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One step ahead

Innovation in core facilities

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Many life science research organizations and institutes have established core facilities to support scientists by providing access to specific technologies and expertise that a single laboratory could not support and maintain [1]. The working model of these facilities is determined to a large extent by the technology. Generation of tools, products or data can be carried out by the facility as a "customer service". Others will offer access to their key technology and expertise through consultancy, collaboration and training. In some facilities, a combination of both models is worked out.

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The first core facilities that were established during the 1990s mainly offered DNA sequencing and/or bioinformatics services. Since then, the number of technologies and services offered by core facilities has greatly increased to include proteomics, metabolomics, electron and light microscopy, high-throughput screening, analysis or sample handling, or synthetic chemistry. Many of these facilities have come of age, and there is a clear tendency to expand services around the key activity. This provides opportunities to work together with and help scientists to explore new technologies and scientific questions but also creates challenges for facilities that depend on constant innovation and development. This article discusses some of potential benefits and challenges of constant innovation for academic core facilities.

Expanding services

Expanding the range of services is a general trend in many businesses. Thirty years ago, airlines just flew a passenger from one airport to another. Nowadays, airlines offer customers a broad array of other services related to travelling: renting a car, booking a restaurant, or train or taxi shuttle to another city. Even though a core facility is a different entity than a commercial airline, there are similarities in how both had to adjust their portfolio. Many facilities were originally established to offer a particular service usually based on a single technology or device, such as DNA sequencing. Today, however, the needs of scientists have changed. Technologies are generally getting more user-friendly, but at the same time more demanding in terms of sample preparation and data analysis. Moreover, tweaking or adapting the protocols allows for applying a certain technology to a different field of research than it was originally developed for. In addition, there is a constant turnover of techniques and technologies that requires core facilities to assess and adopt new opportunities.

> *"Scientists as "customers" have clearly stimulated core facilities to develop and offer "whole-package" services..."*

Scientists as "customers" have clearly stimulated core facilities to develop and offer "whole-package" services that include many or all steps from experimental design, sample preparation, data generation to data analysis and presentation. Many commercial facilities and technology firms offer similar ease-of-use or whole-package services often at competitive prices; scientists could, for instance, send an environmental sample to a sequencing company and obtain the full microbial metagenome along with

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bioinformatics analysis and ready-to-use illustrations for publication. This creates pressure on academic core facilities to innovate and keep ahead of new developments, technologies and their applications.

Moreover, scientists increasingly need to align services from different core facilities to combine different technologies, such as FACS and light microscopy to sort and analyse individual cells followed by single-cell exome sequencing. It therefore makes sense for core facilities to link or combine separate activities. For instance, more and more facilities offer light and electron microscopy or FACS and light microscopy as a single service unit. Generally, new workflows can originate from combining different applications. This is very prominent for the emerging single-cell approaches where the combination of sorting, advanced imaging and sequencing help to link spatiotemporal *in situ* events to mutational drift in the genome.

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New ideas are not necessarily a bottleneck, but choosing where to innovate—whether it is a new technology or a working model—is, and it requires input and help from scientists. Since it is the users of a core facility who will judge an innovation by making use of it or not, their opinions and requirements are important for determining which aspect requires innovation or improvement.

Incubators for new ideas

In addition to improving existing services and scouting for new technologies and applications, it is also possible to innovate from the point of idea creation onwards. This would expand core facilities' roles as service providers to become incubators for new technology. Here, a close connection to research laboratories is key. Indeed, many technological innovations originated in research laboratories and found their way to facilities where they were made accessible to the wider research community. One example is single plane illumination microscopy (SPIM) [2], which is based on an illumination scheme that was first described at the beginning of the last century. SPIM microscopes are now part of the instrument park of many light microscopy facilities, either as a commercial device or custom built, which is facilitated by open source projects [3,4]. Another example is the structural and mechanistic studies of the bacterial nanopore CsgG that led to the nanopore sequencing technology offered by Oxford Nanopore [5]. Cryo-EM is another disruptive innovation that has contributed to the so-called "resolution revolution" and was awarded with a Nobel prize for the scientists who laid the groundwork for this technology [6,7]. All over the globe, institutes are now massively investing in Cryo-EM facilities and expertise to offer access to this technology.

