Translating your research discoveries into practice: It takes a village!

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Cancer Immunotherapy: It Takes a Village!

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- Basic scientists who did the fundamental scientific research to provide the foundation for the field
- Scientists in academia and industry who designed and tested the molecules for the targets to turn the concepts into potential real medicines
- Physicians who did the clinical trials
- **Patients who participated in the clinical trials**

It takes a big village!

Academic Research, Invention and Innovation at the University of Michigan

- **Academic Research**
  - **What we do very well at the University of Michigan**
  - **$1.34B research expenditure in 2012-2013 (#1 among American public universities)**
- **Invention**
  - **Turning money into ideas (patents)**
    - **421** new invention disclosures in 2013 received by UM OTT
    - **128** patents issued by the US Patent and Trademark Office
- **Innovation**
  - **Turning patents into money**
    - **108** License/Option Agreements in 2013
    - **9** New Business Startups in 2013
    - **$13.4M** Royalties in 2013

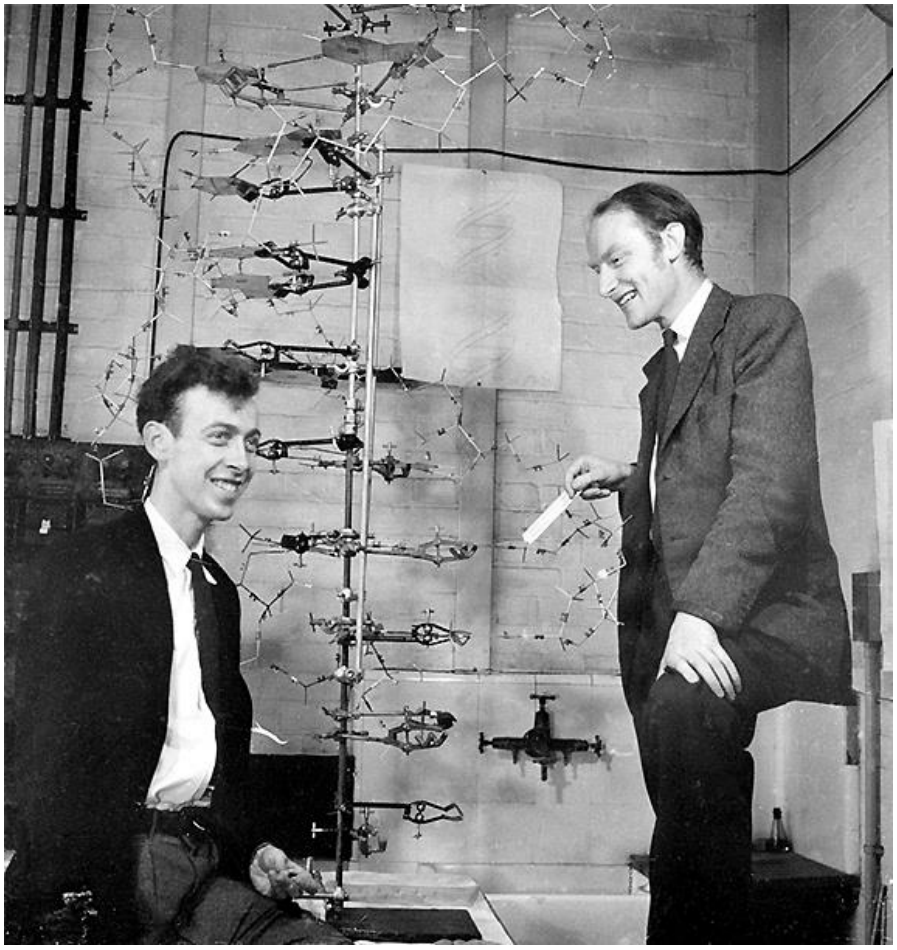
Academic Research: Basic *versus* Applied

- **Basic Research** (Wikipedia)
  - also called pure research or fundamental research, is a systematic study directed toward greater knowledge or understanding of the fundamental aspects of phenomena **without specific applications** or **products** in mind.

- **Applied Research** (Wikipedia)
  - Applied research is a form of systematic inquiry involving the practical application of science. It accesses and uses some part of the research communities' accumulated theories, knowledge, methods, and techniques, for a **specific**, often state-, business-, or client-driven **purpose**.

