UK SPINE KE Conference

Improving collaboration to accelerate drug discovery for healthy ageing

Full recordings of talks and panel discussions can be found at our YouTube channel and Website.

The first annual UK SPINE Knowledge Exchange conference on the 16th and 17th April 2019 brought together 106 delegates to discuss knowledge exchange and ageing over two days. 18 different companies and 19 universities were represented amongst the delegates, as well as 5 funders, 7 charities, and 6 delegates from the healthcare sector. This demonstrates UK SPINE's ability to bring together expertise from relevant stakeholders to accelerate the development of new therapies to improve health in old age. These Experts discussed issues relating to ageing, health, and affordable medicines. The prestigious surroundings of the British library provided an appropriately learned setting for a series of though-provoking talks and lively discussions.

Day 1: Accelerating Drug Discovery

The conference was open by talks from **Dr. Beverley Vaughan**, UK SPINE Programme Director, and **Prof. Sir Mike Ferguson**, co-director of the University of Dundee's Drug Discovery Unit (DDU). Dr Vaughan provided an introduction to the UK SPINE initiative, describing how it will bring together the expertise of the five UK SPINE hubs to accelerate the development of new therapies. Prof. Ferguson inspired the audience by discussing the successes of the DDU's open drug discovery projects; advancing assets in an academic setting before transferring to external partners for further development.

Following these opening remarks, the focus turned to the challenges of achieving effective knowledge exchange in drug discovery. **Dr. Martino Picardo**, who has a wealth of experience in operating UK science parks, shared his views on how to create environments where ideas flow freely and businesses are given support to grow. This was followed by a panel discussion on how to achieve frictionless knowledge exchange, chaired by **Dr. Barbara Domayne-Hayman**, Entrepreneur in Residence at the Francis Crick Institute. The panel consisted of experts from academia, industry, and tech-transfer, alongside Dr. Picardo. The lively Q&A included a debate on whether it was desirable to have frictionless knowledge exchange. "If you don't have a bit of tension you are not being truly innovative" suggested one audience member. However, the panel was in agreement that the UK shouldn't underplay it strengths in incubating new businesses, this is something the UK is very good at. Instead, the UK should look at how a better environment can be created to support these businesses in scaling up.

'You need people, you need infrastructure and you need money and without one component of those you are going to be frustrated and disappoint a lot of people.'

- **Dr. Martino Picardo, Chairman at Discovery Park - Sandwich, Kent**

The next panel session focused on the challenges and opportunities of open science in drug discovery. The panel was chaired by **Dr. Wen Hwa Lee**, CEO of Action against AMD, and contained experts from industry, academia, and primary health care. Amongst the fascinating

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discussion, **Prof. Trish Greenhalgh** wisely reminded everyone that in a complex system, there will be no perfect answers.

After a break for lunch and networking, the conference resumed with four parallel sessions focused around IP, building networks, managing CCF Proof of Concept portfolios, and ageing. The leaders of these sessions used these sessions to listen to and challenge the delegate's views. The discussions held in these sessions can be found at the end of this document.

The delegates returned to the main auditorium, where **Dr. Rob Salguero-Gomez**, Associate Professor of Zoology at the University of Oxford, reminded us of the breadth of ageing research that takes places across the full range of departments and faculties at universities. Dr. Salguero-Gomez described how the society could benefit from researchers from the arts and humanities working together with social, physical, life, and medical scientists.

The day ended with a brilliant talk (expertly delivered via Skype due to a French train strike) from **Prof. Sarah Harper**, Director of the Centre of Population Ageing at the University of Oxford. Prof. Harper used a series of beautiful graphical representations of data to express the staggering challenges – and also opportunities – that will be created by a rapidly ageing society over the next 30 years. A truly inspiring end to the day, which left all in no-doubt about the size of the challenges ahead, but excited about the great potential societal good that new therapies could deliver.

Left to right: Prof. Frank von Delft (NDM, Oxford), Dr. Daria Donati (GE Healthcare, Life Sciences), Dr. Barbara Domayne-Hayman (Entrepreneur-in-residence at The Francis Crick Institute), Dr Iain Thomas (Head of Life Sciences at Cambridge Enterprise), Dr. Martino Picardo (Chairman at Discovery Park - Sandwich, Kent).

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Day 2: Affordable Medicine

Day two of the conference focused on the need to assure that new medicines are affordable. With it made clear from the outset that 'affordable' does not necessarily mean the same as 'cheap'. The day was opened by **Prof. Chas Bountra**, Pro-Vice Chancellor for Innovation and UK SPINE Project Lead at the University of Oxford. **Prof. Sir Jeremy Farrar**, Director of Wellcome then provided a global perspective on the affordability of medicines, including a reminder of how the global economic landscape is changing.

