Studies in Arts and Humanities **VOL**03/**ISSUE**02/2017
IN FOCUS (INTERVIEW) | sahjournal.com

Genomic Insights and the Irish Travellers: An Interview with Professor Gianpiero Cavalleri

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Abstract

Professor Gianpiero Cavalleri is Associate Professor of Human Genetics at Department of Molecular and Cellular Therapeutics at the Royal College of Surgeons in Ireland and is the lead author of a 2017 study into the genetic structure of the Irish Traveller community. The study provided an estimate of when Irish Travellers split from the 'settled' population in Ireland. This population-based genetic research project involved researchers from the Royal College of Surgeons in Ireland, University College Dublin, the University of Edinburgh and the Hebrew University of Jerusalem and looked into the history and structure of the Traveller population in the context of 'settled' Irish as well as neighbouring European and Roma Gypsy groups.

A full-text version of the study first published in the journal Scientific Reports can be accessed here.

This interview took place at RCSI on Tuesday 21st November 2017.

CM: *This is an example of collaborative research involving a number of university researchers in Ireland, the UK and Israel. Can you explain how the project came together?*

GC: Liam McGrath, a documentary film producer from Dublin initially contacted David Croke at RCSI about some research that David had done into some of the medical disorders that are seen in the Traveller Community. David knew I was interested in population structures from the perspective of genetics and he passed the contact on to me. Jim Wilson, Professor of Genetics at the University of Edinburgh, is a colleague of mine. We have similar interests and we have worked together a lot in the past and I suppose we have complementary skills. As a result, we did some analysis that appeared in an RTE documentary called *Blood of the*

Travellers (2012) but I was always conscious that for this research to have an impact for the community in policy terms, it would have to be more than a television documentary. A peer-reviewed paper is a little bit more robust and could be something that a politician or a health-care planner could hang their coat on. Another colleague, Professor Dan Bradley at TCD suggested that we publish it as well. A few years later, a student Edmund Gilbert (first author on the paper) joined us and we thought this could be a good data set for him to push through to manuscript and publication. As part of that process we came to the issue of dating the point of isolation and there was an individual at the Hebrew University in Israel (Shai Carmi) who had developed a particular technique that we wanted to apply and that was well suited to the nature of the data and the question that we had. Sean Ennis at UCD came in as the co-supervisor for Edmund Gilbert.

HMcD: *Your research suggests that Travellers split from the 'settled' population in Ireland in the mid-1600s. What does that tell us about the origins of the Irish Travellers?*

GC: To be honest, not a whole lot. It just really points to the date of separation, the point at which they became isolated as a community. This is absolutely not to say that Traveller culture started at that point but it says that something happened at that point where that community became isolated. They started to marry within the community and stay within the community in a social sense and that is the signature that we are picking up at a genetic level today.

HMcD: *Is there any particular reason as to why this might have happened at that point? Or is this a question for an historian more than a geneticist?*

GC: I don't see myself as an historian but multiple historical events that had a significant impact on society occurred around that period. I think it's really for the historians to comment on. One qualifier with that dating is that we assumed that the Travellers are one population. We had to make that assumption because our data set was of a relatively small size. Ideally, you would be able to split the sample according to the structure that we could detect within the Traveller Community because it's quite possible there were separate times when parts of the population became isolated but we had to assume them as a single group. We know that this is actually not the case. We know that there are several sub-groups within the Traveller Community. Our data points to that and work that we have done since this paper also backs that up but for that dating analysis we had to assume they were one group.

HMcD: *Can you elaborate on the nature of these sub-groups?*

GC: The groups are basically reflecting kinship between individuals. If you take any two Irish people they are going to show more genetic relationship, more kinship than if you took an Irish person and a Finnish person. What we are trying to detect is kinship or genetic similarity between individuals and what you see within the Travellers firstly is that there is a very high level of kinship within the community generally, but also that there is structure within that community whereby we see higher levels of kinship between certain individuals reflecting marriage and breeding patterns and ultimately kinship and social affinity. We can see much higher kinship within and between some sub-groups than we see across the whole group.

