Concept Clearance:

Development of Translational Animal Models for Rare Diseases

Franziska B. Grieder, D.V.M., Ph.D.
Director
Division of Comparative Medicine
Office of Research Infrastructure Programs
DPCPSI

Background:

Rare Diseases – Conditions affecting fewer than 200,000 individuals or <0.1% of the US population. Thousands of conditions.

Examples – Bloom Syndrome, Crohn's Disease, Leigh syndrome, Midas syndrome, Nemaline myopathy, Noonan syndrome, and many others.

Comparatively few research studies are conducted, because there is little profit incentive for pharmaceutical companies and only few basic scientists studying these diseases.

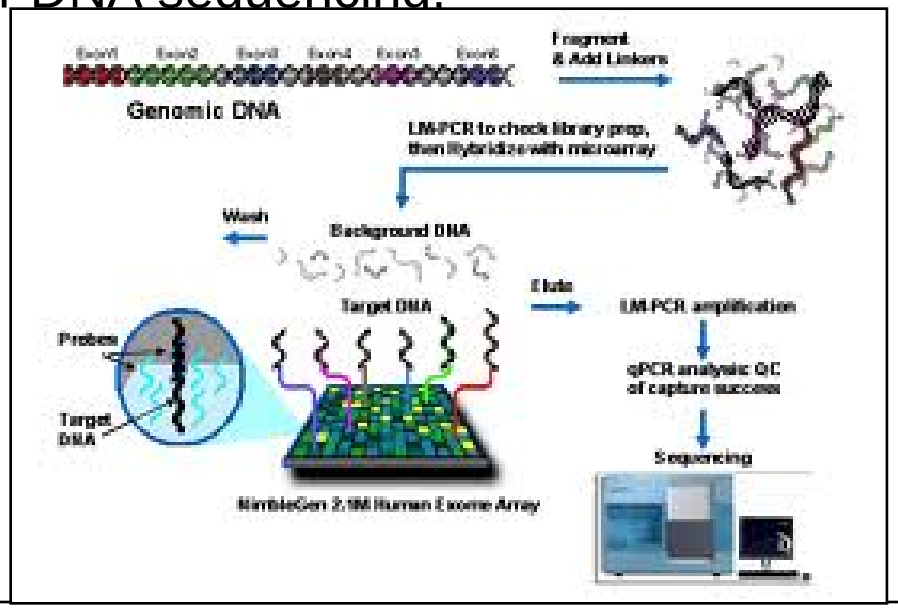
Office of Rare Diseases Research – a portal for information.

Therapeutics for Rare and Neglected Diseases (TRND) within NCATS encourages and enhances the development of new drugs for rare diseases.

Current Technological Advances:

An expanding repertoire of genetic technologies make animal models extremely valuable in bridging the gap between genetic associations and translational model systems that help understand the cause of disease and search for therapeutics.

Technologies include
- Discoveries through the Human Genome Project
- Development of faster and cheaper DNA sequencing:
  Exome sequencing (also known as targeted exome capture)
- Advances in genetic manipulations of numerous model organisms (ranging from bacteria to pigs and non-human primates)



Proposal:

Initiative to support grants/centers that will produce and characterize genetically-modified animals carrying specific mutations analogous to the mutations in patients suffering from these rare diseases.

- Genetically-modified animals (from yeast to non-human primates) will be tested for phenotypes analogous to those observed in human patients.
- