
Collaborative
Research and
Development with
the Industry

Topics

- Experience/examples
- Importance of Academia/Industry Co-operations
- Advantages/Disadvantages
- Things to take into consideration
- How to establish contacts, find the right partner
- Potential funding

Experience and Examples

- Dennis Carson, MD
- *Inventor and Scientific Advisor*

- Currently working on adjuvant discovery and vaccine research
- Played key role in founding Dynavax, IDEC, Telormedix, Vical and others
- About 600 papers published
- Professor Emeritus, Moores UCSD Cancer Center
- Member of the National Academy of Science


Inspired by Nature
KUPANDO

Thalidomide -a drug that changed almost everything…….and Basic Research could have helped to prevent it

- 1953: Gruenenthal created the drug Thalidomide for morning sickness and as a sleeping pill
- 1958: Since compound had no side effects in animal models, it came as an over the counter product on the market
- 1961: An Australian doctor, William McBride, writes to the Lancet medical journal after noticing an increase in the number of deformed babies born at his hospital, all to mothers who had taken thalidomide. The drug is withdrawn later the same year.
- 1961: The drug was taken off the market
- 1961: Germany establishes first law that still does not regulate the drug approval process. That happens only in 1976.
- 2004: Thalidomide is made available on a named patient basis, meaning doctors can give it to patients only on a case-by-case basis and at their own discretion, under strict controls.
- 2008: the drug is approved for the treatment of multiple myeloma by the European Medicines Agency.
- **2009:Scientists at the University of Aberdeen claim they have solved a "50-year puzzle" after discovering how thalidomide causes limb defects. They found that a component of the drug prevented the growth of new blood vessels in developing embryos, stunting limb growth.**

Thalidomid – Lessons Learned

- State of the art development could have prevented the disaster
- Basic research, understanding the mechanism of action would have stopped the development at an early stage

Blockbuster Drugs discovered by Academia, developed by Industry

Example 1

James Allison discovers CTLA4 mAB

Medarex develops it as treatment for melanoma, FDA approval in 2011

CTLA mAB became a blockbuster drug

Allison is awarded Nobel prize in 2018

Blockbuster Drugs discovered by Academia, developed by Industry

Example 1

James Allison discovers CTLA4 mAB

- **B**ack in the ’90s, immunologist James Allison wasn’t trying to develop a cancer drug. “I was doing just really **fundamental research trying to understand T-cell regulation**,” he says. But in the course of that work, performed at the University of California, Berkeley, Allison discovered that a protein receptor called CTLA-4 negatively regulated T-cell responses to antigens, and that inhibiting that receptor with an antibody enhanced T-cell activity.
- The clinical applications were obvious. “I had the idea that you might be able to exploit that to get immunological responses, T-cell responses, to tumor cells,” says Allison, now chair of immunology and director of immunotherapy at the University of Texas’s MD Anderson Cancer Center. In a 1996 Sciencepaper, he and his colleagues reported that, in mice, this approach worked: rodents treated with an anti-CTLA-4 antibody rejected tumors. “I thought this was pretty cool. **We patented it**,” says Allison. “I thought everybody would jump at it.” But everybody—in particular pharmaceutical companies—did not.

Lesson learned

Example 1

James Allison discovers CTLA4 mAB

- He filed a patent
- He did not give up

Blockbuster Drugs discovered by Academia, developed by Industry

Example 2

Michael Jung led the UCLA research team whose discoveries resulted in the development of a leading prostate cancer drug.

Prof. Jung worked with Drs. Charles Sawyers and Howard Scher of the Memorial Sloan Kettering Cancer Center to develop the anti-androgen drug enzalutamide (Xtandi), which has been found effective in slowing or stopping the progression of late-stage prostate cancer for several months and received FDA approval in August 2012. The product was developed by Medivation. At the end of a battle between Roche, Gilead and others Pfizer acquired the company for 14 billion USd

UCLA is using its share of the proceeds — approximately $520 million — to support research programs aimed at generating additional discoveries that lead to medications and other products that serve the public good. UCLA also supports undergraduate scholarships and graduate student fellowships, a campus priority.

Lesson learned

Example 2

Michael Jung and Xtandi

- If a cooperation is successful the tax payer , the patient will benefit
- If a cooperation is successful there is money for everybody, the company, the inventors, the university

Drugs discovered by Academia, developed by Industry

Example 3

- **The BCG replacement vaccine VPM1002: from drawing board to clinical trial**
- **Stefan HE Kaufmann,** Department of Immunology, Max Planck Institute for Infection Biology, Berlin, Germany et al.

