12. Innovation and Translation

Introduction

One of EMBL's core missions is the development and transfer of know-how and technologies to academia and to industry and commercial entities in order to facilitate further research, innovations, and commercialisation for the benefit of society at large. To fulfil this mission, a range of activities and interactions between EMBL scientists, industry, and other academic institutes are needed, from investment and support of spin-out companies to the development of partnerships with industry in order to develop technology further and for knowledge-exchange.

The technology transfer activities of EMBL are carried out exclusively by EMBLEM Technology Transfer GmbH (EMBLEM), the wholly-owned limited liability company of the Laboratory. Established in 1999, EMBLEM identifies, protects, and commercialises intellectual property developed at EMBL, by EMBL alumni, and by third parties. Together with the associated venture capital fund, managed by EMBL Ventures, EMBLEM also helps in the structuring, creation, and financing of start-up companies in the life sciences in any of the EMBL member states. The proactive and comprehensive technology transfer approach (e.g. licence, collaboration, service, public-private partnerships, start-up creation, proof of concept, and venture-capital funding), closely matched to EMBL's research areas, ensures the rapid commercial development of promising innovations while concomitantly securing the free dissemination of knowledge for basic research purposes.

Throughout this scientific Programme, EMBL intends to:

- Strengthen and expand key innovation and translation activities, both individually and by bridging with local and national networks;
- Expand successful mechanisms to encompass the proposed new research directions

The overarching goal is to ensure that the promising inventions and technologies from EMBL are developed to commercial maturity to benefit scientific endeavour and society. A range of instruments enable the transfer of such technologies including the creation of spin-outs, licensing, public-private partnerships, industry-sponsored research collaborations, knowledge-exchange programmes, and access to public funding programmes.

Building a Portfolio of Innovation and Commercialisation Activities

A number of technologies developed at EMBL have created substantial socio-economic impact throughout recent years. The success of the technology development and transfer activities is reflected not only in the solid development of key performance indicators (Table IT1) but also in more than 400 satisfied commercial licensees of EMBL technologies, more than half of whom are recurring customers interested in establishing a long-term relationship with EMBL and EMBLEM. EMBLEM also manages a portfolio of 150 copyrights and trademarks, over 100 patent families comprising more than 400 individual granted patents and patent applications, and 22 spin-out companies. More than 1,000 EMBL scientists are on record as inventors with over 1,000 invention records.

Table IT1 | EMBLEM Technology Transfer in numbers (2015–2019).

	2015	2016	2017	2018	2019	Total (2015 - 2019)
Income (k€)	8,322	8,364	9,879	11,287	12,160	50,012
Licence & Collaboration Agreement Concluded	318	353	410	365	435	1,881
Invention Disclosures	43	45	36	38	34	196
Priority Patent Application Filed	19	20	23	28	20	110
Copyrights	1	1	1	3	0	6
Patents Granted	19	20	23	28	20	110
Patent Families Reassigned	3	6	2	7	5	23
Gross Patent Costs (k€)	557	677	745	801	819	3,599
Patent Cost Recovered (k€)	254	407	394	355	283	1,693
Net Patent Cost(s) (k€)	303	270	351	446	535	1,905
Spin-offs Created	2	0	1	0	3	6

Four spin-out companies have been incorporated during 2017–2019, creating more than 20 jobs in Heidelberg and Grenoble and raising more than €7 million external investments. Three of the four provide scientific services for the scientific community (both academic and industry) based on platform technologies developed at EMBL. For example, the pioneering spin-out company **Velabs Therapeutics**, launched in December 2017, makes accessible microfluidics technology which allows for fast functional screening of antibodies from natural sources against difficult targets (Figure IT2). The high-throughput screening platform allows for the testing of millions of correctly paired fully natural IgGs from humans and mice for therapeutic effects, rather than just for binding. Velabs offers customised screening services for users worldwide. Besides carrying out service projects, the company also works on establishing a proprietary pipeline of therapeutic antibody candidates and further developing the technology platform.

