Creating Cultures

Leadership Interview with Professor Mark Lowdell

Life Sciences

By
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Amrop

Leaders For What's Next

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The immune system is a fundamental component of all living organisms. It is what keeps us all alive, yet its suppression is a central mechanism in the development of many cancers and neurological diseases.

In this interview we speak with Professor Mark Lowdell, an expert in the field of Immunotherapy, the treatment of cancers and other diseases using substances that stimulate or suppress the immune system. Immunotherapy, a type of Cell and Gene Therapy, is a rapidly emerging field currently transitioning into the realm of mainstream pharmaceuticals.

Mark is an academic, clinical scientist and a co-founder of a number of commercial businesses. The backdrop is an emerging scientific and commercial market, where the push and pull of both sides of the union create truly unique challenges for trailblazing leaders.

Mark discusses the novelty of the field, his experiences as a leader in both the academic and commercial realms, and the challenge of running a business based in a state-run British clinical* facility during the COVID-19 pandemic.

This interview was originally recorded as an episode of the Amrop Coffee First podcast — a series of thought provoking conversations with leaders.

*The NHS (National Health Service)

Mark Lowdell, PhD, is a clinical scientist specialising in translational immunotherapy and regenerative medicine. His work is focussed on the development of cell and tissue medicines for immunotherapy and transplantation.

He is Professor of Cell and Tissue Therapy at University College London (UCL) where he has led a translational immunotherapy group since 1994.

Since February 2009, Mark has also been Director of Cellular Therapy at the Royal Free London NHS Foundation Trust.

Mark is also a co-founder and owner of a number of businesses. At INmune Bio, a clinical stage biotechnology company, he is a co-founder, Chief Scientific Officer and Chief Manufacturing Officer. INmune Bio was founded in 2015 and has reached the landmark go-ahead to undertake human trials for cancer treatments.

He is also a co-founder of Autolomous, a technology company which provides software solutions for the manufacture of cell and gene therapy.

Mark received his PhD in clinical immunology from London Hospital Medical College, University of London in 1992 and is a qualified immunopathologist

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Creating Cultures | Leadership Interview with Prof Mark Lowdell
Key Messages

1 A fast-growing field

Cell and Gene Therapy as a commercial application in the treatment of cancers is burgeoning. Advances in the space began to gain momentum in the early 2000s but it was not until the purchase in 2010 of the CAR-T cell therapy by Novartis that big pharma began looking at Cell and Gene therapy as a viable commercial product.

2 Pioneering on a new front

As a pioneer in the manufacturing of Cell and Gene Therapies, Mark has founded a number of business to solve issues of scale. His company INmune Bio was founded as a manufacturing solution, whereas Autolomous was founded to combat the challenges in safely digitalising manufacturing records for a large number of patient-specific therapies.

3 Leadership needs to blend responsibility and empowerment

Mark is responsible for leading teams in both academic and commercial verticals. To Mark, true leadership is the ability to delegate authority whilst retaining responsibility. Ensuring that you empower your teams to deliver on your behalf. This is the case in both academia and industry.

4 Rank does not automatically determine respect

As an individual thrust into leadership at an early age, Mark was quick to recognise that rank does not determine respect. Respect from your team must be earned on day one, and must continue to be earned.

5 The step into industry demanded a True North

The move into industry, and the creation of Mark's commercial businesses, was driven by ethics. As an academic he felt passionately that new therapies must reach the patients needing treatment. The only way to achieve that is through commercialisation of the intellectual property, rather than purely publishing in an academic journal.

6 A new approach — Hotelling

Mark's commercial businesses have been entrepreneurial, creating the concept of 'Hotelling'. In renting a manufacturing space, Cell and Tissue therapies can be manufactured for a fraction of the cost of building a new laboratory. Mark has created a model that is used internationally for the manufacture of Cell and Gene therapies.

7 Development leads to longevity

The personal development of Mark's team is crucial. Considerable effort is taken to develop the individuals in his team, creating an empowering environment with a longstanding corporate memory and a long-term median term of employment.

8 The driving force

Mark's ethos is to change clinical practice. The success of his commercial businesses is secondary to his life's ambition to change clinical practice either through his own drug, or somebody else's drug that his companies are helping to develop.

