Short and Long-Term Goals for Sequencing in Complex Disease Research

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Obstacles and Opportunities

- Sequencing costs are high, but they are coming down.
- The biomedical IT infrastructure is not up to the task, but this project will be enabling.
- The perfect study sample is not available, but a collection of existing (and emerging) samples sets will likely achieve our goals.
- This should not be seen as a US effort, but rather an international effort.
- This is not the right time because of economic uncertainty, but it will create a widely used research resource, promote a better health care infrastructure, and fuel a therapeutic pipeline.
- Institutional and disciplinary silos will undermine the effort, but the project will only succeed with a result-oriented team effort.
Recognize and Organize Existing Infrastructure

Available samples on well-phenotyped individuals.

Data Sharing

Need to recognize success

- Y142X or C679X variants
  - African-Americans
    - N = 3,363 followed 15 years
  - R46L variant
    - European-Americans
      - N = 9,524 followed 15 years

![Graph](chart.png)

- PCSK9^{142X} or PCSK9^{679X}
  - CHD, (%)
    - No: 28% ↓ LDL; 88% ↓ risk, p = 0.008
    - Yes: 0%

- PCSK9^{46L}
  - CHD, (%)
    - No: 15% ↓ LDL; 47% ↓ risk, p = 0.003
    - Yes: 12%
I am an optimist.....