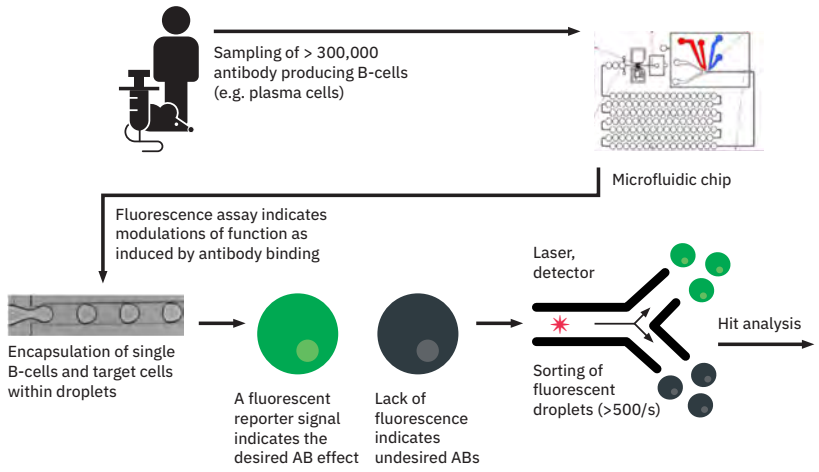

Figure IT2 | Velabs' Droplet Microfluidic Technology.

Velabs technology allows for small amounts of starting material (e.g. patient-derived samples) to be reliably analysed to rapidly generate antibodies against target molecules presented on cellular membrane surfaces or as soluble drug targets.

Similarly, **Araxa Biosciences** was founded in August 2019 to offer protein engineering services for medical, research, and biomaterial applications via a novel platform which paves new ways for the development of highly specific antibody-drug conjugates (ADC) or -radioisotope analogs. In October 2019, **Suricube** was incorporated to commercialise instrument control hardware and software, which allows for highly modular and versatile control of microscopes and other scientific instruments. The design has already been implemented successfully in the commercially available light-sheet microscopy provided by the EMBL spin-out company LUXENDO.

EMBL has also created spin-out companies that focus on the provision of scientific services to industry such as **ALPX** (Figure IT3). The CrystalDirect technology enables full automation of the crystal harvesting process. ALPX was established to provide CrystalDirect for routine services in macromolecular crystallography to pharma companies, enabling them to pursue structure-based drug development at unprecedented speed and quality.

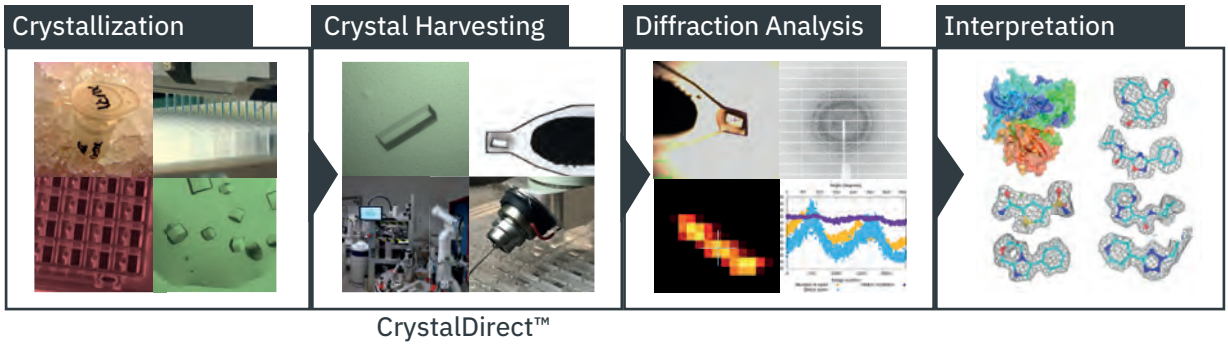

Figure IT3 | ALPX Smart crystallography.
Automated protein crystallography for new structures and small molecule screening. Accelerating structure-based drug discovery using unique EMBL proprietary technologies CRIMS and CrystalDirect.

As EMBL pursues new avenues of research, new technologies and results will be generated. For example, projects within the planetary biology theme may potentially generate new sensors for environmental measurements, biomarkers that can enable evaluations of ecosystem collapse, as well as software and databases that allow for the modelling of ecosystems. Similarly, knowledge about the environmental impacts (physical, biological and social environments) on human phenotypes (Chapter 6: Human Ecosystems), including interactions between pathogens and their human hosts (Chapter 5: Infection Biology), can give rise to novel diagnostics, therapies, and prophylactic measures. Mechanistic understanding about cellular and multicellular systems (Chapter 3: Cellular and Multicellular Dynamics) and the causal relationships behind dynamic changes in tissue structure and morphology and the functional units within the cell and their molecular interactions (gene regulation, metabolism, protein control etc.) in the context of their environments (Chapter 2: Molecular Building Blocks in Context) will stimulate a number of ambitious scientific, medical, and ecological questions to be answered.

An area that will see significant growth in the next few years will be the modulation of the microbiome for the treatment of major human diseases such as infectious diseases, liver diseases, gastrointestinal cancers, metabolic diseases, respiratory diseases, mental or psychological diseases, and autoimmune diseases. In addition, the movement towards a more circular economy and rising concerns regarding sustainability and pollution have also seen significant investments in bioremediation strategies to discover naturally occurring or artificially introduced microorganisms to break down the environmental pollutants to reduce environmental toxicology. Novel enzymes from the mining of metagenomics data, prevention strategies for antibiotic resistance spread, and potential new therapies stimulated by an increased understanding of

bacterial communities as well as their interaction with the human host (Chapter 4: Microbial Ecosystems) are very much needed for microbiome science to have a true industrial and clinical impact.

The commercial potential of these developments can lead to out-licensing to commercial partners or the creation of new spin-out agreements that focus on therapies, prevention strategies or enabling technologies. EMBL will continue to build intellectual property portfolios around key areas of EMBL expertise with specific focus on enabling platform technologies and seamless services. EMBLEM will also actively source inventions and technologies from these new fields and seek to understand market needs through engagement with key stakeholders in the relevant industries, participation in sector-specific conferences/partnering events, and by organising EMBL-industry science days with companies in these sectors, all of which will enable out-licensing. EMBL investments (via the established EMBLEM Technology Development Fund) for proof-of-concept funding of innovations are also essential to rapidly validate, prototype, and develop research results prior to investment by commercial partners. These investments enable development of innovations that are past the lab bench yet are still too early to be embraced by commercial partners, bridging the so-called valley of death and capturing value creation for EMBL and the member states. EMBL's scientific discoveries, knowledge, and evidence in the new areas will be strategically communicated to policymakers (Chapter 15: Public Engagement, Communications, and Outreach). Knowledge-transfer between scientists and policymakers is not only key for evidence-based decision making but it is also an important mechanism for building bridges between experts on all sides.

Expanding Collaboration via Strategic Partnerships

Scientific collaboration agreements between EMBL scientists and industry play a central role in translational science and additional efforts will be made in the next five-year period to trigger more collaborations and expand existing partnerships.

New Public-private Partnerships

Large-scale public-private partnerships (PPPs) bring about increased capacity to research and develop new products and an enhanced reputation for cutting-edge technology development. EMBL and EMBLEM develop large multi-project, multi-partner, multi-year PPPs, each with budgets in excess of £1 million per year.

The first of these was **Open Targets**, a PPP established in 2014 to use extensive human genetics and genomics data to transform how drug targets are identified and prioritised. Open Targets started with EMBL-EBI, the Wellcome Sanger Institute, and GlaxoSmithKline (GSK) as founding partners and was subsequently joined by the pharmaceutical companies Biogen (2016), Takeda (2017), Celgene (2018), and Sanofi (2018). While initiated by EMBL-EBI, in 2018 collaboration opportunities were expanded to all researchers at all EMBL sites, thus bringing institute-wide opportunities to harness and translate research and genomic data/evidence into new medicines and therapies.