'We need more affordable treatments and we need them quickly. When you talk to patients, even tomorrow is too late. Patients want the drug today, they want the treatment or cure ASAP. …. What they don't want from us is excuses, what they don't want from us is us blaming each other. … . They expect us to come up with solutions.'

- **Prof. Chas Bountra, Pro-Vice Chancellor of Innovation, University of Oxford**

The day continued with a panel discussion chaired by **Dr. Chris Schofield**, University of Oxford, in which members of the pharmaceutical industry set out how they were looking to support the development of affordable medicines, and were robustly challenged by the audience. This led on to a series of parallel workshops focusing on impact, the ethics involved in patient and public involvement, and how IP affects business models.

After lunch, **Prof. Mariana Mazzucato**, Director of the Institute for Innovation and Public Purpose gave brilliant plenary talk: "Re-imagining Health Innovation to Deliver Public Value". This talk sparked much debate on the value created by public and private investment in drug discovery, and whether the prices charged by pharmaceutical companies to public healthcare providers adequately reflects the role of public research investment in drug-discovery. Prof. Mazzucato also spoke about mission-orientated public investment, and how that could be used to tackle health challenges created by an ageing society.

Gregory Regano Esq., the CEO of IKU DAO furthermore delivered an excellent talk on his revolutionary block chain driven platform technology that intends to put science back in the hands of scientists. Working with block chain ensures valid transaction and makes inventions traceable in the absence of a third party regulator such as an IP-office or bank. Around the conference there was an overwhelming sense that if this technology catches on, it will be disruptive.

'It's a mad idea until it's proven and this will not happen within existing structures. It will take entrepreneurs and dreamers and idealists and people with vision and then they'll all come, that's what will happen.'

- **Julie Walters, Founder and CEO of Raremark**

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The conference concluded with a final panel discussion with representatives from industry, charity, and Innovate UK, prior to summing up from **Dr. Niven Narain**, CEO of BERG LLC, a Boston-based, "AI-powered biotechnology company".

The conference brought together **experts from academia, industry, the NHS, patients groups, investors and other stakeholders** to discuss how UK SPINE can achieve its goal of accelerating the development of new therapies to improve health in old age. The discussion and debate was rigorous and wide-ranging, and new networks and connections were made between the delegates. We look forward to repeating the success of this event in Birmingham next year.

Sir Jeremy Farrar, OBE, FRCP, FRS, FMedSci, Director of the Wellcome Trust

'I say all of that and it may come across as pessimistic, but I'm actually not pessimistic. I would be pessimistic if this sort of debate was not starting. I would be pessimistic if people were saying: actually the model works and is going to work in 2020, 2030, 2040 and 2050, but I do not think that that is what is being said. I think the start of it has to be the acknowledgement of what the issue is and then the question of who needs to be part of that debate going forward and what role we can all play. Because the truth is that none of us are at the scale that is required to actually change this on our own.'

- **Sir Jeremy Farrar, OBE, FRCP, FRS, FMedSci, Director of the Wellcome Trust**

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Breakout sessions of day 1: Key findings

After a break for lunch and networking on day 1, the conference resumed with four parallel sessions focused around IP, building networks, managing CCF Proof of Concept portfolios, and ageing. The leaders of these sessions used these sessions to listen to and challenge the delegate's views.

Breakout Session 1: Building CCF Networks

A key focus of discussion was around the challenges of getting different academic institutions and disciplines to work with each other. Establishing a common language and definition of terms was vitally important and often barriers to collaboration came down to not having the infrastructure (administration etc.) or leadership/facilitators (e.g. defining the role of a KE lead and finding someone with the right mix of skills in a competitive job market) to support them. The consensus was reached that this process could take up to 6 months but that the necessity of this timeline is often not recognised within funding bodies. The need for regular communication, either by phone or in person, was highlighted as essential for success.

Breakout Session 2: How do we achieve open later in drug discovery pipelines?

This session was led by 3 case studies:

***Case Study A**: A drug for a chronic condition. The target was developed by a small company with input from academics at a prominent university and the target was patented and granted an exclusive licence to develop small molecule therapeutics. This led to the development of Drug A up to the stage of early phase clinical trials. At Phase II the company and assets were bought by a larger international company before being taken through Phase II and Phase III who then sold the drug at high prices, meaning it is used in a limited fashion in the US and Europe. When asked, they said the high price was to recover the Costs of R&D etc.*

Discussion: This is seen as being a quite common scenario. There is a need to improve the interface to translational science to improve this process. Pitfalls include:

- A lack of cost/benefit analysis
- Poor pre-clinical models which lead to early success indicators that do not translate.
- The lack of biomarkers as indicators of therapeutic success
- A difference in international standards requiring extra work

A longer duration of patents might help to spread the costs over time, leading to a longer time to make back the money and reducing costs per time unit. It would be better employ narrow patents of small molecules instead of very broad patents as this leaves the freedom to operate around the target open for others to work on uncovering useful small molecules. This situation could stem from poor advice from a university tech transfer office which were perceived in the room as often quite poor. Standardisation in this area would be beneficial.