Impact of Basic Research

James Watson and Francis Crick

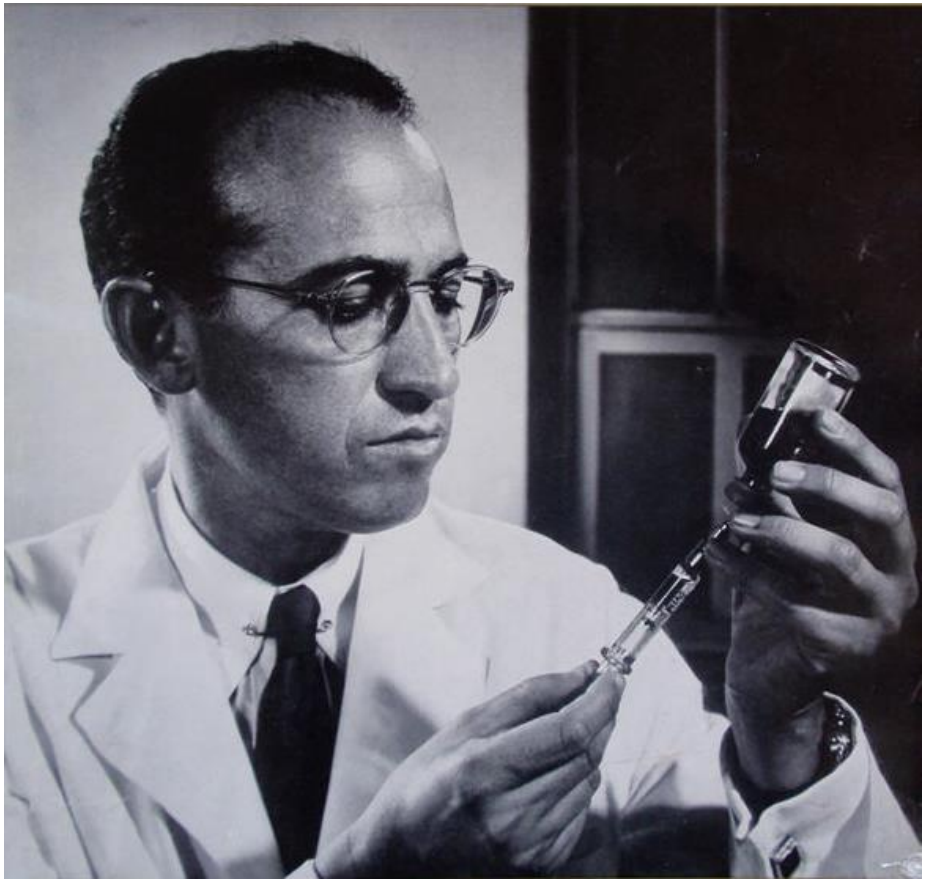


IMPACT

The discovery of double-helix DNA structure by Watson and Crick marked a milestone in the history of science and gave rise to modern molecular biology

Impact of Applied Research

Jonas Edward Salk
(October 28, 1914 – June 23, 1995)



IMPACT

Salk developed the first successful polio vaccine. Before the Salk vaccine was introduced, America's greatest fear was polio, apart from the atomic bomb.

Salk: Inventor but not Innovator?

- "**There is no patent. Could you patent the sun**?", Said Salk, when asked by a reporter if he had filed a patent on his polio vaccine.
- It is estimated that he could have made $7B if he had patented his vaccine.
- But his invention has saved thousands of lives, mostly children.

Why Patents Your Research?
Impact of the 1980 Bayh-Dole Act

- Non-profits, including universities, and small businesses may elect to retain title to innovations developed under federally-funded research programs
- Universities are encouraged to collaborate with commercial concerns to promote the utilization of inventions arising from federal funding
- Universities are expected to file patents on inventions they elect to own
- Universities are expected to give licensing preference to small businesses
- The government retains a non-exclusive license to practice the patent throughout the world
- The government retains march-in rights.

Why Patents Your Research?

- Unlike Salk's era, today, unless you (the university and inventors) have a patent on your discovery, no one will invest into it and turn your discovery into a commercial product for the betterment of humans and human health
  - This is how the capitalism works:
    - **99% investors seek financial return for their investments**

My Own Research:
Academic Drug Discovery

- What is academic drug discovery research?
- What are the opportunities and advantages for academic drug discovery research?
- What are the main differences between academic drug discovery research and drug discovery research in the pharmaceutical industry?
- What are the biggest challenges for academic drug discovery research?
- How to build a successful academic drug discovery research program?