Read on for the full interview.

Mark, due to the technical nature of what you do can you frame your current role, firstly in the academic field?

If we use the term academic loosely, I work one day a week for UCL*, three days a week for the Royal Free London NHS hospital Trust, and one day a week for my company Inmune Bio.

My main role is physically within the hospital, where the trust employs me as Director of Cell and Tissue Therapy. I am a clinical scientist, specifically an immunopathologist (diagnostic immunologist). So my role is to interpret the results of pathology tests and recommend treatment by a specific medical professional.

I lead a team of twenty-one NHS staff and a further twenty University staff. Collectively we run the most active manufacturing space for novel, and increasingly important, cell and gene therapies in Europe. We manufacture cells and tissues into medicines, sometimes with genetic modifications, which makes them a gene therapy. We work in a very specialised facility at the Royal Free Hospital, one which I say is very active. In addition to manufacturing, we support clinical trials across the whole of the academic health centre, which is UCL partners, and further trials across the country and abroad.

You are also a co-founder and consultant for a number of commercial businesses. What is your role outside academia?

The field of Cell and Gene Therapy is burgeoning. The first real cell therapy to make headlines was the CAR-T cell therapy published in TIME magazine back in 2010. This technology has since been acquired by Novartis from a US University, and commercialised into a commercially-available cell drug that is manufactured from a patient's own cells to treat that specific patient.

In order to develop these therapies to get them out to the right number of patients that need them, you've got to commercialise.

*University College London

Cell and Gene therapy is a burgeoning field. In order to get the treatments to the number of patients that need them, commercialisation is key.

At the forefront of manufacturing in an emerging field, you must be entrepreneurial to solve the problems that are preventing therapies reaching patients.

The companies I work with were founded to solve problems identified in the field. We are at the forefront of manufacturing, so you see what is needed and create the solution. Creation of these companies is entrepreneurial and driven by the need to get these crucial therapies out to patients.

One day per week I work for INmune Bio, a US-based Cell and Gene therapy company. I work with Autolomous, a software solution for Cell and Gene Therapy manufacturing, and I'm also co-founder of Achilies, a T-Cell therapy company. We have just treated our first two patients in our first two trials, so that is very exciting.

In addition to my own businesses I consult to a number of other pharmaceutical companies.

So, the businesses you are closest to are INmune Bio and Autolomous. What are these businesses trying to achieve?

Inmune Bio is an immunotherapy company that I co-founded with two colleagues. We went public in 2019 on NASDAQ. Everything we do is focussed on innate immunotherapy — developing therapies using the inflammatory system in the innate response: *the Natural Killer (NK) cell system*. Our work targets a broad spectrum of cancers and neurological diseases, with a focus purely on the innate immune system.

Autolomous was founded to address the issue of scale. Back in 2008 it became apparent to me that we just couldn't create these patient-specific autologous cell therapies at the scale that was needed, simply because the paperwork in manufacturing the drug was too great. The paperwork needed digitalising, but the issue lay in doing that securely. In 2016 I was approached by a blockchain expert and it was clear that we could use blockchain to electronically secure a batch manufacturing record in cell therapies. So, in February 2019, we formed Autolomous as a software solution for Cell and Gene manufacturing. We've just raised our second round of funding and we're just about to announce our first US contract.

Immunotherapy as a cancer therapy really began taking off in the mid 2000s, but the commercial side of that has been slower on the uptake, hasn't it. Why has that been?

Drug companies historically develop internally by taking a compound and randomly changing it to see what it does. That is not the way we work in the field of immunotherapy, and as Cell and Gene therapy is not a traditional pharmaceutical field, their R&D units are not set up to work on immunotherapy.

What we have seen in the field of advanced Cellular and Gene therapies, even now, is that 80-90% of new therapies in development are coming out of academic units and either being bought out by big/small pharma, or spun out as a company. These therapies are not being developed by the pharma companies themselves.

Leadership is the ability to delegate authority whilst retaining responsibility.

The shift to commercialise the field has taken a lot of change and is still quite slow. Jim Allison, who won the Nobel Prize for Medicine in 2018, pioneered this idea that Checkpoint Inhibitors can be used as an immunotherapy. (CPIs are antibodies that prevent cancer sells from switching off the immune system).