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***Case Study B**: A diagnostic test, integrating multiple measurements into a single diagnosis, for responsiveness to treatment in oncology patients contains a portion of the test that is patented by another company. Many diagnostic sites use the overall test and have a mix of both private and public algorithms that they use to analyse the results. The company that has patented part of the test issues a cease and desist order for testing for this gene as part of the overall test despite not offering a similar overall diagnostic test itself. The sites may choose to ignore the cease and desist, remove the gene test from the diagnostic algorithms or cease offering the diagnostic test entirely. The company is unwilling to licence its patented part of the test.*

Discussion: Underlying the case study is the issue relating to access;

- Refusing to licence a patent required for a test
- The use of microarray technology
- The exact nature of the patent in question (the manner of application can alter the way it works),
- The specificity of the assay and it's targets and how that ties in with how you understand the data from an assay (usually via algorithms) and which targets are actually important and which are not

A comparison of the algorithms would be useful as their development and use in the public and private sectors will be very different. The patent should be challenged as it is possible the sequence of the gene is patented but not the gene itself.

If open source science had been used then this could have dramatically reduced the cost of the assay. As Algorithm licences can be very expensive, it would have helped with the aggregation of resources and the use of healthcare systems. Despite reducing the development time, open source work does have the disadvantage in increasing the possible competition to the work.

Moving forward it's important to think about the biology of the situation and work out exactly what kind of assay is needed. Establishing a consortium might help with licencing issues while challenging the patent might be worthwhile especially given that it's unclear what the patent exactly covers. There is also an ethical angle to consider relating to how a licence can be used to control an invention vs. the importance of the invention for public health.

***Case Study C**: A biological agent against a chronic but non-fatal infectious disease has been developed in collaboration with an NGO in a low/middle income country (LMIC) which helped obtain patient samples for research. The drug is approved in western developed countries but is not available in the LMIC's where it is most needed. The manufacturing expense and limited health care system capacity in LMIC's was cited by the company as a reason. The NGO is now calling for cheaper access to the drug in LMIC's. It is unclear if the disease is likely to be classified as a 'public health emergency' which might enable a government use exception from normal patent requirements.*

Discussion: There are three key issues:

- Cost: Not only of production (a balance of profit and recouping costs) but also what people are willing to pay (which will be different in rich and poor countries and thus

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it becomes an access issue). Is it then fair to have differing price structures for different countries dependent upon the local means and/or needs. What is the social responsibility here of rich countries to poorer ones?

- Regulatory burden: If there is no easy way to produce generics then patients with no access will suffer and the disease may become a public health emergency.
- The existing setup of Pharma companies: This is hard to change, although costs can be reduced working with an NGO. They do not want to compete unless a drug reaches phase 2 which would give them a massive advantage over other companies with that testing in hand. To reduce this reluctance why not do everything before phase II as open access?

The consensus reached in the room was that this is a big issue which requires a big systems shift to solve. However, it is at this stage unclear to participants what this shift would need to look like to solve the problem.

Breakout Session 3: Grow MedTech

A consortium of 6 universities is looking to support innovation in medical sciences and technologies, funded by the Research England Connecting Capability Fund. A key issue is linking researchers together but also at an early stage with industry partners. Three stages where development can occur are proof of market, proof of feasibility and proof of concept. This consortium seeks to transition projects along this track. The consortium allows better investment in projects by people, better feedback channels and allows industry input without conflicts of interest occurring.

The key challenges faced include getting academics to engage with end users at the start of the project, the recruitment of technology innovation managers, issues surrounding applicability outside of medical devices, any foray into digital health requires early clinician engagement, issues surrounding regional hubs and the best distribution of partnerships.

Breakout Session 4: Clinical studies in ageing populations

One issue is separating out different underlying causes of multi-morbidities, which have a common measured outcome. The need for concrete, unique readouts (biopsies instead of frailty) is important as many diseases have the same risk factors (e.g. ageing) and some shared components. Key problems with developing new drugs (repurposed or otherwise) include classifying a disease based on pharmacological sensitivity and the complicated nature of older patients already taking many drugs. It is going to be necessary to work together to get trials with large enough numbers to account for the different underlying causes to the same pathologies. The advent of new technologies for wearable data collection and the discovery of new biomarkers points to a future where enough data can be collected for meaningful clinical trials to be run in an ageing population.