BioBeat'18

WELLCOME GENOME CAMPUS

Disrupting biodata healthcare

Summit report

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Introduction

From genetic and molecular information to routinely-collected NHS patient data or novel measurements from clinical trials, biomedical data is everywhere. BioBeat18, held on 15th November at the Wellcome Genome Campus in Cambridge, brought together scientists, innovators, entrepreneurs and investors to discuss opportunities for bringing disruptive biodata ideas to life, including:

- Combining genomic and other large open datasets to improve the hit rate for drug discovery
- The potential for patient-generated data – for example, from wearables or smartphones – to provide more meaningful outcome measures in clinical trials and encourage recruitment and retention of participants
- Using biodata to develop innovative, personalised interventions or treatments in a wide range of diseases
- Mining combined datasets to draw out insights, and facilitating local and international data access
- Developing sustainable business plans that add value and attract investment
- Recruiting diverse, interdisciplinary talent and building an ecosystem for researchers and entrepreneurs

Yet there are hurdles that stand in the way of taking hold of this data deluge and channelling it into a successful, sustainable company. This word cloud was generated from the audience's suggestions of the challenges they think biodata businesses will face as they strive to transform healthcare over the next ten years:

- The spectre of hype looms large, particularly around blockchain-based applications
- There are major concerns about public trust – individual biodata companies that fail to act responsibly and transparently risk damaging the whole industry
- Scalability, interoperability and finding funding – it's no longer enough just to gather biodata, companies must add value and build sustainable business models
- Managing stakeholders and communications around disruptive new technologies
- Data governance – including issues of privacy, consent and regulations, such as GDPR

Genomic approaches for boosting the drug development 'hit rate'

The journey from finding a target and developing a drug to final marketing approval costs upwards of £1 billion and can take 10 years or more. Yet around 85 per cent of candidate drugs fail at some point in the process, mainly because they simply don't work as well as they were expected to.

"Nearly half of all new therapies fail in Phase 3 testing, at a cost of millions of dollars, mainly due to a lack of efficacy. How do we pick drugs that are more likely to succeed?" asks **Maya Ghoussaini, Genetic Analysis Team Leader at the Open Targets initiative, Wellcome Sanger Institute.** "We have to use genetic information."

As an example, a study published in 2015 suggested that using genetic evidence to inform drug development could double the success rate for new agents in clinical trials. Initially, researchers have focused on developing therapies that target rare diseases caused by specific faults in the protein-coding regions of a relatively small number of genes. But this does little to help the much larger numbers of people affected by more common illnesses, including heart disease, diabetes, dementia and cancer, whose condition is influenced by more subtle variations in non-coding regions of the genome.

Ghoussaini points out that the number of genomic regions associated with common diseases has jumped from about a hundred in 2007 to many thousands today, thanks to the exponential proliferation of genome-wide association studies (GWAS) and the increase in sample size. Yet there is little insight into what any of these variants actually do at a biological level, or how they are linked to disease. The challenge now is to identify the genes and pathways that all these individual variations act upon, and to turn this information into relevant insights for drug development.

By integrating multiple datasets, including genomic and epigenetic data and gene expression analysis, Open Targets is bringing together academic and industry expertise to build a comprehensive, open-source portal to link genes to diseases and variants to genes. This will enable scientists from academia or industry to identify novel targets or find new indications for existing drugs with known mechanisms of action, rapidly building testable biological rationales for preclinical work or clinical trials.

Using patient-generated data to improve clinical trials

Elin Haf Davies, CEO and Founder of Aparito, is approaching the challenge of improving clinical trials from the other end, focusing on developing new ways to accurately capture whether individual patients are improving in response to their trial drug. This is particularly pressing for trials in rare childhood diseases, and a staggering 42 per cent of paediatric clinical trials are inconclusive.

"When it comes to healthcare and clinical trials, the design and methodology hasn't changed at all," she points out. "On the one hand companies are investing billions in developing innovative therapies, but they're not putting the same investment into innovative endpoints and outcomes for clinical trials. We need to do much better at collecting data from trials – we might not change whether a drug works, but we're making it more likely to get a definitive yes or no."

As a solution, Aparito has created a tech solution that provides ongoing, real-time monitoring of a range of symptoms, which can then be used to develop meaningful, individual endpoints for clinical trials. More broadly, the development of machine learning algorithms that can analyse 'digital biomarkers' (e.g. photos, videos, voice recordings, wearables and even local weather data) along with real-time capture of symptoms and drug adherence will provide a much better picture of overall health and progression. Additionally, it's highly likely that these tools will increase patient activation, leading to better understanding of their disease, increased motivation to take part in clinical trials, lower dropout rates and better quality of life for participants.

