Preface

Modern science is a discovery as well as an invention

—J.L. Heilbron

Progress in science can emerge in many different ways. Even when a research project, a technical development, or a scientific theory is rejected or replaced, progress is present in the sense of the refinement of the path in the quest for wider and more accurate knowledge and understanding of nature.

A traditional debate juxtaposing basic research—the fundamental scientific activity not intended to achieve a specific practical purpose—and applied research—the scientific activity aimed at producing tangible results—was once ongoing within the scientific community because the two types of research were pursued in spheres and often not interlinked to each other, even in cases when they should have been. However, interdisciplinarity has always existed in science, though the speed of knowledge exchange pertinent to the dissemination of progress has been limited by the available means of communication at any given moment. An illustrative example could be the development of NASA's—and the equivalent former Soviet Union's apparatus—vast space programme in the closing decades of the twentieth century: undoubtedly, innumerable contributions from many scientific disciplines—from basic to applied—were needed to finally accomplish one of the oldest dreams of humanity: reaching outer space. Or, going back forty-six centuries in time, one can also consider the construction of the Giza Pyramids; such a magnificent result can only be envisaged with the participation of the most advanced science (innovative engineering, new materials, evolved communications… even applied astronomy) of that era, and surely with highly qualified and motivated project managers and technical planners. In both cases, of course, a major injection of financial support had to be made and administrated from different coordinated origins with a common final objective.

Nowadays, most scientists agree in the need of sustaining basic research as a source of potential new applications for Science and the final recipients of the results, being individuals, organizations or Society as a whole. Furthermore, it is commonly assumed that—due to the intrinsic complexity, increasing specialization and specific features of each of the stages related to a scientific development—the process has to be fragmented and performed by different stakeholders in order to become more efficient. *Efficiency* in Science means minimizing the resources needed to get a result and having the vision to keep the project under way if some collateral discovery could arise. So, in terms of scientific management, productivity as a straight measure of efficiency has to commune with the capability to anticipate opportunities. And specialization appears to be a natural process to extend the scientific impact to the very last of the aspects of the world. Any of the general branches in science is currently divided in a myriad of subcategories that form a very intricate system indeed, but this is not a negative fact as far as it *forces* researchers to focus on a very specific field of discovery and try to sort out the very last of its hidden secrets—or find out new ones to be studied—in an iterated and cumulative process. This, in opposite to previous periods when scientists used to work on wider areas of knowledge at the same time, is only possible when the critical mass of dedicated staff is large enough and the resources devoted to the progress of science are sufficient. Even the most recent discipline in applied science, Nanotechnology, has already deployed the usual range in subdivisions of activities: nanomedicine, nanochemistry, nanomaterials, nanoelectronics, nanophotonics, nanometrology. Thus, the research system is developed by diverse players that go from individuals to the biggest companies, governments or even transnational organizations, creating a global net of synergies that boost research, both basic and applied, to a point never known before. It is in this rich discovery and innovation ecosystem that the different stakeholders match their role in the big picture regarding their dimension, purpose, sustainability, objectives and interests. Moreover, the instant access to gigantic online contents on a given research provides the mechanism to facilitate the complementarity of research lines and projects: it becomes possible to reach a global view on the state of the art of a subject and check whether a scientific development is expected to contribute to the progress in that specific matter prior to starting the project.

Let us give an example related to the content of this book to illustrate the interaction among activities inside medical research that has been a standard for the last 50 years: the drug discovery process.

It takes 10–15 years for a compound to reach the market in the form of a new drug, after several screening stages—each one of them perfectly regulated and controlled—that refuses 10.000 former candidates as an average. This process involves all the range of scientific possible scientific actors from most basic research to final marketers and needs of a total investment of around 1 billion euros. (DiMasi JA, Grabowski HG. R&D Costs and returns to new drug development: a review of the evidence. In The Oxford Handbook of The Economics of the Biopharmaceutical Industry. eds. PM Danzon and S Nicholson, 2012, chapter 2:21–46. Oxford, UK: Oxford University Press). The number of novel new drugs approval by FDA averages 25 per year in the period 2005–2013 (US Food and Drug Administration, Center for Drug Evaluation and Research, Novel New Drugs 2014 Summary, 2015). General schematic of time range related to drug discovery

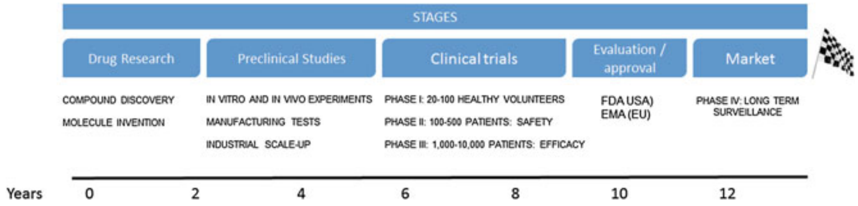

Fig. 1 Drug discovery stages *Image* Endor Nanotechnologies

and use in the market is given in Fig. 1, according to practical experience by Endor Nanotechnologies, company that has business precisely in the area of drug discovery.

