Evolving genes lead to evolving genes

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Researchers have designed a method that can universally test for evolutionary adaption, or positive (Darwinian) selection, in any chosen set of genes, using re-sequencing data such as that generated by the 1000 Genomes Project. The method identifies gene sets that show evidence for positive selection in comparison with matched controls, and thus highlights genes for further functional studies.

The method was employed to test whether any of the genes directly regulated by FOXP2 may themselves have undergone positive selection following the known selection at the FOXP2 genetic region. Human FOXP2 defects have been implicated in speech and language disorders, and altered versions of the gene have been selected several times during human evolution. Have these evolutionary changes in FOXP2 function or expression exposed its target genes to novel selective pressures?

The study used three gene sets regulated by FOXP2 that had been identified by previous genomic screens in mice and humans. These sets were compared with matched controls using this method.

"Our method worked well and overall, there was strong evidence for selection of FOXP2-regulated genes in the Europeans, but not in the Asian, or African populations," says Dr Qasim Ayub, first author from the Wellcome Trust Sanger Institute. The subset of FOXP2-regulated genes that were selected in Europeans play roles in neural cell development, cellular signalling, reproduction and immunity."

The selection in the Europeans might be due to local adaptations to

environment or pathogens. Some of the genes, such as CNTNAP2 and RBFOX1, showed strong signals of selection in all populations examined. Intriguingly, both these genes are highly expressed in the brain and have been implicated in neurodevelopmental disorders, including autism.

"Our study highlights how genes can acquire and adapt to different roles in human evolution. We should never underestimate how complex human biology can be." says Professor Simon Fisher, a co-author from the Max Planck Institute for Psycholinguistics. "A next step could be to test whether variants in the selected genes are associated with risk of human neurodevelopmental problems, like language impairments and autism spectrum disorders. Genetic networks can give us powerful insights into the biology underlying these important disorders, which make a major impact on modern human society."

"We have already started using this method to look for selection in various other gene sets such as those associated with diabetes and viral infections", says Dr Chris Tyler-Smith, lead author from the Wellcome Trust Sanger Institute. "Our method is opening new doors to understanding how modern humans have genetically adapted to their local environments and finding candidate genes to study biological function. This approach is a practical and successful way to screen for positive selection and adaptation signals in different gene sets and populations using whole-genome sequencing data."

More information: Qasim Ayub, Bryndis Yngvadottir, Yuan Chen, Yali Xue, Min Hu,1 Sonja C. Vernes, Simon E. Fisher, Chris Tyler-Smith (2013). 'FOXP2 targets show evidence of positive selection in European populations' Advanced online publication in *American Journal of Human Genetics* 18 April, 2013.