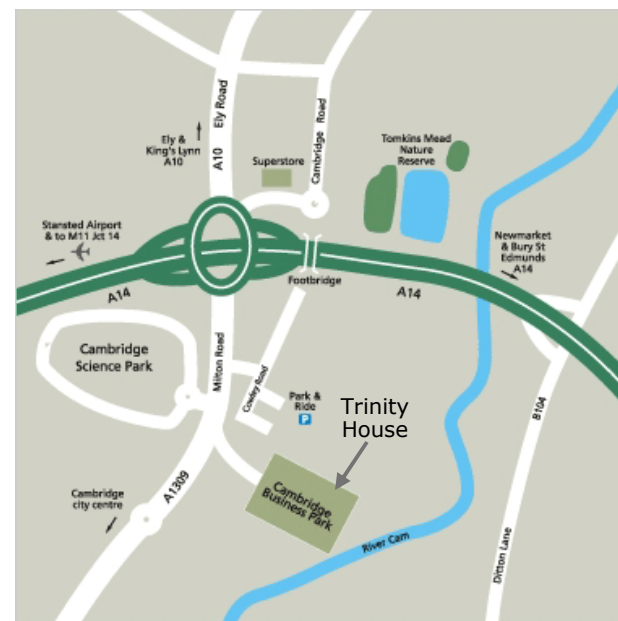
Professor Wehling has authored >200 scientific publications and several books, received prestigious awards (e.g. Heisenberg scholarship by Deutsche Forschungsgemeinschaft) and his scientific contributions to the identification and analysis of nongenomic steroid actions coined a novel science segment. He is also an experienced clinician with experiences in invasive cardiology (appr. 4000 cardiac catheters and interventions) and runs an outpatient clinic for geriatric pharmacotherapy. Martin joined the 4D Advisory Board in Q1 2008.

CHANGE OF ADDRESS

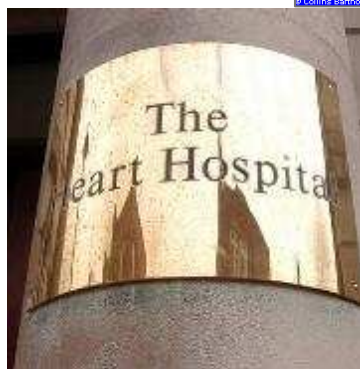
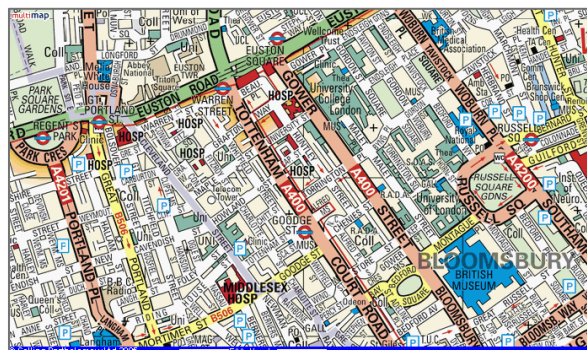
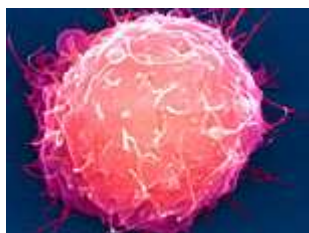
Please note that with effect from Monday 25th February 2008
4D Biomedical Ltd, 4D Cleantech Ltd and 4D LLP have moved to:

