July 2021

Printing Organs and Tissues

After years in the making – will the printed organ revolution arrive?

3D printing as a technique has been ground-breaking in the food industry, fashion industry, construction, education sector and biotechnology but how close is it to saving people's lives? 3D printed organs and tissues has been a hot topic for years, but they are still not readily available to the public.

Although the introduction of 3D printing in the medical field has been recent and is still in its infancy, current and future applications of medical 3D printing are found across many specialisations and provide a solution to problems of ranging significance. 3D bio-printing functions is an assistive tool for replicating vascular anastomosis, building cells, blood vessels, dental prosthetics including a jawbone and constructing sugar-based stents to join veins. This is a game-changing development as it allows surgeons to quickly fabricate stents that are totally customisable to the geometry of the patient's vessels. The most ground-breaking application of this manufacturing technique is that it can use the patient's cells to 3D print full replacement organs.

This is the time to take a step back and reflect on the inventions and innovators powering 3D bio-printing, but also investigate what the inventive landscape can teach us about what is to come.

The pace of invention has grown rapidly in the past 10 years but recently appears to be stagnating. After seeing so many new inventions being protected, this stagnation could indicate that many of these technologies are coming of age and might be ready for implementation within the healthcare sector.

An initial study of the inventive landscape of 3D bio-printing doesn't show any lack of invention or investment into this technology; however, the limited progress in offering these solutions to patients at risk suggests otherwise. The regulatory framework regarding the classification of this technology is unclear. It is described both as 'biological' and a 'medical' device. Perhaps this, coupled with the fact that the regulatory framework is unable to keep up with the pace of research advancements and public needs, are the main reasons hindering progress in this technology area.

The end of organ shortage

The demand for printed bio-structures is high in cases that need organ transplantations or smaller tissue structures such as burn victims. In the last 26 years the number of patients waiting for an organ donor has multiplied five-fold in the U.S and the number of people in Europe registered on the waiting lists has reached over 150,000. Since 3D bio-printing of organs and tissues is done using the patients' own cells, the side effects of the immune response are prevented along with the costs and side effects of the immunosuppressive therapy. In addition, this process can be carried out when needed and can be continuously generated according to demand, putting an end to the organ shortage issue.

Despite the advances and buzz around this technology area, the bladder is the only organ that has been 3D bio-printed and transplanted to a human so far.

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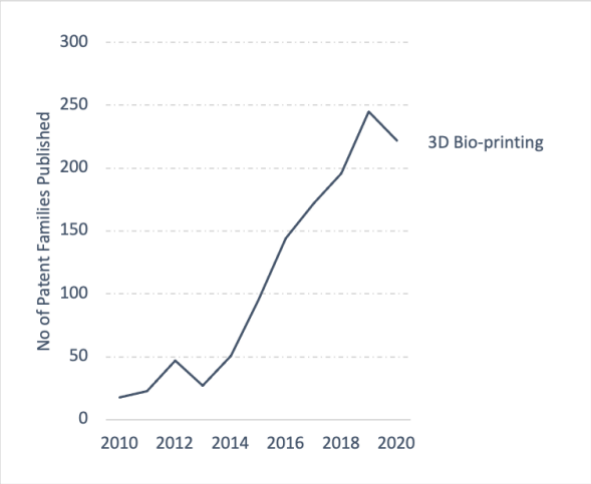
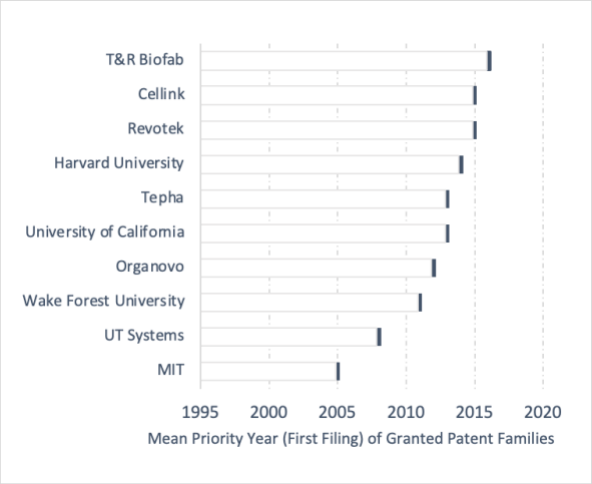
A growing field, but challenges persist

This young, upcoming technology area has seen a huge growth in terms of protected inventions over the past 10 years. However, this trend is not reflected in the number of solutions available to the public with the bladder being the only example of a successful transplant of a bio-printed organ. This happened 15 years ago and was done by Wake Forest University. Between 2015 and 2020, the number of published inventions increased on average 19% per year.

Pace of Invention: *US & Europe*



Invention Age: *US & Europe*



As measured by patent families either granted or pending in US and Europe

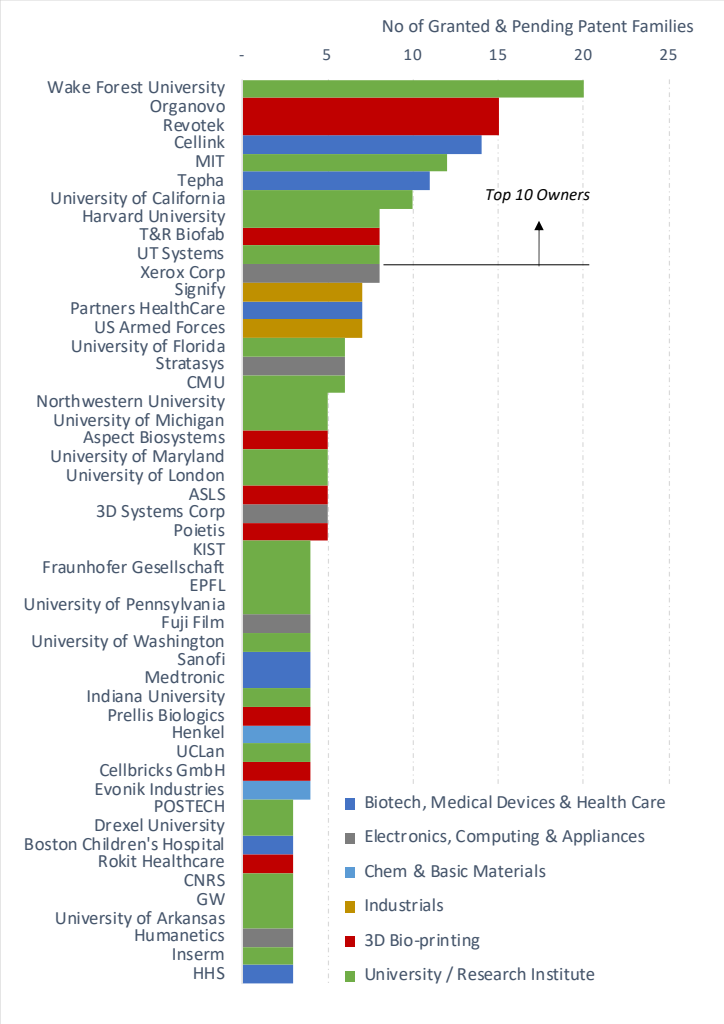
There is clearly investment and invention within this field, from both research institutions and organisations. There are however challenges involved which are technical, regulatory and safety related. The technical challenges to the technology being fully operational are primarily due to the limited availability of biomaterials such as biocompatible synthetics and natural bio-inks. Further improvements need to be made regarding the resolution and speed of the technology as well as the requirement of a vascular system, for tissues beyond 150 micrometres thick to be manufactured, being a challenge.

Gaining regulatory approval when bio-printing entire organs constitutes a challenge as these solutions are a combination treatment that can be described both as 'biological' as it is derived from autologous cells, or as a 'medical' device. The regulatory authorities remain undecided on how to address the potential risks. The governments of Canada, the US and European Union (EU) have produced guidance documents on the manufacturing of 3D printing technologies, but none include any provisions pertaining to 3D bio-printing. There is a lack of clear and predictable rules and standards relating to this new area of medicine, as well as significant ambiguity regarding the classification of these technologies. Current regulations deem methods that rely on the destruction of human embryos unpatentable. This poses challenges for organisations wishing to bring bio-printed solutions to the market. Further, the migration of the implanted materials or cells and the degradation of the biomaterials causing cytotoxicity of degraded by-products are some of the concerns regarding the safety risks of bio-printed organs.

