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Cancer Pharmacogenomics:
Setting a Research Agenda to Accelerate Translation

Workshop Overview & Objectives

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Trans-NCI Pharmacogenomics and Pharmacoepidemiology Working Group (PPWG)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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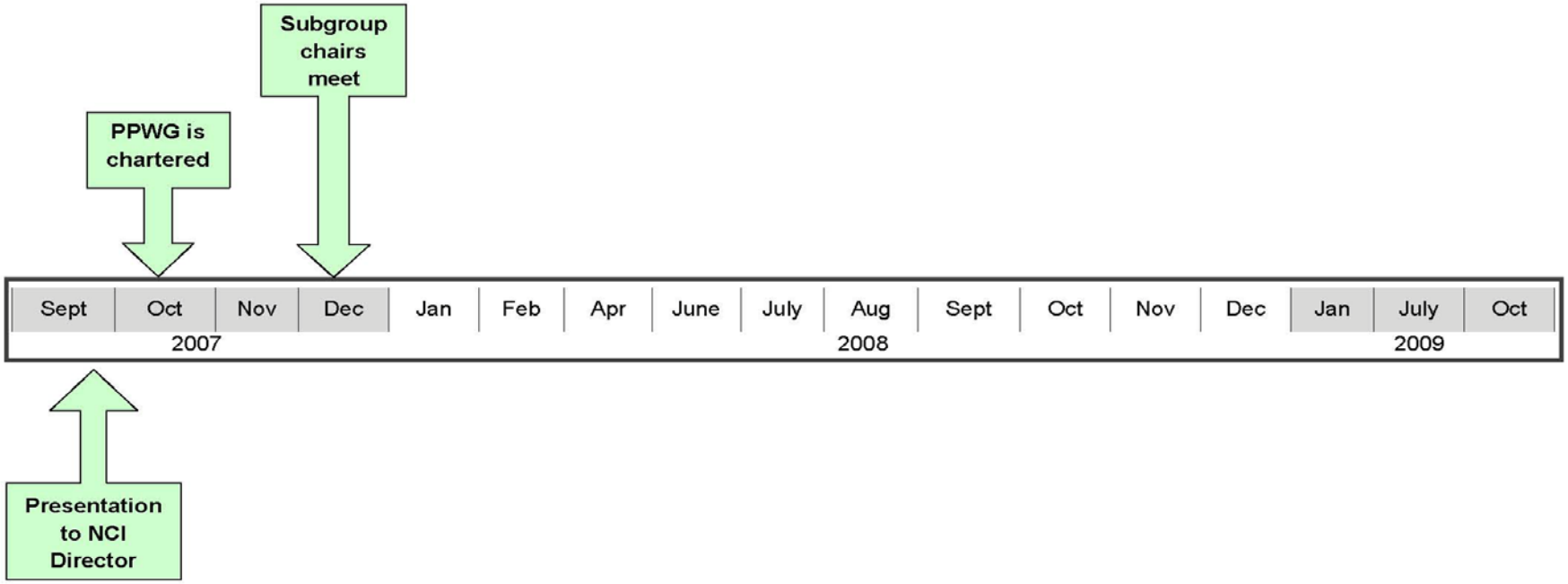
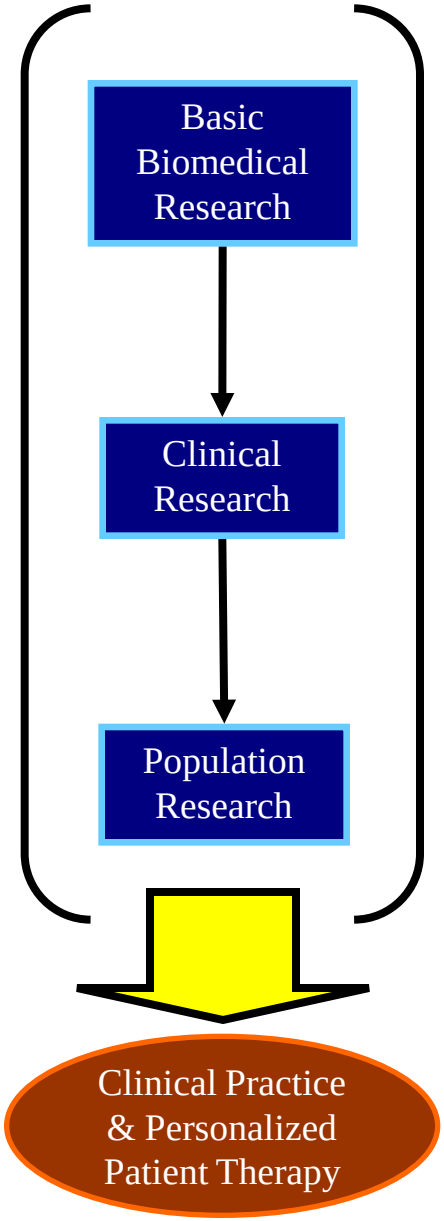
Outline