While Aparito and other companies are working on data-driven solutions for clinical monitoring, the regulatory environment and healthcare providers are playing catch-up. Davies argues that there is a need to move away from single 'go/no-go' decisions to more iterative approval and reimbursement mechanisms based on an evolving body of evidence of meaningful patient benefits.

Building a sustainable business

Investors are becoming much more aware about the potential power of biodata, says **Elisa Petris, Partner at life science investment trust Syncona.** It's no longer enough to base a company around gathering massive datasets – an effective business idea should focus on driving value for the company and its investors. "Biodata is a hugely exciting area with mass applications, but investors are becoming more specialised and savvy," she warns. "I want to know what your business model is and how are you going to monetise the value in your data?"

The entrepreneurs on the panel spoke about the need to be flexible when faced with reality – as **Liberty Foreman, CEO and Co-founder of DynamX Medical (formerly Beamline Diagnostics),** says, "People call it 'pivoting', but it's really just realising when something isn't working and switching to doing something else." In Foreman's case, this has meant renaming and conceptually overhauling her entire company. Or it might involve trying different models for income generation, as **Fiona Nielsen, CEO and Founder of Repositive** has done.

Alternatively, as **Jo Pisani, Partner at PwC Strategy&**, points out, some companies may need to switch their research and development focus to a more immediately marketable interim goal. "Successful start-ups might have a deep conviction of something they know will eventually come to fruition, but in the meantime they might need to go for an easier or financially less risky therapeutic area or platform as a step along the way," she says.

"Ultimately, the only person who really knows your business is you," says Nielsen. "One of the key differentiators of success is how fast you can make those decisions, but you also need to make sure you're communicating effectively to your team to make sure you're still all heading in the same direction."

Attracting talent

Another essential aspect of sustainable business development raised by the panel is recruitment and retention of talent, and all the CEOs taking part in the summit stressed that they were actively recruiting talent.

For Nielsen, crossing into the biodata start-up world has meant she is now drawing from a talent pool in which she's competing with major tech companies that can pay big salaries for data specialists, machine learning engineers and web developers. The panel advises dipping in the biggest pool possible, considering people with backgrounds and experience in industries that may seem unrelated to bioscience, such as e-commerce or even more diverse technology sectors – Nielsen gave examples of how Repositive has made hires from places as varied as Badoo (online dating) and JDR Cables (oil and gas industry) for their team.

Wellcome Sanger Institute Associate Director Julia Wilson showcased the Genome Campus as a hub for collaboration in her introductory remarks. "Genomic science is now at a time when it can have a direct impact on human health," she explains. "The ingredients we have in this country, this region and on this site make us part of the largest technology cluster in Europe."

Employers must also adapt to trends in the workplace in order to attract and retain good people, such as the increasing desire for flexible working. For example, Foreman gives the example of one of her employees who lives and surfs in Swansea, appearing daily in the company's Oxford office as an online rather than physical presence. The biotech community will benefit in the long run from promoting the benefits of moving into biodata careers to undergraduates and encouraging gender and ethnic diversity in STEM subjects at school.

Developing disruptive technologies

Another theme emerging from the panel discussion was the challenge of introducing disruptive technologies based on biodata. In the case of Repositive – an online marketplace for genomic datasets – Nielsen has taken the existing e-commerce concept and applied it to biological data. But, as Petris points out, investors are becoming ever more niche and it can be difficult to find funders with broad enough knowledge to see that something is a good bet, so entrepreneurs must work on having a clear, coherent story that sells their idea.

Understanding how a product drives clinical decision-making and who the stakeholders are is key, particularly if a new technology or product has the potential to remove specific roles or existing sources of revenue. There is a risk of backlash with any disruptive technology, which needs careful stakeholder management and communication. As an example, Foreman raised £2.5 million to develop a cancer diagnostic device that uses infrared spectroscopy biochemical analysis to identify the difference between healthy and cancerous tissue, which has the potential to replace much of the work done by trained pathologists.

Faced with a backlash from the medical community, concerned that this would result in job losses and deskilling, Foreman has concentrated on the biggest problem in pathology right now: 90 per cent of analysed samples turn out to be normal, taking up valuable time and resources from an already-understaffed profession. By focusing on developing a protocol that can identify and screen out the majority of normal or benign samples (so-called 'resect and discard'), she aims to reduce the workload for overburdened histopathologists by around 50 per cent – a much more enticing prospect to sell to potential users.

Data governance and public trust

Unlike the pharmaceutical industry, which has a well-worn regulatory path, the regulatory framework for fast-emerging data-driven technology companies is much less clear. Governance and regulations are often thought of as a roadblock to companies wishing to work with data, although **Natalie Banner, lead for Understanding Patient Data at Wellcome,** explained the much-feared GDPR has actually become an enabler. Rather than data compliance being seen as an IT issue, new regulations are forcing organisations to think about governance, transparency and fairness all the way up to board level, weaving good practice into company culture rather than trying to bolt on compliance afterwards.