The idea of using antibodies as reagents that are made in a huge batch like any other drug, and that are shipped, prescribed and taken like any other drug, meant that pharmaceutical companies could commercialise the field. The CPI story fitted into a model that already existed in big pharma. Cell and gene therapy, is more personalised than CPIs. That model did not exist in big pharma, and has been a real challenge.

At my tiny facility at the Royal Free [Hospital] we are currently manufacturing a drug for a big pharmaceutical company. Whilst they have the resources, they don't have the skills to make it. There are a number of positive outcomes from this. The [healthcare] Trust is receiving income, my lab is receiving kudos from the community, and it is great for the patient because they'll get a drug that is manufactured much more quickly, because we know how to make it. Big pharma find these things very difficult, because they do not have the skillsets in-house. They are chemists and pharmacists, we're cell biologists, and there is a big difference.

Moving onto leadership, this falls into two camps for you; split across the academic and commercial, so what does leadership mean to you?

Leadership is the ability to delegate authority whilst retaining responsibility. You've got to be able to lead your team and allow them to develop with the security that if they make a mistake it's your mistake. So the most important part of leadership that I see is not so much the delivery, but empowering the team to deliver on your behalf.

Your first real taste of leadership came very early when you were 27. Not long after that, at 32, you become Associate Professor and Senior Lecturer. How did you find that experience?

I was very lucky in that at 27 I had to step up and take over ownership of a technical department. I turned up as a very young senior lecturer, by far the youngest in the department, with no history whatsoever in Haematology, and yet I had to try and get the people who were there to believe in me.

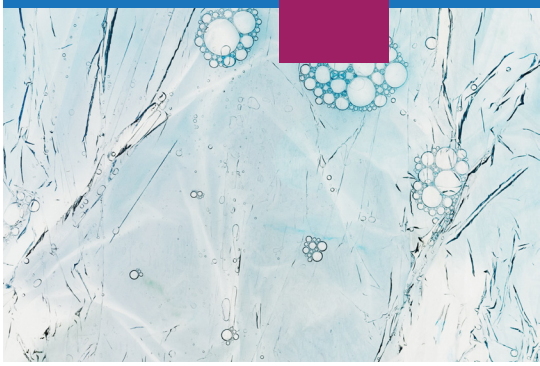
Although I had a team working for me, I came from outside their field. I had a clinical lecturer working for me who knew far more about haematology that I ever did, and probably still does. Yet I had to persuade him that when I determined the experimental plan, he should risk his research time in joining me.

There was a lot of challenge leading that department. The early years were certainly very stressful, but the NHS is very good when it comes to leadership training. One of the great courses I attended was called "Getting Things Done". It was about change management, which is something I think that leadership regularly gets wrong. It was a great experience to be taught about change management at such an early age.

So leadership and rank are totally different things, one doesn't necessarily follow the other?

Yes. The biggest problem I have seen with junior staff working for me is when people get to a position in management and think that this gives them an immediate right to respect. Whenever this happens it is important to reinforce that respect is earned, it doesn't come with the title. You've got to earn that respect not just at the beginning, you have to continue earning it. If you don't have integrity, or don't support your team, it is very easy to lose your team's respect. That's the biggest issue.

Being in a leadership role is not an automatic route to respect. A good leader must earn the respect of your team on day 1, and continue earning it.



Let's talk now about your two current businesses, and particularly the leadership challenges. Firstly, what made you take the step out of academia into the commercial world?

It sounds twee but this is absolutely true, it was ethics. Nearly every cell therapy we make is patient-specific, so there are no good animal models. Take chemotherapy, for example. As a treatment this has been put into an animal model to determine the maximum dose before you start to see side effects. In Cell and Gene therapies the first patient you treat is a real guinea pig, and it's a huge responsibility to relay that message to a patient.

When we did the first NK Cell trial with my own IP (intellectual property) I sat down with my first patient, a lady named Joanna, to explain that whilst we had created a medicine that I was very passionate about, we really didn't know whether it was going to do her any harm or not. Joanna made me realise that agreeing to take the therapy was not just for herself, it was also about the learning from the trial that will potentially have a fundamental impact on other patients in the future. And this has been true for around 90% of the patients we have treated since.

