



PROPHSY: Proteome in Pulmonary Hypertension Assay Score

A model score calculated from levels of circulating plasma proteins for the diagnosis, prognosis, and treatment optimisation of Pulmonary Arterial Hypertension.

Proposed use

- Point of Care test: Pulmonary Arterial Hypertension diagnosis/prognosis – risk stratification
- Pulmonary Arterial Hypertension treatment response and optimisation monitoring/evaluation

Problem addressed

Pulmonary arterial hypertension (PAH) is a rare condition that continues to be associated with a high morbidity and mortality burden. Because patients with PAH have very variable responses to standard therapies which is difficult to predict, as well as monitoring the effectiveness of such therapies. The N-terminal pro-brain natriuretic peptide (NT-proBNP), is a biomarker of cardiac origin already used to risk stratify patients with pulmonary arterial hypertension (PAH) but has its limitations, including poor sensitivity to early vascular pathology. The plasma proteome can inform prognosis beyond established factors in PAH and may provide a more sensitive and quicker measure of therapeutic response.

Technology overview

An aptamer-based assay targeting over 4000 proteins was used to measure plasma proteins in two idiopathic/heritable/drug-induced-PAH patient cohorts.

Discovery-validation survival analyses permitted identification of approximately 30 proteins associated with PAH that could reproducibly inform prognosis independent of established prognostic factors NT-proBNP and 6-MWD.

From the 30 proteins a weighted combination score of 6 biomarker proteins (selected by LASSO) was developed and validated at baseline and follow-up study.

The value of this score permits, independently of established clinical targets, discrimination between:

- Low/intermediate/high risk of PAH progression/death
- Response to therapy
- Development of PAH in at-risk individuals

Benefits

- Accessible point-of-care test for earlier diagnosis of PAH.
- Non-invasive test
- Easy to interpret single measurement
- More sensitive measure of risk / therapeutic response / disease progression
- Complements established clinical measures / risk algorithms
- Reflects underlying pathobiology rather than late-stage heart failure

Development Stage

- TRL 2/3
- Model developed using SomaLogic SomaScan v4 data in UK PAH Cohort
- Model validated in external cohort from Paris, France
- 4/6 proteins validated by commercial ELISA measurements

Contact

Imperial College London
Industry Partnerships and
Commercialisation

Imperial College London

South Kensington campus

London, SW7 2AZ

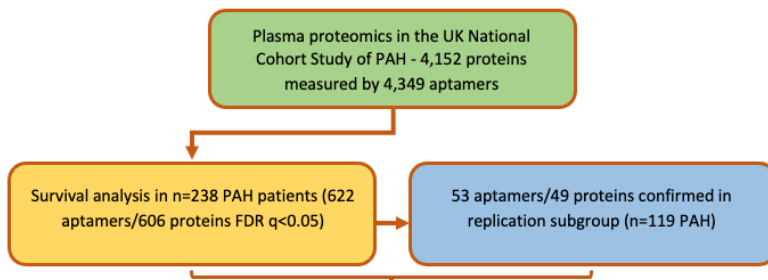
Amritha Nair

e: a.nair@imperial.ac.uk

t: +44 07543305229

Technology reference: 10746

Stage 1: Identification of prognostic proteins



Stage 2: Selection of independent prognostic proteins and model development

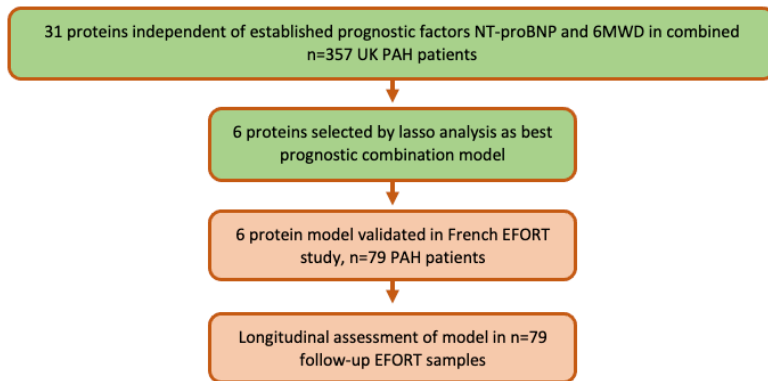


Fig 1: Study Flow Chart

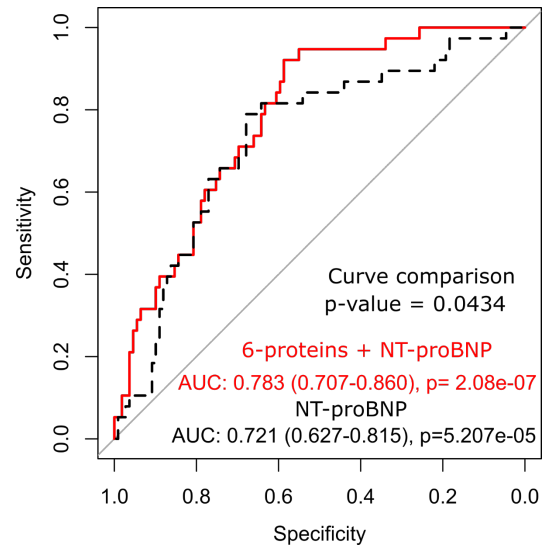


Fig 2 : ROC analysis of NT-proBNP individually and combined with 6 protein model score in data from the replication group of the UK PAH Cohort study and the French EFORT study. A composite endpoint of death or lung transplantation at 5-years follow-up was tested.

Intellectual property information

A PCT Patent application has been published (WO2022/079448), covering the PROPHSY score and associated biomarkers. A national patent application has also been filed at the EPO.

Link to published paper

Rhodes, C.J., Wharton, J., Swietlik, E.M., Harbaum, L., Girerd, B., Coghlan, J.G., Lordan, J., Church, C., Pepke-Zaba, J., Toshner, M., Wort, S.J., Kiely, D.G., Condliffe, R., Lawrie, A., Gräf, S., Montani, D., Boucly, A., Sitbon, O., Humbert, M. and Howard, L.S. (2022). *Using the Plasma Proteome for Risk Stratifying Patients with Pulmonary Arterial Hypertension*. American Journal of Respiratory and Critical Care Medicine. [online] Available at: <https://www.atsjournals.org/doi/pdf/10.1164/rccm.202105-1118OC>.

Inventors

Professor Martin Wilkins: Martin R. Wilkins is Professor of Clinical Pharmacology at Imperial College London. He is Vice Dean (Research) for the Faculty of Medicine, a role he combines with Director of the British Heart Foundation Imperial College Centre of Research Excellence and Director of the National Institute of Health Research Imperial College Clinical Research Facility at Hammersmith Hospital.

Dr Christopher Rhodes: Dr Rhodes is British Heart Foundation Intermediate Basic Science Fellow and Senior Lecturer in Pulmonary Vascular Diseases in the Centre for Pharmacology and Therapeutics. His research focus involves integrated studies of -omics profiles in patients with pulmonary hypertension (PH). This includes working on whole genome sequencing data as part of the NIHR BioResource project, with pulmonary arterial hypertension (PAH) being one of the key rare diseases studied.

Dr John Wharton: Dr Wharton is an Honorary Senior Lecturer for the National Heart and Lung institute Imperial College Faculty of Medicine. His research within the Cardiovascular Group has been focusing on adopting an integrated approach to study the mechanisms of pulmonary vascular disease and identify therapeutic targets, taking studies with human vascular cell cultures through to whole animal models and proof-of-concept studies in patients.