Cite as: Mairi Shepherd, Catherine Elton, Qkine: improving growth factors for stem cell science and the fast-moving organoid and cellular agriculture fields
Innovation & Impact, 2021
URL: iai.digital/2021/Qkine

Qkine: improving growth factors for stem cell science and the fast-moving organoid and cellular agriculture fields

Mairi Shepherd, Catherine Elton*

* Corresponding author: catherine.elton@qkine.com

Qkine Ltd. 152 Cambridge Science Park Cambridge, CB4 0GN, United Kingdom

Abstract: Stem cells are transforming our understanding of basic biology, fast-tracking drug discovery with better models of human biology, and are set to enhance global sustainability through the emerging cultured meat industry. Qkine manufactures growth factors, essential reagents for all stem cell culture. These highly pure and bioactive proteins have the power to control the signalling cascades that define stem cell fate. At Qkine, we are improving reliability and reproducibility of growth factors, and addressing the need for fundamental innovation to tailor the proteins themselves to support the demands of the rapidly expanding stem cell industry. Spun-out from the Biochemistry Department at University of Cambridge in 2016, Qkine currently has a team of ten people and is based on the Cambridge Science Park. Our loyal early customer base in both the academic and biotech sectors reflects the truly global nature of stem cell science. Alongside expanding our product portfolio, we are establishing the commercial infrastructure to support and extend our customers and their science.

Keywords: Growth factors, cytokines, proteins, stem cells, regenerative medicine, cellular agriculture, organoids, drug discovery models, 3D-cell culture, UK manufacturer

Mairi Shepherd, Catherine Elton, Qkine Ltd. 152 Cambridge Science Park Cambridge, CB4 0GN, United Kingdom
Email: catherine.elton@qkine.com
© Mairi Shepherd, Catherine Elton, published under the Creative Commons Attribution 3.0 License.

1. The success story

Stem cells hold extraordinary promise: they are transforming our understanding of basic biology, fast-tracking drug discovery with better models of human biology, and are set to enhance global sustainability through the burgeoning cultured meat industry.

However, for all of these applications stem cells are taken out of their natural niche and cultured in an artificial setting, like a plastic dish or bioreactor. Under these conditions, stem cells are entirely reliant on the cell culture media to provide the complex environmental cues essential for them to grow, self-renew, differentiate and develop the characteristics of the cell type of interest. The most important component of the media for control and direction of these highly complex processes are the bioactive signalling proteins, also known as growth factors.

At Qkine, we manufacture growth factors, highly pure and bioactive proteins with the power to control the signalling cascades that define cell fate. Given the right combination of growth factors, stem cells can be used to produce any cell type, such as liver, nerve cells, or any other of a multitude of specialised cells for research, drug discovery and therapeutics, or muscle, fat, or even lactating cells, for the cellular agriculture industry.

There are only a handful of manufacturers of growth factor proteins globally. Historically, there has been limited innovation in the commercial sector to tailor the growth factor proteins themselves to support the demands of specific stem cell applications. We are changing this at Qkine.

Since spinning out from the University of Cambridge in 2016, we have redefined the industry leading standards in protein quality, purity and reliability. In addition, we have used our protein engineering expertise to innovate; for example, to successfully bring the worlds first totally animal-free version of TGF beta 1 to the market. TGF beta 1 is a core growth factor that is especially relevant in cell therapy manufacture and any induced pluripotent stem cell culture that needs carefully defined media conditions.

Qkine's laboratories are located on the Cambridge Science Park and we currently employ a team of 10 people. We have attracted a loyal customer following from both leading biotech and pharmaceutical organisations, as well as world-class academic institutions. Stem cell science is global and from the outset, our customers and collaborators have spanned the globe. In 2020, while laboratories across the world were quiet, we focused on expanding our protein range and strengthening our ability to support our customers by established distributors across Asia and Europe. As researchers return to the lab post-pandemic, we are ready and excited to support their research as we enter the next thrilling phase in our company growth.

2. How did we start

When Dr Marko Hyvönen established his academic laboratory in the Biochemistry Department at the University of Cambridge in 1998, he needed to produce large quantities of highly pure Activin A protein for X-ray crystallography. However, this growth factor superfamily is notoriously difficult to make with sufficient yields and purity for structural studies. Using his

expertise, a huge amount of patience, and long hours in the laboratory, he developed protocols that not only solved this challenge[1] but serendipitously also would impact the nascent Cambridge Stem Cell community for the next decade and beyond.

