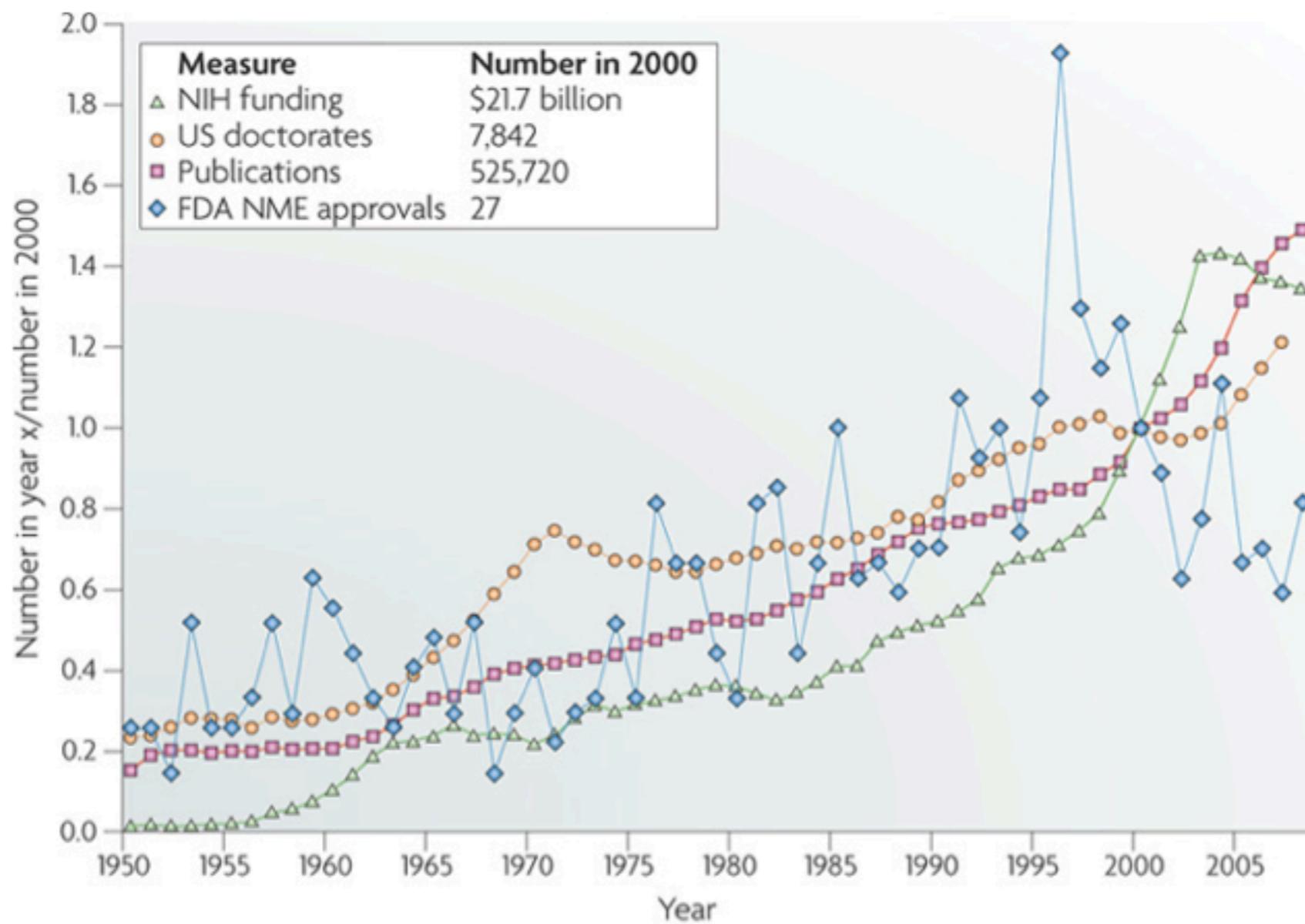




“Opening-Up” Academic Medicine: Experiments in Biomedical Research

Eva Guinan (HMS), Kevin Boudreau (LBS), Griffin Weber (HMS), Karim Lakhani (HBS)

