SPARK

Reducing the Barriers between Bench and Bedside

Kevin Grimes, MD, MBA

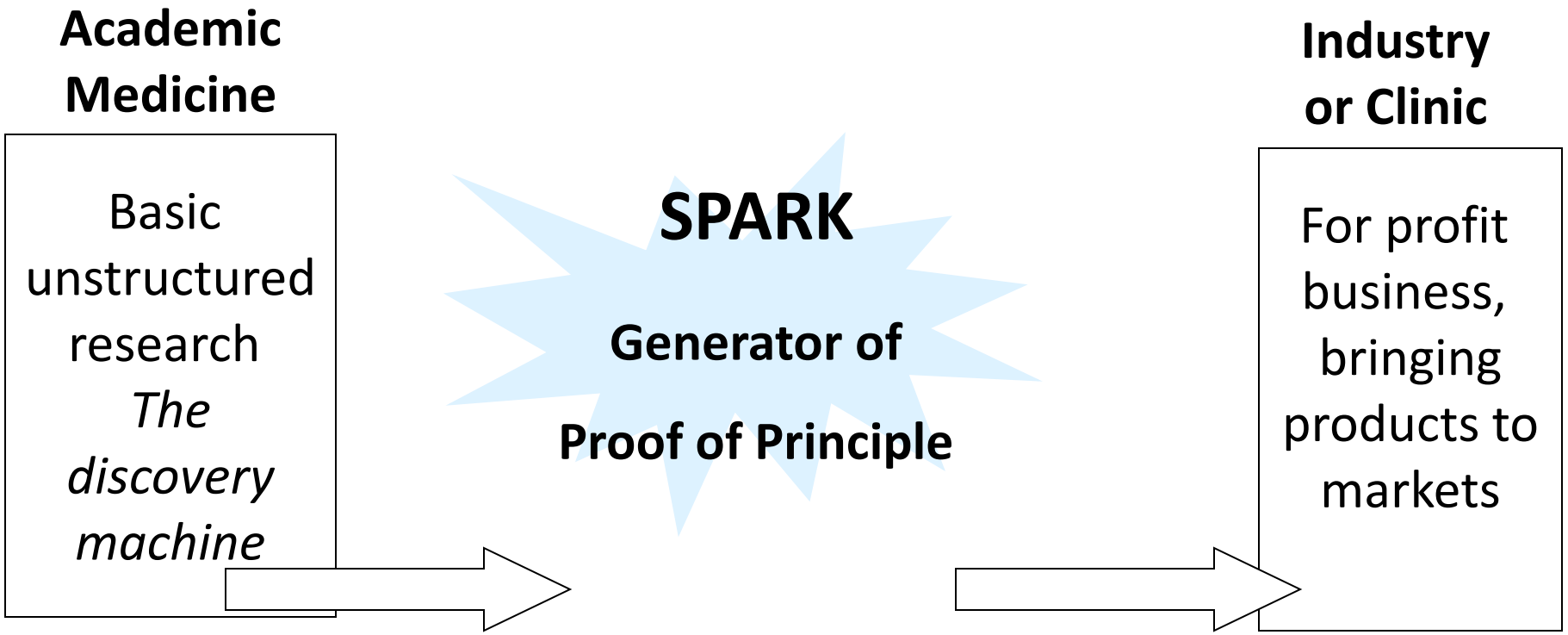
October 3, 2012

STANFORD
SCHOOL OF MEDICINE

Problems for Academic Researchers

- Super-specialized
  - Lack knowledge & expertise regarding the drug development process
- Incentives
  - Career advancement depends on publications and research grant funding; bias to positive results
- Availability of funding for applied research
  - Government grants funded basic research and clinical trials
- “Curing rodents is easy”
  - models are not predictive

From Discovery to Human Benefit



STANFORD SCHOOL OF MEDICINE

SPARK Mission

Partnership between university and industry to:

- Educate faculty, fellows and graduate students on the translational process (discovery and development) for therapeutics and diagnostics
- Advance promising research discoveries to the clinic and commercial sector
- Innovate efficient and cost-effective approaches to discovery and development

SPARK Selection Criteria

Therapeutic or diagnostic for any clinical indication:

- Address unmet need
- Novel approach
- Advance to commercial sector or clinic within 2-3 years
- Special consideration to orphan and neglected diseases

STANFORD
SCHOOL OF MEDICINE

SPARK Selection Process

Academic-industry selection committee

1. Initial review of promising discoveries from Office of Technology Licensing database (n≅150-200) and proposals from across the university (n≅50)
2. Invite 20 finalists to present to selection committee
3. Select ~ 10 projects each year

Once selected, projects are funded for up to 3 years

STANFORD
SCHOOL OF MEDICINE

SPARK Approach

- Money: Provide directed funding that is tied to achievement of milestones
- Education: Year-long seminar on drug and diagnostics development
  - topics range from assay development to commercialization
- Mentorship: local biotech, VC experts, Stanford faculty
- Matchmaking: introductions to possible investors/collaborators

STANFORD
SCHOOL OF MEDICINE

The Industry Mentors

SPARK Approach – Lower Barriers

Project Management

- Target product profile
- Funding - tied to achievement of milestones
- Quarterly project updates