- Trans-NCI Pharmacoepidemiology and Pharmacogenomics Working Group (PPWG)
  - Formation, Structure and Progress
- Goals of the PPWG and Subgroups
- Development of the PPWG Recommendations
- Goals and Objectives of the Workshop

Trans-NCI PPWG Progress



Translation of Cancer Pharmacoepidemiology and Pharmacogenomics



Description	Funded by:	Examples:
Basic Science Subgroup		

• **Drug Development**
  • In vitro and In vivo and preclinical testing
• **Pharmacogenomic Variability**
  • **Pharmacokinetics**: absorption, distribution, metabolism, excretion
  • **Pharmacodynamics**: receptors, target proteins enzyme regulation
	• Pharma
	• NIGMS
	• NCI
		• PGRN
		• SPOREs
		• RO1s
		• CCR
		• DCB
		• Pharma

Clinical Trials Subgroup		
• **Clinical trials** • **Phase 0**: Metabolism- FHIT- 10-15 subjects • **Phase 1**: Safety, metabolism- 20-80 subjects • **Phase 2**: Efficacy, dose, safety- 20-300 subjects • **Phase 3**: Efficacy and safety for approval- 300-3000 subjects	• Pharma • NCI	• NCI trials • SPORES • CCR • DCP • DCTD • Pharma
Population Science Subgroup		

• **Registries**
• **Pharmacoepidemiology**
  • Etiology
  • Identifying new risk & preventive factors
• **Passive surveillance: FDA AERS**
• **Phase 4 trials: Pharmacovigilance**
  • Safety, effectiveness
  • Case-control studies
  • Prospective studies
	• Pharma
	• FDA
	• AHRQ
	• NCI
		• CERTs/DEcIDE
		• Health Plans
		• Insurers
		• VA
		• DOD
		• CMS
		• Academic & Community Systems
		• DCCPS
		• DCEG
		• Pharma

• **Dissemination, implementation**		

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Trans-NCI Pharmacogenomics & Pharmacoepidemiology Working Group (PPWG)

- **Goals:**

- Develop recommendations to support the development of a comprehensive and interdisciplinary pharmacoepidemiology (PE) and pharmacogenomics (PGX) cancer research program in order to accelerate the translation of discoveries in basic, clinical and population research to enhance personalized therapy
- Provide support for the discovery of clinical, epidemiologic and genomic factors that are associated with:
  - adverse effects and enhanced response of cancer prevention and treatment therapies
  - commonly-prescribed pharmaceuticals and risk of cancer

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Basic Science Subgroup Goals

Chair: Doug Figg, Ph.D.

- Facilitate the development and application of pharmacogenomic technologies for drug discovery and diagnostic development
- Identify novel genetic variants and expression profiles involved in drug metabolism
- Relate genomic associations observed in clinical and observational studies to protein function

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Clinical Trials Subgroup Goals

Chair: Lori Minasian, M.D.