Despite the challenges and the stagnation of inventive pace, this area is expected to see a large growth in the coming years. According to Grand View Research in 2020 the global 3D bio-printing market size was valued at USD 1.4 billion and is forecast to increase at a compound annual growth rate (CAGR) of 16% from 2021 to 2028. They also predict that during this period invention growth within tissue and organ generation is expected to achieve the fastest CAGR, that of 19%. Time will tell if this holds true. What we can see, based on previous invention trends within 3D bio-printing from 2015 to 2020, is that the tissue and organ generation field had a global CAGR in the pace of invention of 23%.

Universities and pure 3D bio-printing organisations take the lead

The Companies: *Number of Inventions Owned*
3D Bio-printing US & Europe



The list of owners in US and Europe is diverse, in terms of size, geographical headquarter and function. The owners range from universities and research institutions to pure 3D bio-printing companies.

MIT being among the top 5 owners comes as no surprise given that the concept of 3D printing was first introduced in this institute and later applied to various research areas. This also explains why out of the top 10 owners, MIT was the earliest owner to file for protection of inventions in this technology, in 2005. Most of these owners had the first filing of protected inventions after 2012, which is when inventive pace within this space really took off.

The leader in this field is Wake Forest University, the scientists of this university were the first to manufacture organs growing in a laboratory environment and successfully implant them to patients. Wake Forest University is heavily funded by the Armed Forces Institute of Regenerative Medicine as one of the current aims of researchers in regenerative medicine is to apply their proficiency to wounded soldiers.

Revotek, an industry leader

In the US and Europe, it comes as no surprise that Revotek is one of the top leaders. Revotek is a 3D bio-printing company and in 2016 they became the first company in the world to print 3D bio-printed blood vessels. Looking at US and European inventors, Wake Forest is in the lead. However, if also including inventions from the rest of the world, Revotek is a bigger inventor.

Revotek was established in 2014 in China and as expected, 80% of their inventions are protected in China. As a young company the protections of their inventions will expire from 2035 onwards, maintaining their current active portfolio size for more than a decade from now. It is interesting to note that even though Revotek is a key player globally, with the second largest portfolio size in the US and Europe, compared to the top 10 owners in these regions, it has one of the lowest mean Portfolio Value IndeX (PVIX) scores that of 49. An observation regarding the strong quality of the protected inventions is that Organovo, which has the same number of assets as Revotek in these regions, has the highest PVIX out of all top 10 owners. This American-based early-stage research company, Organovo, has carried out cutting-edge research in the production of organs and tissues for transplants since its launch in 2007.

Other organisations and institutions, such as Cellink, MIT, Tepha and University of California are also growing investors in this technology. Companies and institutions from all around the world protect inventions in 3D bio-printing with 74% of patent families having grants in China. Cellink is well known within this space due to their bio-printers such as Bio X6. Developed in 2019, this is the most advanced 3D bio-printing device currently available. Lumen X, another Cellink bio-printer which manufactures vascular structures, has been extremely beneficial for COVID-19 drug and vaccine testing.

Key factors that are driving the market growth in 3D bio-printing include an ageing population, a limited number of donors, chronic conditions and advancements in technology. Thus, there is a great need for further development and implementation of these types of solutions. There are several obstacles to overcome such as regulatory frameworks and further technical and operative advancements needed. We expect pure 3D printing organisations to drive progress and impact in this space, not large, diverse organisations. Once regulatory authorities catch up with the pace of invention within this field the revolution in printed organs will be truly upon us, resulting in these organisations having a serious advantage in the playing field.

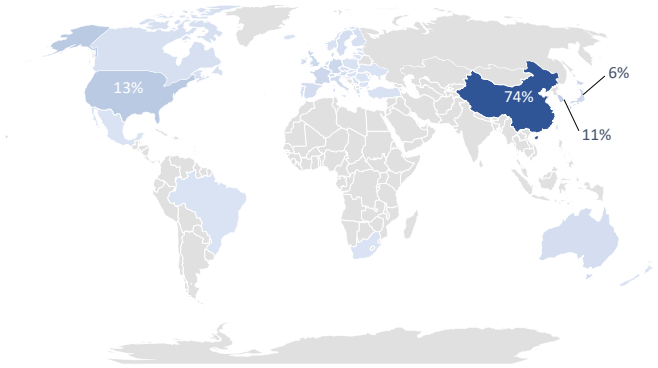
For reference & attached: Innovation Lens Snapshots