It is important that we realise, when we are asking patients to take these medicines, that whilst they may have fatal leukaemia with a life expectancy of six weeks, this medicine may reduce that lifespan to six hours, and that is very powerful. Also, if we are going to do these high risk studies with patients who are brave and generous enough to take an experimental medicine, we need the capacity to treat every patient that needs the treatment if it is successful.

As academics you must consider the ethical implications of your work. The real value is in creating a therapy that can reach the number of patients requiring treatment. The way to do that is through commercialisation — not just publishing a paper in an academic journal.

As academics there is an ethical dimension to consider. We can't just treat ten patients, publish the results, and wait for someone else to turn the therapy into a drug. You have to be able to look at the big picture and commercialise the therapy. You can do that either by creating your own company, or by selling the IP to a company. My businesses have emerged as nobody has been brave enough to buy anything I've invented, so I have commercialised the IP myself.

So from your experience in both academia and the commercial space, is leadership the same experience for you?

Yes and no. In running my commercial businesses I've had to learn a lot of skills that I didn't have, but they are not necessarily leadership skills, they have been different managerial skill sets.

Of course the financing sources are completely different in the two scenarios, but I don't think leadership *per se* has been different. Whether the team working for me is paid for by INmune Bio or whether they are paid for by a research grant doesn't really matter.

This is such a specialised field that people are being sucked out of academia, so the sort of people that we get into companies are not substantially different from the people we get in our academic groups. Nearly every company that I've been involved in has been staffed by people taken from my lab, or other labs, so their mindset is the same, making it less of a leadership challenge.

As big pharma have been slow entering the field, Cell and Gene therapy as an industry is very much built around smaller, agile, businesses. Would you say that your businesses are entrepreneurial in nature?

Definitely. There is a particular business model for spin-out companies in this field, which is: file the IP with the University or yourself, find a venture capital firm to provide funding to start the company, and employ staff, to run the business as you would with your own research lab.

With INmune Bio we took a different approach. Our CFO, David Moss, managed to use an awful lot of contacts to raise millions from small investors, enabling us to retain a large chunk of ownership as founders of the company. Without any venture capital we filed directly on the NASDAQ, and the only way to do that with a small amount of money is to do an awful lot of work. For example, all of our R&D around my therapy is actually done in UCL University space that we rent. We pay the University to do a research project for us that I run and that is done in my lab and by staff under my employ. The University takes their overhead so they are very happy. Meanwhile we don't have to pay a huge amount of money for a whole research team.

In being nimble and entrepreneurial, Mark has created the system of 'Hotelling' now utilised as an international manufacturing model.

So we have been very nimble and dynamic. In reality, the company is six people running a number of clinical trials, which is remarkable when you consider we are able to pay the Royal Free for the manufacturing space. It is a completely different route and has been a very exciting, different way of running a company.

The process of 'hotelling' that you created is another great example of your businesses being entrepreneurial in nature. Could you tell us more about that?

Yes, back in 2007 Gregg Sando (an ex-banker from Deutsche Bank) and I formed a company called Cell Medica. When it came to manufacturing that drug I suggested that the company rent time in my hospital facility when the facility was not being used. So, instead of Cell Medica raising money to build their own manufacturing suite from scratch at the cost of millions of pounds, we in effect rented the manufacturing suite in the Royal Free when there was down-time. Cell Medica could operate under the Royal Free manufacturing license and quality system, drugs were legally signed off by the Royal Free, but clinical trials were operated by Cell Medica.

The hotel system worked extremely well. At the Royal Free now, we use the system for a number of different companies, including my own companies Achillies and INmune Bio, as well as companies I am not involved in. The income generated is used to subsidise the academic trials run out of the Royal Free, and the trust makes profit out of it.

We have been so successful that the system has been promulgated elsewhere, turning it into an international model.

Speaking of the context of today, this interview has been conducted during the COVID-19 pandemic. A large portion of your team is based inside NHS facilities. How has the experience been for them, and how has it been for you?

It has been very challenging as a team. The government instruction was that you should work from home if you can. Now that my teaching commitments are gone, 99.9% of my work, even when I'm at the Royal free or UCL, is sitting behind a desk. I can do that from home, so it hasn't impacted me too much as an individual.