The partnership runs multi-partner projects in informatics, oncology, immunology, respiratory, and neurodegenerative disease that comprise a portfolio of more than 60 projects, 48 with EMBL involvement. Across EMBL more than 25 groups are actively engaged in Open Targets projects and more than 40 publications have resulted from Open Targets work, including three recent (2019) landmark publications on large-scale functional genomics studies in oncology and immunology.

Another EMBL drug discovery collaboration builds on the close interaction with Cellzome, an EMBL chemoproteomics spin-out company that was later acquired by GSK in 2012. The **EMBL and Cellzome-GSK**

alliance formed in 2017 aims to jointly develop and apply cutting-edge technologies to help address key questions in drug discovery, like which biological pathways to target and what drug candidate molecules to choose. The current framework comprises 12 collaborative projects in which 11 postdoctoral fellows and two PhD students work jointly across EMBL and GSK, co-funded by both organisations.

Current projects within this partnership include the application of cryo-electron microscopy in lead optimisation; the development of droplet microfluidics for the functional characterisation of antibodies modulating GPCRs; exploration of potential synergies of drug combinations for new antibiotic effects against *Shigella flexneri*, the cause of bacterial diarrhoea, shigellosis; and ion channels to explore how inhibition of the compound PI3Kdelta attenuates rhinovirus-induced damage of human COPD small airway epithelium *ex vivo*.

In the past two years, this collaboration has led to five joint publications in high impact journals with several more anticipated in 2020. The success of the collaboration is also demonstrated by the fact that GSK and EMBL agreed to expand the scientific footprint of GSK's presence on campus by the construction of a new research building that Cellzome-GSK will move into in 2021.

Partnerships for Innovation

As EMBL moves into new directions under the Molecules to Ecosystems Programme, EMBL aims to establish new single-sector PPPs with other pharmaceutical, agritech, biotech, and food industries. Modelled on the Open Targets experience, these new relationships will leverage and further expand existing collaborations with companies in the agritech, green chemistry and food industries (e.g. Unilever, Lesaffre, Nestlé, Bayer Cropsciences, Syngenta). This could lead to PPPs and collaborations that aim to develop solutions to address global societal challenges, including the development of novel antibiotics, carbon footprint reduction, plastic degradation, and bioremediation.

The experimental workflows and quantitative assays systems to study the dark proteome or the effects of environmental pollutants developed by the Chemical Biology Core Facility (Chapter 10: Scientific Services) will offer further opportunities for collaborations with the pharmaceutical, environmental, and energy sectors. Data and reagents generated during the process such as recombinant proteins, crystal structures with fragment hits, or validated probe molecules and associated activity data can enable a portfolio of intellectual property to be developed very early in the research process which, via EMBLEM, can form the basis of EMBL spin-outs.

Data Resources for Industry Use Cases

The use of public data resources such as those hosted by EMBL-EBI has been shown to have a large effect on the productivity of knowledge-driven organisations. From the industry perspective, this is especially true in organisations in the biomedical space, such as pharmaceutical companies, where the main drivers are the need to reduce the time-to-market and lower the costs of drug discovery. A 2015 independent survey of academic and industry users of EMBL-EBI's data resources found EMBL-EBI's public molecular data and services contribute benefits worth £920 million every year to the wider realisation of future research.

One of the major achievements of the Open Targets partnership is the development of the Open Targets Platform and more recently an accompanying Genetics Portal (Figure IT4). These provide comprehensive and robust data integration systems for access to and visualisation of potential drug targets associated with disease. Both platforms bring together multiple genetics and genomics data types from EMBL-EBI data

resources and other sources, to assist users in identifying and prioritising targets for further investigation. Other EMBL-EBI data resources have also arisen from industry requirements, including the Patient-Derived Xenograft Finder resource to capture patient-derived xenograft models and their data, and tools such as the Ontology LookUp Service. More recently, EMBL's COVID-19 Data Portal, launched in partnership with the European Commission, has proved vital for both industry as well as public health agencies, enabling the sharing of available research data, including DNA sequences, protein structures, data from pre-clinical research and clinical trials, and epidemiological data.

