People of the British Isles Project

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Dr Ron Dixon is involved in a national project to build a genetic map of the British Isles to better understand the causes of hereditary diseases. A team from the University of Oxford's 'People of the British Isles' project have come to the University of Lincoln as they embark on the second stage of their study to work with volunteers who are providing genetic information which could prove vital in future medical research.

The project, launched 7 years ago with funding from the Wellcome Trust, has already seen more than 4,000 blood samples taken from volunteers in rural locations across the UK, including almost 300 from Lincolnshire. The samples, which are anonymised so cannot be traced back to individuals, provide a 'control group' for medical researchers looking to identify genes responsible for certain diseases.

The Oxford team won further funding from the Wellcome Trust to extend their original project by re-visiting volunteers in Boston, Grimsby, Sleaford and Lincoln posing further questions which will shed more light on the British people's genetic characteristics. Dr Bruce Winney, from the University of Oxford, said:

> *"We have gone back to our original volunteers who have already given blood samples and asked them a series of questions, such as whether they are left or right handed, whether they can roll their tongue – even whether they like the taste of Marmite! We are also taking 3D photos of their faces. By doing this, we are hoping to find the genes involved in normal variation, such as facial features like the shape of the nose or the size of the forehead."*

Understanding the genetic make-up of Britain's rural populations is central to the success of the People of the British Isles project. This is because the task of identifying the genes responsible for diseases is complicated by the influence of invasions and migrations on people's DNA (Figure 1). By mapping out the genetic traits seen in rural locations like Lincolnshire, where families can often trace their roots back for generations, the team hope to untangle the effects of history and geography from their studies of disease.

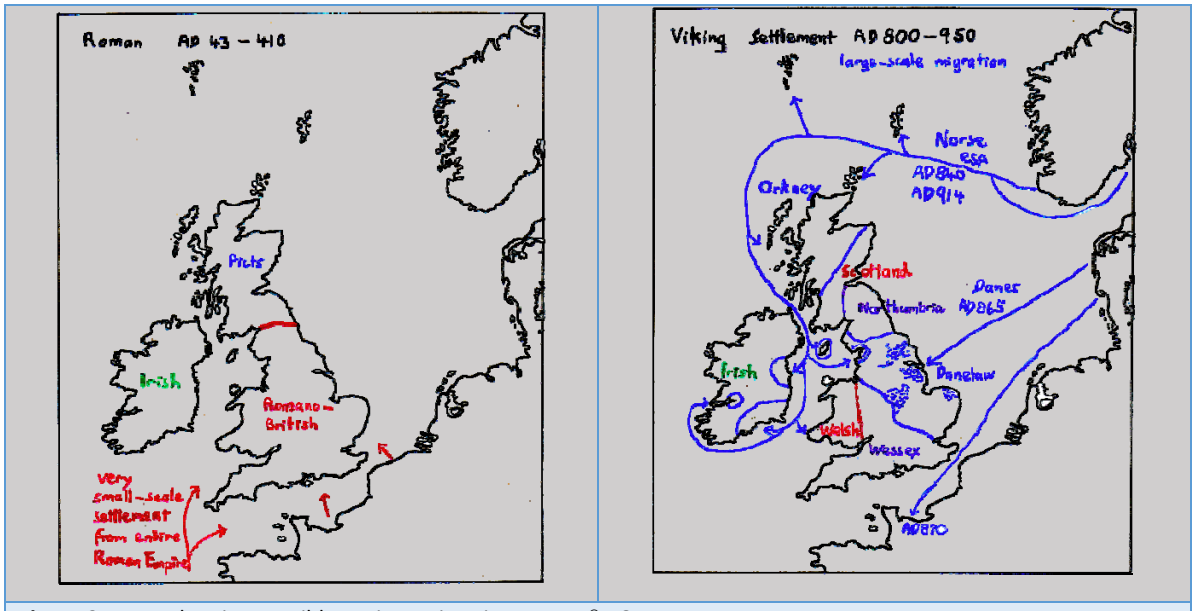


Figure 3: Maps showing possible ancient migration routes ® POBI

The University of Lincoln has been collaborating with the Oxford team for several years by collecting blood samples from Lincolnshire people. To be eligible for the study, volunteers had to show they, their parents and their four grandparents were born in the area (Figure 2).

Dr Ron Dixon, Reader in Biomedical Sciences, said:

> "We thought Lincolnshire would be important to this study because historically it is an agricultural area and people stay with the land. It was not too difficult to find volunteers who had four grandparents born in the area. In fact, we found people whose families had farmed the same land since the 17th Century."

Principal investigator on the People of the British Isles project, Prof Sir Walter Bodmer of the University of Oxford (Figure 3), said:

> *"All the genetic data that we have collected is being maintained as a resource for future medical research. It's a sort of genetic map of the British Isles. At the moment our interest is in the basic science, but in the future, who knows? We may be able to use a person's DNA to reconstruct their face, or identify genes that when seriously disrupted cause severe abnormalities."*

Figure 2: Volunteer session, University of Lincoln

Figure 3: Professor Sir Walter Bodmer (right) at Lincoln

For more information on the project, visit: www.peopleofthebritishisles.org

People of the *British Isles*

Newsletter Issue 5 - June 2012

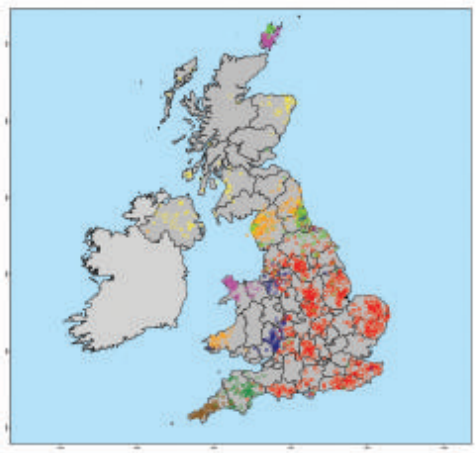
Welcome

Well it is time for the annual newsletter of "The People of the British Isles". We would like to update you on our progress over the last year and tell you about an exciting event we are taking part in. We have spent a fruitful year returning to our volunteers and collecting 3D face photographs and our first paper (People of the British Isles: preliminary analysis of genotypes and surnames in a UK-control population) was published in the European Journal of Human Genetics earlier this year. It is available for download from our website. This effectively announces PoBI to the scientific world and attracted a favourable commentary from Chris Tyler-Smith and Yali Xue. The link to that paper is also on our website. This is a good start and we are now currently preparing a major paper based on analysis of about 2,000 samples. More about that later.

