Get to know the speakers of the BioData World Congress 2016: VA Precision Oncology Project

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With the advent of revolutionary high-powered computing architecture and the exponential decrease in the cost of sequencing, this new era has now truly begun with the likes of **Genomics England's 100k Genome Project** taking centre stage.

That's why, with the help from our partners we're once again hosting the **BioData World Congress USA** , US's leading event for pioneers working in Big Data, genomics and precision medicine.

Held with the support of the **Wellcome Trust Sanger Institute, EMBL-EBI, Global Alliance for Genomics and Health, Babraham Institute, Farr Institute, Crick Institute, Cancer Research UK and the Broad Institute** will:

- examine the science and technology that is shaping and revolutionising our understanding of complex biological processes
- review the game changing innovation, roadblocks and critical success factors in the utilisation of genomic data in personalised medicine
- highlight how big data is driving developments in medical research
- bring senior scientists within academia, pharma and biotech companies in order to facilitate discussion and partnerships

This event is where innovation and expertise are showcased, solutions are found, and learning done. Join the world leading life science research institutions at BioData World Congress USA and help make personalised healthcare a reality.

DNAdigest- official supporters of BioData World Congress Series interviewed one of the event speakers- Louis Fiore, doctor, scientist, manager, innovator at the Department of Veterans Affairs (VA) in Boston Massachusetts, Executive Director of the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC). Louis will be speaking about the Precision Oncology Project at BioData World Congress USA 2016

Take a look at the short Q&A session:

1. Could you please tell us about your background and your role at VA?

I've been working for VA for almost 36 years. The department of VA takes care of approximately 20 million people, who served in the Armed Forces and are now retired. VA has a network of more than 150 hospitals across the country, they provide all types of healthcare services to veterans. VA has three missions: 1) care for veterans; 2) educate the next generation of healthcare providers; 3) provide research opportunities to improve healthcare of veterans first, and of the greater community as well.

The group that I run, MAVERIC, has over 140 employees and works across four divisions: epidemiology and data mining, clinical trials, biobanking and informatics. We have three national profile projects: Million Veteran Program (MVP), Point of Care Clinical Trial (POCCT) program, and Precision Oncology Program (POP).

2. At BioData World Congress USA 2016 you will be presenting the Precision Oncology Program. Could you tell us more about its history, aims and implementation?

Yes, this is our third program and it takes the lessons learnt from the first two – MVP and POCCT – so let me first briefly introduce these two programs.

At MVP, we are enrolling up to one million veterans into a genomic cohort where they agree for us to access and share their medical data from the electronic health record (EHR) and case report form data, and they also allow us to access their DNA. We are currently performing microarray analysis and we have also performed some whole genome and whole exome sequencing. In this project, we analyse germline mutations, not somatic mutations. The purpose of that is strictly to do research, discovery, and validation of important associations between mutations and health or disease or response to treatment. All these resources are aggregated and are available to intramural and soon, to extramural researchers. We have enrolled almost half a million participants, so about 50% of the way to completion of the project.

The second national program that we are executing is the Point of Care Clinical Trial program. Simply stated, this program is there to perform comparable effectiveness randomised clinical trials within the clinical ecosystem, thus eliminating the need for a parallel world of research staff and equipment to conduct clinical trials. In this model, as patients are cared for in the healthcare system, they are offered opportunities to seek treatment on a randomised basis. If they agree to that, we collect data from the healthcare system databases to assess whether a randomised intervention was successful or not, which randomised intervention is superior to the other. The questions we can study in this fashion involve products that are already in use and where the toxicity is well known. It cannot be done for Phase I, II or III studies but is highly effective for Phase IV studies.

The third national project, the Precision Oncology Program, leverages both of the first two programs and puts them together to create a third program that I like to think of as a complete learning healthcare system enterprise program. At its core, we identify newly diagnosed cancer patients (initially concentrating on lung cancer) and ask their clinicians if they think that sequencing of the target panel of genes, known to be potentially causative for the cancer, could be beneficial for the patients. By and large, clinicians are interested in learning what picking into the DNA of a patient can add to the case. If the doctor agrees, we collect the samples, do the analysis and return the results to the clinician via the medical record. We also provide consultation services through the VA SCAN-ECHO system. The clinician is counselled by an expert in precision oncology who can tell them what to do with the results. There might be important changes to care that might be driven by the results of mutation analysis. We created this clinical component of the program to assist clinicians to deliver high quality care and to democratise precision oncology such that the same skills would be afforded to clinicians who work in the facilities not near an academic clinical centre and do not have expertise in this area.