**Trinity House
Cambridge Business Park
Cowley Road
Cambridge
CB4 0WZ
01223 393 522**

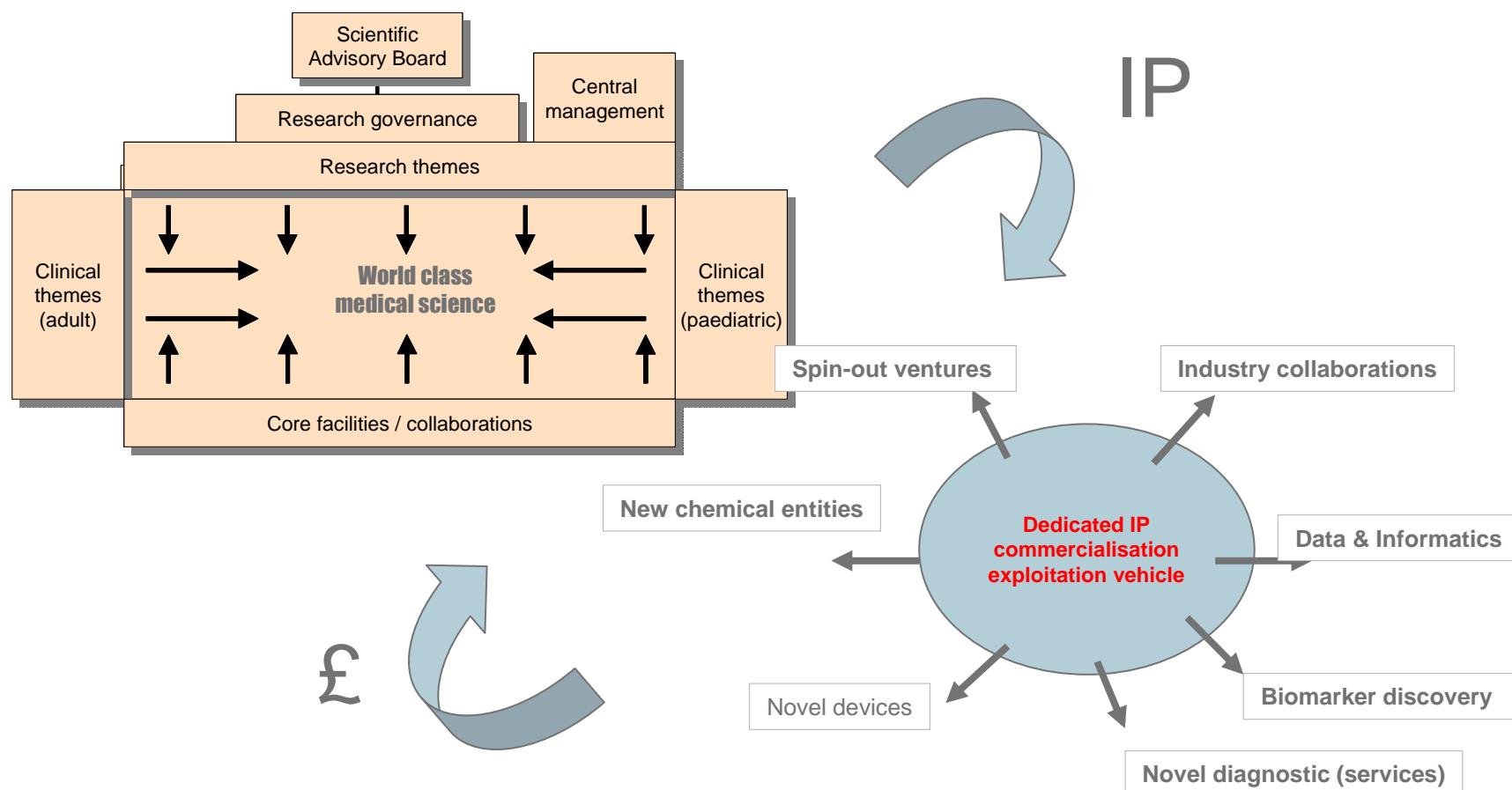
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The Cardiovascular Research Institute. A Partnership preventing heart disease for the next generation.



Phase 2: a specialist cardiovascular commercialisation vehicle



What do we mean by 'translational medicine'?

Fundamental integration of research and clinical practice

Cite this article as: BMJ, doi:10.1136/bmj.38693.435301.80 (published 20 January 2006)

Research

Chronic stress at work and the metabolic syndrome: prospective study

Tarati Chandola, Eric Brunner, Michael Marmot

Abstract

Objectives To investigate the association between stress at work and the metabolic syndrome.

Design Prospective cohort study investigating the association between work stress and the metabolic syndrome.

Participants 10 508 men and women, aged 35-55, employed in 20 London civil service departments at baseline (the Whitehall II study); follow-up was an average of 14 years.