Academic Drug Discovery Research

- Entire spectrum of drug discovery research
  - Assay development
  - “Hits” and “leads” identification for drug targets or pathways
  - Lead optimization
  - Drug-target interaction
  - Target validation with lead compounds
  - Efficacy and toxicity studies in animal models

Opportunities for Academic Drug Discovery Research at the University of Michigan

- World-class research university with top ranked research programs in all disciplines
- Extensive clinical expertise in different disease areas
- Cutting-edge science and deep knowledge on many new and exciting disease targets
- Basic infrastructures and cores available for drug discovery research

Some Main Differences between Academic and Industry Drug Discovery Research

Academia

- **You choose a project to work on**
  - Freedom! You are the boss as long as you can get funding.
- **Publications rank as the top priority**
  - "Publish or perish"
- **Less stringent timeline**
- **New targets and cutting-edge science**
  - High risk projects and high innovation

Industry

- **You do what you are assigned**
  - Limited freedom but funding provided
- **Publications rank low and are often discouraged**
- **Stringent timeline**
- **Not always new targets or new science**
  - Breaking other people's patents are common practices in companies

Some of the Biggest Challenges for Academic Drug Discovery Research

Basic Academic Research

- Individual science
- Single discipline
- Publication is the final product
  - Taking one-year
  - High rate (>90%) of success
- **Translation is not needed**

Drug Discovery Research

- **Team science**
- **Many disciplines**
- **Medicine is the final product**
  - **Taking 7-10 years**
  - **High rate (>90%) of failure**
- **Translation is needed and not easy**
  - **Stuck in preclinical stage**

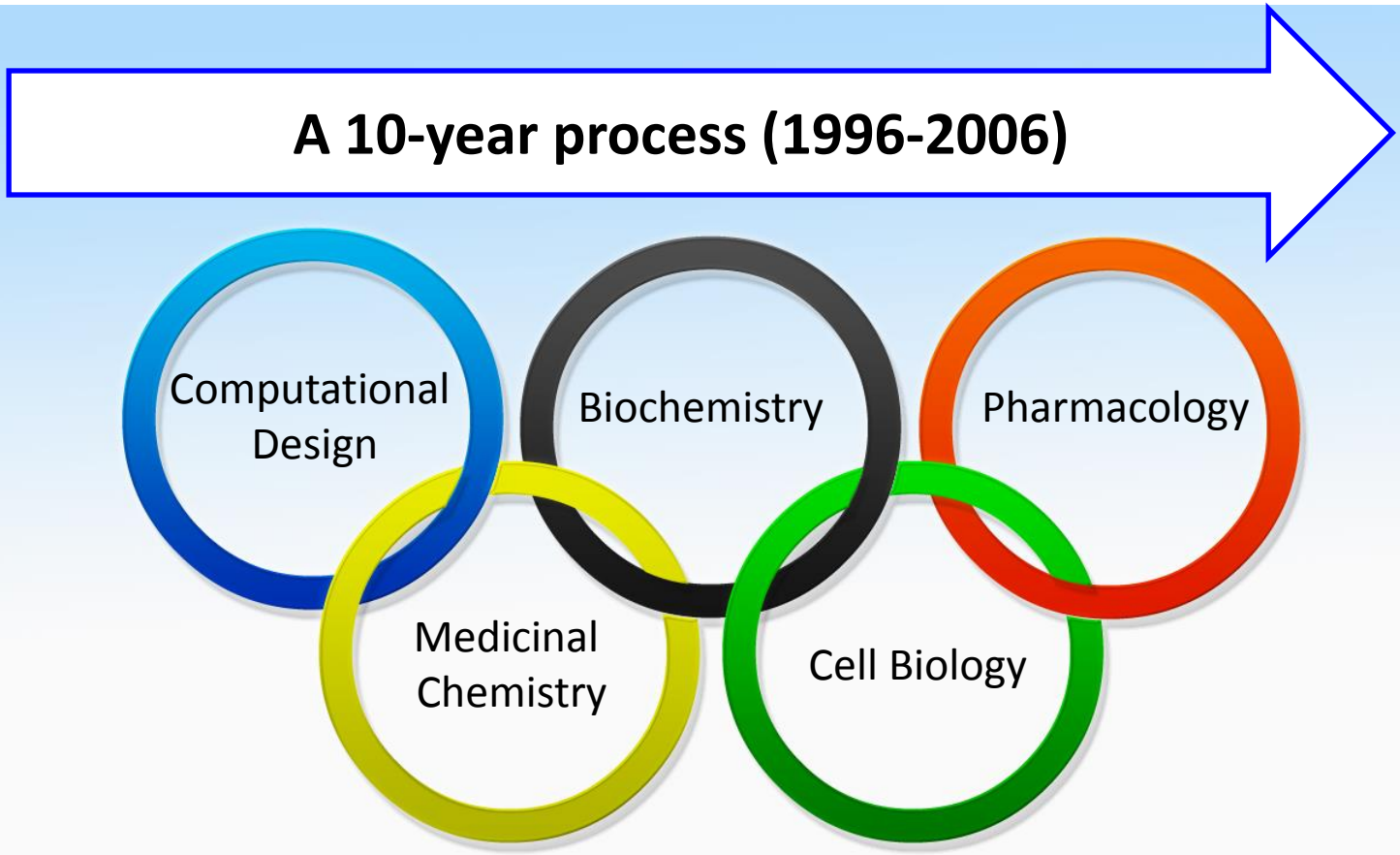
Given These High Hurdles, Why Do We Do It?