The main stakeholders in the drug discovery value chain take their role in the play where they can contribute properly:

- Academia. The general source for the discovery and invention of compounds. A continuous feed of new development possibilities. At this stage, the market is several years ahead, so the scope of the projects relies on excellence in science and widening the technical frontiers beyond current limits.
- Universities. The organizations that bring academic discoveries to a formal stage. Usually, first intellectual property protection for basic developments is carried out at Universities. When a technology transfer office is present, not only IP registration and follow-up are done but also commercial negotiations on developments suitable for exploitation by the rest of organizations involved in the drug delivery process. In this case, the interest for the industry is gaining early access to potential disruptive compounds at a lesser cost compared to more advanced stages.
- Spin-offs/start-ups: Both concepts are applied in many different ways and variations (university spin-off, tech-based start-up, J.M Beraza Garmendia/ A. Rodríguez Castellanos), and currently in a much vaster and more flexible sense. For the scope of this introduction, the assumption is that the act of ‘starting up’ is wider and inclusive of ‘spinning-off’ (this is, *starting up* from an already existing organization) and, at last, the role and place in the value chain is equal not regarding nomenclature. Thus, here the term ‘start-up’ tries to sum up complementary concepts: a university-born entrepreneurial initiative to take benefit of an advanced knowledge representing a clear innovation, with a critical potential impact in the market, often in the initial form of a micro-small private company. The typical role of this kind of start-up company in the drug development process is completing the preclinical and/or Phase I of the development.
- Investors, funders. Regarding the project stage, there are different denominations for the funding partakers: *Seed Capital, Business Angels, Venture Capital…* They bring financial support and often business counselling from initial start-up investments to the next expansion financing rounds up to the first public offering of shares. These specialized professionals used to have a

peripheral vision of the whole sector they invest in and can boost synergies in several areas while participating in the decision boards of their invested companies. Crowd funding is a peculiar new way of reaching financial resources from granular small contributions instead of a one-time, one-source disbursement, and specific online platforms for drug development funding have emerged recently.

- Contract research organizations (CROs). CROs play a central role in the whole chain of the drug development. They usually complement the areas of activities that are not in the core of the research company and can be outsourced to these specialised organizations: regulatory affairs, industrial scalation, clinical trials, market studies; they can collaborate with any of the other stakeholders involved in the development.
- National/Transnational Official Agencies. Any new drug going into the market has to be approved for human use by the official agency that holds the authority over the drug commercialization. The process for approval may vary in every country, but the aim is to keep a close control on the marketed products. This is inclusive of potential long-term undesired side effects, toxicology surveillance and alert protocols in the case of a serious issue affecting patients. The two main agencies that lead the regulatory affairs worldwide are the FDA (Food and Drug Administration) in the USA and the EMA (European Medicine Agency) in the European Union.
- Pharma companies/industry. The pharmaceutical market holds one of the highest volume in sales worldwide. In 2011, the global revenues for this market surpassed $1.000 billion for the first time. The industry is not only interested in brand new developments but also reprofiling and repositioning, pertaining to the different further applications of drugs initially developed for a specific different therapy. Moreover, among pharmaceutical companies providing generic drugs (those with expired patents and thus available for open manufacturing and selling), the business opportunity is still heavily present. A pharmaceutical company can become a licensee in any of the stages of the development, depending on the degree of innovation, effectiveness or business potential can be seen.

On a very different way, the discovery of graphene in 2004 at a university laboratory (Electric Field Effect in Atomically Thin Carbon Films. K.S. Novoselov, A.K. Geim, S.V. Morozov, D. Jiang, Y. Zhang, S.V. Dubonos, I.V. Grigorieva, A.A. Firsov, 2004) was not exactly what we could call a standard process. It is indeed a good example of how basic research on a novel material that started appearing in scientific literature by 1947 in a conceptual level (The Band Theory of Graphite Phys. Rev. 71, 622. P. R. Wallace. 1947) becomes one of the most promising industrial applications beyond fundamental nanotechnology. So promising that the European Union launched its *biggest ever research initiative* called Graphene Flagship in 2014 involving 142 partners in 23 countries by 2015. The consortium behind the organization is, again, composed by stakeholders from university to big industries, including start-ups that have just been founded for the production and processing of graphene itself.