Tuberculosis remains a major health threat and vaccines better than bacillus Calmette-Guérin (BCG) are urgently required. Here we describe our experience with a recombinant BCG expressing listeriolysin and deficient in urease. This potential replacement vaccine has demonstrated superior efficacy and safety over BCG in *Mycobacterium tuberculosis* aerosol-challenged mice and was safe in numerous animal models including immune-deficient mice, guinea pigs, rabbits and nonhuman primates. Phase I clinical trials in adults in Germany and South Africa have proven safety and a current Phase IIa trial is under way to assess immunogenicity and safety in its target population, newborns in a high tuberculosis incidence setting, with promising early results. Second-generation candidates are being developed to improve safety and efficacy.

Lesson learned

Example 3

Stefan Kaufmann and modified BCG

Basic research facilitated the discovery of an important vaccine

Drug development is about quality, efficacy, safety and……..

the prize

Find the right partner……

Difficulties to Overcome

- The success of those partnerships is far from guaranteed. Differences in **institutional cultures**, on top of the scientific challenges of translating academic results into clinical treatments.

- **SPEED**:Academic researchers generally receive grants to pursue given projects over several years, industry labs tend to expect faster results and are quicker to abandon projects that don't show immediate promise.
- But where there's a will there's a way.

Difficulties to Overcome - Reproducibility

- One of the major problems in translating research from academia to industry is a lack of reproducibility.
- According to studies by pharmaceutical companies Bayer and Amgen, when industry labs try to reproduce academic results they are unsuccessful approximately 80 percent of the time, as McGill University ophthalmologist Leonard Levin and coauthor Francine Behar-Cohen note in a 2017 *Trends in Pharmacological Sciences* editorial.

Difficulties to Overcome – Reproducibility – What to Do

- Likely various reasons for this reproducibility problem get “lost in translation” :

- Insufficiently detailed methods in published studies
- The use of different animal models
- The use of different statistical approaches in academic vs. industry labs.

- Recommendation:
- Write more detailed methods
- Hold data to highest statistical standard
- Start co-operation at an early stage in development
-

Academia and Industry, Differences

Industry Priorities	Academia Priorities
Patents	Publication
Safety	Mode of action
Efficacy	
Quality (GXP)	
Prize	
NPV – making money	
USP	

Difficulties to Overcome – Publish or Secrecy

- This problem exists every day.
- Companies publish only once patent has been filed and the publish some topics not at all.
- Manufacturing information gets rarely patented by the industry, because patens get published.
- Solution: ? A long term relation ship that secures funding

- As described in a 2012 article in the *MIT Sloan Management Review* by the University of Bath's Ammon Salter and Imperial College London's Markus Perkmann, who both research academic-industry collaborations, short-term, confidential projects would ordinarily not appeal to academic researchers. But in the context of a longer, more open collaborative project, academics might find short-term secret projects more palatable.

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Difficulties to Overcome – Basic Science or Drug Development including Prizing

- Harvard, for example, engages in long-term collaborations, called strategic alliances, with company partners. The multi-project agreements that govern these collaborations serve to expedite collaborative research, Caroline Perry, director of communications at Harvard's technology transfer office, tells *The Scientist* in an email. Such long-term agreements can also help resolve the conflict between academics' wish to publish results and industry's preference for secrecy.

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Academia and Industry, Common goals

- Identify and develop tools for better health care, drugs, devices, diagnostic markers etc.

Disadvantages and Risk

- Pharma partner shelves projects at times
- Pharma partner discontinues project for strategic and not for scientific reasons. New CSO does not like technology, acquisition or merger leads to a new portfolio etc etc – milestones in the contract
- Contractual negotiations delay project - master agreement

Funding Opportunities

- In cooperation with “big pharma” funding will be provided by the company in most cases, which compensates for the ”secrecy”, is one point of view
- Another one was published in the London Business School :To test the actual impact of collaboration, he used the twin-papers approach again – multiple scientists making roughly the same discovery around the same time. (It’s worth noting that to find 33 twinned discoveries, the researchers put significant effort into sifting through millions of scientific publications.)“Instead of reducing the quantity of publications, academic-industry collaborators had greater output than their non-collaborating peers.” More financial and equipment resources?