- There are many unmet medical needs and millions of patients urgently need new medicines
  - We live longer and many age-related diseases (cancer and Alzheimer's disease) are now the biggest medical problems in health care
- This is a golden era of drug discovery in human history since there are many new drug targets for every single human disease
  - Biology evolution
- Big pharmaceutical industry is cutting back on their investment in early-stage drug discovery and focusing on late-stage drug development
  - Big pharma are laying off scientists by the thousands every year but their early pipelines are drying up
  - Academia and small biotech companies are there to fill the void

My Journey for Academic Drug Discovery Research at UM

- Building a complete team
- Doing it systematically
- Choosing your targets carefully
- Being innovative
- Identifying and bringing on key collaborators to your research to solve key challenges
- Being patience and persistent
  - Determination and resolve

Building A Basic Team



Doing it systematically

- For a promising target, we drive it all the way to the finished line by advancing one or more drugs into clinical development
- We work on more than one target at a given time (e.g. 8-10 targets) but focus on 2-3 projects to make the most impact
- We triage our projects based upon science
- We constantly bring in new and exciting targets through collaboration

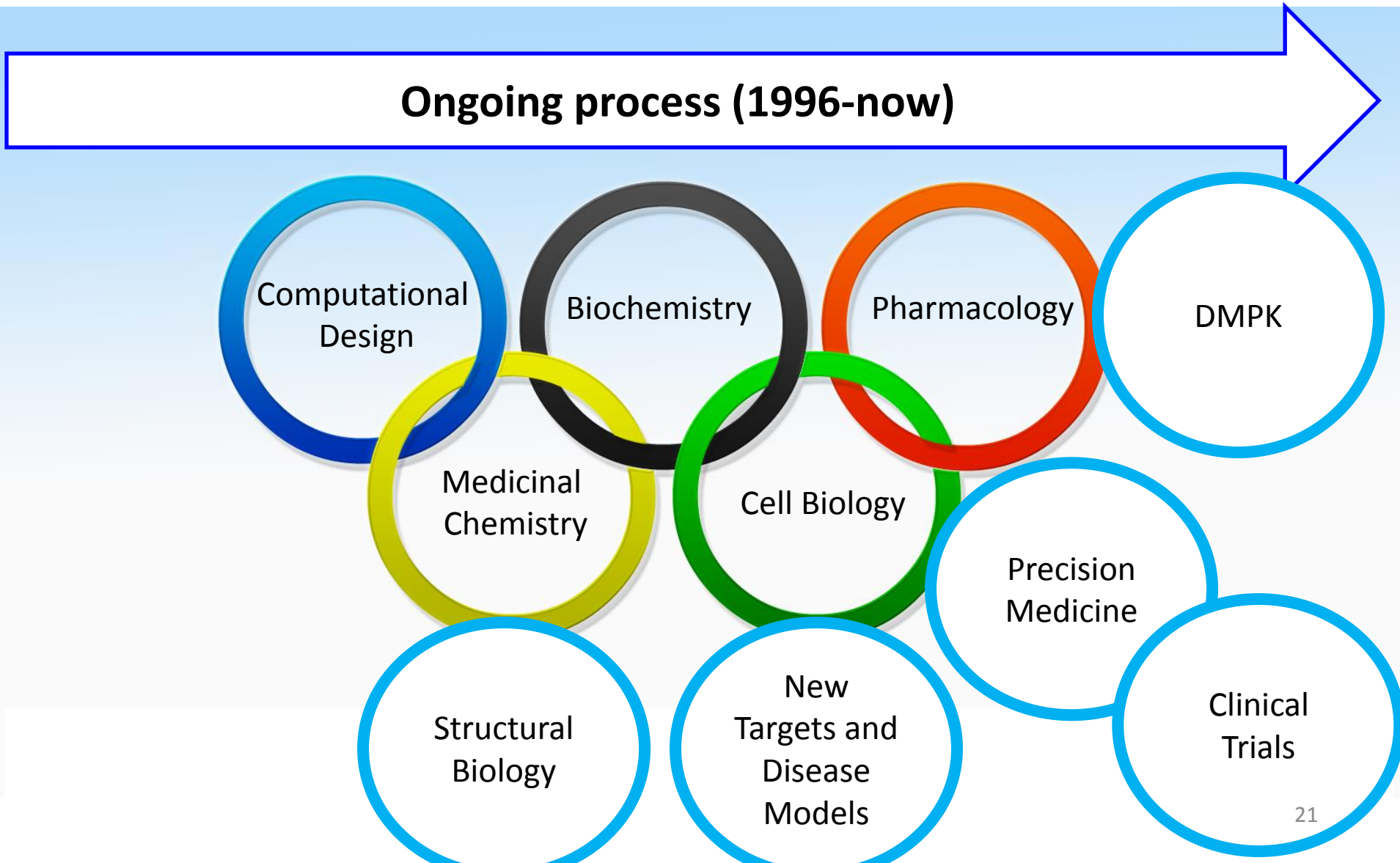
Choosing your targets carefully

- **Highly clinically relevant**
  - If we are successful, how much impact can we make for this disease (impact to patients)
- **Cutting-edge science**
  - If we are successful, how much can we contribute to science (impact to science)
- **High impact but maybe difficult targets**
  - We can afford a longer timeline

Being Innovative

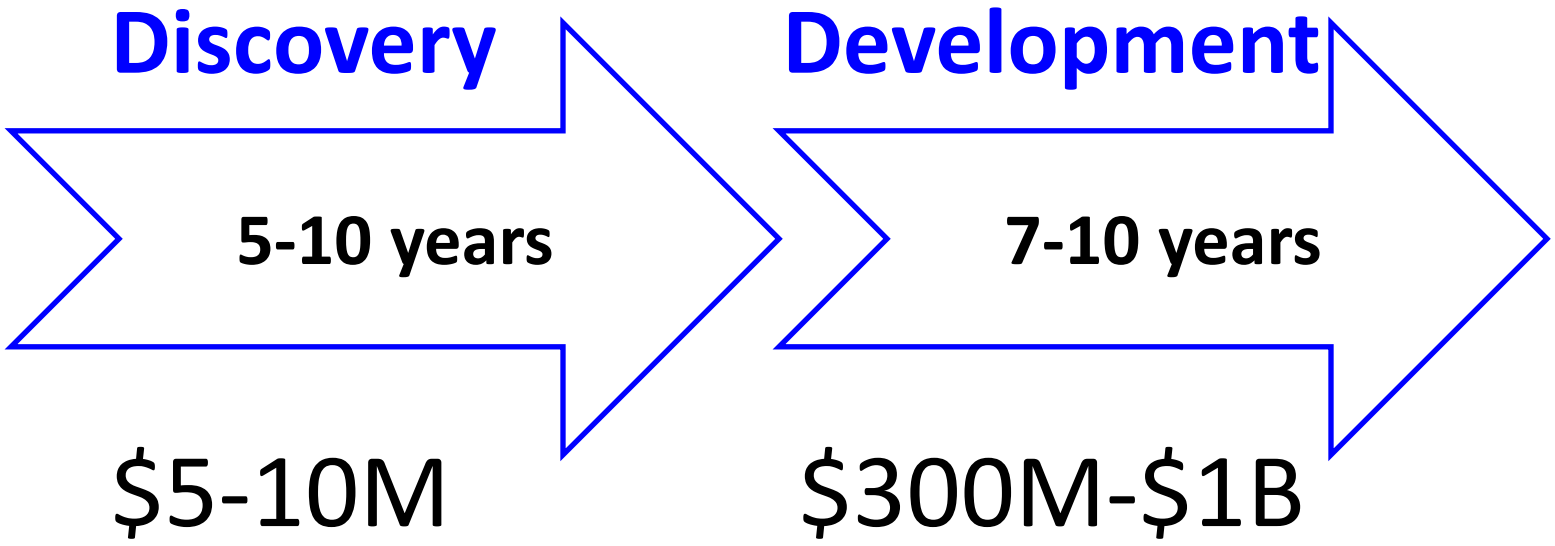
- We won't be able to compete with big pharmaceutical companies on a given project based upon resources alone
- We need to be highly innovative (creative) with new ideas and new approaches in order to compete
- **Be the best**
  - First and the best
  - If not first, be the best

Yes, You Need Collaborators!