Main outcome measures Work stress based on the iso-strain model, measured on four occasions (1985-99). Biological measures of the metabolic syndrome, based on the National Cholesterol Education Program definition, measured in 1997-9.

Results A dose-response relation was found between exposure to work stressors over 14 years and risk of the metabolic syndrome, independent of other relevant risk factors.

Employees with chronic work stress (three or more exposures) were more than twice as likely to have the syndrome than those without work stress (odds ratio adjusted for age and employment grade 2.25, 95% confidence interval 1.31 to 3.85).

Conclusions Stress at work is an important risk factor for the metabolic syndrome. The study provides evidence for the biological plausibility of the link between psychosocial stressors from everyday life and heart disease.

Introduction

Stress at work has been linked with coronary heart disease in retrospective and prospective studies.¹ The biological mechanisms remain unclear.² Plausible pathophysiological mechanisms involve direct neuroendocrine effects and indirect effects mediated by adverse health behaviours.³⁻⁵

The metabolic syndrome is a cluster of risk factors that increases the risk of heart disease and type 2 diabetes.⁶ Characteristics of the metabolic syndrome are abdominal obesity, atherogenic dyslipidaemia (raised triglycerides, small low density lipoprotein particles, and low concentrations of high density lipoprotein cholesterol), high blood pressure, insulin resistance (with or without glucose intolerance), and prothrombotic and proinflammatory states (table 1). Previous studies found a social gradient in work stress and the metabolic syndrome,⁷⁻⁹ suggesting that the social gradient in the metabolic syndrome and heart disease could in part be explained by greater exposure to work stress among less advantaged social groups. Cross sectional studies have linked work stress with components of the syndrome,¹⁰⁻¹² but this association is not consistent.¹³

A major limitation of previous studies is the lack of information on the duration of exposure to work stress. Repeated meas-

urements of work stress over a person's career provide a more accurate representation of exposure to psychosocial stress, and its cumulative effect on health.¹⁴ Here, we report the association between work stress (measured in four phases) and the metabolic syndrome over 14 years of follow-up, and we test the hypothesis of a dose-response association. If the prospective stress-metabolic syndrome relation is robust to adjustment for confounders (such as social position) and potential mediators (such as health behaviours) a stronger causal inference could be made.

Methods

The Whitehall II study recruited participants from 20 civil service departments in London from 1985 to 1988 (phase 1). Surveys consisted of postal questionnaires in 1989 (phase 2), 1991-3 (phase 3, which also included a clinical examination), 1995 (phase 4), and 1997-9 (phase 5, which also included a clinical examination). The phase 4 questionnaire collected no information on work stress or health behaviours. Full details of the screening examinations are reported elsewhere.¹⁵

Variables

Data on the components of the metabolic syndrome were collected at phase 5 (1997-9) during the clinical examination, using the definition of the National Cholesterol Education Program (adult treatment panel III) (table 1).⁶ The syndrome was defined by the presence of three or more risk factors. Components of the metabolic syndrome were not measured at baseline. We used obesity (defined as body mass index > 30) at baseline as an indicator of risk for the syndrome.

We measured self reported work stress using the job-strain questionnaire.¹⁶ Work stress was present when participants' responses to questions about the job demands were high and

Table 1 Definition of the metabolic syndrome.* These risk factors need to be present

Risk factor	Defining level
Abdominal obesity (waist circumference)	
Men	≥102 cm
Women	≥88 cm
Triglycerides	≥150 mmol/l
High density lipoprotein cholesterol	
Men	<1.03 mmol/l
Women	<0.85 mmol/l
Blood pressure	≥160/95 mm Hg
Fasting glucose	≥6.11 mmol/l

*From the National Cholesterol Education Program recent panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III).⁶



Discussion Theme: new business models for new medicines

1. Can the **NHS model** deliver modern healthcare?
2. Is **over regulation** driving medicines discovery out of the UK?
3. Will the rise of personalised medicine inevitably drive a shift in the balance of power **from Pharma to devices**?
4. Can the crisis facing Pharma R&D be solved through new **translational models**?
5. Is there a sustainable **financing model** in biomedical venturing?