IBD genetically similar in Europeans and non-Europeans

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The first genetic study of inflammatory bowel disease (IBD) to include individuals from diverse populations has shown that the regions of the genome underlying the disease are consistent around the world. This study, conducted under the auspices of the International IBD Genetics Consortium, included nearly 10,000 DNA samples from people of East Asian, Indian or Iranian descent and an existing set of 86,640 samples drawn from across Europe, North America and Oceania.

The observation that genetic effects on disease risk are consistent across diverse populations is an important one because it suggests that the biology underlying disease is also consistent. This could have profound consequences for the treatment of IBD because drugs developed based on insights from genetic studies in one population could be used worldwide.

"The prevalence of IBD has increased dramatically in Asia over the last 50 years, probably due to lifestyle changes brought about by economic growth" says Dr Carl Anderson, a corresponding author from the Wellcome Trust Sanger Institute. "We are now able to compare genetic risk profiles of IBD across diverse populations to find out how similar they are. Discovering differences can provide us with biological insights that would be missed if we were to focus our efforts on just a single population. In turn, this can lead to the identification of new drug targets."

"In our study we found little difference in the genetic risk of IBD across

the populations we studied. This is a very important finding because it suggests that biological lessons learned by studying the genetics of IBD will be relevant globally."

More than 163 variants in the human genome have already been associated with increased risk of IBD, the most common forms of which are Crohn's disease and ulcerative colitis, but this research has only been conducted at a large scale in Europeans.

By including 10,000 non-European samples alongside the existing European samples, the team were able to detect 38 additional regions of the genome that influence susceptibility to IBD. Because the genetic effects were largely consistent across populations, the researchers hypothesized that the reason they were able to discover these new regions was the big increase in sample size, rather than because the additional samples were drawn from non-European individuals.

"We've already seen the benefit of using trans-ethnic approaches to understand complex diseases such as type-2 diabetes and rheumatoid arthritis," says Dr Jimmy Liu, a first author from the Sanger Institute. "This study demonstrates the importance of collecting trans-ethnic data on IBD, firstly because any increase in the number of samples improves our ability identify regions of the genome influencing disease risk, and secondly because we can gain new insights into the biology underlying IBD by comparing results across the diverse populations."

Despite the wide-spread similarities, the study did confirm previously identified differences between IBD risk in European and non-Europeans. There are genetic variants in a gene called NOD2 which increase risk of IBD in Europeans that are simply not present in Asian populations. It remains to be seen if there are IBD risk-increasing variants in NOD2 that are only present in Asia. At another gene, called TNFSF15, the IBD risk increasing variants are at a similar frequency in

both Europeans and East Asians, but the variants seem to have a much stronger effect on disease risk in East Asia. The team have suggested this finding could be due to subtle differences in the environment or genome structure.

"This study is testimony to the need for large-scale international collaborations that enable us to answer questions that would not be possible using samples drawn from a single population," says Dr Rinse K Weersma, a corresponding author from University Medical Center Groningen. "We thank every individual who donated a DNA sample to the study and the clinicians within the International IBD Genetics Consortium who collected these, particularly those outside of the US and Europe.

"The finding that the biology underlying IBD is consistent across populations is hugely important, it tells us that we can use insights from genetic studies of IBD to develop globally relevant drugs with the potential to improve disease management around the world."

More information: Liu JZ, van Sommeren S, et al. (2015). Association analyses identify 38 susceptibility loci for inflammatory bowel disease and highlight shared genetic risk across populations. *Nature Genetics*. DOI: 10.1038/ng.3359

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