Being Patience and Persistent!

- Drug discovery and development is a costly and lengthy process



Bridging the "Valley of Death" in Academic Drug Discovery

You are here with your drug candidate

You need to be here to put your drug into patients

The only problem: it will cost $2-3 millions for IND-enabling studies and another $5-10M for a phase I trial. What do you do?

Bridging the "Valley of Death": How to Bring Your Drugs to Clinical Development?

- Working with a development partner early-on
- The best development partner is your own company
- Be Entrepreneurial!

Building a Win-Win Relationship between Our Laboratories and UM Start-Up Companies

UM Laboratories

- We focus early, science-driven discovery research
- We generate intellectual properties (patents), owned by the University of Michigan
- We work closely with the company every step along the way
- We are their discovery partner

UM Start-up Companies

- They do everything needed for advancing the projects into clinical development
- They license UM patents through licensing and research agreements on defined areas
- They are our development partners
- They raise funding to support research and clinical development

Three Companies: Three Different Models

- **Ascenta Therapeutics Inc.**
  - **Founded by Shaomeng Wang, Dajun Yang and Marc Lippman in 2003 with HQ in San Diego, CA**
  - **All technologies licensed from UM**
  - **Traditional Venture-Funded Company**
    - Raised ~$100M
    - Advanced first drug (Bcl-2 inhibitor) into >10 Phase II clinical trials for different types of cancer
    - Advanced second drug (IAP inhibitor) into Phase I clinical trial and then licensed out to DebioPharm
      - Three trials ongoing for different types of cancer and more planned
    - Licensed third drug candidates (MDM2 inhibitor) to Sanofi, which advanced it into clinical development
      - Two trials ongoing, more planned

Three Companies-Three Different Models

- **Ascentage Pharma Group**
  - Founded by Shaomeng Wang, Dajun Yang and Ming Guo in 2009, with HQ in Hong Kong, China
  - Most of technologies from UM (5 out of 7)
  - Supported by initial investment from 3S*Bio (a public-traded company on US NASDAQ) and grants from local and central governments in China
    - Advanced two cancer drugs into clinical trials
    - IND-enabling studies ongoing for three other drugs

Three Companies-Three Different Models

- **OncoFusion Therapeutics Inc.**
  - Founded by Shaomeng Wang, Arul Chinnaiyan and Kenneth Pienta in 2012, Ann Arbor, Michigan
  - All technologies from UM
  - Started with seed funds from founders and close colleagues
  - Completed a licensing and research agreement with Medivation in March 2014
    - BET bromodomain inhibitors for oncology and others
  - Plan to advance 4-5 drugs into clinical development through partnership or by itself within the next few years

UM's Progressive Policy

- These start-up companies are possible because of UM's progressive policy in technology transfer and COI management
  - UM has one of the most progressive policies among all American universities
  - Faculty can found companies and
  - Faculty can serve as officers and directors of the board
  - Companies can invest into faculty's research under research agreements, in turn for the rights to license inventions
  - Faculty's outside activities are publically disclosed and managed by conflict of interest (COI) committees

OTT Is Our Best Friend and Partner!

- UM's Office of Technology Transfer (OTT) is superb in supporting new, start-up companies
  - Robin Rasor: Director of Licensing

The Best Days Are Still Ahead!

- **We are getting better every year in what we do!**
  - Targeting selection
  - Our research to deliver drug candidates for clinical translation
- **We are doubling our lab size to 45-50 researchers!**
- **We have close collaborations with many laboratories at the University of Michigan!**
  - Arul Chinnaiyan, MCTP
  - Yali Dou, Pathology
  - Duxin Sun, CoP
  - Jeanne Stuckey, LSI
  - Yi Sun, Radiation Oncology
  - Many others
- **With our successful track-record in academic drug discovery, pharmaceutical partners are eager to work with us!**

Other Labs at UM Can Do It!

- If we can do it, you can do it!
- Medical School's Fast Forward Medical Innovation (FFMI) provides funding for therapeutics discovery and translation
  - **Therapeutics Champion**
- UM is investing into drug discovery research!
  - Provost, Medical School, CoP, LSI, Departments of Pathology and Internal Medicine, EBS have put together resources to invest into early drug discovery research

Wang Laboratory, January 2014