Education – so translation becomes second nature

- Seminar - from assay development to commercialization
- Project updates – common lessons
- Graduate student course

STANFORD
SCHOOL OF MEDICINE

SPARK Approach – Lower Barriers

Access to facilities

- Stanford core service centers
- Academic collaborators
- Commercial contract research organizations

Mentorship

- Industry volunteers from pharmaceutical, biotechnology, non-profit, and investment community
- From overall development strategy to specifics (e.g. medicinal chemistry)

SPARK Approach – Lower Barriers

Building bridges – introducing partners for the next step

- Clinical collaborators
- Pharmaceutical/biotechnology
- Commercial contract research organizations

SPARK Projects

- 60 projects to date (during first 6 years)
  - 33 active
  - 27 graduates
- 7 student-led programs
  - NIH funding, C-IDEA, SPARK
- 11 new projects in SPARK 6

SPARK 6

- Chinese botanical for inflammatory bowel disease
- Diagnostic/mAb for treatment of sarcomas
- Oncotherapeutic targeting scaffold protein
- Non-antibiotic treatment for C *dificile* colitis
- Drug treatment for celiac disease
- mAb for treatment of muscle atrophy
- Protein treatment for rare pediatric skin disease
- Repurposed drug for pulmonary hypertension
- Repurposed drug for preventing lung transplant failure
- Repurposed drug for lymphatic malformations
- Diagnostic test for pre-eclampsia

The Path Forward

- Hand off to industry for new chemical entities and biologics
- Hand off to public private partnerships for global health therapeutics
- Internal development/investigator-initiated trial for repurposed drugs

Metrics of Success

- Projects advancing to the clinic
- Projects that are licensed
- Follow-on grants enabled by SPARK participation
- Publications
- Education of faculty, post-doctoral fellows, graduate students

STANFORD
SCHOOL OF MEDICINE

SPARK So Far

27 projects have completed SPARK

- 10 projects licensed (7 in the clinic)
  - 7 as start-ups (4 SBIRs, 1 applying)
  - 1 to existing small business (1 SBIR)
  - 2 to existing large companies
- 4 projects in clinic but unlicensed

STANFORD
SCHOOL OF MEDICINE

SPARK Project Example

Jean Tang, MD, PhD (PellePharma, Inc.)

Repurposing drug as topical HH inhibitor for BCCA and basal cell nevus syndrome

- Conducted POC clinical trial showing benefit in sporadic BCCA
- Conducted POC clinical trial showing benefit in basal cell nevus syndrome
- Developing topical formulation with SPARK funding
- In discussions regarding commercialization

STANFORD SCHOOL OF MEDICINE

SPARK Project Example

Che-Hong Chen, PhD (Aldea, Inc.)

Small molecule activators of wild-type and mutant ALDH2

- Optimized assay and conducted HTS at Stanford core
- Performed SAR with medicinal chemist to optimize hits
- Conducted POC animal studies showing effect in ethanol intoxication, radiation dermatitis, Parkinson disease
- Conducted preliminary non-GLP safety studies
- Obtained venture funding for start-up company

STANFORD SCHOOL OF MEDICINE

SPARK Project Example

Craig Garner, PhD (Balance, Inc.)

Small molecule GABA inhibitors

- Optimized Down syndrome animal model for measuring ability to learn
- Conducted POC animal studies in transgenic mice and identified active compounds
- Conducted preliminary non-GLP safety studies
- Obtained venture funding for start-up company
- Enrolling subjects in Phase 1/POC trial

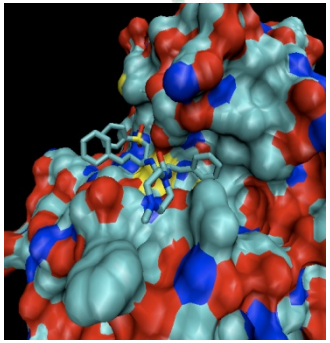
STANFORD SCHOOL OF MEDICINE

Challenges

- Marked decrease in venture funding for new biotech companies

- Cost of later stage development expensive for academia
  - Promising lead to Development Candidate
  - GLP studies
  - GMP material to enter clinical study
    - 3 projects on hold

NIH Funded Student Global Health Projects



- Chagas' DNA vaccine – trivalent DNA vaccine induced both cell-mediated and humoral immunity in mice. Murine parasite challenge study underway at UCSF. Collaborating with industry partner Ichor Medical Systems (electroporation)
- Chagas' drug repurposing – identified candidates using ligand-based screen targeting parasite protease. Demonstrated activity in cell-based screen at UCSF – carvedilol most potent, but not hitting target *in vitro*. Testing against suspected new target with collaborators in Argentina. Testing therapeutic activity in mice with JHU collaborator in Peru. Screening additional beta-blockers and MOA with Novartis.
- TB drug repurposing – targeting mycobacterial proteasome pathway. Assay developed and screening to begin at Stanford HTS this month.

STANFORD
SCHOOL OF MEDICINE

Finding Better Drugs and Diagnostics

An expanded role for academia