- Identify opportunities, resources, and methodologies needed to incorporate genomic biomarkers and genomic tests in the design and analysis of clinical trials
- Identify NCI-sponsored Phase II/III trials that have prospectively collected biospecimens
- Explore the opportunity to develop electronic pooling of adverse event data
- Establish funding mechanisms and guidelines for standardized sample collection, storage, and processing of biospecimens

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Population Sciences Subgroup Goals

Co-Chairs: Leah Sansbury, Ph.D., & Nathaniel Rothman, M.D., M.P.H.

- Identify opportunities and data infrastructures to investigate clinical and epidemiologic factors related to the response and toxicity of pharmaceuticals used in the treatment and prevention of cancer
- Provide a platform to conduct targeted observational studies to identify genomic variants related adverse events and enhanced response of cancer prevention and treatment therapies
- Provide evidence for clinical utility of these novel genomic markers

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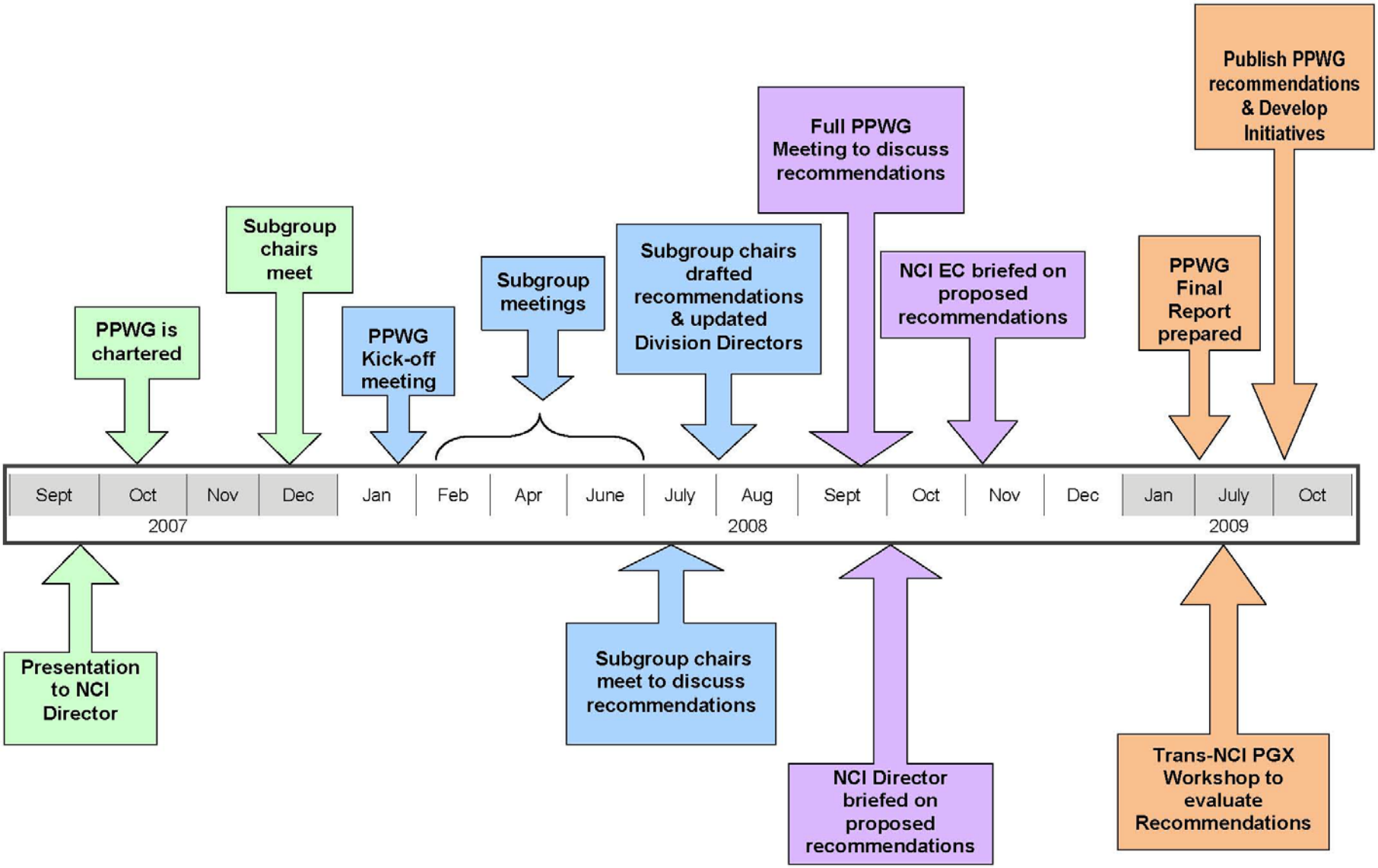
Additional Goals of the PPWG

- Enhance communication, coordination, and collaboration of PE and PGX research across NCI
- Engage other NIH ICs and federal agencies in PE and PGX research
- Identify infrastructures and resources that are needed to advance PE and PGX cancer research
- Leverage existing research efforts by other HHS agencies
- Partner with federal healthcare delivery agencies to conduct and support PE and PGX research
- Plan a workshop to review recommendations
  - Include other government agencies, extramural community, and industry


PPWG is chartered
Subgroup chairs meet
PPWG Kick-off meeting
Subgroup meetings
Subgroup chairs drafted recommendations & updated Division Directors
Full PPWG Meeting to discuss recommendations
NCI EC briefed on proposed recommendations
PPWG Final Report prepared
Publish PPWG recommendations & Develop Initiatives
Sept
Oct
Nov
Dec
Jan
Feb
Apr
June
July
Aug
Sept
Oct
Nov
Dec
Jan
July
Oct
2007
2008
2009
Presentation to NCI Director
Subgroup chairs meet to discuss recommendations
NCI Director briefed on proposed recommendations
Trans-NCI PGX Workshop to evaluate Recommendations

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Workshop Objectives

- To evaluate the recommendations of the Trans-NCI PPWG in order to develop a comprehensive and integrated scientific agenda to accelerate the translation of this research from discovery to application

- To ensure the PPWG's recommendations help NCI focus on the most promising research opportunities that will move the field of pharmacogenomics forward in the areas of basic science, clinical trials and the population sciences