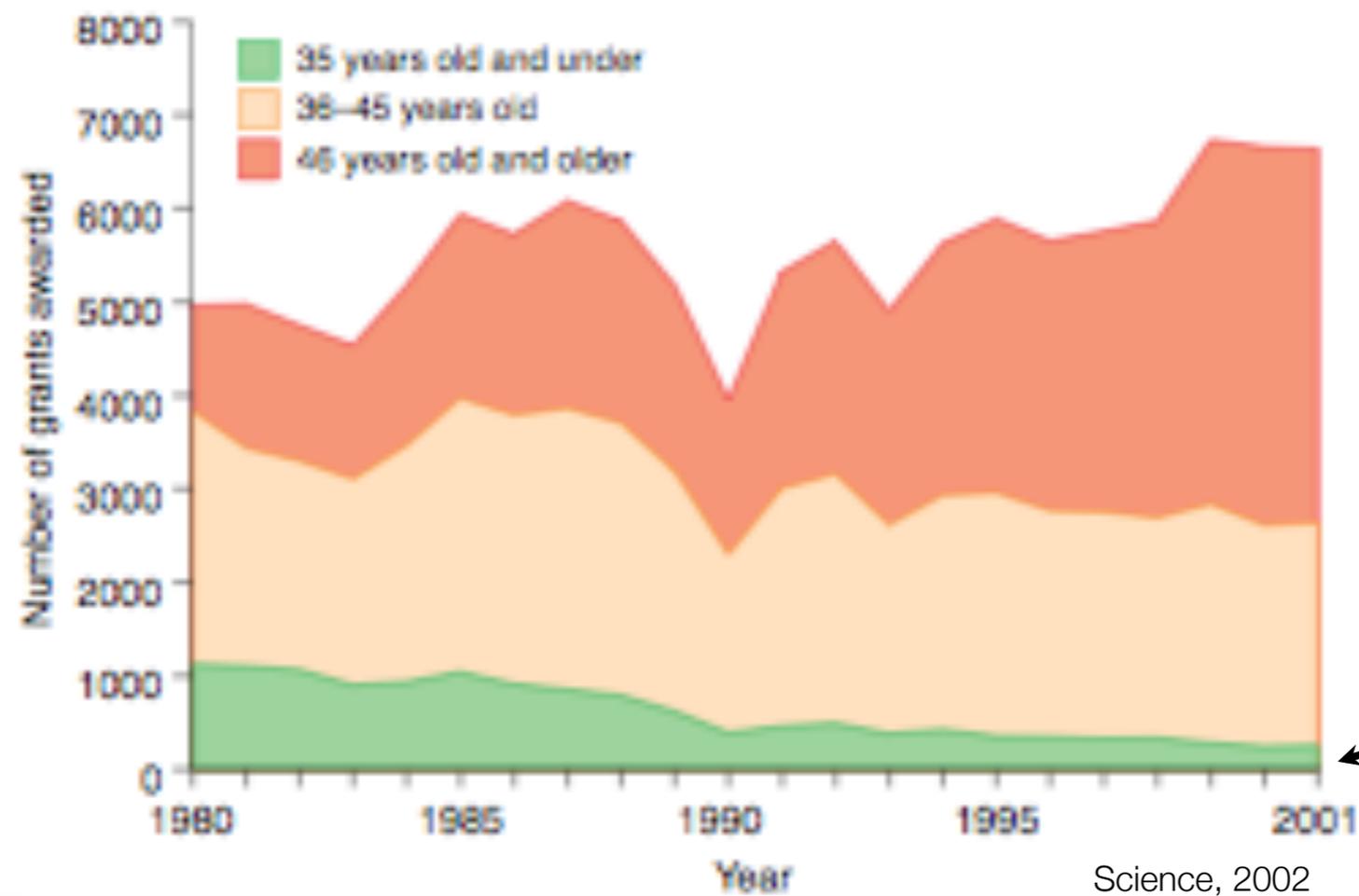
Development of novel therapeutics has stalled