The real challenge has been around stopping my team from overworking. The team were still manufacturing products and wanting to be present in the lab to do their job, but it became clear that commuting in was not feasible for everyone. A big part of leadership is saying to people *you can't come in when it is not safe to do so*, and stopping people from overworking, and over-commitment.

Investing in the personal development of the team has been key in creating businesses with huge corporate memory, and longstanding median terms of employment.

Stopping your team from that over-commitment must have been a huge pressure as a leader, to make sure that you're looking after your team as well as the business.

Yes, my principle role is as their employer, so my responsibility is to my staff. When we make a cell therapy in clinical trial we don't know if it's going to work. However I can at least manage the risk around someone coming in to work during what was considered then to be a highly infectious episode. There are two things I'm proud of in terms of leadership. First is the people I've developed who have gone on to really lead in their fields, and second is the fact that the median duration of employment in my team is nearly eleven years now.

We put a lot of effort into personal development of the team. Some of them go away and come back, but ultimately we keep a team that has a huge corporate memory, which is massively valuable. Most hospitals don't recognise the importance of this corporate memory, as it prevents us from making the same mistakes over and over again. It makes me very lucky that my team are as brilliant as they are.

Given the overlap between academia and industry, is getting talent into the commercial side of this space challenging due to the inherent nature of academics?

Yes. When you're trying to fund research in either a university or hospital space you've got two routes. You've either got a conventional academic grant, which is what the universities want you to get, or you've got commercial collaborations.

On the academic side, the idea of getting money in from a company has always had this smell about it. It is considered to be "dirty money" because you didn't compete for it against millions of people, or undertake a peer review by the MRC [Medical Research Council]. You got the money because a company wants something done. The work could be truly academically poor, but they're going to throw money at it regardless.

And so, for junior staff developing their career, it is very difficult to take them out of an academic funding stream, and put them into a commercial stream without potentially damaging their career prospects. One of the great things we see in the field of Cell and Gene therapy is that so much of it is coming out of academia into these spin-out companies. So many of these are actually part-owned by universities. It is forcing academia to change their attitude a little bit, and is certainly empowering junior postdocs and graduates to follow a route in industry, opposed to a more traditional academic career. But yes, until the last few years the concept of being in both camps was actually seen as very detrimental to your career.

So is there a fundamental difference in the mindset and approach of individuals in academia vs commercial?

Academia is very aggressive and there are very few top slots. You are dependent upon a research grant being awarded, and your field being interesting enough to continue receiving grants. So it is a pyramid that doesn't have much room in the middle, leaving a lot of people with nowhere to go. In our field, Biopharma, those people now have a home.

The mindset in academia is focussed on delivering research to answer a specific question without necessarily worrying about whether the work will have any patient benefit or application. It is a different sort of person we bring across to industry, the individuals that can translate their research into something that is going to have an effect.

My ethos is that I want to change clinical practice. Whether it's my drug, or with somebody else's drug that we are helping to develop, it has to change medical practice.

So how would you sum up the challenges that you face as a leader in your two businesses, INmune Bio and Autolomous?

In INmuneBio the challenge is organisational. We're running trials globally, with multiple different companies involved, so relationship building and management is key. INmune Bio is such a small company that we have to rely upon all these different parties. Ensuring that my employees are part of that mission and understand the importance of the relationships we are building is a huge challenge.

At Autolomous there are four co-founders, each with very different skills. I have no skills whatsoever in coding, or programming but I do know what the programme needs to do, so my role is to act as the client with the coders. The challenge here is in the teaching. Because they are providing a service to people like me, it is key to emphasise the contribution they are making to medicine — which they have no knowledge of at all - explaining the importance of immunity and cell and gene therapies. If I can inspire them to put in the sort of hours that my team in manufacturing do, I have successfully gotten the message across, and so far it works! They are incredibly dedicated, I'm so impressed by them in terms of the speed they turn things out, it's just remarkable.