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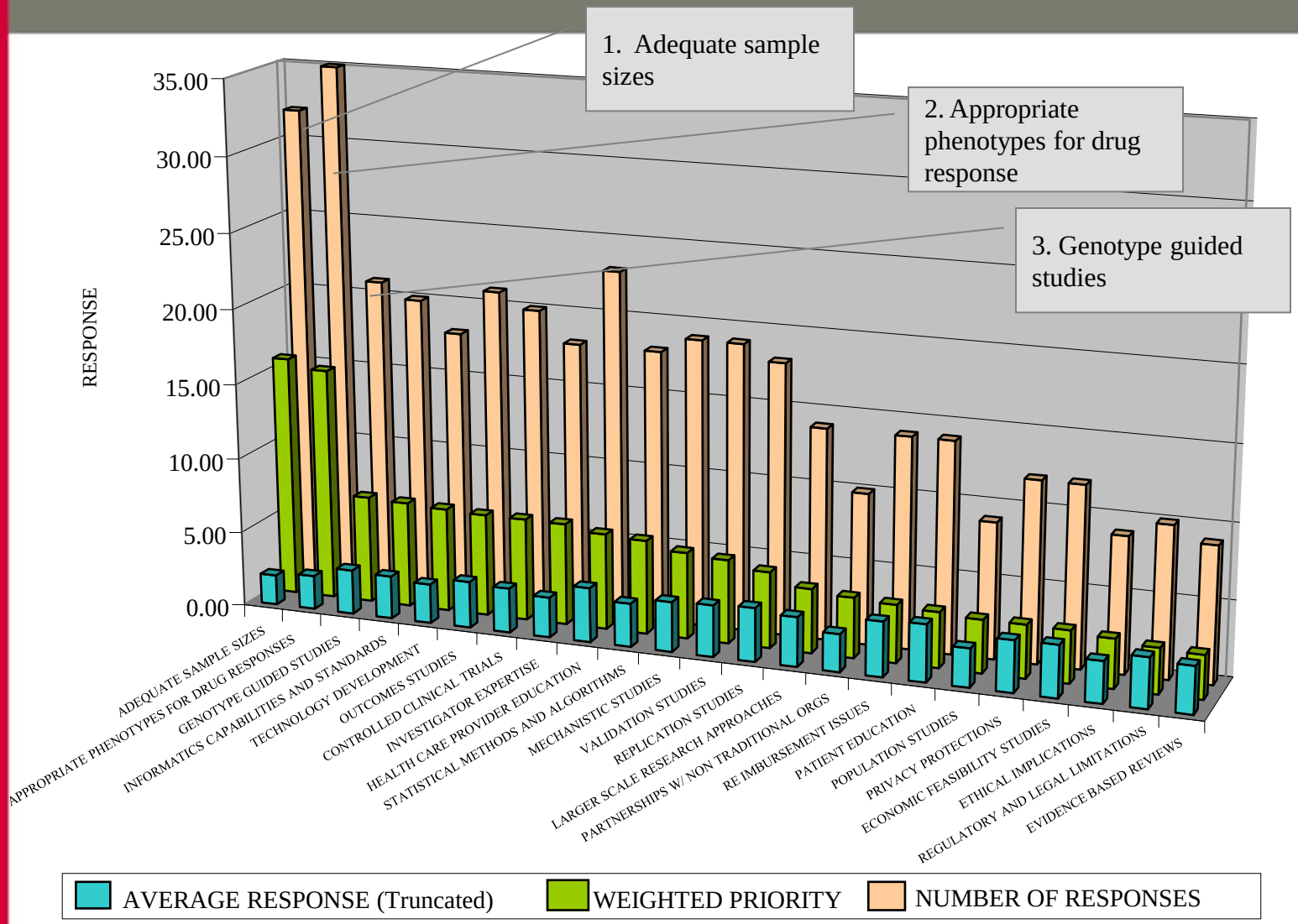
Responses to NIH Pharmacogeomics Working Group Request for Information



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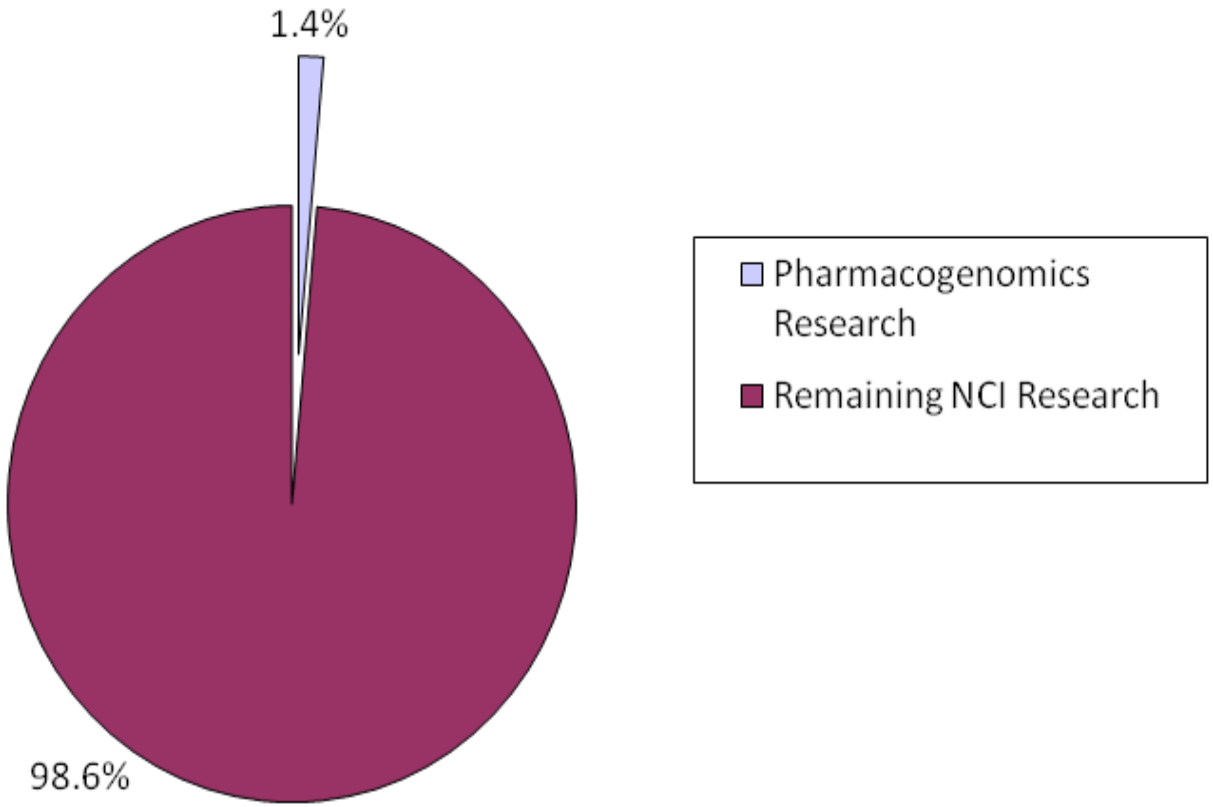
Current Pharmacogenomics Support at NCI

