
SPARK

Reducing the Barriers between Bench and Bedside

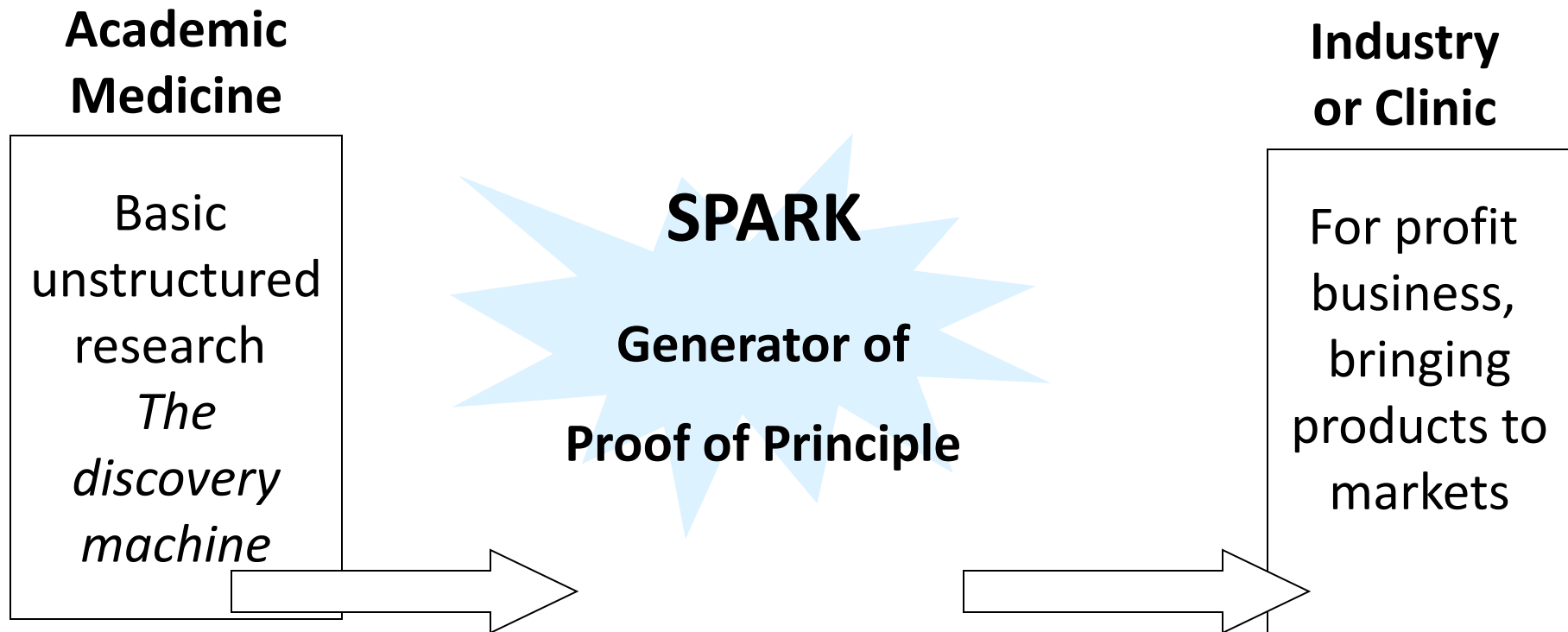
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Problems for Academic Researchers

- 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



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

SPARK Selection Process

Academic-industry selection committee

1. Initial review of promising discoveries from Office of Technology Licensing database ($n \cong 150-200$) and proposals from across the university ($n \cong 50$)
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

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

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

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 difficile* 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

SPARK So Far

27 projects have completed SPARK

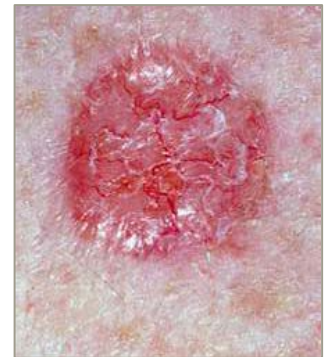
- 10 projects licensed (7 in the clinic)
 - 7 as start-ups (4 SBIRs, 1 applying)
 - 1 to existing small business (1 SBIR)
 - 2 to existing large companies
- 4 projects in clinic but unlicensed

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



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



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



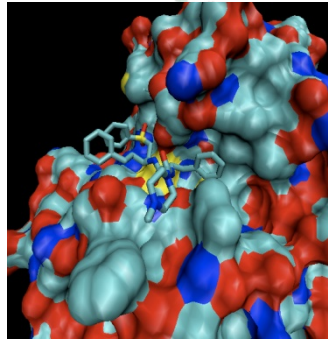
Challenges

- 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.



Finding Better Drugs and Diagnostics

An expanded role for academia