Dr. Niccolò Mencacci
Department of Neurology
Feinberg School of Medicine
Northwestern University
Chicago, USA

DAVID MARSDEN AWARD WINNER PRESENTATION:

"A Missense Mutation in KCTD17 Causes Autosomal Dominant Myoclonus-Dystonia".

Studying genes causing inherited dystonia has yielded important clues about why the neurons do not function properly in dystonia.
Myoclonus-dystonia (M-D) is a rare familial movement disorder characterized by a combination of myoclonus (jerky contraction of groups of muscles) and dystonia. Mutations in a gene called epsilon-sarcoglycan are found in about 30-50% of familial M-D cases, suggesting that mutations in other genes responsible for this condition are yet to be discovered.
To identify a novel genetic cause of M-D, I studied a large British family with many individuals affected with M-D, but without mutations in epsilon-sarcoglycan. Through the combination of different genetic techniques, I identified a mutation in a gene called *KCTD17* as the only possibly disease-causing mutation.
A subsequent analysis of other familial M-D cases without a genetic diagnosis revealed the same mutation in a different family of German origin, confirming KCTD17 as a novel dystonia gene.
The precise function of KCTD17 is unknown, as is how the mutations actually cause dystonia.
KCTD17 is very abundant in the brain and in particular in the putamen, a brain region which is known to be critical in the neuronal circuits that are dysfunctional in dystonia patients.
Preliminary work to understand the function of KCTD17 showed that KCTD17 contributes to regulate (1) the effect of dopamine (one of the neurotransmitters critical in the development of dystonia) and (2) intracellular turnover of calcium (one of the most important signaling molecule in neurons).
Future studies are warranted to further characterize the molecular function and the interactors of KCTD17 as a step towards identifying new pharmacological targets to effectively treat dystonia.