At that time, Professor Roger Pedersen and his then post-doc Ludovic Vallier (now Professor of Regenerative Medicine and co-deputy Director of the Cambridge Stem Cell Institute) were demonstrating a role for Activin A in maintaining stem cell pluripotency. Marko spotted their paper and said he had a freezer full of exceptionally pure Activin A and would they like to try it. In true Cambridge fashion, Marko delivered his Activin A by bicycle to the Laboratory of Regenerative Medicine down the road. Marko's protein was highly bioactive in stem cells and Marko has supplied the Cambridge Stem Cell Institute with Activin A from his University laboratory for over a decade supporting world-class research and high impact publications [2-4].

As alumni established themselves across the world, Marko received growing numbers of requests for his growth factors. He worked with Cambridge Enterprise– the technology transfer arm of the University of Cambridge – to commercialise his research. In 2015, he was introduced to Dr Catherine Elton (now CEO) by Cambridge Enterprise. Her experience in the early phases of successful life-science supplier, Abcam's, growth, combined with the immense promise of the growing stem cell sector allowed them to attract seed investment from a quintet of experienced angel investors and the University of Cambridge. Qkine – which stands for 'quality cytokine' – was born.

3. Our technology

Qkine builds on the core protein production and engineering technology developed in Marko's laboratory to tackle new supply chain and innovation challenges faced by the stem cell industry. Some of our products, like the original Activin A, are standard proteins produced to exceptionally high purity in an animal-free system with in depth biochemical quality testing. Others are optimised to address particular limitations or customer needs.

This process of optimising growth factors, which may involve identifying the ideal protein fragment for an application, refining proteins for manufacture yield or indeed using protein engineering to manipulate the fundamental biological properties of the protein, allows us to bring an entirely new set of tools to market for biotechnology companies and researchers developing stem cell applications.

Early in Qkine's journey we secured Innovate UK funding to apply our technologies to growth factors using in organoid culture. Organoids are 3D clusters of cells that come together and emulate the basic physiology of an organ but on a micro scale, whether that be liver, kidney, heart, gut or other organs. Organoids can also be grown to mimic diseases such as cancer and brain disorders and over the last 5 years their potential as animal-replacement technologies in drug discovery and basic research has been firmly established. There is a pressing need for better reagents for organoid culture.We have been applying our R&D efforts towards this area and have developed a diverse and expanding range of growth factors for organoid cultures. We recently established an Innnovate UK-funded collaboration with Cardiff-based organoid

company, Cellesce, and peptide 3D scaffold specialists Manchester BIOGEL to tackle the next big challenge in organoid culture; the need for fully synthetic, chemically defined 3D scaffolds that more accurately mimic the physiological environment in the human body and enable manufacture scale-up and improved reproducibility of patient-derived organoids.

Recently, we have started exploring the scientific needs of the unique and fast-moving cellular agriculture sector, where growth factor supply has been identified as one of the principle challenges to successful commercialisation. This sector is poised to disrupt the traditional meat market and is likely to have a concrete impact on global sustainability in the next decade. If we can be a small part of making this a reality, that would be a worthwhile application of the expertise and technology we are building at Qkine.

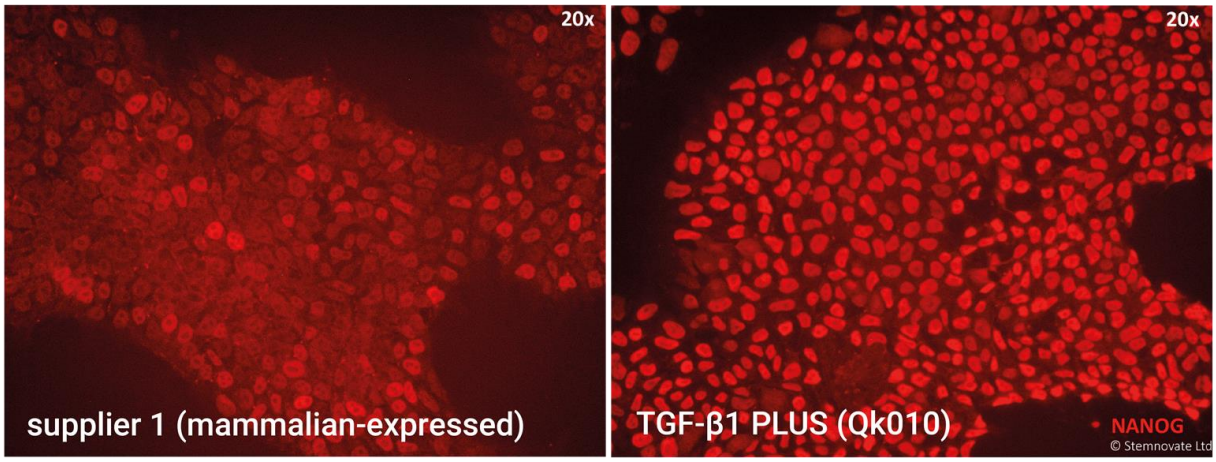

Figure 1. Comparison between Qkine TGF-β1 PLUS (animal-free) and mammalian expressed TGF-β1 sourced from another commercial supplier. TGF-β1 PLUS promotes efficient maintenance of iPSCs at just 1ng/ml, with highly homogeneous expression of the pluripotency marker, Nanog.