The Royal Society Summer Science Exhibition 2012

The project has been invited to be one of 21 that will be exhibiting their work at the Royal Society Summer Science Exhibition in July. This is a week-long event at the Royal Society open to the public and includes two evening soirees, which are open only to Royal Society fellows and invited VIP guests. This is an annual event that has been running in one form or another since about 1778 with the aim of showing off cutting edge science to the public. We will be displaying some of our genetic maps from our latest analyses and will also have the 3D camera there. The Exhibition will be open to the public from Tuesday 3rd July until Sunday 8th from 10am to 9pm (apart from Wednesday, Thursday and Sunday when it closes at 5pm or 6pm). If any of you are around in London during that period and want to pop in, we would love to see you again! You can get further details from **http//sse.royalsociety.org/2012/exhibits.** We are the "Genetic Maps" exhibit and will be in the main hall.

Prof. Peter Donnelly, Director of the Wellcome Trust Centre for Human Genetics, and Professor of Statistical Science, University of Oxford, has been a co-applicant on the grants funding both phases of the project. Peter organised the genotyping of the samples and has led the statistical analysis of geographical structure from genetic data, for the forthcoming paper



A genetic map of the UK. Each symbol is the place where a sample comes from. Individuals who belong to a genetically similar group are distinguished by colour

Our forthcoming paper

We are working on final analyses and writing up of a really exciting paper. It is based on 2,031 of our samples on which we have examined about 500,000 genetic markers across the genome. We have used a new approach to group individual samples together by genetic similarity into a number of clusters. These are then colour coded and placed on a map of the UK at the average position of where the grandparents were born. This new method of analysis, combined with our careful collection strategy, means that we can detect amazing fine scale population structure within the UK (see map). Indeed the detail of the geographic differences astonished us. For example, the genetic boundaries between Cornwall, Devon and the rest of England remarkably fall on the County boundaries, whilst in Orkney there are obvious differences between Westray and Mainland. This level of detail is unprecedented in human population genetics - until now it has been difficult to even differentiate reliably between North and South Europe.

Furthermore, by collaborating with a couple of other large projects (within the Wellcome Trust Case Control Consortium 2), we have access to genetic data from about 6,300 more samples from throughout Europe. With these, we are currently looking to see if we can detect those European regions that contributed to the clusters that we observe in the UK. The results are looking promising and will be an important part of our paper.

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ARTICLE

People of the British Isles: preliminary analysis of genotypes and surnames in a UK-control population

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There is a great deal of interest in a fine-scale population structure in the UK, both as a signature of historical immigration events and because of the effect population structure may have on disease association studies. Although population structure appears to have a minor impact on the current generation of genome-wide association studies, it is likely to have a significant part in the next generation of studies designed to search for rare variants. A powerful way of detecting such structure is to control and document carefully the provenance of the samples involved. In this study, we describe the collection of a cohort of rural UK samples (The People of the British Isles), aimed at providing a well-characterised UK-control population that can be used as a resource by the research community, as well as providing a fine-scale genetic information on the British population. So far, some 4000 samples have been collected, the majority of which fit the criteria of coming from a rural area and having all four grandparents from approximately the same area. Analysis of the first 3865 samples that have been geocoded indicates that 75% have a mean distance between grandparental places of birth of 37.3 km, and that about 70% of grandparental places of birth can be classed as rural. Preliminary genotyping of 1057 samples demonstrates the value of these samples for investigating a fine-scale population structure within the UK, and shows how this can be enhanced by the use of surnames.
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INTRODUCTION

During the last 10 years there has been much interest in a fine-scale population structure, particularly in the UK, both as a signature of historical immigration events[1–6] and because of the effect population structure may have on disease association studies,[7,8] although this depends on the magnitude of the associations.[9] Fine-scale population structure is principally the outcome of historical movements of people into Britain following the last ice age about 10 000 years ago, with the major subsequent detectable influences likely to be from Anglo-Saxon, Norse and Norman admixture.[10] Although population structure appears to have a minor impact on the current generation of genome-wide association studies,[9] it is likely to have a significant part in the next generation of studies designed to search for rare variants.[11,12] It is, therefore, important that suitable control population cohorts are available for such studies. In this study we describe the collection and preliminary analysis of a set of carefully chosen samples, to represent the areas of the UK from where they have come.

A powerful way of detecting a fine-scale population structure is to control and document carefully the provenance of the samples involved. This can be carried out by, for example, ensuring that volunteers are chosen for whom all four grandparents were born in the same rural area. This approach should maximise the probability of recruiting individuals whose families have been stable inhabitants of the area for many generations, as most recent migration has been into larger towns and cities. Genotyping a collection of such samples from throughout the UK should then allow identification of high-quality ancestrally informative markers and enable a detailed analysis of population structure. These samples can then be used to assess the impact of population structure on disease and other phenotype association studies, particularly when searching for rare variants. The resulting body of data will also provide an excellent basis for

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