The Academic Gerontocracy

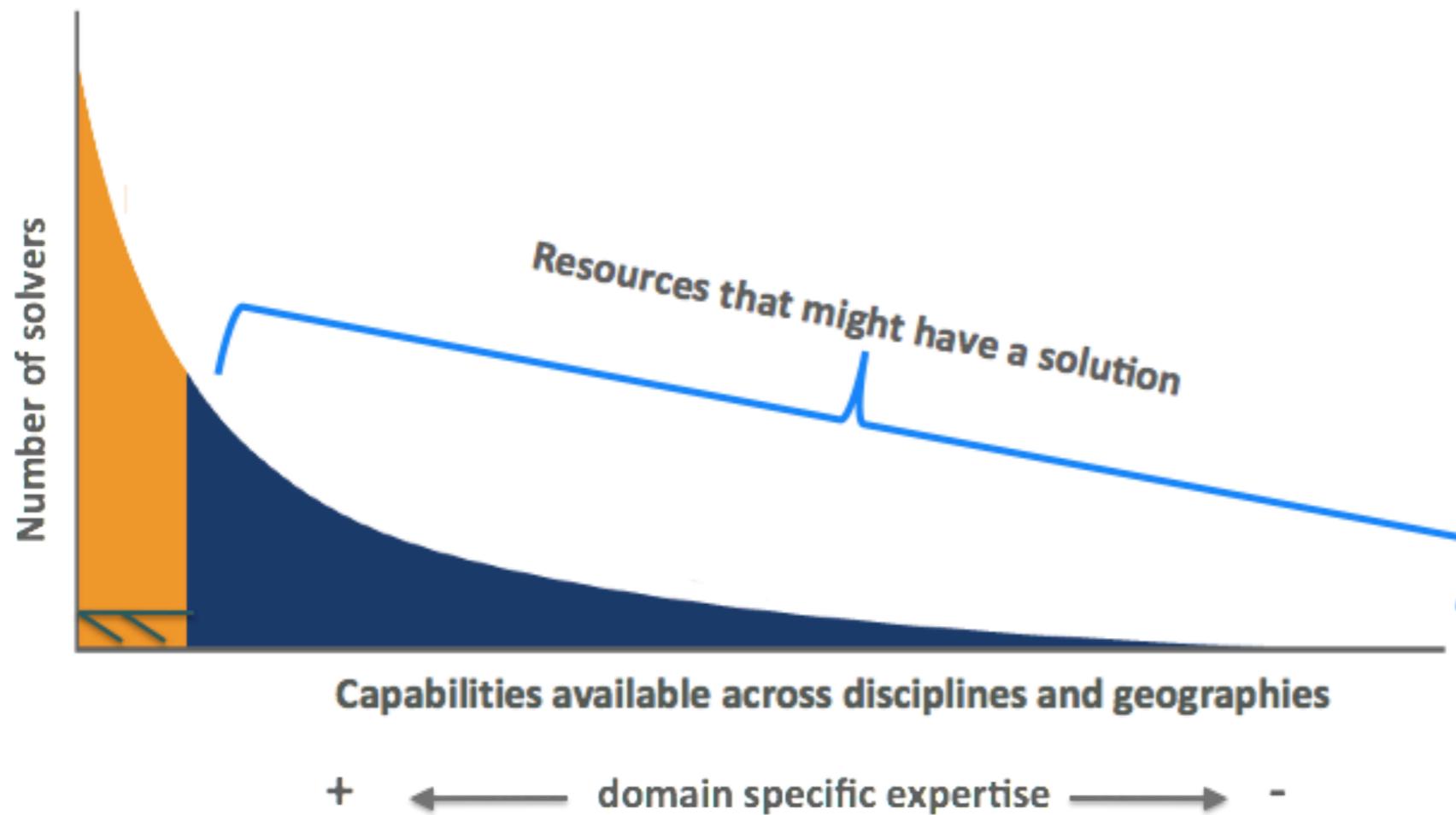


New competing NIH grants

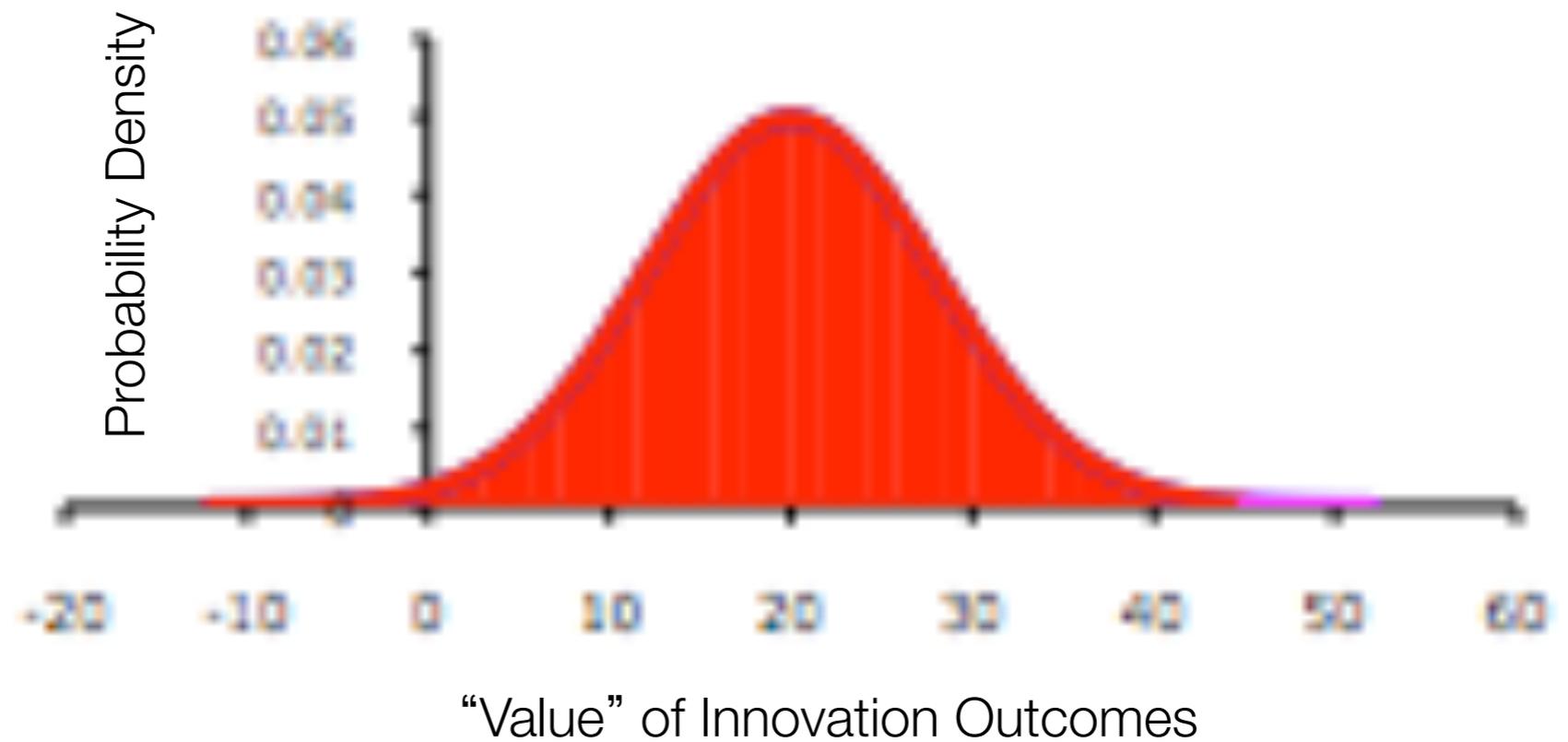


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The Long Tail of Innovation



Accessing “Extreme Value” Key to Innovation



First Step in Opening Up the Research Process



- ❖ **Expand the Solution Space (Reduction to Practice)**
 - ❖ Provide example of engagement to academic community
 - ❖ Feasibility of sourcing a problem
 - ❖ Experience in framing a challenge statement
 - ❖ Develop an argument for a practical/concrete deliverable
 - ❖ Demonstrate ability, creativity and speed of an external solver community
 - ❖ Wide, active broadcast to *untraditional* solvers