- *Technology Screening: 3D Bio-printing*
- *Company Screening: 3D Bio-printing*
- *Company Snapshot: Revotek*

Technology Screening: 3D Bio-printing

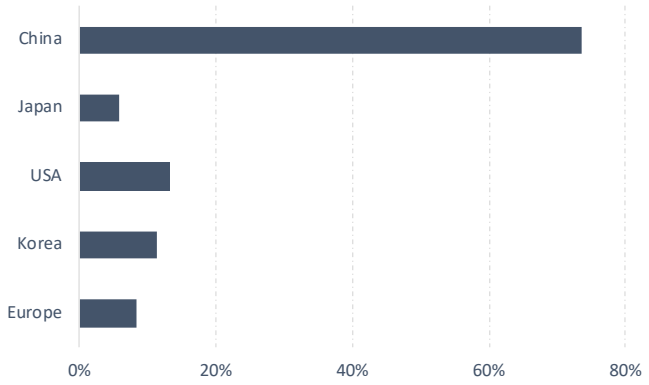
Technology Areas: **3D Bio-printing**

Geographies Protected: *By Country across the Tech Area*



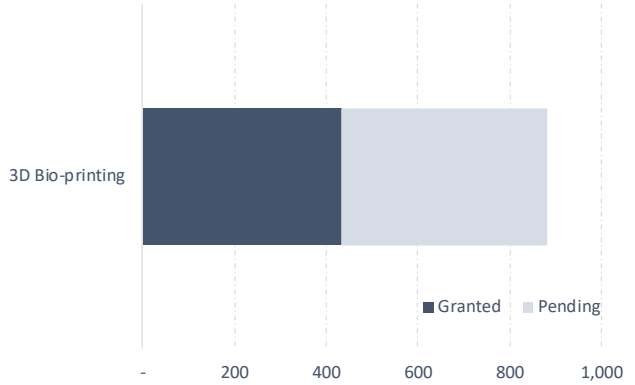
Patent Families with Grants by Country as a Percent of the Total Granted Families

Geographies Protected: *By Key Region / Countries*



Patent Families with Grants by IP5 Region as a Percent of the Total Granted Families

Number of Inventions: *US & Europe*



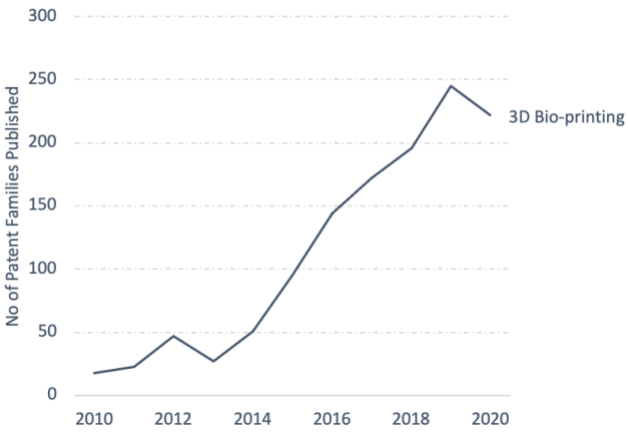
No. of Patent Families with grants / applications in the US / Europe

Companies: *Top ranked by Inventions owned, US & Europe*

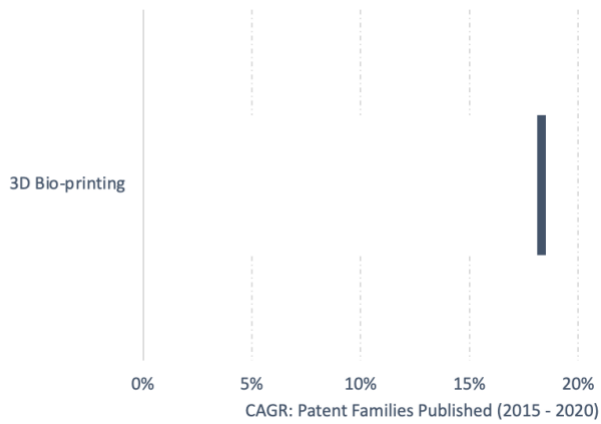
Rank	3D Bio-printing
1	Wake Forest University
2	Organovo
3	Revotek
4	Cellink
5	MIT
6	Tepha
7	University of California
8	Harvard University
9	T&R Biofab
10	UT Systems
11	Xerox Corp
12	Signify
13	Partners HealthCare
14	US Armed Forces
15	University of Florida