Working with ”big pharma”, how to find the right partner

- One needs an internal champion, somebody who supports the project/cooperation within the organization, secures the budget, secures internal resources etc. That person does not need to be high in the hierarchy. That person has to be ready to fight and has to be a supporter of the project
- Very common: The not invented here syndrome, in some organizations a huge problem
- Pharma Organizations might have a change in leader ship, change in strategy, merger and acquisitions. A project might be terminated despite the fact that it is promising from a scientific point of view – secure rights, define milestones

How to find the right partner – more innovation originates from small companies

- In 2009, small pharma was responsible for discovering 31% of NMEs; now jump to 2018, when 64% of all NME approvals originated from small pharma, a 103% increase over 2009.
- Marketing and sales will be the strength of “big pharma”

- Development stage of your project should be taken into consideration, when searching for the right partner. Development costs as well.

Attention: Patents and Ownership

- In any given cooperation one has to define by a contract the ownership for newly generated patents
- In a service agreement setting the newly generated IP typically belongs to the party that pays for the service
- In a research agreement the newly generated patents can be jointly owned. That correct wording should be in the contract

Attention: Patents and Ownership cont.

Any results generated by Company and/or University
and/or by the Parties jointly (regardless of inventorship), particularly
but not limited to compounds that combine the Company Technology
and/or Materials and the Univeristy Technology and/or Materials Results shall be deemed joint results and shall be jointly owned ("**Joint Results**"). The Parties shall jointly file patents on inventions included in the Joint Results ("**Joint Inventions**") and share equally the costs thereof. Neither Party shall be entitled to use the Joint Results and/or grant licenses thereunder to third parties without the prior written consent of the other Party.

A second paragraph should be included addressing the topic publication, e.g. that the Company has the right to review publication, but with a defined time frame like 6 weeks.

SME- What is it?

‘Jobs, growth and investment will only return to Europe if we create the right regulatory environment and promote a climate of entrepreneurship and job creation. We must not stifle innovation and competitiveness with too prescriptive and too detailed regulations, particularly when it comes to small and medium-sized enterprises (SMEs). SMEs are the backbone of our economy, creating more than 85 % of new jobs in Europe and we have to free them from burdensome regulation.’

Jean-Claude Juncker, President of the European Commission

In 2019, the pharmaceutical industry spent $83 billion dollars on R&D

R&D spending in the pharmaceutical industry covers a variety of activities, including the following:

- **Invention**, or research and discovery of new drugs;
- **Development**, or clinical testing, preparation and submission of applications for FDA approval, and design of production processes for new drugs;
- **Incremental innovation**, including the development of new dosages and delivery mechanisms for existing drugs and the testing of those drugs for additional indications;
- **Product differentiation**, or the clinical testing of a new drug against an existing rival drug to show that the new drug is superior; and
- **Safety monitoring**, or clinical trials (conducted after a drug has reached the market) that the FDA may require to detect side effects that may not have been observed in shorter trials when the drug was n development. Congressional Budget Office

SME- A good Partner for Academia

- The mindset and the culture is similar and entrepreneurial
- There are ways of receiving funding for joined projects

SME- A good Partner for Academia

Eurostars is the largest international funding programme for SMEs wishing to collaborate on R&D projects that create innovative products, processes or services for commercialisation. Your consortium must spotlight an innovative SME as the main project participant.

29%
APPLICATIONS RECEIVE FUNDING

1.75B€
PUBLIC/PRIVATE INVESTMENT SINCE 2014

45%
OF PARTICIPANTS REACH NEW MARKETS

84%
OF PROJECT PARTNERS FORM LONG-TERM RELATIONSHIPS

Alternative: Incubators

- The incubator concept within large pharma started gaining ground about three years ago.
- “Large pharma companies started to create their own incubators and attract talent to those incubators,” he says. “I’ve seen many cases where top scientists from the academic space have shifted over to large pharma incubators where they’re still doing the same thing but the opportunities to advance their science and technology are better, because of the infrastructure that a large pharma company can provide.”
- JLABS at J&J is only one example. Many VCs (Kurma eg.) and companies (eg. Evotec and Kurma) are establishing incubators, which will facilitate innovation.

Summary

- Define the project: non clinical, research, clinical, drug, devices, diagnostic biomarker
- Estimate timelines and funding requirements
- Identify potential interested big pharma or SMEs
- Personal goals
- Patent protection
- Make it work. It is essential for the development of new medical means

Relationships are successful when the two parties understand each other's needs and concerns . . . and reach a structure and a conclusion that is acceptable to all," says Isaac Kohlberg, chief technology development officer of Harvard's Office of Technology Development.