Percentage of NCI's 2007 Research Funding Dollars from NCI's 6 Divisions* Relevant to Pharmacogenomics Research



*NCI Divisions include: CCR, DCB, DCCPS, DCEG, DCP, DCTD

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Portfolio Analysis

Percentage of NCI's 2007 Research Funding Dollars from NCI's 6 Divisions* Relevant to Pharmacogenomics Research

Pharmacogemomic Research Portfolio Summary

Total Pharmacogenomic Portfolio	
Number of Relevant Awards in 2007	98
Percentage of Total NCI Awards*	1.2%
2007 Funding ($ in millions)	$38.8
Percent of Total NCI Budget*	0.8%
Funding to Six Divisions/Centers in 2007 ($ in Millions)	$2,815
Percentage of FY 2007 Pharmacogenomic Funding to Research Funding across Six Divisions/Centers	1.4%

*Total NCI portfolio in FY 2007 was 8,302. Total NCI budget in FY 2007 was $4.8B.

*NCI Divisions include: CCR, DCB, DCCPS, DCEG, DCP, DCTD

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Ongoing and Developing Activities in Pharmacoepidemiology and Pharmacogenomics

- Basic Science
  - Pharmacogenetics Research Network (PGRN)
    http://www.nigms.nih.gov/Initiatives/PGRN
    - Effect of genetic variants on the pharmacokinetics and pharmacodynamics of anticancer agents
    - Contribution of genetic variants to the efficacy and toxicities of endocrine treatments for breast cancer
    - Pharmacogenetics of Phase II Drug Metabolizing Enzymes

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Ongoing and Developing Activities in Pharmacoepidemiology and Pharmacogenomics

- Clinical Trials
  - NCI-sponsored pharmacogenomics correlative studies
  - RIKEN collaboration
  - The Breast Cancer Intergroup (TBCI)
    - Pharmacogenomics meeting, March 2008
    - Support correlative studies
  - MARVEL lung cancer trial

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Ongoing and Developing Activities in Pharmacoepidemiology and Pharmacogenomics

- Population Science
  - HMO-CRN cardio toxicity and breast cancer treatment demonstration project
  - PGRN population science supplements
  - NCI-VA Study on Erythropoietin (EPO)
  - SEER-Medicare study of biologic therapies for cancer
  - PGx website (http://riskfactor.cancer.gov/tools/pharmaco)