So, it is a general feature that in any activity concerning discovery, new applications and innovation a start-up niche appears. Thus, we should consider what is the role and the reason for a start-up to be created and why is it such a common thing to happen in the university environment. Start-ups aim at transforming conceptual research and basic development into applied innovation. They are the links that allow university research groups to step into the market, since as far as usually, regarding local dispositions, a university itself cannot act as direct promoter, founder or shareholder of an independent private company. Additionally, start-ups can bring to light the rich flow of intellectual knowledge originated in public organizations which are usually left on standby for an applied advance. The dimensional advantage from this point of view is crucial—no big investment nor infrastructure is needed to start-up—just one single potential innovation, a balanced combination of will and intelligence and, possibly, a little bit of good luck, or let us say 'opportunity'. The key point in this know-how transfer system to expand is the high iteration speed: as far as in a start-up ecosystem a business idea can become an incorporated company in a matter of days, this helped by the favourable environment given by Universities and Science Parks themselves. The same ecosystem is quick and efficient in *clearing* start-ups that do not find a demanding match for their offer: the failure rate is very sharp among start-ups. It is a high-risk bet and a very volatile environment. If repeated time after time, once in a while a start-up succeeds in going beyond the survival point, growing rapidly and turning into, or being sold to a big company and an example, as well as an incentive, for new similar initiatives. Because when a start-up succeeds, it is a really big deal. These are just a few of the several so-called *unicorns* in the recent years, start-ups that have achieved a post-money valuation of at least 1 billion dollars. The post-money valuation is the value of the company after a new private investment round or at the completion of the Initial Public Offer—IPO—at the stock market. It fixes the number of equity shares gained by every shareholder after the increase of capital (Table 1).

One of the singularities concerning start-ups is the way of financing the first steps into autonomous activity. This is usually the wage for the first employee and the very least operative expenses concerning basic administration. No traditional financing formula from banks can easily be achieved, regarding two main reasons: a high-risk business plan and no historical backup from the lender's point of view. At this stage, funds support from other organizations rather than banks is crucial. Company Incubators, Science Parks, Technology Transfer Offices, Public Institutions, Private Investors (Seed Capital, Business Angels, Venture Capital, Big Companies, etc.) play a fundamental role in keeping the source of new start-ups flowing. And the shorter the way from the business idea to the market application, and the bigger the market, the easier and faster financial resources can be achieved and multiplied.

This particular aspect—the importance of the expected time to market—can be observed in the profile of the projects granted by the European Union through the Frame Programmes for Research, Development an Innovation and its evolution.

Table 1 *Unicorns* from different countries and industries, listed by the year of foundation

Company	Area of activity	Year of foundation	Country of origin
Vertex Pharmaceuticals	Pharmaceutical	1989	USA
Avast	Software	1991	Czech Republic
Skyscanner	Travel	2001	UK
Portola Pharmaceuticals	Biopharmaceutical	2003	USA
BlaBlaCar	Transportation	2004	France
Mascoma	Biofuel	2005	USA
Spotify	Music streaming	2006	Sweden
Adyen	Financial services	2006	The Netherlands
Opfthotech corporation	Biopharmaceutical	2007	USA
Flipkart	E-commerce	2007	India
Dropbox	File hosting	2007	USA
Avito.ru	E-commerce	2007	Russia
Airbnb	Accommodation	2008	USA
Uber	Transportation	2009	USA
Kik	Communications	2009	Canada
Xiaomi	Electronics	2010	China
Ultragenyx Pharmaceutical	Biotechnology	2010	USA
Delivery Hero	Catering	2011	Germany
Global Fashion Group	E-commerce	2014	Luxemburg

The *7th Framework Programme for Research and Technological Development* that lasted from 2007 to 2013, assigned € 50.521 million assignated and included five general pillars: Cooperation, Ideas, People, Capacities and Nuclear Research. Mainly based on collaborative projects to join academia, research groups and industry to reinforce the strengths of the European Union on the topics that were considered of the major importance at the time the Frame Programme was designed. For the new Frame Programme, Horizon 2020, that will grant € 80.000 million and last from 2014 to 2020, directives show that the general aim is to grant projects that are closer to market than in the previous Frame Programme, using a specific indicator, the *Technology Readiness Levels*—TRL—to measure the distance between a development and the real application:

