Research breakthroughs advance understanding of genetic causes of vascular disease

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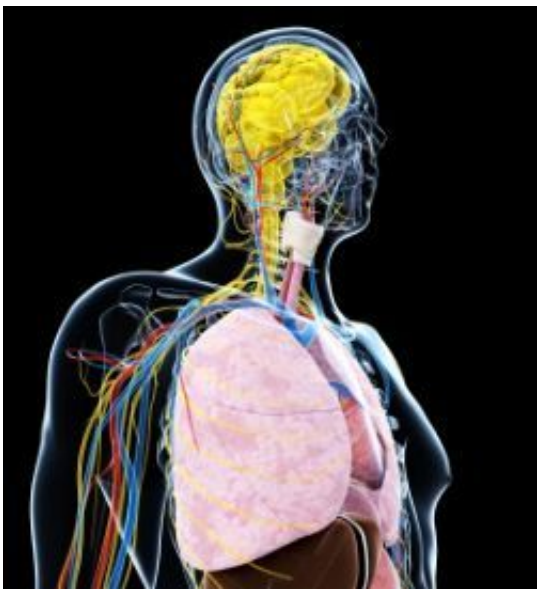

(Medical Xpress)—The world's leading voices in the fight against pulmonary hypertension have compiled a special publication detailing the breakthrough research into the causes of this debilitating vascular disease.

Co-author Dr Rajiv Machado, from the School of Life Sciences, University of Lincoln, UK, attended the World Symposium on

Pulmonary Hypertension in 2013 as an invited member of the symposium's genetics and genomics task-force.

Papers arising from this conference, which brought together the most respected clinicians and scientists in the field, have now been compiled in a special edition of *Journal of the American College of Cardiology*.

The symposium, which discussed several forms of resistance in lung vessels including those associated with common disorders such as congenital heart disease and HIV, resulted in a powerful consensus around key issues and recommendations.

The replication and extension of these studies should serve to further define the genetic landscape surrounding vascular disease.

Dr Machado said: "The aim of the symposium was to report new information and how this could then be translated into clinical medicine by providing novel targets for therapy. The results have now been published as the definitive scientific consensus on this area of disease."

Dr Machado's main research focuses on pulmonary arterial hypertension (PAH), a progressive disorder characterised by abnormally high blood pressure (hypertension) in the pulmonary artery, the blood vessel that carries blood from the heart to the lungs. Symptoms include shortness of breath, dizziness, swelling (oedema) of the ankles or legs, chest pain and a racing pulse.

Dr Machado was part of a team that discovered the primary gene that causes PAH and has since gone on to investigate the disease pathway, isolating more contributory genetic mutations.

As reported at the symposium, Dr Machado's investigation of 300 patients with disparate forms of PAH - the largest study of its kind -

resulted in the identification of three novel genes which appear to cause pulmonary dysfunction.

A process called next generation sequencing (NGS) was used to exclude the likelihood of the observed genetic variation being present in the general population.

In a separate study, colleagues reported two additional genetic causes of disease present only in PAH patients and, intriguingly, a genetic variant enriched among patients but present in all of us.

Dr Machado said taken together the findings presented promising new avenues for research.

"It is extremely rare to find this form of variation in a disease like this," he said.

"Identification of this alteration may provide a new target for PAH treatment. It has wide ranging significance to our understanding of lung disease. It all contributes to the genetic architecture of the disease and our understanding of what causes it."

Dr Machado is now working on population-specific genetic patterns, looking at two subsets of PAH, including an Indian group which has no family history of the disease. He will use next generation sequencing to drive a baseline genetic profile of this previously unstudied population.

Dr Machado will also carry out full DNA sequencing to interrogate the causes of childhood PAH, a particularly severe form of disease which is currently not well understood.

More information: The full paper, "Genetics and genomics of pulmonary hypertension," can be viewed at content.onlinejacc.org/article

Provided by University of Lincoln