HMcD: *Can you tell us a little about your methods for data collection for this study?*

GC: We recruited individuals who had at least three grandparents with surnames associated with the Traveller Community. There have been a number of surveys conducted with members of the Traveller Community over the last 50 or 60 years and those surveys list surnames associated with the community and we created a list of surnames that were consistent across these studies. To enter into our study you had to have at least three of your four grandparents carrying one of these surnames. Then we looked to identify just one individual per family with as much of a geographic spread across the country as possible and indeed beyond. In this way, each individual that entered our study carried the maximum amount of information, as distinct from simply recruiting 50 people from one particular family in one particular area, which would not have reflected population as a whole. We then generated very dense genetic data on each sample, around 600,000 data points per individual (these are points in our DNA where we differ from one another, they occur on average every 1 letter in 1000 of our DNA, which is made up of 3 billion letters) and those data sets give you a lot of power to infer kinship between individuals.

HMcD: *What about the ownership of that data and data protection issues?*

GC: Ultimately the data belongs to the individuals who contributed the DNA. It is their genetic sequence. Data protection is now a legal issue. It's the law and will be binding from May 2018. The genetic data is safely secured under our roof here at RCSI. We are very conscious of working with the community in a way that they would be happy with on a community level but also critically on an individual level. If anybody wanted to pull out of the study or remove their data, they would just need to contact us. Current legislation means that you can't just share data like you might have been able to at one stage. Now everything is guided by data protection and the specific consent that was provided. It's actually an interesting area because funders and governing bodies around science generally push for the sharing of data because the more you share data, the more likely discoveries can be made. However, data protection pushes for the opposite and so for the moment, you could be about to publish a paper and the editor will ask you where you are going to deposit the data. You'll reply that you can't deposit the data because data protection doesn't allow me and I don't have the consent to do that. I think that the scientific community hasn't quite caught up yet with the reality of data protection. The governing principle is consent. Take the following example: if you came to us and wanted to be part of the RCSI Irish DNA Atlas Project (the study of Irish ancestry), we have consent documentation where we ask you a series of questions to see if you were happy for us to do X, Y or Z with your data. We have to act specifically under the guidelines of the consent you provide or we probably have to go back to you for more information or for further consent. If you say to me that I am allowed to use your data with any company in the world or publish it publically, then I can publish it publically. But if you do not give me that specific consent, I can't do that. In the past, things were much vaguer. It's not that scientists were being devious; it was just that the gold standard for consent at the time was what it was. Things have changed now with data protection legislation. More papers are being published on ethics and the gold standard is constantly becoming more and more stringent, which is a good thing. Ultimately, what we can do with your data is governed by the permissions provided by you at an individual level.

HMcD*: Were you doubly conscious of these issues when dealing with a community like the Travellers for this this study?*

GC: Yes, personally I am very conscious of that. The travellers can teach us a huge amount not only about Irish history but also about genetics and I see it as their gift to us in providing that. As researchers, we have to be very conscious of the vulnerability of the community and in that context it needs to be driven by them. The work should really be driven by them. The work needs to be driven by them as a community. I think this work that we did was very much driven by them. Francis Barrett approached Liam McGrath (Scratch Productions) with the idea of shedding more light on Traveller history. Francis helped with all the recruitment and it couldn't have happened without him. I like to think it was something that they wanted to do as a community, and we just facilitated it.

HMcD: *Were you conscious of the health disparity between Irish Travellers and the rest of the population when undertaking this study?*

GC: To be honest, I wasn't aware of that when I started this study and since then I've read the work of Cecily Kelleher at UCD and it sends shivers up your spine when you read it. A Traveller male has a lifespan 10 years less, a female 12 years less than the general population. Suicide rates in Traveller males at 7 times the level you see in the general Irish population. Diabetes, cancers, I wasn't aware of that detail. I was aware of an increase in rare Mendelian disorders due to consanguinity in the population but I wasn't aware of the larger health issues. Now I am aware of this and I'm trying to think of ways to shed light on that as a geneticist.