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An Experiment in Genomics Algorithm Development

- ❖ Objective: Improve on MegaBlast algorithm for nucleotide sequence alignment
- ❖ Experiment: Facilitate and evaluate external solver participation in development of gene-sequencing tools
- ❖ Calculate levenshtein distance between query string and original string (DNA sequence annotation and prediction)
- ❖ Two week long competition - \$2000/treatment for \$6000 prize pool
- ❖ Treatments: Fully Competitive – head to head competition | Fully Collaborative – full information sharing, individual submission | Hybrid – competition for one week, collaboration for one week

Experimental Results

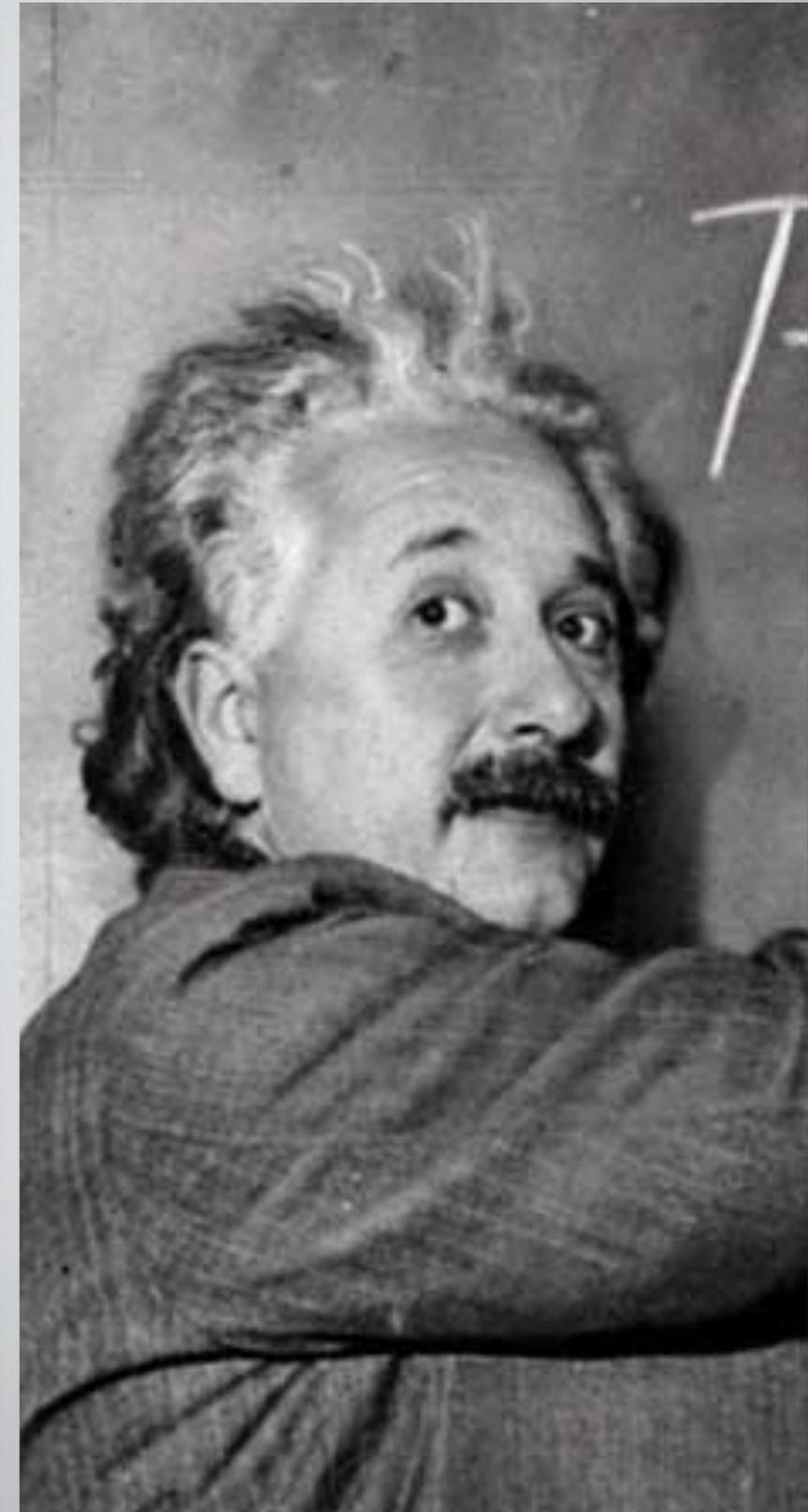
- 733 coders registered and were assigned to 1 of 3 treatments
- 122 coders made 654 submissions
- Top 34 coders exceeded state of the art in computational biology by factor of 10^2 to 10^5
- 9 different approaches to solve problem identified
- Winners from Russia, France, Egypt, Belgium and US



Motivation for Type 1 Diabetes Experiment

“To raise new questions,
new possibilities, to
regard new problems
from a new angle
requires creative
imagination and marks
real advance in science”

