Translational Science: From the Bench to the Clinic (and beyond)

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Foundation Fighting Blindness
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Developing products to prevent/treat human disease is a resource intensive activity

- Most recent Tufts survey pegs costs of developing new drug at $2.588 billion in 2013 dollars:http://csdd.tufts.edu/news/complete_story/tufts_csdd_rd_cost_study_now_published
- Actual costs depend on many factors.
- Decisions to fund/proceed still made on case by case basis, in a transparent manner.
- Initial goal is to identify and manage risks

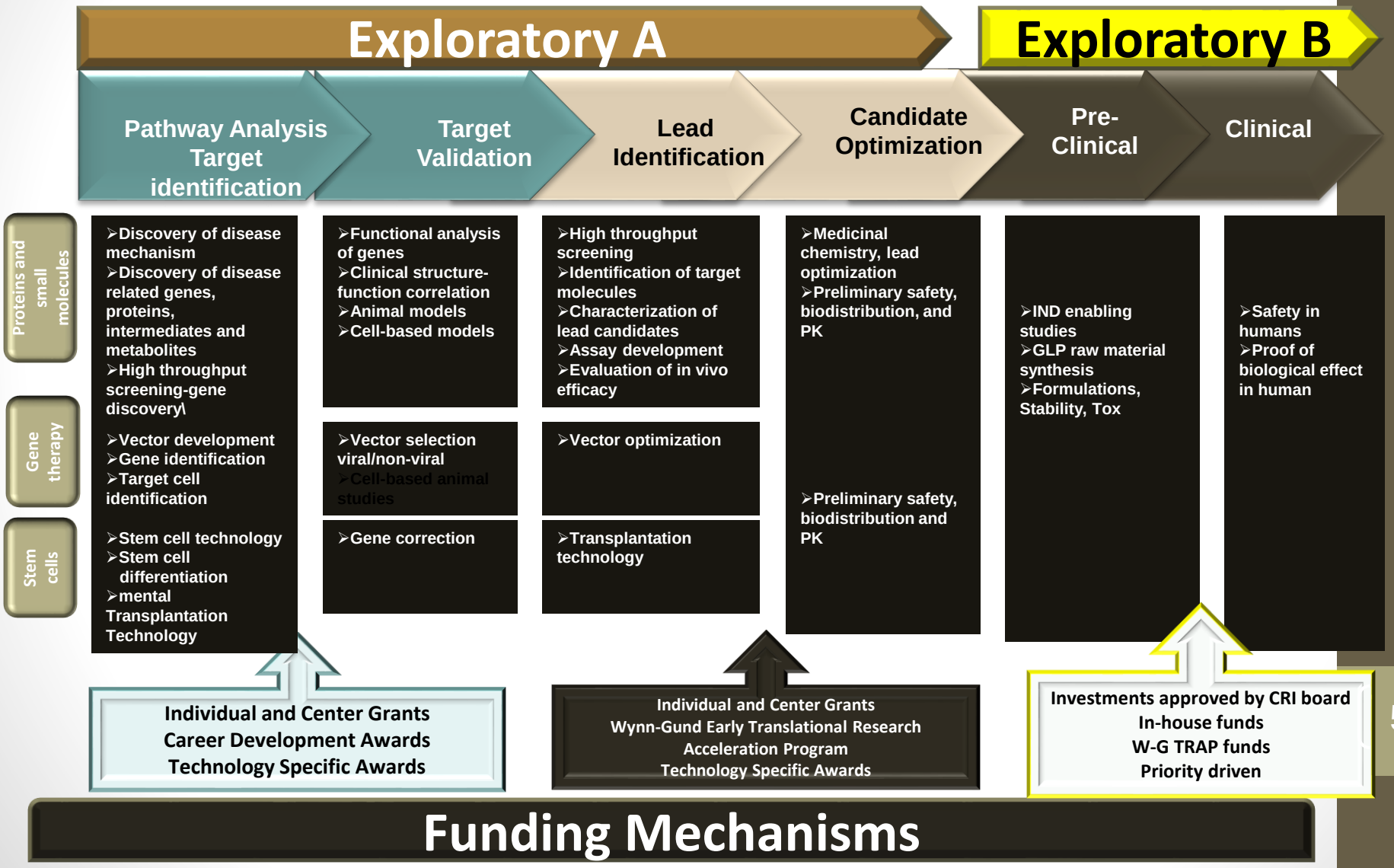
Transition from Research to Development – what is needed?

- Lead compound identified
- *In vitro*/*in vivo* efficacy - Proof of concept in relevant animal model
- Methods for making/testing API
- Ideas for clinical use – Target Product Profile
- Product development plan

Funding Translational Activities

- Early funding from non-profits is critical to the creation of new therapies
- Attracting funding from government and non-government sources depends on generation of early data
- We fund high risk, high reward activities that would not occur otherwise – failure is an option and is OK

FFB Science Pipeline and Funding Mechanisms



Lessons learned from funding TS programs to date

- Translation to clinical studies is slow and costly – educate investigators
- Lack of clarity on how to get to clinic
  - Lack of understanding of quality, regulatory issues
  - When/how to engage/manage CRO
  - Missing key aspects in early development (formulation, etc.)
  - Disconnect between theoretical therapy and clinical practice
- Projects where we provided independent consulting did better
- Oversight of integrated activities requires active project management
- Funding translational activities without supplying expertise leads to waste of scarce resources

Investigators need

- CMC Support
- Pharm/Tox support
- Regulatory Support
- Project management support
- Clinical support

Gund Harrington Initiative

- The primary goal of the Gund Harrington Initiative is to identify promising therapies that can benefit from acceleration and provide:
  - Funding
  - Experienced commercial project management
  - Access to senior pharma expertise (no cost)
- The overall effort seeks to create a comprehensive package to facilitate raising funds for further development

Harrington Discovery Institute
University Hospitals | Cleveland Ohio

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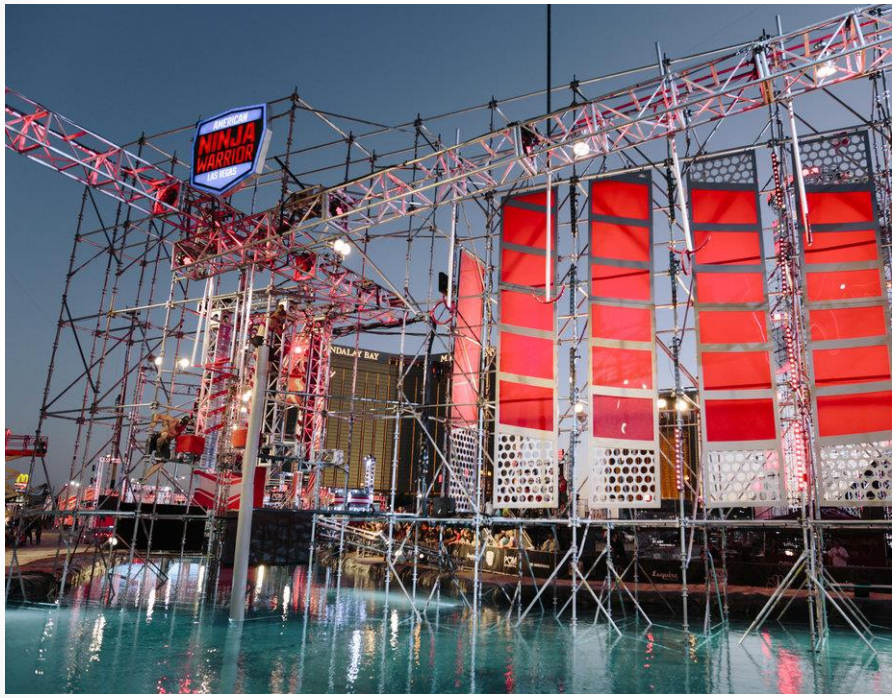
Tools for Management of Translational Activities

- No one approach works for all diseases, products

Does your development path look like this?

- **Low-Moderate $**
- **Moderate training/ expertise required**
- **Streamlined path with explicit rules (well worn path)**
- **Low risk of failure, multiple entries possible**