"Nobody was talking about data a few years ago, but now we are having a 'data moment'," she says. "People are increasingly aware of issues of data use, rights and privacy, and asking questions about who has access to their data and what they are doing with it. There is a significant risk of undermining public trust in legitimate research using data that is trying to do good things, and all businesses will suffer if trust is lost."

Research by Wellcome and other organisations, shows that while the public broadly accepts the need to use patient data for research, they become more suspicious when commercial interests are mentioned. Banner says, "Companies have to build trustworthiness into the system and give the public good reason to trust them. Are you doing what you said you would with this data? Are you being consistent in your application of the rules? What is your motivation and your business model? And what are the benefits that you want to bring to patients and the wider public?"

Getting this right will have big benefits: patients, trial participants and the public are much more likely to hand over data and advocate for research that they feel will make a big difference to people's lives, as long as they trust the organisations that they are giving it to. The recent controversy and suspicion around Google apparently moving patient data from DeepMind back into the parent company highlights the potential risks to the whole industry from getting this wrong.

Only once did we hear the 'B-word' – not Brexit, but blockchain, about which the panel generally expressed scepticism. "Blockchain is a solution in search of a problem and I worry that people are charging ahead trying to apply it in a health data context without understanding quite what it's supposed to fix," says Banner. "Blockchain allows people to control data in a trustless 'Wild West' environment but we need data to flow around the health system, so the idea of full patient control isn't feasible."

Opportunities ahead

Using biodata to develop biological insights, accelerate drug discovery, personalise therapy and develop bespoke products for individual patients are major areas of interest. Large, open, curated datasets like those provided by Open Targets are likely to provide fertile ground for entrepreneurs seeking novel ideas that could be developed into beneficial healthcare innovations, while expanding out from individual genes and variants to understanding genetic networks and potentially druggable targets within them could provide valuable new insights.

Diagnostics usually have a shorter path to approval than pharmaceutical interventions, but this area is often seen as unprofitable and tends to be avoided by investors. However, Petris argues that this probably has more to do with the fact that most new products are no better than current tests and techniques.

"Performance is just the starting point," she says. "You have to put things through a narrow and strict lens to find things that are truly valuable from a healthcare perspective and generate the clinical data to convince people to pay for it. This will be different in different diseases – you need to have a deep understanding on a case by case basis."

This doesn't mean that clinical trials have to be hugely expensive: Foreman and her team ran a 400-patient trial over four sites with three people at a cost of £150-200 per patient by working out the minimum amount of data required for regulatory approval, engaging early adopters at trial sites, and offering devices for free.

There are significant opportunities that will come from using AI technologies, such as deep learning and neural networks, to crunch together big datasets and see what shakes out. It's likely that this will be a rich source of testable insights and hypotheses in the healthcare arena, which would be unlikely to emerge through more conventional approaches.

"Biodata is becoming increasingly interoperable as systems talk to each other and datasets are linked," says Banner. "There is huge potential if we can add in patient-generated data too – there is limited richness in things like electronic health records but if we can add in patient-generated data then that could be very useful."

"It's going to be even more exciting when we learn to harness our 'data dragons' and combine them," agrees Foreman. "Right now, companies are gathering their own separate datasets – I'm producing spectroscopy data while you might be generating genomic information – we haven't yet learned what we can do together."

There are significant opportunities for companies that can facilitate access to data wherever it is located in the world. "There's a huge demand for all sorts of biodata but it can be hard to get hold of – if you can facilitate access and compliance with transparent and easy-to-understand contracts then people will want it," says Nielsen. "For example, Chinese law says you can't export genomic data out of the country, so how do we make insights from that data available to people who are conducting research outside of China? There is a business opportunity there for companies that can provide this kind of service."

The future looks promising for biodata-driven healthcare, not only for entrepreneurs with bright ideas but also for people wishing to work to work with them. According to founder Miranda Weston-Smith, "Collaboration sits at the heart of everything BioBeat stands for, and the result is the potential for new ideas and breakthroughs – great ideas attract great partners!"

Despite challenging economic times, the world of biodata has been democratised, from AI and cloud computing to large open 'omics' datasets and digitised health records. However, while the barriers to entry are lower than they have ever been, the industry as a whole should guard against 'data cowboys' and operate transparent and ethical data management and regulatory compliance. The Cambridge scientific ecosystem is fuelling an incredible ferment of activity, providing unparalleled access to datasets that can be translated into healthcare benefits for patients, and we have the opportunity to do things that will have global significance in the years to come.