Top Owners of Patent Families with grants / applications in the US / Europe

Pace of Invention: *Trendlines, US & Europe, includes WIPO*



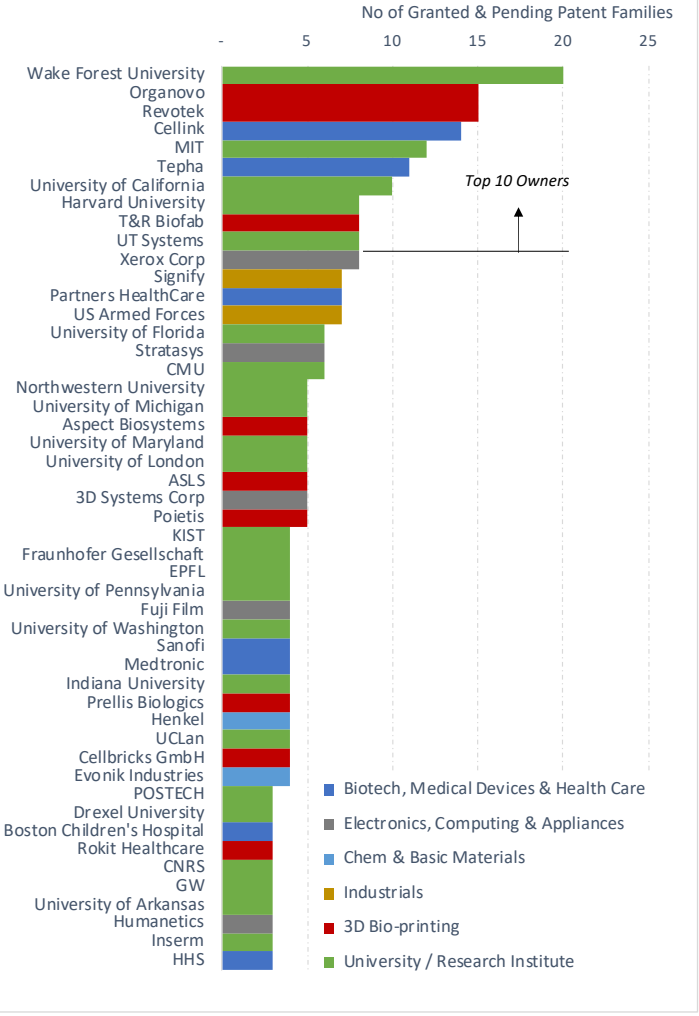
Pace of Invention: *CAGR 2015-2020, US & Europe, incl. WIPO*



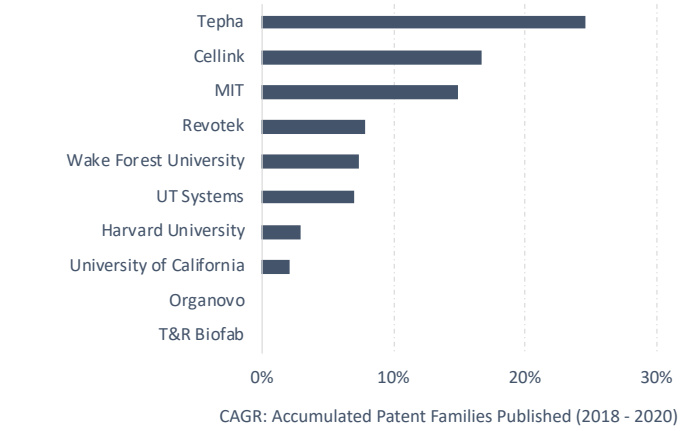
Company Screening: 3D Bio-printing

Technology Area: **3D Bio-printing**
Region: **US & Europe** *granted/pending patent families (inventions)*

