Discovery of novel gene solves mystery of scar formation

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(Medical Xpress)—The study, in a South African-British-French collaboration which led to the discovery of the little-known novel gene called FAM111B, brings hope to millions of families across the world who pass on this debilitating gene to one another. It saw researchers team up from The University of Manchester, UK, the University of Cape Town, South Africa and University of Nantes in France.

Professor Nonhlanhla Khumalo, one of the lead investigators from the University of Cape Town and Groote Schuur Hospital, said that the study represents a breakthrough in the fight against fibrosis and scar formation.

"The elucidation of the mechanisms by which FAM111B gene mutations cause fibrosis is likely to lead to the development of new drugs to treat fibrosis in the affected families and possibly prevent fibrosis in other diseases such as scleroderma,' she says. Scars are areas of fibrous tissue (fibrosis) that replace normal tissue after injury. A scar results from the biological process of wound repair in the skin and other tissues of the body. Thus, scarring is a natural part of the healing process. With the exception of very minor lesions, every wound (e.g. after accident, disease, or surgery) results in some degree of scarring.

Unfortunately, scarring is a major cause of disease and death following infections such as tuberculosis. In some people, scarring of several organs of the body occurs for no obvious reason. For example, in a disease called scleroderma, there is spontaneous scarring of the skin, the

lungs, the gut, and blood vessels, leading to shortness of breath, difficulty with swallowing, pain and hypertension. Until now, the cause of this condition has been a mystery. There is no treatment for these severe forms of scarring, and they lead to death and disability for millions of people in the world.

In 2006, Professor Nonhlanhla Khumalo and her colleagues from the University of Cape Town (UCT) discovered a family with inherited fibrosis involving the skin, tendons, and the lungs. This disease had already claimed two members of this family through death from lung fibrosis. The Cape Town group worked with Professor Bernard Keavney from The University of Manchester in the United Kingdom to identify the genetic cause of this condition. In 2012, Dr Sandra Mercier of the University of Nantes in France contacted Professor Khumalo about a series of patients from France who had the same clinical condition of inherited skin and organ fibrosis. The groups from the three universities teamed up to solve the mystery of this condition, with UCT colleague Dr Gasnat Shaboodien conducting all the South African genetic tests.

This South African-British-French collaboration has led to the discovery of a novel genetic cause of fibrosis due to a hitherto little known gene called FAM111B. The findings of this study will be published in the *American Journal of Human Genetics* on 21 November 2013.

Professor Bongani Mayosi, the Head of the Department of Medicine at UCT and Groote Schuur Hospital, where the discovery was made, said that this discovery illustrates the power of collaboration between clinicians and affected families on whose generosity this type of scientific endeavour depends. He also emphasised the value of collaboration among clinicians and scientists across different countries and disciplines with varying resources and expertise in achieving major advances in science.

Professor Bernard Keavney, Director, Institute of Cardiovascular Sciences at The University of Manchester, said: "Families with this particular condition are very rare, but it is possible that by identifying this new gene of essentially unknown function our team has discovered a new pathway involved in the formation of abnormal scar tissue in other more common conditions."

The researchers plan to build on their South African-British-French collaboration with a view to the development of a cure for scar-formation in the future.

More information: "Mutations in FAM111B Cause Hereditary Fibrosing Poikiloderma with Tendon Contracture, Myopathy, and Pulmonary Fibrosis." Sandra Mercier, Sébastien Küry, Gasnat Shaboodien, Darren T. Houniet, Nonhlanhla P. Khumalo, Chantal Bou-Hanna, Nathalie Bodak, Valérie Cormier-Daire, Albert David, Laurence Faivre, Dominique Figarella-Branger, Romain K. Gherardi, Elise Glen, Antoine Hamel, Christian Laboisse, Cédric Le Caignec, Pierre Lindenbaum, Armelle Magot, Arnold Munnich, Jean-Marie Mussini, Komala Pillay, Thahira Rahman, Richard Redon, Emmanuelle Salort-Campana, Mauro Santibanez-Koref, Christel Thauvin, Sébastien Barbarot, Bernard Keavney, Stéphane Bézieau, Bongani M. Mayosi. *American Journal of Human Genetics* - 21 November 2013. DOI: 10.1016/j.ajhg.2013.10.013

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