4. The journey so far

Founded in 2016, Qkine has secured investment totalling £2.2m, with the support of an exceptional angel investor base including Andy Richards, Jim Warwick and Jonathan Milner; Cambridge Enterprise; and leading life science funds Parkwalk, Martlet Capital and o2h Ventures.

We joined the inaugural cohort of the Accelerate@Babraham programme in 2018, a superb experience leading to long-term and highly valued collaborations. Expanding the product portfolio from the original four proteins developed in Marko's laboratory, Qkine is expecting to complete the build of its core catalogue comprising fifty proteins by the end of 2022, and has plans to expand into related areas, all focused on helping deliver the potential of stem cell science and regenerative medicine.

Although 2020 was a challenging year for many with research laboratories and biotech companies impacted by the pandemic, Qkine has continued to build traction and has collaborations and customers in world-leading stem cell research institute and biotechnology

companies world-wide. Supported by our new global distribution network, we are progressing to full commercialisation and expansion post-pandemic.

5. Looking to the future

Improving reliability and reproducibility in science is imperative. Far too much time and money is wasted on poor quality or poorly characterised reagents. Qkine will continue to put strong scientific principles at the heart of what we do and advocate for greater transparency, more data, innovation and enhanced quality in the global stem cell and regenerative medicine supply chain to help deliver the promise of these technologies.

References

[1] Harrington, Adrian E., et al., "Structural Basis for the Inhibition of Activin Signalling by Follistatin", The EMBO Journal, vol. 25, no. 5, Mar. 2006, pp. 1035–45. embopress.org (Atypon), doi:10.1038/sj.emboj.7601000.

[2] Yiangou, Loukia, et al., "Cell Cycle Regulators Control Mesoderm Specification in Human Pluripotent Stem Cells.", Journal of Biological Chemistry, vol. 294, no. 47, Nov. 2019, pp. 17903–14. DOI.org (Crossref), doi:10.1074/jbc.RA119.008251.

[3] Ragheb, Ramy, et al., "Differential Regulation of Lineage Commitment in Human and Mouse Primed Pluripotent Stem Cells by the Nucleosome Remodelling and Deacetylation Complex.", Stem Cell Research, vol. 46, July 2020, p. 101867. DOI.org (Crossref), doi:10.1016/j.scr.2020.101867.

[4] Ortmann, Daniel, et al., "Naive Pluripotent Stem Cells Exhibit Phenotypic Variability That Is Driven by Genetic Variation.", Cell Stem Cell, vol. 27, no. 3, Sept. 2020, pp. 470-481.e6. DOI.org (Crossref), doi:10.1016/j.stem.2020.07.019.

The company

Qkine

Qkine Ltd
152 Cambridge Science Park
Cambridge, CB4 0GN
United Kingdom
https://qkine.com/

Investment Rounds (collected in May 2021)

Pre-seed | April 2018 | 5 angel investors, University of Cambridge | £120k |
Seed | April 2019 | angels and University of Cambridge | £550k |
Series A | April 2020 | Parkwalk, Martlet Capital, o2h Ventures, angels and University of Cambridge | Amount | £1.5m

Main facts (collected in May 2021)

The Company started November 2016
The first product was delivered in 2017
The company currently employs 10
The next milestone is global commercialisation and expansion

Catherine Elton is CEO at Qkine, which she co-founded in 2016. Educated at King's College and Corpus Christi College, Cambridge, she earned her PhD in the biochemistry of platelet-collagen interactions in 2003. Following her PhD, she joined Abcam, then a small disruptive antibody supplier. Under her leadership, the Abcam in-house laboratory responsible for antibody design, manufacture and characterisation grew from 4 to 40 staff. She assisted with their successful IPO on AIM in 2005 and was a member of the senior management team. Following a career break, she returned to academic research as a Daphne Jackson research fellow at the Wellcome Sanger Institute where she studied the role of surface proteins in parasite infection. During this fellowship, she co-founded Qkine to address challenges in the growth factor and complex protein supply chain and support innovations in stem cell science and regenerative medicine, areas she believes underpin future advances in human health and wellbeing.

Mairi Shepherd is Stem cell specialist. Mairi joined Qkine in 2020 after earning her PhD in the University of Cambridge Stem Cell Institute. Her research focused on the heterogeneity of malignant haematopoietic stem cells. Having spent 5 years growing single stem cells in culture, Mairi knows only too well the importance of high quality, reliable, growth factors in the stem cell community!