Assessing High Risk, High Reward Research at the National Institutes of Health (NIH)

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High Risk, High Reward

- High Risk - research with an inherently high level of uncertainty
  - Many unknowns
  - Hypothesis may not be achieved
  - Often involves innovative ideas or approaches

- High Reward - capacity to produce major impact on important problems in research
  - EX: vaccine research
  - Returns often long term

Current Issues at NIH

- Science and R&D inherently full of unknowns and path unclear
- Programs increasingly multi-site and multi-disciplinary, like systems
- Hypotheses can fail but still generate valuable knowledge

Current Issues at NIH

- Funded research projects may adjust scope to match budget and no longer align with goals and objectives in original RFA
  - Project demonstrates met stated objectives, not overall program objectives
- Higher risk projects judged by same criteria as lower risk projects
  - No scale for assessing risk level of project
  - No incentive for high risk or ambitious projects

Challenge to Evaluation

- Emergent topics (difficult to plan and predict)
- Complex, large, diverse programs
- Dynamic
- Discovery mode – results unknown
  - Undetermined amount of time to reach goals
  - Cost unknown
  - Impact assessments take time post project
- Serendipitous or failed results may lead to advancements not included in project scope

Alternative Approaches

- Assess management of science; science assesses itself
- If science must be assessed, use corrective strategies and adaptive measures
- Develop new methodologies to assess complex high risk, high reward research

Alternative Approach: Assess Management, Not Science

- Process of science assesses itself
  - Results are statistically tested
  - Validation and replication part of scientific discovery process
- Peer Review also assesses science
  - Selection process for funding
  - Publications

Alternative Approach: Assess Management, Not Science

- Overall program objectives achieved, in addition to individual project or site objectives
- Objectives align with overarching program goals
- Scope and/or budget adjusted appropriately
- Adaptive measures that follow path of scientific discovery
- Credit for serendipitous results
- Expectations match level of risk or difficulty

Alternative Approach: Corrections, Adaptive Measures

- View corrective strategies as progress when based on scientific discovery
  - Goal revision
  - Goal extension
  - Target adjustment
- Allow adjustment of prospective annual targets to ensure best science
  - Require sound scientific justification
  - Hence adaptive measures

Alternative Approach: Corrections, Adaptive Measures

- Extend targets in addition to reporting as not met, met, or exceeded
  - Need additional time to achieve target
  - Requires scientific justification
  - Report performance in future
- Capture serendipitous or other important results in performance narrative
  - Report more performance than just achievement of target
  - Capture corrective strategies to depict best science

Alternative Approach: Corrections, Adaptive Measures

Develop path/goal → hypothesis fails → knowledge generated → employ corrective strategies and adapt path/measure

- Original goal: By 2007, demonstrate the feasibility of islet transplantation in combination with immune tolerance induction for the treatment of type 1 diabetes in human clinical studies.
  - Key drug agent failed
  - NIH adapted path to continue conducting best science for research area
- Revised goal: By 2015, evaluate islet transplantation in combination with immune modulation strategies for the treatment of type 1 diabetes in clinical trials.

Alternative Approach: New Methodologies

- Weight assessment by risk level
  - High risk projects assessed differently than low risk projects
  - Criteria needed to evaluate risk level
- Include knowledge generation as measure of success
  - Serendipitous results, failed results, null hypotheses all yield knowledge
  - Criteria needed to evaluate knowledge generation

Alternative Approach: New Methodologies

- Develop system assessment methodologies to assess large complex multi-site, multi-disciplinary programs
  - Not sum of individual project assessments
- Develop benchmarks for R&D
  - EX: average time to develop vaccine
  - Can signal when corrective strategies needed

Conclusion

- Traditional evaluation approaches do not work for high risk, high reward research projects
- Best approach is to use correctives strategies and adaptive measures
- New approaches needed to:
  - Assess stewardship and management
  - Assess high risk, high reward programs