Industry-driven use cases can drive the development of new biology-specific portals that can be used by the entire scientific community. The combination of industry expertise with the deep research knowledge of academic scientists can enable significant scientific advances in open innovation. As data volumes grow, there are several opportunities for EMBL to work with many other industries that need to organise large, unstructured biomolecular data collections, in order to increase productivity and reduce the time to create new products. EMBL's experience in large international collaborations both for experimental research and for data coordination make EMBL a sought-after collaborator. With companies funding, analysing, and openly sharing health and agriculture resources such as the UK Biobank or the Reference Wheat Genome project, projects under human ecosystems and planetary biology will also be attractive to industry partners. The reengineering of EMBL-EBI data services, in coordination with industry partners, to support the greater degrees of integration required for industrial use cases, such as the proposed data platforms for microbial surveillance and functional data (Chapter 4: Microbial Ecosystems; and Chapter 5: Infection Biology), will result in benefits for all users internationally. EMBL aims to work with industry in sharing the challenges, resources, risks, and rewards, whilst also building the systems to turn these data into knowledge and then making them openly available for the scientific community to use. The Data Sciences strategy will also stimulate natural collaboration with AI companies and information technology sectors for methods development, computing, and storage infrastructure (Chapter 8: Data Sciences).

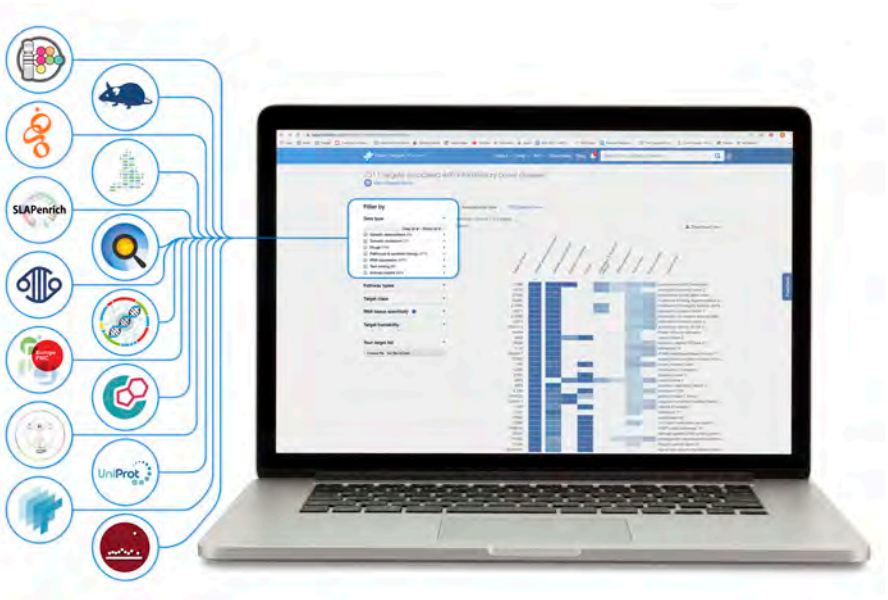

Figure IT4 | The Open Targets Platform.
The platform enables researchers to intuitively search for genetic and other evidence that links a gene (drug target) to a disease. Multiple data types from various sources (left) for genetic associations, somatic mutations, drugs, pathways and systems biology, RNA expression, text mining, and animal models are made interoperable and integrated to be available via a single portal.

Partnerships for Technology Development

EMBL has a long history of engaging in collaborations with technology companies that enable the industry partner to test the value of EMBL technology platforms (e.g. in core facilities) for their own R&D or generate proof of concepts for future development of new products. There is much value in such individual, bespoke projects since they allow rapid prototyping or the fast delivery of solutions to industrial partners. Equally, they provide value for the scientific community at large as results are published jointly or, if data is an output, that data is released into the public domain.