A core facility is a perfect hotspot of expertise around a key technology and therefore a good place for ideas to improve upon the technology or to develop alternative methods. However, one has to be cautious to start implementing ideas in a closed environment, because it is risky to put time and efforts into something that may not be of value to its users. Developing a solution in need of a problem is not helpful to the research community and a waste of resources. Co-creation, together with researchers and a technology vendor, therefore helps to assess the wider usefulness of a technique early on, because the partners look at the innovation from the end-user's perspective. This kind of collaborative effort fits into the concept of open innovation [8], used successfully in several businesses, including the life sciences, pharma and health care.

In this setting, scientists cooperate in a way that is different from the typical research collaboration whereby teams join forces with a core facility to use established services. A scientist has a different role as a customer of a service, compared to being involved in developing a new technology or working method. When a scientist comes to a core for established service there is a certain guarantee that he or she will get the results. In innovation, the collaboration between the user and the core facility is a riskier project, aimed at troubleshooting a technique or method, with no guarantee of a positive outcome. Managing expectations is essential because such an innovation-driven collaboration is not focussed on answering a biological question. A good start is to understand the trigger and scope of the innovation: Is it the scientist's research question that prompted the need, the core seeing potential for an innovation or, alternatively, a technology provider that wants to test a new tool or method? Depending on who the driver is, the partners have different roles. The core can either act as the innovation initiator that teams up with the scientist and/or vendor, or as partner in an alliance from academia and industry.

Beware of the gaps

Open innovation typically fails when it is only driven by the requirement of one of the partners. An example is a user who wants to solve a very specific problem that is not relevant to the broader community. To be successful, partners need to align their interests, and frequently, the project lead will not be the responsibility of one partner, but shared between the contributors. Moreover, innovation is an assignment that cannot be done as part of the routine business, but requires its own time and resources [9]. Scouting, testing, evaluating and implementing technology or work methods must be separate from the daily business by different timelines, budget, skills and goals. Time pressure could result in superficial testing, too little flexibility, and therefore may cause a project to fail. In many business environments, innovative projects are therefore carried out by different profiles than those involved in the key activities. Running the core activities requires precise work, sticking to robust procedures, working in a reliable context, while innovation needs flexibility, creativity and being able to adapt to unexpected developments.

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It is essential that this distinction is clear to staff and users. In reality, though, the staff members who are providing the daily service are also involved in testing and implementing novel technologies. When a core facility embarks on technology and methods development, there are different degrees of organization: either development is carried out by different people than the ones that do the service, or all core members have development projects and allocate a dedicated time to this separate from their service tasks. Regardless of how it is structured, the bottom line is that service and innovation are different assignments.

One also has to realize that the criteria to evaluate innovation are different from those used to score standard service. Unlike for routine service, a so-called negative outcome—in the sense that it may not result in a final product or method—is not necessarily a failure in innovation projects, because the end goal is not necessarily to "get a job done" but to acquire knowledge and experience. This requires a different mindset and for most core facilities a change in culture.

Even if a facility has a clear outline for an innovation project with all operational means to carry it out, innovation requires dedicated management. This is different from managing the daily business that has to focus on keeping on track, assuring quality, applying robust processes, and making operations run smoothly. Innovation management is not restricted to managing a project, but also calls for flexibility, ambition and co-operation from different parties. It needs a clear endorsement from everyone involved, as well as other levels within the organization. It is hard to achieve if the social culture is not ready for it; it is the support from the entire facility that is necessary to make it a success.

Managing innovation

Innovation management has many facets that need to be brought together: this entails strategic planning, the right skills in a team, the necessary infrastructure and project management. Other, less rational factors that are required to move the project forward are maintaining partnerships, team spirit and motivation and support from all levels in an organization. For a core facility, this means that the scientists, the core staff and management endorse innovation as one of its tasks. Endorsements are difficult to translate into measurable and rational means but can become more obvious from clear mandates and expectations.

The challenge is to bring all these aspects and factors together in a balanced manner. If one or several factors are not sufficiently appreciated, innovation has little chance of succeeding. The timing of bringing all these elements together is crucial too. Ideas that are implemented too soon may flounder and lose support, while missing the boat is a recipe for becoming redundant. Momentum and preparing for innovation are very much intertwined and can steer each other.

