PREDiCT:5th Annual

3D ONCOLOGY & TISSUE MODELS SUMMIT

Speaker Interview

Marcin Krzykawski

CEO

Real Research

*Leading up to the **5th PREDiCT: 3D Oncology & Tissue Models Virtual Summit**, we have had the pleasure of catching up with **Marcin Krzykawski**, CEO at **Real Research**. Marcin and his team are dedicated to developing new types of protein-based hydrogels for 3D cell cultures. Their goal is to change the way people carry out research – moving it away from inefficient 2D cell cultures to the much more reliable 3D cultures.*

Marcin, I do not think anyone would disagree in calling you an entrepreneur – would you share your journey of founding Real Research with us? What have been the highlights and lowlights?

Starting Real Research was one of the most exciting moments of my professional life. A few years before we had made a breakthrough discovery which led us to our first great product: LifeGel. The story of LifeGel is in fact strange and I always go back to with a lot of sentiment.

With a very basic version of our prototype hydrogel product we aimed high and wanted to perform an angiogenesis test. For half a year we got negative results and with the last 50ml of the cell culture media we were quite convinced it would not work. I was planning to make an experiment on Saturday but since I was quite depressed with all the failures I did it on Monday… and it worked!

We made a full documentation and wanted to repeat the experiment however it failed again. It took us over 3 months to establish the manufacturing protocol and make it reproducible. With these results we decided to take the risk and start the company. We could see success ahead of us but had to learn the hard way that business is a totally different story and that we will have to start from scratch.

It took us 3 years, with hundreds of meetings and multiple ups and downs to find an investor. After this, we saw that success was in reach but again, we had to learn the hard way that running a company requires a completely new set of skills which we were just starting to acquire. In about two years we have managed to grow the company from the two of us to ten people currently and doubled the lab/office space.

We are now facing our next tipping point where we have already patented our core technology and developed multiple products. We feel like the next milestone is just around the corner again – third time lucky? We will see, but whatever happens we will continue because we believe Real Research can make the 3D revolution happened.

> ***"In our new device, we will showcase how we can mimic almost every type of pharmacokinetics in vitro to expose the growing tumor to the same drug concentrations as in vivo. This can be used for drug screening, but it is going to be especially useful in hit confirmation tests"***

You have worked on several interesting projects backed by the European Funds, such as the development and implementation of an innovative research service testing therapeutic regime in 3D tumor culture, could you tell us more about this?

Testing the 3D therapeutic regime is one of our most exciting projects in development. During the *PREDiCT: 5th Annual 3D Oncology and Tissue Models Summit*, we are excited to show the results for the first time. The product premiere will be mostly to find the right partners and present what we are working on. Therapeutic regime testing provides a new level of tumor testing as usually drugs are tested on cell cultures in a very short time window.

In real life, a patient gets the same drug multiple times over a few weeks. On top of that, a patient gets a dose of the drug but the tumor receives a diluted concentration with different pharmacokinetics for every drug. In our new device, we will showcase how we can mimic almost every type of pharmacokinetics *in vitro* to expose the growing tumor to the same drug concentrations as *in vivo*.

This can be used for drug screening, but it is going to be especially useful in hit confirmation tests. When one of our clients reaches a stage where there are several potential drug candidates to enter clinical trials (or even before animal studies), they will be able to test this drug in an almost *in vivo* like setup with highly humanized cell culture. We look forward to revealing our readouts with the audience!

It seems we have reached an inflection point in the industry for 3D models and 3D cell cultures, but there are still challenges to be overcome, such as reproducibility, cell line quality, high throughput screening. How can you and the Real Research team help?

In my opinion the scientific community has just started to adopt various 3D cell culture solutions. I see an inflection point in the availability of original ideas because companies very often make a lot of noise about their new products that is just a minor iteration of the previous one. Still, the true modern 3D cell culture is yet to come. For example, everybody works on miniaturization of assays and part of the reason is high throughput screening.

