PRESS RELEASE

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Scientists identify novel genes linked to motor neuron disease

An international consortium of scientists, led by King’s College London and the University Medical Center Utrecht in the Netherlands, has identified novel genes which increase the risk of developing amyotrophic lateral sclerosis (ALS), the most common form of motor neuron disease.

Published today in *Nature Genetics*, the study reveals three new risk genes for ALS and one of these - *C21orf2* - increases an individual’s risk of developing the disease by 65 per cent. These results could aid the development of personalised treatments for people with ALS by using gene therapy - an approach which involves replacing faulty genes or adding new ones.

One in every 400 people will be diagnosed with amyotrophic lateral sclerosis (ALS) at some point in their lives, yet its causes are largely unknown and effective treatments are therefore lacking.

In ALS, motor neurons in the brain and spinal cord degenerate causing the muscles they control to weaken and waste away. Symptoms normally start in mid-life and eventually affect all movement including swallowing and breathing. Average life expectancy from symptom onset is two to five years.

Variations of the genes we all carry are an important cause of ALS, even though most people do not have an inherited form of the condition. The researchers set out to discover new genes for ALS to find out why the disease develops and how to design new treatments.

Using genetic data from *Project MinE*, comprising 15,156 ALS patients and 26,224 healthy controls from 15 countries, the researchers combined ‘snapshot’ genetic information with whole genome sequencing of 1,861 individuals. Whole genome sequencing involves reading every single one of the six billion letters in the human genome. In total 8,697,640 variants across the genome were tested for the risk of developing ALS.

The researchers identified three new risk genes for ALS. One of these, called *C21orf2*, appeared to be particularly important as a risk factor for ALS. The exact function of *C21orf2* is still unknown, but it appears to be part of a system in cells related to their own movement and their internal skeleton. They also found that for any one person, just one or two genes had a substantial effect on whether they developed ALS, which is different from most other conditions in which lots of genes each have a small effect.

Professor Ammar Al-Chalabi from the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) at King’s College London, said: ‘This tells us that ALS is not the result of a few common gene variations that each contribute a little to the risk. Rather, any
one of many rare gene variations contributes a large risk for ALS development. This insight is crucial as it affects the types of treatment strategies that might be effective.’

Professor Jan Veldink from the University Medical Center Utrecht said: ‘Most genetics studies in ALS focus on the familial form of the disease. Project MinE is an innovative approach to find genetic causes of all ALS cases. In this study we have found a total of three genomic regions where genetic variation in these regions increases the risk of ALS. One of these regions included a gene named C21orf2. This gene was subsequently shown to harbour rare mutations that directly increase ALS risk. This makes the C21orf2 gene extremely interesting for future studies to shed light on the mechanisms that lead to ALS and possibly future therapeutic strategies.’

Professor Ammar Al-Chalabi added: ‘Pinpointing genes which increase the risk of ALS will help us develop new treatments that can stop or improve symptoms of ALS in the future. The more we understand about the genetic basis of ALS, the closer we are to revealing new treatment targets and effective therapies.’

Brian Dickie, Director of Research Development at the Motor Neurone Disease (MND) Association said: ‘We are pleased to have been involved since this approach to gene hunting was in its infancy a decade ago. It’s so encouraging to see how the collaboration, catalysed by Project MinE, has grown and is now delivering results that will open up new avenues of research across the world.’

The study was funded by the Motor Neurone Disease (MND) Association, Project MinE, the ALS Association and the EU Joint Programme on Neurodegeneration Research through the Medical Research Council (funding of the STRENGTH European consortium).

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Notes to editors

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About King’s College London - www.kcl.ac.uk

King’s College London is one of the top 20 universities in the world (2015/16 QS World University Rankings) and among the oldest in England. King’s has more than 26,500 students (of whom nearly 10,400 are graduate students) from some 150 countries worldwide, and nearly 6,900 staff. The university is in the second phase of a £1 billion redevelopment programme which is transforming its estate.

King’s has an outstanding reputation for world-class teaching and cutting-edge research. In the 2014 Research Excellence Framework (REF) King’s was ranked 6th nationally in the ‘power’ ranking, which takes into account both the quality and quantity of research activity, and 7th for quality according to Times Higher Education rankings. Eighty-four per cent of research at King’s was deemed ‘world-leading’ or
'internationally excellent’ (3* and 4*). The university is in the top seven UK universities for research earnings and has an overall annual income of more than £600 million.

King's has a particularly distinguished reputation in the humanities, law, the sciences (including a wide range of health areas such as psychiatry, medicine, nursing and dentistry) and social sciences including international affairs. It has played a major role in many of the advances that have shaped modern life, such as the discovery of the structure of DNA and research that led to the development of radio, television, mobile phones and radar.

King’s College London and Guy's and St Thomas’, King's College Hospital and South London and Maudsley NHS Foundation Trusts are part of King’s Health Partners. King's Health Partners Academic Health Sciences Centre (AHSC) is a pioneering global collaboration between one of the world's leading research-led universities and three of London’s most successful NHS Foundation Trusts, including leading teaching hospitals and comprehensive mental health services. For more information, visit: www.kingshealthpartners.org.

King’s fundraising campaign – World questions | King’s answers – created to address some of the most pressing challenges facing humanity has reached its £500 million target 18 months ahead of schedule. The university is now aiming to build on this success and raise a further £100 million by the end of 2015, to fund vital research, deliver innovative new treatments and to support scholarships. The campaign’s five priority areas are neuroscience and mental health, leadership and society, cancer, global power and children's health. More information about the campaign is available at www.kcl.ac.uk/kingsanswers.