- Albert Einstein and Ledlow Enfeld

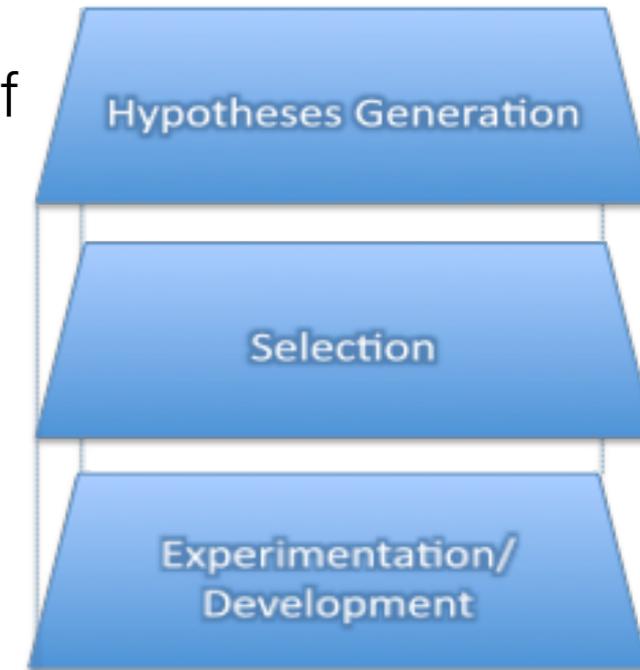


Systematically Open Up the Research Process



Phase 1 - Expand the Hypothesis Space ("Ideation")

- Six-week challenge to submit hypotheses (prize of \$25,000)
- Wide, active broadcast to *traditional* and *untraditional* solvers