HMcD: *Have you been able to identify genetic vulnerabilities within the population studied?*

GC: Our study was not focused on disease, but rather population structure and ancestry. But, it is known that there is an increased frequency of recessive Mendelian diseases in the Traveller population, however that is only going to impact a tiny percentage of the population as a whole. There is no evidence to suggest that there are other genetic liabilities associated with the community. There is no evidence to suggest that there is specifically and exclusively a genetic factor in the increases we see in cardiovascular disease, diabetes, etc. – conditions known to be observed at an increased frequency in the community. There is probably a large environmental component. I would say it is multi-factorial. You have a combination of genes that in a particular environment might create increased risk for disease. There is no evidence to say that it is exclusively genetic. To the best of my knowledge there is no evidence to suggest that there is a genetic component at all, but I suspect that there will be because the diseases involved are known to have a genetic component (as well as environmental). It could be that some genetic factors have drifted to a higher or lower frequency and that in combination with environment you see a higher frequency or incidence.

HMcD: *Did you come across any evidence as to how the Traveller Community access medical care as compared with the rest of the population?*

GC: No, we didn't engage at that level at all with the population. My understanding is that there are issues in this regard but I think that Cecily Kelleher would be much better placed to inform on that issue.

HMcD: *Do you think there is an element of fear or suspicion in how the Travellers relate to medical care systems?*

GC: I don't feel fully informed to answer that question but my understanding is that it's not so much a fear of engagement but that the language that is used between clinician and patient can have different requirements between the Traveller Community and the rest of the general population. The bridge between clinician and patient is not always the same. It could be something as simple as the language used on a prescription form or on a drug box. There can be literacy issues or the terminology used may be unclear to some, resulting in an inadequate treatment experience Again I would refer you to the work of Cecily Kelleher on this subject.

HMcD: *Do you think that the genetic component of your work in this area will help health care providers to better understand and to improve treatment of the Traveller Community?*

GC: I think it will, yes. If you go back to the kinship point that we discussed earlier, firstly there is greater kinship within the Traveller Community than there is in the general Irish population because it's a small isolated community and secondly there is structure in kinship groups within the Traveller Community. If you then think about a recessive Mendelian disease where you need to have two copies of the diseased gene, what we can infer from our results is that the Mendelian recessive diseases will structure with those sub-populations within the community. So, recessive disease 'X' you might see in sub-group 'A' because of the very high level of kinship in that group. There is a greater chance of the two diseased genes coming together because of consanguinity in that sub-group of the Traveller population. In that context, I think the work can help guide clinicians. However, it should be noted that the point I make is only relevant to recessive disease, which makes up a tiny fraction of the health burden experienced by the community as a whole.

HMcD: *You mentioned that you see this study is a 'gift' from the Traveller Community. Can you elaborate on that point?*

GC: I see DNA as a resource, whether at a national or a community level. I think that as researchers, we have a responsibility to recognise that when people participate in our studies they are providing a valuable resource. The Travellers are unique as a population and I think they are particularly interesting in that they are isolated within Ireland and they have increased incidences of certain diseases, etc. They have a resource that geneticists and researchers can work with. It is in their gift to provide that resource for us to work with. It is our responsibility to handle the design, data, analysis and results of a study in a manner in keeping with their interests as a community. Data protection is the same for any study. We have to be compliant with GDPR (General Data Protection Regulation). But I personally think that with a vulnerable community like this there is an additional responsibility on the researcher to really work with the community in their very best interests.

CM: *Your paper has had a significant media impact here in Ireland. Where will you take it from here?*

GC: The paper has been well received in the general media. On a political level, it has had an impact. I'm told it was discussed by the government at Cabinet level, and I like to think of the work as a small cog in the wheel of discussion around the Traveller ethnicity question. I would love to work further with the community but again, it is entirely within their gift and we'll wait and see what comes through in the future.