Building on such collaborations, EMBL aims to expand existing strategic partnerships with technology companies into the new research fields in order to develop new sample preparation methods, instrumentation, workflows, analytics and associated data resources. These partnerships would not only support EMBL's technological leadership, they would also increase the visibility and attractiveness of EMBL to other professionals such as mechanical and electrical engineers, physicists, chemists, and software developers, thus cross-fertilising across the entire EMBL community and increasing interdisciplinarity. Efficient commercialisation strategies of newly developed technology and workflows, dependent on how IP was generated (jointly with the involved industry partner or independently via spin-out companies), will also need to be created to realise the broadest dissemination of new technologies most effectively.

EMBL Imaging Centre Partnerships

Part of the technology development vision for the upcoming EMBL Imaging Centre, currently under construction at the EMBL campus in Heidelberg, is to be the European Hub for introducing the latest pre-commercial imaging technologies to ground-breaking life sciences applications. EMBL has already partnered with industrial partners (currently Leica, Carl Zeiss, Thermo Fisher Scientific, Abberior Instruments; interest by Bruker) to drive early-stage next-generation technologies from industry with biological applications, leading to the development of new instruments and methods. Another example of open innovation at EMBL, this novel model of collaboration with industry aims to drive longer term partnerships and framework agreements. It also provides a great opportunity to mobilise funding for such PPPs from the European Commission under the framework of the new Innovative Medicines Initiative (IMI) programme that explicitly wants to broaden to the imaging sector. These partnerships will also benefit from close relationships with EMBL research groups that develop new microscopy technologies and applications, ranging from novel sample preparation, via single instrumentation development and workflow development to correlate/integrate several instruments, to novel image analysis tools, enabling new biological applications as early as possible to a broad user community.

Going forward, there is also a pressing need to bring genomics, imaging, and engineering together to spark the next wave of biological breakthroughs. EMBL's unique mix of cutting-edge expertise at the forefront of genomics and imaging technology in combination with long-standing industry collaborations stands to advance genomics methods and biological discovery. Workshops that embed engineers and genomics specialists within laboratory space will stimulate unique co-developments in this area, in addition to potential new intellectual property.

Multi-sector PPPs

Multi-sector PPPs for the development of integrated technologies suitable in different application areas (e.g. to tackle climate change, pollution, or antimicrobial resistance) can also be envisaged. The United Nations Sustainable Development Goals have served as a rallying point, bringing together academics, NGOs, social entrepreneurs, companies and governments to develop solutions. Multi-sector PPPs could be structured as

a core partnership between EMBL and technology companies onto which application-oriented partnerships with companies (pharma, environmental management, agritech) could be docked as satellites.

The outcome of the developments pursued under these partnerships would include new technologies for better molecular understanding of ecosystems. The results would not only lead to significant socio-economic impact via the generation of new products and technologies exploited either by the collaboration partners or via EMBL start-ups created from these partnerships, but would also concomitantly strengthen all other EMBL missions by impacting on scientific publications, training, and development of new scientific services.

Developing an EMBL Innovation Culture

EMBL also intends to continue fostering a vibrant innovation culture across the organisation. The scientific culture at EMBL is rooted in an ambition to conduct and enable truly excellent research. The EMBL-wide appetite for investigation and excellence, paired with a necessary acceptance of risk and failure, has led to impactful discoveries which have notable scientific and societal benefits (Chapter 1: Introduction). This approach and culture will be encouraged across EMBL's missions and research areas, with a renewed focus on innovation. An entrepreneurial and risk-taking spirit will ensure people within EMBL are empowered and equipped to be creative, collaborative and innovative. To foster an innovation culture at EMBL, novel training formats and topic areas, collaborative space (both physically and figuratively), cross-border and cross-sector expertise and networks, and a widespread encouragement to be visionary need to be nurtured. Particularly in light of EMBL's new scientific research directions, it is imperative that people at EMBL are capable and inspired to be innovative to drive scientific discovery which in turn can lead to essential planetary health impacts.