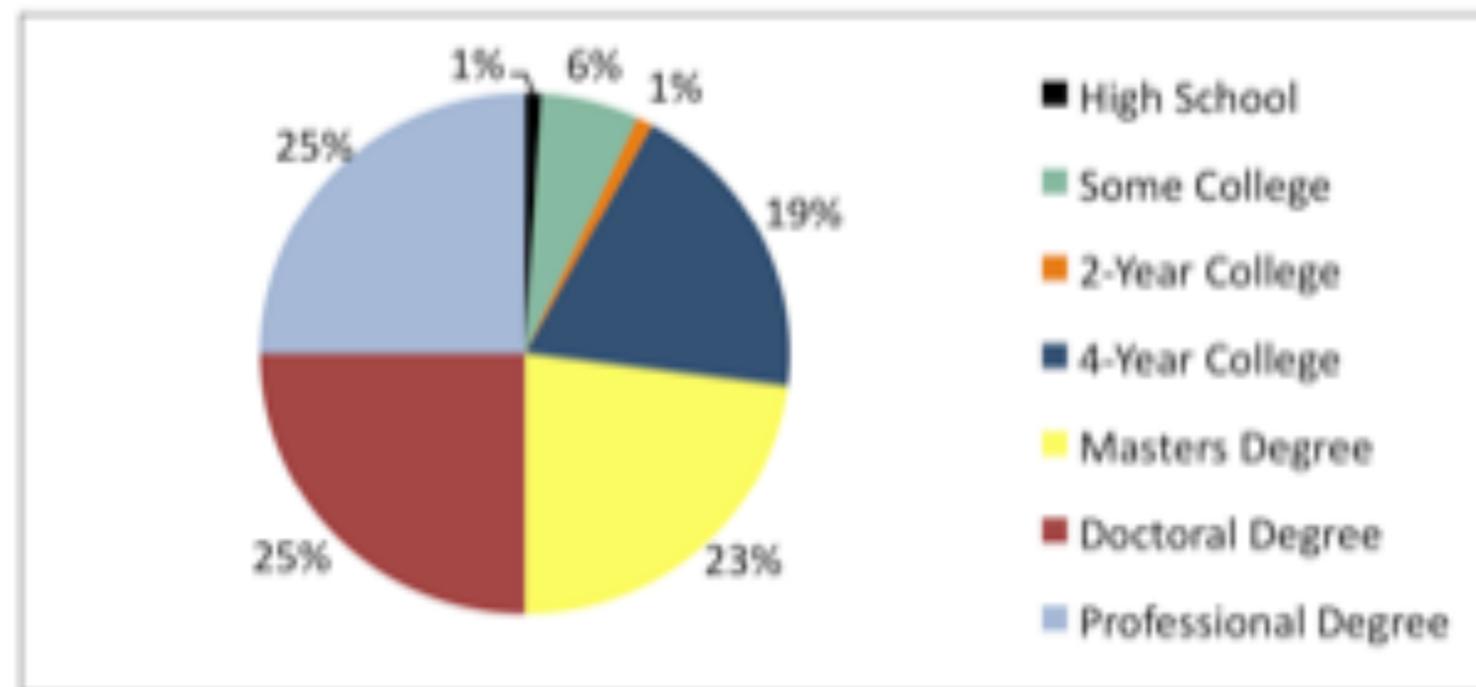


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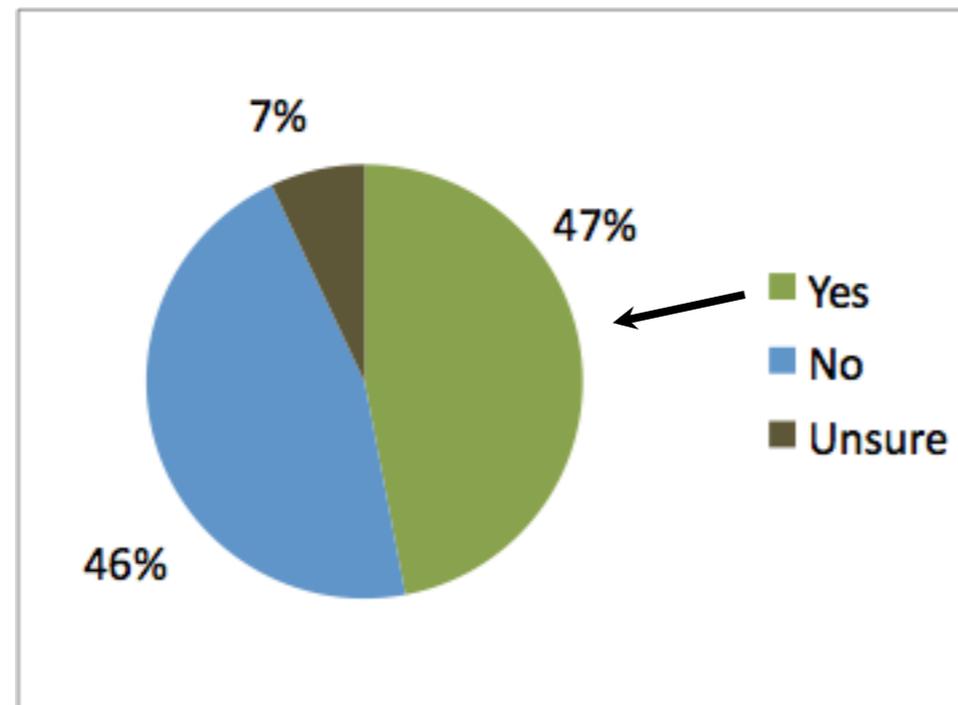
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Who came to the table?

Self report of 'the highest academic qualification received'



Do you or a close family member have Type 1 diabetes?



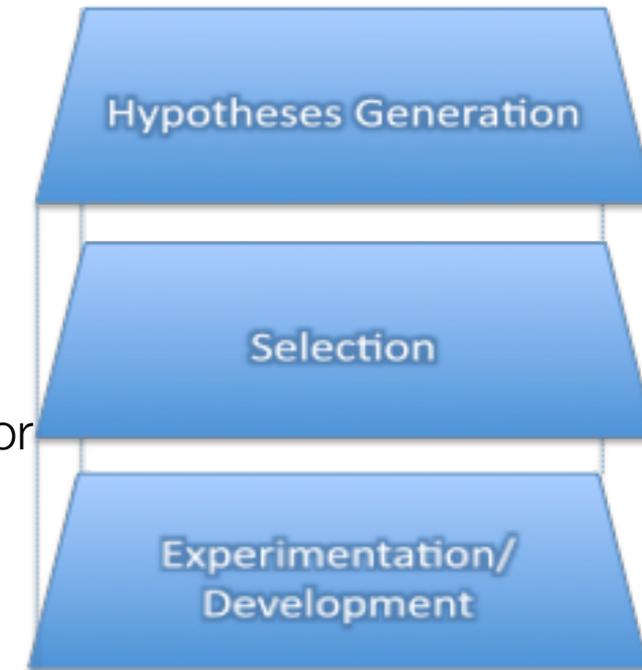
Systematically Open Up the Research Process



- ❖ **Phase 1 - Expand the Hypothesis Space (“Ideation”)**
- ❖ Six-week challenge to submit hypotheses (prize of \$25,000)
- ❖ Wide, active broadcast to *traditional* and *untraditional* solvers