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Nokia is a textbook example of such a failure although all ingredients for successful innovation were available. Until 2007, Nokia dominated the mobile phone market with a share close to 70% until Apple introduced the iPhone and quickly came to dominate the new smartphone market. The rapid downfall from a globally dominant and innovative telecommunications company has of course several reasons, but some are clearly related to a lack of innovation. Nokia had been focussing on technological know-how and optimizing production and marketing, but failed to recognize that the market shifted towards mobile devices to access the Internet along with online services and mobile phone apps. Furthermore, Nokia's leadership failed to translate their strategic insights on disruptive innovations and technological developments into new products until it was too late. They were not able to foster a culture of innovation based on customer demand when the disruptive technology of the smartphone became available.

Another illustrative example is the cascade of innovations in sequencing after the completion of the human genome sequence. It took 10 years and US$ 2.7 billion, and profoundly changed the life sciences. Suddenly, this breakthrough impacted all stakeholders: scientists, core facilities and especially sequencing companies. The market potential for technology providers was huge, but so was competition. The challenge was to introduce a new sequencing technology as quickly as possible without jeopardizing ease of use and quality. Several companies—Roche, Life Technologies, Pacific Biosciences, Illumina and Oxford Nanopores—entered the market within a few years, which made it difficult for core facilities to implement the right platform(s) at the time. Sequencing facilities had to convince their institutional management to invest in highly expensive platforms with price tags as high as 1 million €, train their staff at unprecedented speed, find out which particular platforms would withstand competition over time, and handle the massive cost that comes along with the rapid turnover of these platforms. The complexity was so high—as was the speed at which this happened—that to be successful, a core had to have all innovation elements right at once to survive. Those who made it went through a speed-course of innovation and are likely well prepared for the next innovation wave that single-cell approaches will bring along. For the sequencing companies, the battle was even harder: so far, Illumina succeeded with a 75% market share, but it is challenged by Oxford Nanopores and others.

Outlook

Life science research has made enormous progress during the past decades, and core facilities have been an integral part of it. The completion of the Human Genome Project represented a profound disruption for the life sciences with a focus on high-throughput data generation and analysis. The vast increase in technology-demanding projects requested the set-up of centralized state-of-the-art core facilities. Initially, their main task was to facilitate access to sophisticated technology platforms, either as an open-access facility or by generating data as a service. Over the past 10 years, the focus shifted to an all-in service model where the core often acts as a consultant for a whole experimental workflow. Nowadays, core facilities are also asked to innovate to create new methods and applications together with the PIs. This is not an easy task and requires a cultural change to handle all aspects of innovation equally well.

In a conservative environment, innovation is frequently slowed down; it is therefore necessary to establish an open innovation ecosystem that relies on the complementary strengths of different actors. Here, the user often plays a central role and liaises expertise from cores with tech providers. Leading institutes have realized that innovation has become a novel and extra mandate for their cores on top of the daily service activities. Not to

Box 1: Where to innovate?

Several facets of a core facility can lead to innovation. For device-driven services, the obvious subjects for innovation are the devices that can be improved or adapted for specific applications. Methods also require innovation [10]. Sequential innovations of workflows can help to determine the full potential of a technique to generate the final data set or deliverable, for instance, preparation of 3D organoids in transgenic facilities or optimization of CRISPR/CAS gateways in protein cores.

On a different level, core facilities may have to change their working model from handling specific devices to an all-in-one service that covers a whole workflow from experimental design to data analysis. While originally, the specifications of the equipment park determined the value of a facility, nowadays, more value is created from the expertise of the team. A specific challenge is to determine the best working model for new applications that emerge from combining different existing technologies and expertise across core facilities.

With the focus on expert knowledge, the relationship between the core and the principal investigators will shift from a service–user interaction to a collaboration in which both parties equally share their expertise. This entails that a facility must change its mindset: instead of keeping all the know-how locked in house, it will become more valuable when it shares its knowledge.

innovate is no longer an option if you want to stay in the game.

Conflict of interest

The authors declare that they have no conflict of interest.

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