- TRL 1—basic principles observed
- TRL 2—technology concept formulated
- TRL 3—experimental proof of concept
- TRL 4—technology validated in laboratory
- TRL 5—technology validated in relevant environment
- TRL 6—technology demonstrated in relevant environment
- TRL 7—system prototype demonstration in operational environment
- TRL 8—system complete and qualified
- TRL 9—actual system proven in operational environment

Table 2 Horizon 2020 structure

Main pillars	Excellent science	Industrial leadership	Societal challenges
Areas	• European Research Council • Future and Emerging Technologies • Marie Sklodowska-Curie Actions • Research Infrastructures	• LEIT, Leadership in enabling and industrial technologies (ICT, Nano, new materials, Biotechnology and Space) • Acces to Risk Finance • Innovation in SMEs	• Health • Food • Energy • Transport • Climate • Inclusive Societies • Security
Transversal programmes	Spreading excellence Science for society European Institute of Innovation and Technology—EIT Joint Research Centre—JRC Euratom		
Industrial pilot (2015–2016)		Fast track to innovation	

Source European Commission H2020 website

What is more important, for the first time single Small and Medium Enterprises (SME), also including start-ups, can apply for individual grants to get funds for their projects in a competitive scheme with the rest of applicants. This tells us about the priority that the European policies bestow to the applied innovation and the kind of incentives to modulate the whole process of technological transfer to the industry. Just to mention the current pillars, Horizon 2020 deploys Excellent Science, Industrial Leadership and Societal Challenges (Table 2).

In conclusion: big companies willing to carry on with innovative projects cannot afford to be present in every little hidden corner of scientific activity, and in this niche is where small start-up companies arise and contribute with cutting-edge developments potentially interesting for the industry. This book is about that particular form of progress in Science.

This book is the result of the contributions from several experts and professionals in the matter, from academia to business managers and entrepreneurs. The focus is on practical aspects of the start-up role, conception and execution from a university environment, though many of the topics can be applied to other fields. We are including articles about some of the desirable features that a scientist that becomes an entrepreneur should have: creativity, flexibility, interdisciplinarity, simplicity and patience, along with willingness and knowledge to adopt innovation. The book covers the areas pertaining to the transfer of technology from research to society. When transferring technology, two main ways may arise: licensing out the further exploitation rights straight from the university departments to the industry and go together with the technology step beyond into market applications for products abd services development, through spin-off and start-up companies. This book has focused on the second process and stakeholders involved, and with several study cases from real life.

Profiles of research entrepreneurs are described, along with categories and the general characteristics of entrepreneurial infrastructure. Different phases of launching university ventures are presented, as well as currently perceived technology transfer systems, important practical considerations for Intellectual Property (IP) protection are included: legal and regulatory affairs, as part of the formal requirements for a business to adopt, complemented with IP rights and strategy aimed to protect and strengthen the know-how. Some aspects of new technologies and their impact on new entrepreneur activities and frameworks are considered since advancements in ICT and nanotechnologies have provided the most significant influence on rapid growth of start-ups nowadays. Within university environment, collaboration with industry and business sector is of the utmost importance for boosting entrepreneurship among young people and researchers to tranfer the technology to the market. New ICT solutions as a support to companies, especially small and medium enterprises (SMEs) can boost competitiveness.

Innovation towards real market product is especially important in nanotechnology where newly generated knowledge is still in laboratory stages, and many new issues can arise related to real applications and company foundation. However, successful stories of starting up a company in nanotechnology sector exist already and this is the novelty making our time. We believe that, beside general theoretical chapters, these successful stories about companies that were founded and do business based on research results are very important for young researchers and professionals willing to start up a tech-based company in the university environment, to motivate them and showcase the possibilities. Accordingly, real business case studies of research transfer and real examples of stakeholders in the system for several successful companies, related to nanotechnology, biomaterials and magnetic sensing applications, as well as practical guide on IP protection, are given at the final chapters.

This work is the result of joint efforts of different companies, academic, and research institutions participating in the large international project, WIMB Tempus, 543898-TEMPUS-1-2013-1-ES-TEMPUS-JPHES, “Development of Sustainable Interrelations between Education, Research and Innovation at WBC Universities in Nanotechnologies and Advanced Materials where innovation Means Business”, cofunded by the Tempus Programme of the European Union.

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