- ❖ **Phase 2 - Alter the Evaluation Process (228 evaluators)**

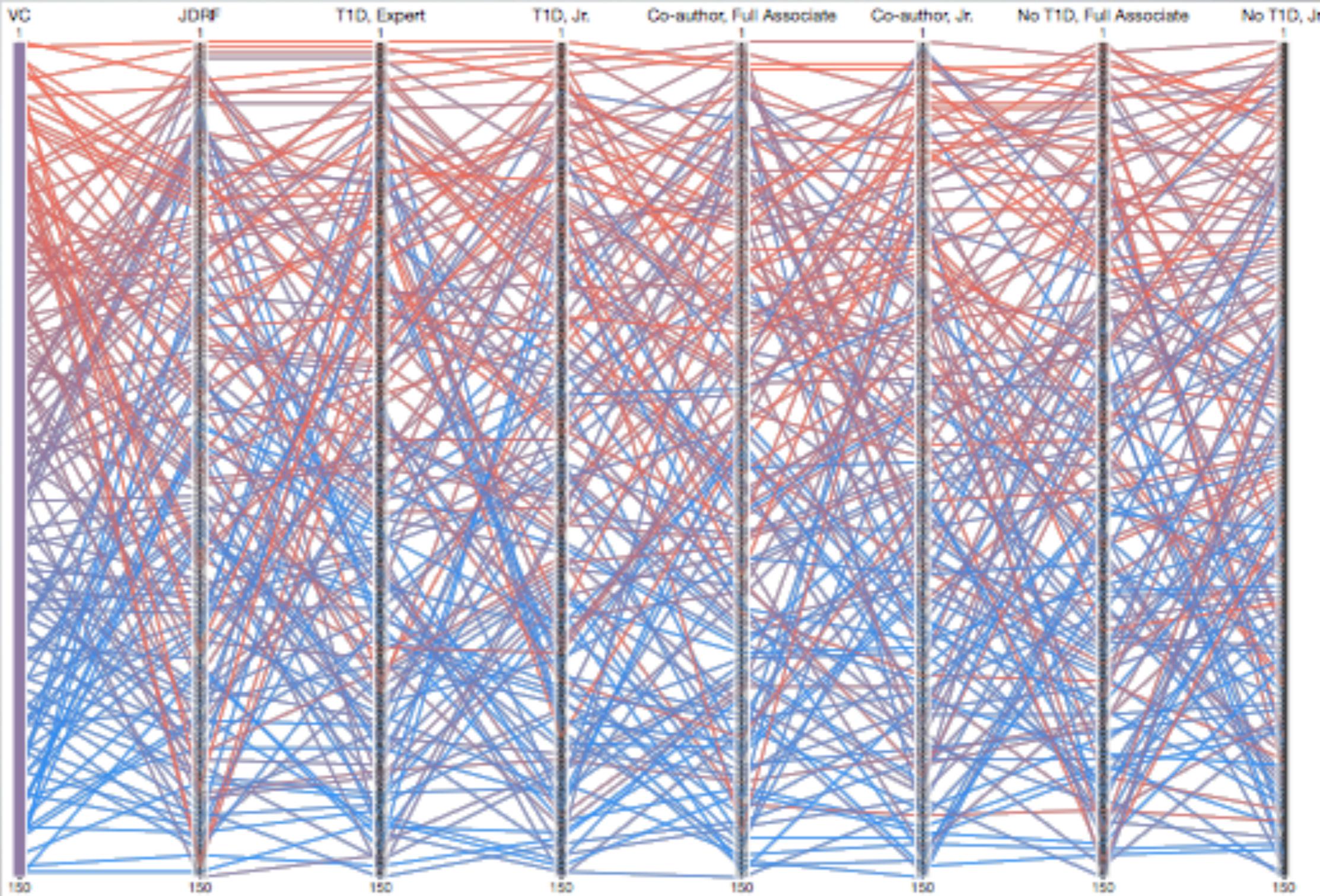
- ❖ *Traditional*: senior T1D researchers/collaborators
- ❖ *Untraditional*: junior T1D researchers/collaborators, senior/junior academic non-experts, VC/Pharma, JDRF



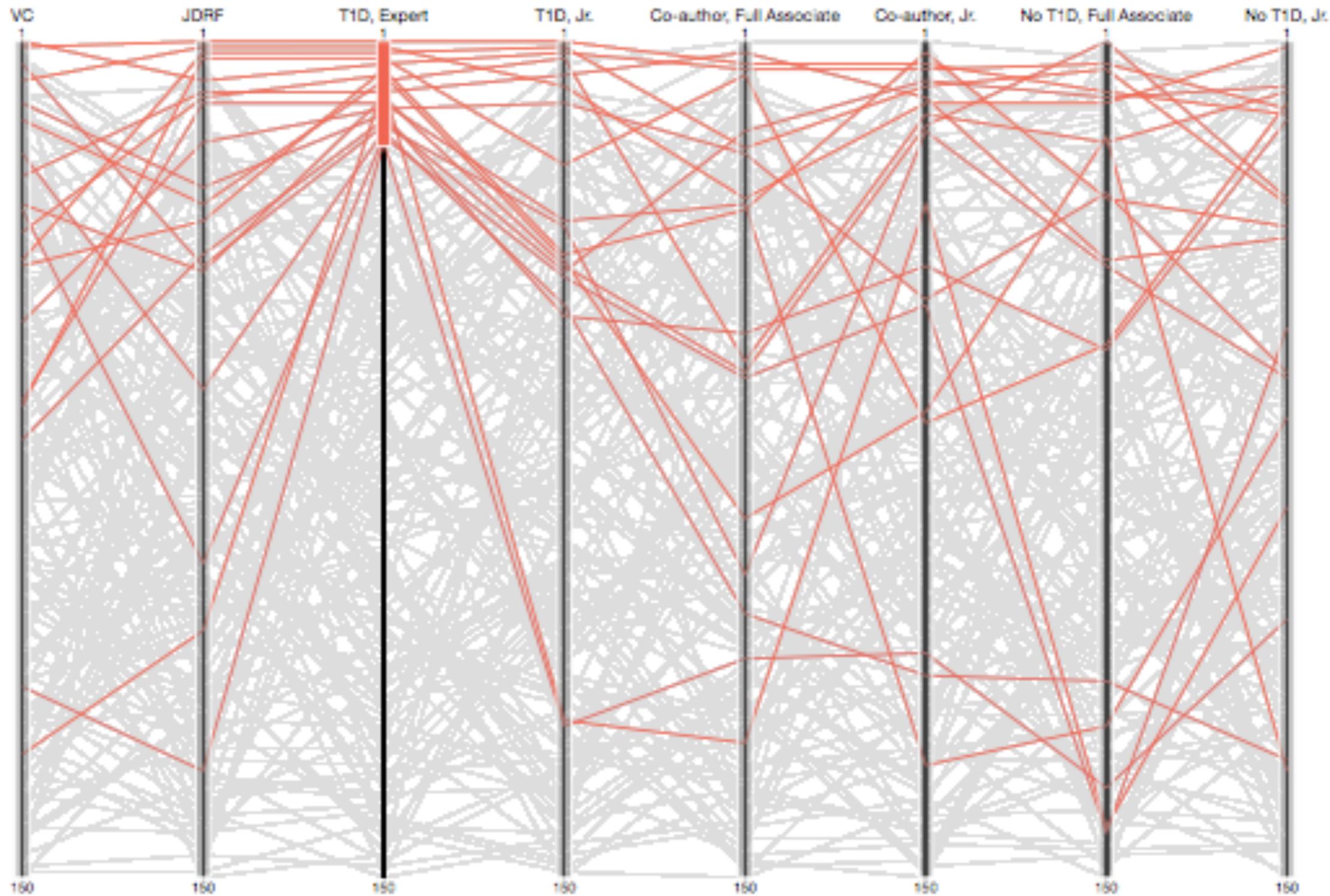
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Wide Diversity of Evaluations