As well as growing initiatives, EMBL plans to implement a number of new activities which seek to facilitate a mindset and culture change that will lead EMBL towards an innovation ecosystem and increase impact (Figure IT5). These activities include learning from industry and commercial leaders drawn from EMBL's expansive network of corporate partners and connections via an annual lecture series, career development support, as well as networking events (Chapter 11: Training). EMBL alumni who are entrepreneurs or hold positions in industry can be instrumental in sharing and increasing appreciation of additional research paths available to EMBL scientists that connect EMBL science to innovation and translation. Competitions to spur start-up ideas as well as hackathon-type events that enable EMBL researchers and industry scientists to tackle cutting-edge scientific challenges can also stimulate new ideas and approaches as well as increase awareness and engagement. EMBL's new **Career Accelerator for Research Infrastructure Scientists (ARISE)** programme is a novel training programme for future research infrastructure (RI) scientists (Chapter 11: Training; and Chapter 14: People, Processes, and Places). Through the ARISE programme, the RI scientist will have the opportunity to mutually benefit from **intersectoral secondments** with industry partners (Figure IT5).

Going forward, EMBL plans to further engage with biotech hubs at EMBL sites, working with regional networks such as BioRN in Heidelberg, the DESY innovation campus in Hamburg, and organisations such as the Cambridge New Therapeutics Forum in Cambridge UK to increase industry links.

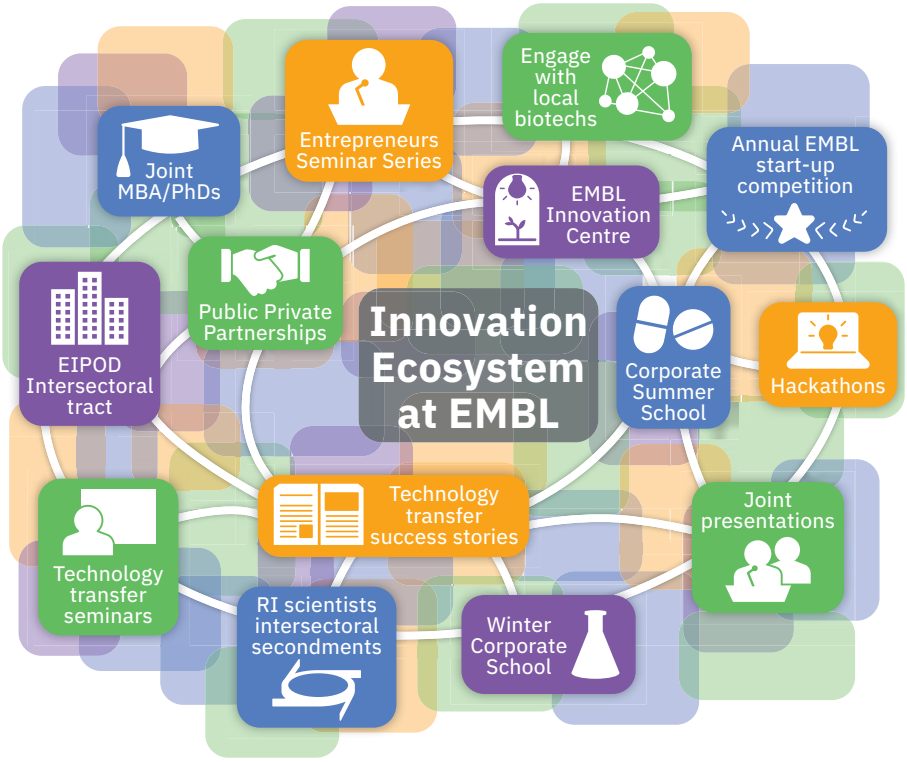

Figure IT5 | Towards an Innovative Ecosystem at EMBL.
EMBL plans to implement a number of new activities and strengthen existing ones which seek to facilitate a mindset and culture change that will lead EMBL towards an innovation ecosystem and increase impact.