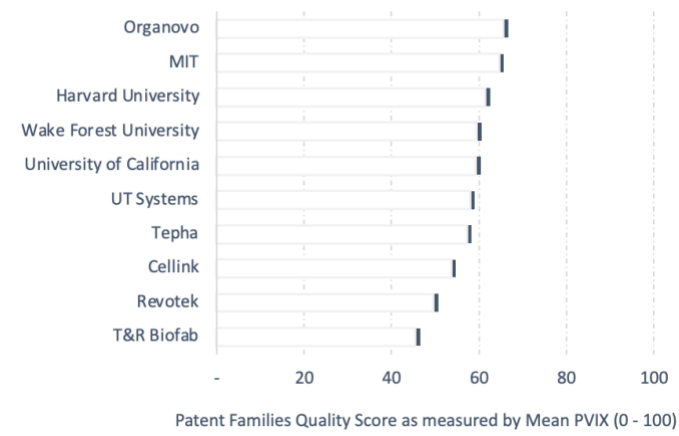
Companies: *No of Inventions Owned, 3D Bio-printing*



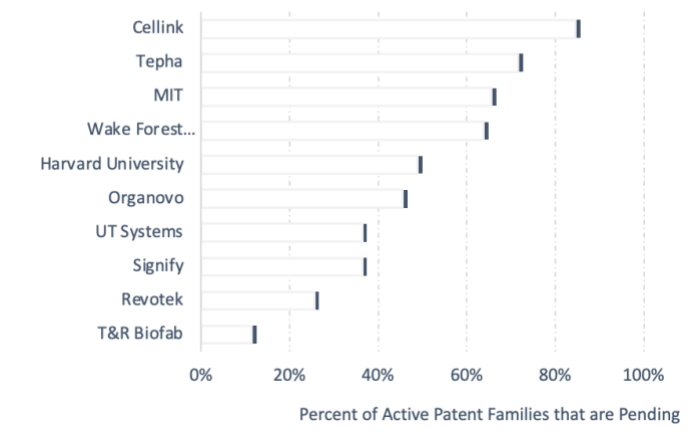
Pace of Invention: *CAGR 2018-2020, 3D Bio-printing*