Top Ten Evaluations of T1D Experts Through Other Eyes





Diversity of Winning Solutions: Attacking T1D on all Flanks

- ❖ (Danwei Huangfu, Ph.D.) A **Cell-Electronic Approach** to Insulin Therapy
- ❖ (Carlos O. Mendivil-Anaya, M.D.) Integral Treatment of Type 1 Diabetes using **Smart Liposomes**
- ❖ (James Mulvihill, D.M.D.) Development of a **Non-Invasive Blood Glucose Monitor**
- ❖ (Dirk Moore, Ph.D.) **Family-Based Association Studies to Identify Gene-Environment Interaction and Genomic Imprinting** in Type 1 Diabetes
- ❖ (Srinivas Viswanathan, Ph.D.) **Post-Gastric Bypass Nesidioblastosis** as a Model for Understanding Beta-Islet Cell Neogenesis
- ❖ (Kevin Dolan, M.S.) Type 1 Diabetes, **Patient Maintenance and Care**



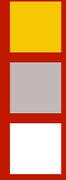
Diversity of Winning Solutions: Attacking T1D on all Flanks

- ❖ (David Friedman, M.D.) A Quiet **Role for Platelets and Eosinophils in Pathogenesis** of Type 1 Diabetes?
- ❖ (Jason Gaglia, M.D.) In-Depth **Analysis of T Cell Repertoire** During the Development of Type 1 Diabetes in **Pancreatic Islet Infiltrating** and Peripheral CD4 T Cells
- ❖ (Matthew Meyerson, M.D., Ph.D., David A. Hafler, M.D., Joonil Jung, Ph.D., Sally Kent, M.D., Alex Kostic, B.Sc. and Akin Ojesina, M.D., Ph.D.) **Hunting for Microbial Genomes** in Type 1 Diabetes by Next-Generation Sequencing
- ❖ (Ms. Megan Blewett) **Lipid Autoreactivity** in Type 1 Diabetes: Clue to Etiology, Co-Occurrence, and Drug Discovery
- ❖ (Anonymous, Professional, Non-medical Field) The Diabetes Triangle: A Systematic Approach to **Align Diabetes Classification with Diabetes Management**
- ❖ (Mark W. Feinberg, M.D.) **Synergistic System Targeting** for Type I Diabetes



The Voices of the Solvers





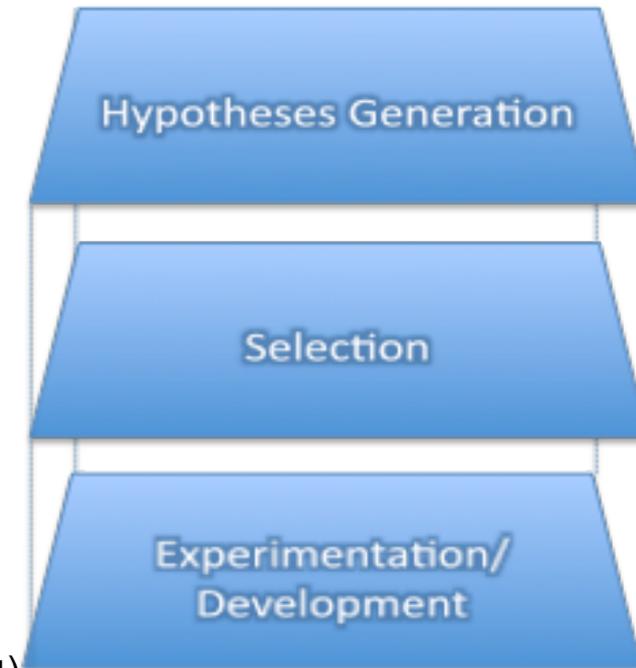
The Voices of the Solvers



Systematically Open Up the Research Process



- ❑ **Phase 1 - Expand the Hypothesis Space (“Ideation”)**
 - ❑ Six-week challenge to submit hypotheses (prize of \$25,000)
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- ❑ **Phase 2 - Alter the Evaluation Process (228 evaluators)**
 - ❑ *Traditional*: senior T1D researchers/collaborators
 - ❑ *Untraditional*: junior T1D researchers/collaborators, senior/junior academic non-experts, VC/Pharma, JDRF
- ❑ **Phase 3 - Reconfigure the Development Space**
 - ❑ Generate RFA from winning hypotheses (\$1M Helmsley Trust)
 - ❑ Contrast *Traditional* (control) “naturally forming” teams; matched pool of *untraditional* “perturbed/engineered” teams



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Process becomes progress

Drs. Turka and Sharpe,

Thank you so much for the good news and especially for your hard work. I know these dollars are precious and how much work goes into this type of program. Doug Melton's team and my team met this week, and we're going to do everything we can to turn this into something that works for patients. (We've actually made substantial progress since the presentation to the reviewers!). I know that our project is a bit crazy, but if it works, it will be cool that it happened here. :)

Rich Lee