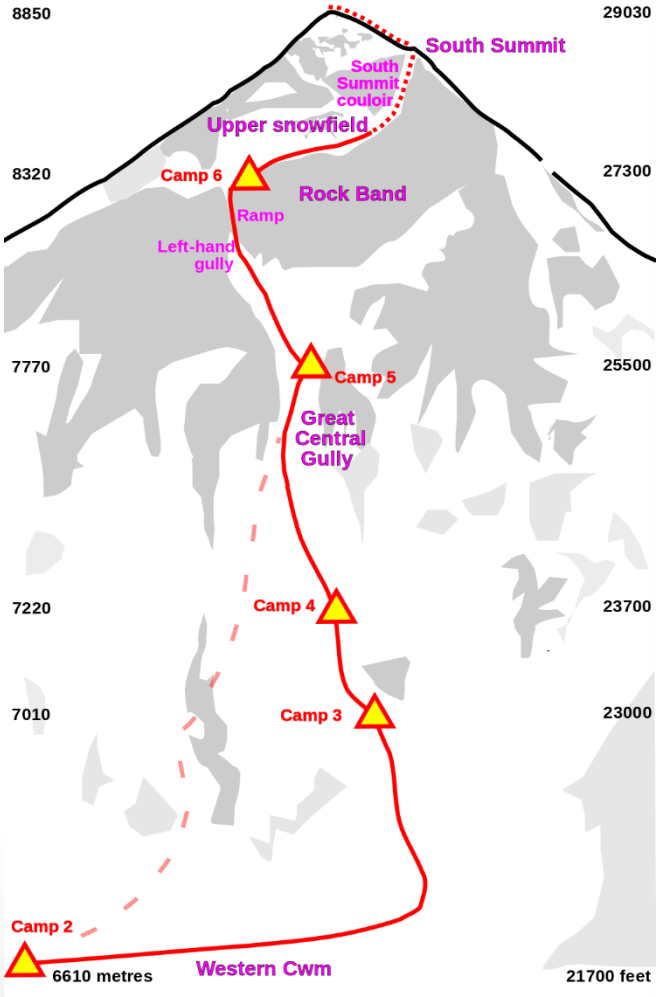
OR this?



- **Moderate $$**
- **Training/expertise required**
- **Multiple different obstacles**
- **No one approach works for all**
- **High risk of failure, but not fatal**

http://www.nbc.com/american-ninja-warrior/photos/season-8/behind-the-scenes-national-finals-week-3/2917643

Or this?



- **Moderate – high $**
- **Extremely high level and diversity of training/**
- **expertise required**
- **Long and arduous**
- **High risk of failure, potentially fatal**

Strategies to Reduce Risk

- GAP analysis to identify and mitigate risks
- Product development planning (TPP, PDP)
- Learn from others' mistakes and manage expectations of team members
- Invest in expertise (regulatory, CMC) as early as possible
- Outsource carefully, with appropriate oversight (compliance audit, quality review by sponsor).

Target Product Profile

- *"Beginning with the goal in mind."* The TPP is a useful tool for planning research and development activities throughout development.
- Identifies characteristics of marketed product
- Living document that changes as new information is obtained
- Can help all stakeholders focus on consensus goals and also understand the end results of the development efforts.
- FDA Guidance: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm080593.pdf

TPP Attributes

- **Indications and Usage**
- **Dosage and Administration**
- **Dosage Forms and Strengths**
- Contraindications
- Warnings and Precautions
- Adverse Reactions
- Drug Interactions
- **Use in Specific Populations**
- Drug Abuse and Dependence
- Overdosage
- **Description**
- Clinical Pharmacology
- Nonclinical Toxicology
- Clinical Studies
- References
- **How Supplied/Storage and Handling**
- Patient Counseling Information
- **Endpoints for clinical evaluation**

Product Development Planning

- A PDP is a tool for assessing and planning development path (road map)
- Include assessment of expertise residing in investigator laboratory
- Intellectual Property assessment
- Feasibility – can product be manufactured GMP
- Living document with iterative review (milestone based) to maximize utility
- NOT one size fits all
- Can be used by investigators to obtain funding, by funders to establish pipeline priorities and future funding needs

Components of PDP

- Background – disease, treatments, market landscape
- Overview of development to date
- Gap analysis
- Risk mitigation approaches
- Plans for development with cost and timeline – the “package”

Have PDP, Time to Start a Company?

- G-H partners such as FFB's CRI, HDI's BioMotiv, and commercial funding partners (such as Takeda) may support or co-partner development.
- Venture philanthropy model to fund commercialization of novel therapies
- Matchmaking with other pharma partners serves the mission just as well as direct investment

Investments Made Since 2008

- ACT
- AGTC
- Genable
- Mitochem
- ReNeuron
- Sparing Vision
- Spark

Strategies for leveraging investments in product development

- Invest in platforms that apply to multiple indications or solve issues that apply to >1
- Sharing of information – “lessons learned” in forums such as HRA
- Working together to bring common issues to light and resolve them, e.g. workshops

Questions after the meeting

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