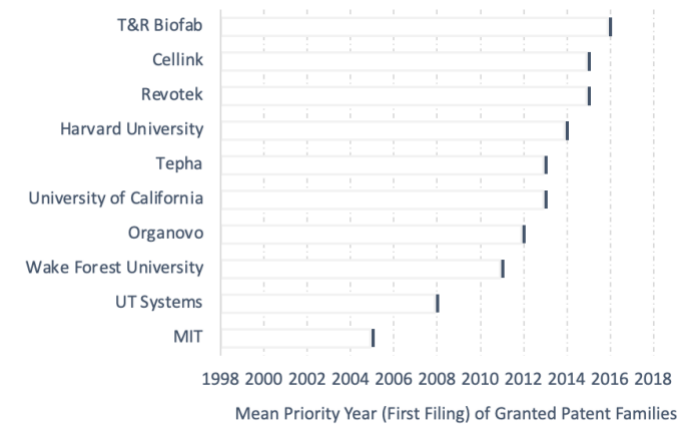
Quality of Invention: *3D Bio-printing*



Invention Pipeline: *3D Bio-printing*



Invention Age: *3D Bio-printing (First Filing Date)*

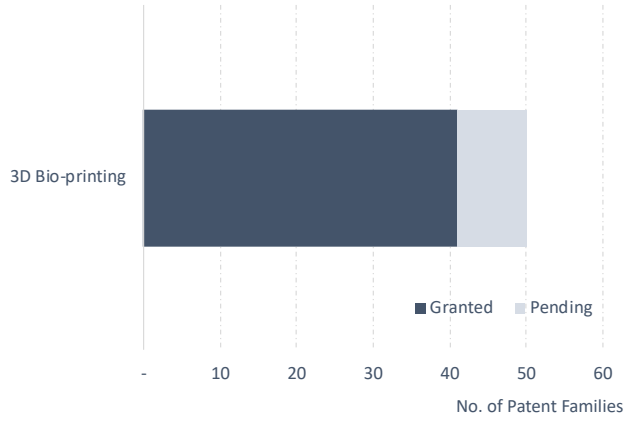


Company Snapshot: Revotek & 3D Bio-printing

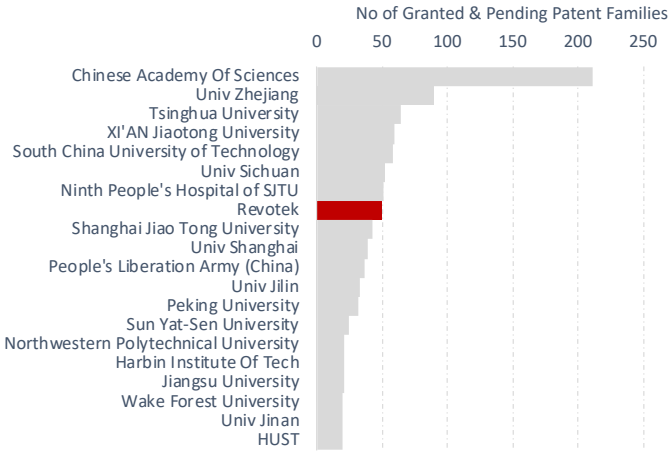
Technology Areas: **3D Bio-printing**

Region: **Global** *all granted/pending patent families (inventions)*

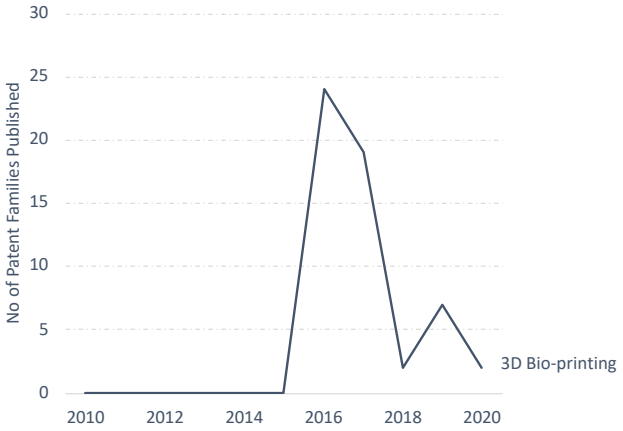
Number of Inventions: *Revotek*



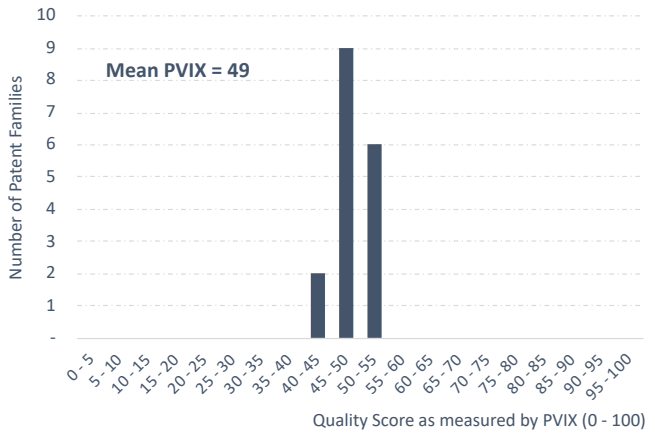
Companies: *Number of Inventions Owned*



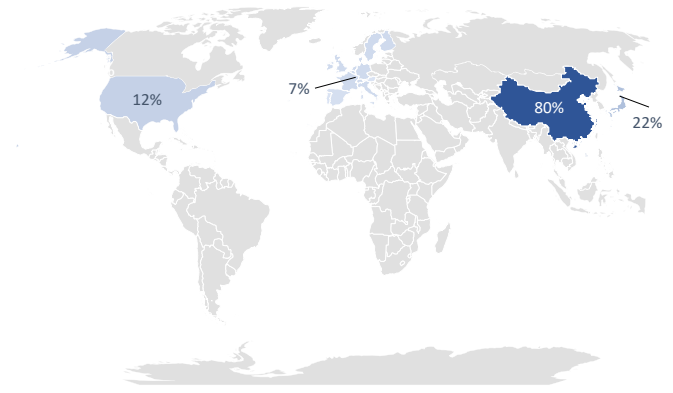
Pace of Invention: *Revotek*



Quality of the Inventions: *Revotek*



Geographies Protected: *Revotek*



Patent Families with Grants by Country as a Percent of the Total Granted Families

Invention Age: *Revotek (Expiry Date)*