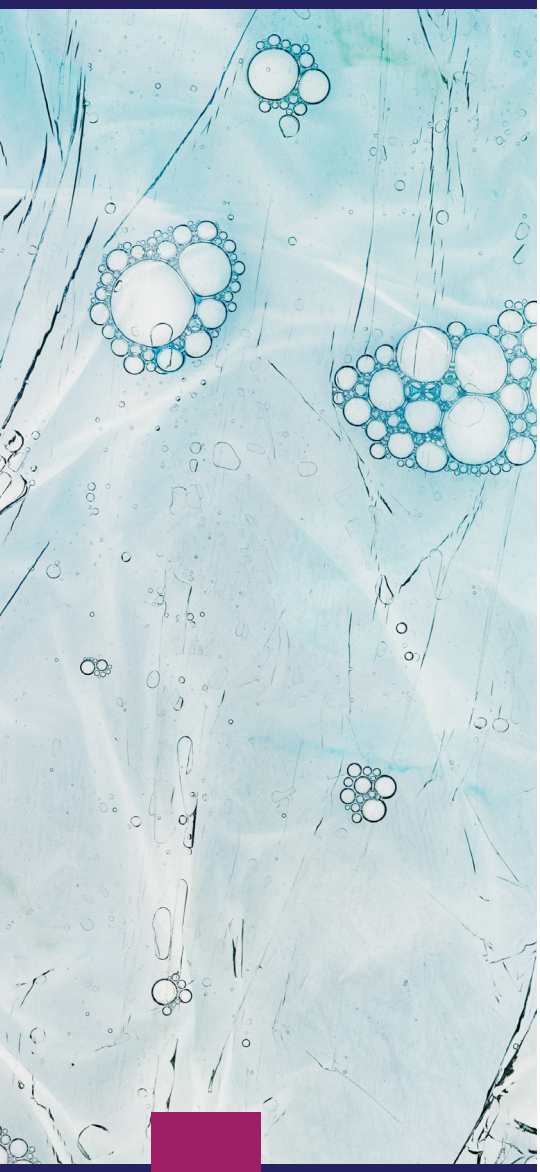
So Mark, I'm keen to understand what drives you. If your business failed commercially tomorrow but your therapy was proven to be successful and have application, would that be a good day or a bad day for you?

My ethos is that I want to change clinical practice. That is what gets me out of bed in the morning, Whether it's my drug, or somebody else's drug that we are helping to develop, it has to change medical practice.

It is a question I ask everybody who comes to me with an idea. I ask whether they want to publish a paper in Nature Medicine, or change clinical practice?

The beauty of my post is that I'm funded by the hospital mostly. I only do one day a week for University and the University has no oversight of my facilities. It's entirely hospital. So if I don't want to support bizarre academic studies, I can just say "terribly sorry, I'm too busy". And I have that luxury, so we only do things that we think can change clinical practice.

Build consensus. The time you spend communicating is just as valuable as the time you spend working.



You've been chasing this goal for 25 years. What makes it so exciting and challenging? What keeps you running at the speed at which you are clearly still running?

I am extremely lucky in that I'm not an academic driven to "become the expert". I am passionate about my invention, my discovery, my field, but if I just focused on that, the risk would be enormous. I still haven't proven that my therapies work, and I may never prove that, which I would say would be a waste of a career.

What keeps me running is being able to facilitate other people's work as much as developing my own. It's all about changing clinical practice, and that's what's exciting, whether it be my therapy or anybody else's.

So what happens next? Is there a bigger goal that sits behind your current focus, if your therapies are proven to work and your businesses become a huge commercial success?

Reading Richard Dawkins' *The Selfish Gene* is what started this passion. I had the sheer amazing luck of bumping into Richard Dawkins at Heathrow some years ago, we sat down and I told him my story, and how the immune system was a perfect model of evolution. I was so proud that I could say I had taught Richard Dawkins something he didn't already know.

So, I would love to write the 'Selfish Gene' of immunology. I think the lay public needs to understand the importance of the immune system, and to get rid of some of the quackery around immunology and immune therapy.

Writing that book is a real retirement ambition.

And to finish, Mark, what piece of advice would you give your younger self if you could go back in time?

Be better at building consensus. The two biggest failures that I have experienced have been because I haven't realised that other people had hidden agendas, and were more Machiavellian in working behind the scenes to stop me doing something I saw as perfectly logical.

It is as much about the time you spend working, as it is the time you spend communicating and pressing the flesh.

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