Empowering the Generation of EMBL Fellows

The EMBL Interdisciplinary Postdocs (EIPOD) initiative includes an **intersectoral tract** which is designed to foster exposure to the applied/commercial side of science (Chapter 11: Training). These interdisciplinary research projects involve an EMBL supervisor who acts as the coordinator, another EMBL group leader at another site, and either one industry partner or active involvement of the EIPOD in IP generation, out-licensing and, if applicable, in the first steps towards a spin-out activity. EIPODs can also participate in the **Corporate Summer School** module which involves lecturers from industry (Figure IT5). The module is aimed at giving the participants a broad overview of the life sciences industry from start-ups to big pharma, insights into the product development pipeline in different life sciences sectors, and some understanding of how research is done in industry.

In addition to a non-academic internship programme for predoctoral fellows, EMBL will cooperate with various local business schools to establish a curriculum that will allow selected predoctoral fellows to pursue an **MBA/PhD** (Chapter 11: Training). This is an ambitious project that EMBL will undertake in order to train the next generation of industry leaders and entrepreneurs. EMBL's **Winter Corporate School** also offers PhD students insights into different, non-academic career options. The course provides a wide-ranging overview of R&D in large pharma companies and some practical training for starting up a business (Figure IT5). A broad range of speakers come to EMBL to share their knowledge and experience of life sciences R&D. The course addresses the growing need of PhD students in life sciences to be informed and prepared for a variety of career options after their PhD.

Co-location

One of the key factors for the success of the Open Targets collaboration is the co-location of academic and industry researchers to jointly work on projects, with core project personnel physically located together in dedicated innovation and translation space within the EMBL-EBI facilities. This allows for an intense exchange of ideas and access to specialist expertise and knowledge which tangibly increases the efficiency and delivery of consortia projects. Co-location also leads to intangible secondary benefits for EMBL researchers. The direct exposure to industry science has enabled greater career mobility between academia and industry, with national companies benefiting from EMBL's turnover scheme.

To spur innovation development and translation opportunities generated by the new EMBL Programme, EMBL plans to develop dedicated infrastructure. One to two new EMBL spin-out companies are established from EMBL annually. Initially, for the first three years maximum, these spin-outs need to be located on site, close to the mother laboratories from which the technology/intellectual property derives in order to ensure a rapid knowledge transfer and future development(s). It is envisaged that the **EMBL Heidelberg Innovation Centre** will host large PPPs, spin-out companies out of EMBL (incubator), proof-of-concept projects, academia-industry collaborations, technology developments, and industry placements.

Training and Knowledge Exchange

Companies also benefit from EMBL's external training, both the Course and Conference and Scientific Visitor programmes. Technology **training courses** are also jointly organised by EMBL Core Facilities and technology companies with students from academia or industry. Technology companies contribute financial resources, equipment, reagents, and training experts for training in cutting-edge technologies and applications.

EMBL-EBI's subscription-based **Industry Programme** serves large multinational companies, which are significant users of EMBL-EBI's bioinformatics resources and benefit from a bespoke programme of **bioinformatics workshops**. With a current membership of over 20 companies representing most of the top pharmaceutical companies as well as several major agri-food, nutrition, and healthcare companies, the scheme has been an important and vibrant part of EMBL-EBI since 1996. The annual programme of workshops, hackathons, and tailored tutorials aids help companies keep abreast of innovations in EMBL-EBI service provision and, at the same time, helps EMBL-EBI remain agile in meeting the needs of the fast-moving data-driven industrial R&D (Figure IT5).

Within the new EMBL Programme, there will be increased demand from companies within the member states across sectors to learn from and benefit from EMBL expert scientists and service providers. Due to the complexity of these emergent scientific areas, **secondments within academia** are seen as an agile mechanism to boost the skills, knowledge and career development for industry scientists. EMBL, with its missions in research, service and training, is in a unique position in Europe to be able to provide these opportunities and not just intensify knowledge exchange between industry and academia, but also add value to the life sciences sector and the European economy by increasing productivity.

Sharing **best practices in technology transfer and open innovation collaboration** strategies is an important contribution by EMBL to the scientific community, especially for member states. EMBL and EMBLEM will continue to do this via provision of on-site and off-site training and advice for research institutes in member states, internships with EMBLEM, as well as participation in the Horizon Europe Open Innovation pillar to help the EU become a leader in breakthrough innovations in the health and environmental sectors.