Obviously, vasculature is a key factor but very few people know that normal cell lines put in a 3D environment will stop growing on top of each other after reaching a certain size. So many scientists are trying to block tumor growth which is already slowing down. There is certainly a problem using the right growth factors and hormones, but it is a surprise that the same cell line will grow indefinitely in 2D models but will reach a STOP point in 3D ones. Since we know already that the gene expression profile in 3D is much closer to *in vivo*, we also know that *in vivo* tumors do not grow that fast.

Tumors *in vivo* are also inhibited and can wait for months and years before they will start to grow. It seems that we are observing a similar situation in 3D, which is generally good because we managed to recreate the *in vivo* observations, but for research and development we need to understand more of the tumor biology in terms of 3D cell culture.

At Real Research we have been mimicking multiple types of environments and see a huge difference in cell morphology and behaviour. In one microenviroment, cells are creating precious 3D structures whereas in the other the morphology will be different, and growth will be blocked for few weeks. Our understanding is that those different environments are different niches of the tumor and when you want to test your drug you should test it in all niches. Cells need to re-program and this will also be followed by different drug sensitivity. Cancer biology is hard but by mimicking different microenvironments we can make a huge step towards better understanding.

One hesitation towards 3D model adoption in oncology is speed and time. Conventional 2D and animal models offer drug developers the comfort of 'reassurance' and 'well validated' – what are your thoughts?

It is indeed comforting to work with something you understand and are already used to. Let us break it down into 3 parts:

1) 3D cell culture models take more time to grow and the experiments can take longer but you can address this issue by purchasing RTU 3D cell cultures to your lab or through a CRO.

2) 3D cell cultures are more expensive and usually less sensitive to drugs but when you look at the overall costs of failures in clinical trials you will see that it is better to fail fast and save the funding for other projects.

3) 3D cell cultures are less reproducible – this opinion was true when scientists were using mainly hydrogels contaminated with growth factors and irreproducible from batch-to-batch, nowadays there are many solutions available (including the key product of Real Research, LifeGel) and the repeatability is not an issue if the model was well designed.

When you are facing a decision between 2D and 3D cell culture it is a lot like choosing easy and comfort but with little chances of success VS more work and harder questions but with great vision and hope for an amazing success.

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We are excited to have your and Real Research's support at the *5th PREDiCT: 3D Oncology & Tissue Models Summit* in September and look forward to a robust roundtable discussion.

Ahead of the meeting, what is your best tip for the audience when they are evaluating the possibility of 3D cell culture?

My best tip would be “Go for it!”. But being more serious, it is challenging to find the right 3D cell culture model but if you find one it is worth the effort. You need to understand the disease you want to model and the target your drug is aimed at.

My advice would be to be very critical of what your models deliver. From my observation a good model answers one question well and for the next question you need to adapt it. Instead of doing this complicated analysis, for somebody new to 3D cell cultures it may be tempting to choose 2D cell culture.

There are many CROs well suited to easily outsource the experiments. Be careful it can be a trap. Your drug discovery phase may look expensive, but you must keep in mind that based on the initial investment you are going to make decisions that will be followed by much bigger investments. A thorough evaluation in the drug discovery and preclinical phase can save you a lot of time and money down the road.

At the same time 3D cell culture model will return much fewer drug candidates (and these candidates could be rejected in 2D cell cultures) but the probability of those candidates to reach clinical trials is much higher to succeed and become the new drugs.

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REAL RESEARCH

Exhibition Partner

Real Research is a biotech company devoted to making 3D cell culture models standard in industry and academia. We have already launched our first product LifeGel - a ready to use, growth factor free, reproducible and customisable hydrogel for 3D cell cultures. We are launching our second product LifeCube, that facilitates fully automated long-term pharmacokinetically relevant drug therapy research in 3D cell culture models. Let’s make the shift from 2D to 3D cell culture models together!
www.real-research.com

Marcin Krzykawski and Real Research are joining us as Exhibition Partner at the *Digital PREDiCT 5th Annual 3D Oncology & Tissue Models Summit*

Download our event program here

September 30 – October 1 | Exclusive Virtual Event | 9am – 6pm EDT | 6am – 3pm PDT