A Streamlined Integrated Process to Predict Genetic Risk of Alzheimer's Disease

*Paula Daunt[1], Greg Davidson[2], **Alex Gibson[3]**, Anthony Hill[3], Olusegun Oshota[1], Eftychia Bellou[4], Valentina Escott-Price[4], Ganna Leonenko[4], Rebecca Sims[4], Julie Williams[5], John Hardy[6], Maryam Shoai[6], Zsuzsanna Nagy[7] and Richard Pither[3]*

(1)Cytox Ltd, Manchester, United Kingdom, (2)Ledcourt Associates Ltd, Cambridge, United Kingdom, (3)Cytox Ltd, Oxford, United Kingdom, (4)MRC Centre for Neuropsychiatric Genetics & Genomics, Cardiff University, Cardiff, United Kingdom, (5)UK Dementia Research Institute at Cardiff, Cardiff, United Kingdom, (6)UCL Institute of Neurology, London, United Kingdom, (7)University of Birmingham, Birmingham, United Kingdom

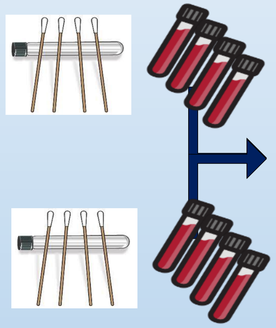
CYTOX
Defining Genetic Risk for Dementia

Funded by Innovate UK

Acknowledgements: We would like to thank all patients that have contributed samples used in this research, our colleagues at AKESOgen, Eurofins, Ramaciotti Centre and Thermo Fisher Scientific and Innovate UK, the UK's innovation agency who co-fund this research.

Background

The development of diagnostic tools to identify disease risk is critical to enable selection of suitable individuals for inclusion into clinical trials and cohort studies. The utility of Polygenic Risk Scores (PRS) is gaining increasing attention for generating an individual genetic risk profile and subsequent estimation of future disease risk in Alzheimer's Disease. Cytox continues to work on the implementation of its proprietary platform, SNPfitR™ as part of a streamlined integrated process, taking DNA from either a blood or saliva sample, through genotyping and PRS calculation to produce an estimation of risk of Alzheimer's Disease.



*varia*TECT ™

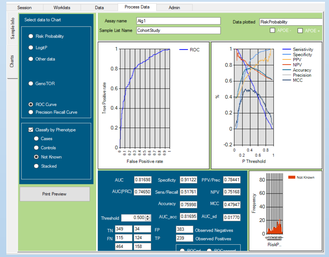
Matched blood and saliva samples generate near identical genotyping on the *varia*TECT ™ array and therefore near identical risk prediction in SNPfitR™

Use of non-invasive sampling procedures facilitates easier and larger sample set collection.

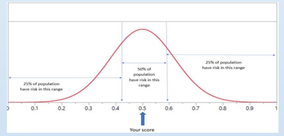
AKESOgen eurofins

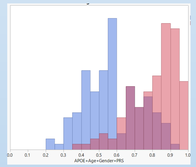
Ramaciotti Centre for Genomics

Genotyping data delivered globally through validated genomic service labs generates the data required to drive the algorithms within SNPfitR™



***geno*SCORE™**
PRS assessment of risk with respect to general population Validated in AD vs Cog Normal Cohorts





***geno*TOR™**
generates individual score profiles at a molecular pathway level with linkage to drug mechanism

IDENTIFY clinical trial participants more likely to decline cognitively to:
- Reduce clinical trial subject numbers
- Reduce clinical trial costs
- Increase chances of demonstrating a therapeutic effect

STRATIFY beyond APOE to:
- Select the highest risk APOE3/E4 subjects mostly likely to develop AD
- Identify highest/low risk APOE3/E3 subjects for inclusion/exclusion in clinical studies
- Benefit either preclinical or MCI trials

EXPLORE genomic study data to:
- Understand/identify study sub-groups who progress more rapidly, respond to treatment, or have common genetic profile associated with certain molecular pathways

CARDIFF UNIVERSITY | UNIVERSITY OF BIRMINGHAM
PRIFYSGOL CAERDYDD | UCL

Conclusions

The Cytox integrated process, combining the use of a proprietary array and the SNPfitR software package, offers a simple and high-quality route from sample collection to AD risk assessment. This could provide an efficient, cost-effective methodology for subject enrichment in clinical trials and reduce reliance upon expensive PET imaging or invasive CSF measurement procedures.

Visit us at Booth 202
in the Exhibit Hall
www.cytoxgroup.com