However, sequencing patients' tumours and advising is not nearly enough, we must deliver effective therapies to make the program useful and while some therapies are approved (there are several for lung cancer), there are many more that are under development. Therefore, giving patients the option to participate in clinical trials is a critical feature of this program. We are in negotiation now with Novartis, other big pharma houses, the National Cancer Institute (NCI), the National Institute of Health (NIH), the American Society of Clinical Oncology, to be able to deliver drugs to veterans who meet the eligibility criteria. You are one of the official speakers at the BioData World Congress. What are your expectations for the event? What topics will you be presenting in your talk?

3. Why in precision oncology and why now? Why should you be granted an exception to a long-established principle of research in clinical trials?

I've been thinking about this recently, trying to rationalise it for regulatory-minded people, but this is not a mature idea (yet). Usually, clinical trials help patients indirectly only, by discovering new products that can be used in the future. They may benefit patients directly who are randomised to the active arm, but generally, the incremental improvement is only modest when you are comparing one statin medication, for example, to a new statin medication or a new flavour of an antibiotic to an existing one. The increase that you need to see to make it marketable is small for any particular patient, but it may be a large difference in healthcare delivery across a population of patients. That type of research is not really convincing for a patient to volunteer for. Because they want to contribute to the general knowledge, they want to help the world at large, but their own care is of minimal impact. And that is the majority of clinical trials. That has been true for cancer as well, because cancer clinical trials, although patients are desperate for care, until now, are concentrating on substituting one very toxic substance for the other, looking for very marginal increments in effectiveness and in safety profiles. It's been said that if you have a patient with a cancer for whom there is no effective standard therapy, patients should be given an opportunity to participate in clinical trials. And we all are really biased there because of this concept, that's why clinical trials are so hard to fill in. Most doctors think that to send a patient to Sloan Kettering Cancer Centre in New York, four hour trip each way once a month, to get a compound that may or may not be marginally better, and would probably be just as toxic, is not worth it. Within POP, biological therapy is designed to affect that particular patient based on their own mutation status, so it is more likely that the drug will be more effective or significantly less toxic. So, there is this transition in clinical trials from contributing to medical knowledge generally for the next generation to actually being helpful to the individual patients sitting in front of you.

4. What has been the biggest challenge in this project? Is it easy to recruit participants and get consent from them?

Every step is a real challenge!

It is generally not difficult to get patients to consent, but it is hard to get the regulators to understand that. All that patients want to know is that measures are being taken to protect their data. They are not really concerned about all these layers of regulation. But this is just one issue.

I think breaking down silos is a really huge issue. Clinical people usually tell me: “This sounds like research and I don’t have time for that”, even though their patients would benefit directly from it. This is a cultural divide. Researchers hear all this and they want to own stuff, automatically. “What do you mean, anyone can have the data?” This sounds antithetical to the research world. For researchers, their currency is publications. To think that they would just be doing something that improves healthcare as the product, for them is incomprehensible because that doesn’t lead to promotions, pay raises, grants. So how do you incentivise researchers to contribute to a combined research-clinical care ecosystem? And how do you get clinicians to embrace research methods like randomisation, to enhance their own ability to learn and to accelerate that? These two worlds are disparate, and then you have the health care administration world which wants to deliver care but as cheaply as possible. Now we are saying to them that they should bear the burden of sequencing patients and they say that it is going to be mostly research. We say that research cannot afford to do it and they are not going to know what to do, or be able to learn, without it. The paradigm here is that the clinical world depends on researchers to inform them how to do their business. This is insane, because the business of taking care of patients is learning how to do it better. It is not discovering and validating, that is what the research world does best. The clinical world does not take responsibility for understanding which of two treatments they commonly use is better. This is what we are doing in the POCCT program. They say the research community should tell them which of these two drugs, both of which are in use, is superior. The research world tries to do that but it costs $100 million to do one study because they have to replicate the clinical care ecosystem in a heavily regulated research environment, which is insane.

I think it is bringing these very disparate worlds together that is the biggest challenge. It is complicated because each has their own vector and they do not align, they are orthogonal to each other.

I have to bring these three worlds together but they speak three different languages, have three different value systems. I have to make them recognise that through breaking down of silos and collaborating together, they can do what has to be done and the reason now is because of the very word “personalised”. That changes the game and I think in 20 years, what I am saying will be obvious and executed. Otherwise, personalised medicine, or better, precision medicine, is not going to happen, because of these new barriers that have appeared, and because our current structure is completely unprepared and inadequate to deal with it. It will require change in structure — and it is already happening.