



**NTP**  
National Toxicology Program

# Host Susceptibility Initiative

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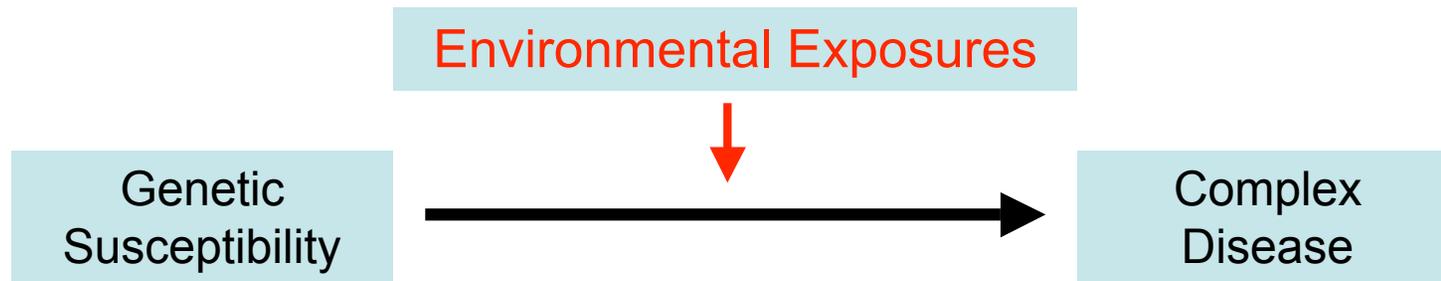
[pritcha3@niehs.nih.gov](mailto:pritcha3@niehs.nih.gov)





## Overview

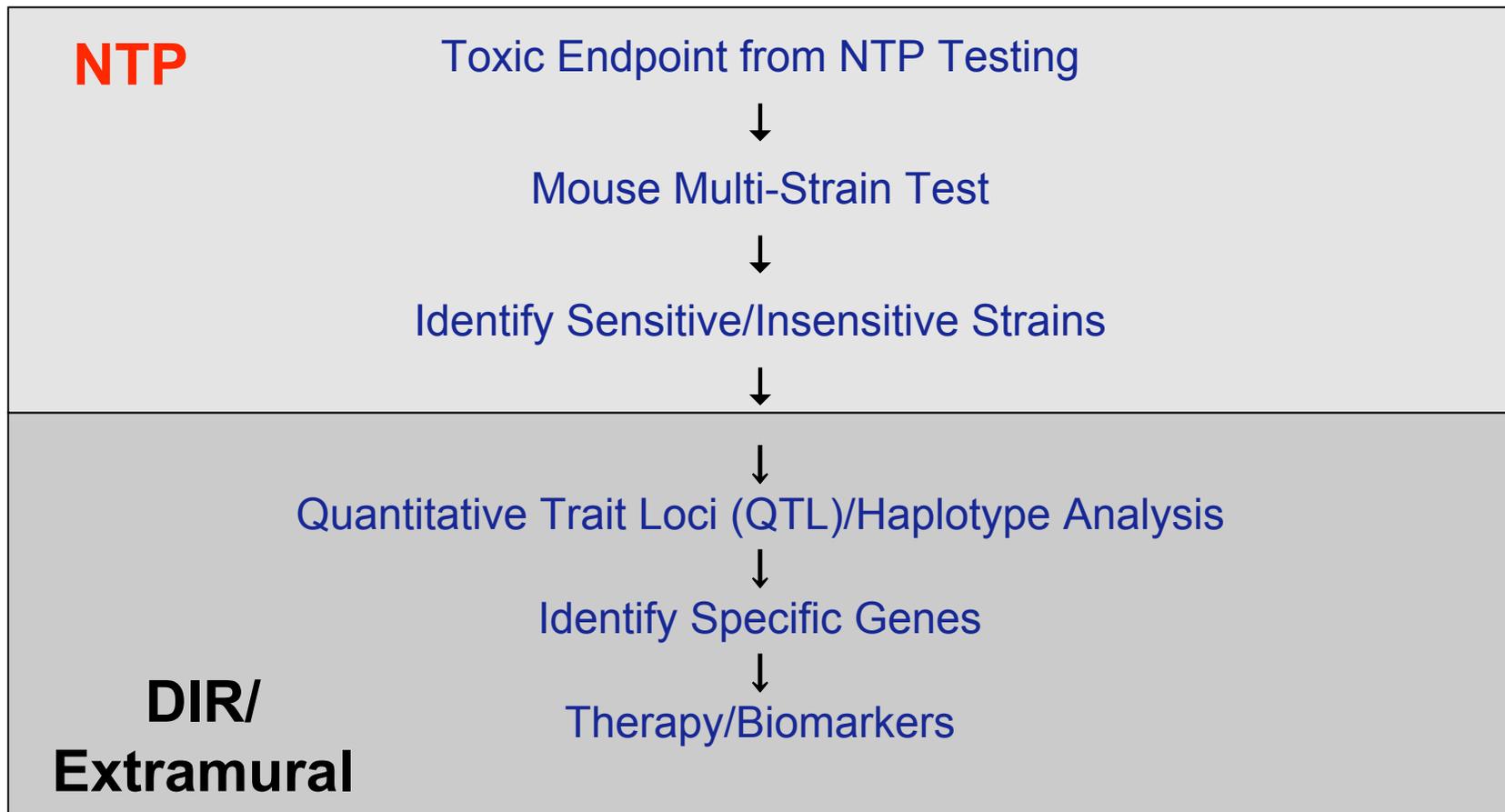
- Part of the general focus on Gene-Environment Interaction



- In the Host Susceptibility Initiative the focus is individual susceptibility to environmental agents, i.e., via the combination of interactions between environmental agents and:
  - **specific genes**, but also
  - **diet**
  - **other disease**
  - **age**



# The Approach





# Approach

- Select Strains
- Identify Endpoints for Further Testing
- Perform Strain Tests
- Communicate to DIR and Extramural Scientists



## Select Strains

- Identify Mouse Genetics Experts for Consultation
  - Dr. Kenneth Paigen, Jackson Laboratory
  - Dr. David Threadgill, University of North Carolina
  - Dr. Robert Williams, University of Tennessee at Memphis
  - Dr. Tim Wiltshire, Novartis
- Meet with NTP Staff (July 21, 2006)
- Some of the Issues
  - How many strains
  - Which strains
  - Are different strains needed for different endpoints
  - Statistical issues



# Identify Endpoints

- **Desired Characteristics of Endpoints**
  - Important effect in critical system
  - Clear link to human disease/toxicity
  - Appropriate to test in mouse
  - Duration of test
- **Others Characteristics to be Considered?**



## Perform Multi-Strain Testing

- Build on NTP expertise, infrastructure, and collaborative culture
  - Team approach
  - Lead scientist ideally the NTP scientist responsible for original tests on that chemical or endpoint
  - Analysis of data utilizing NTP standards of rigor
    - Chemistry/toxicokinetics
    - Statistics
    - Pathology (if appropriate)
    - Other



# Dissemination

- Critical and Not Fully Developed
- Certainly Via:
  - Publications, including NTP Reports
  - Public presentations – e.g., Meetings
  - Targeted activities
    - Workshops
- Other Suggestions?



## Summary

- A new initiative to leverage NTP expertise and data to gain insight into critical genes contributing to the response of individuals to environmental exposures.
- Intended to foster greater use of NTP findings in the understanding of complex human disease.
- Ultimately, to increase our understanding of Gene-Environment interactions leading to identification of new biomarkers for detection of exposure to damaging agents and new candidates for clinical intervention.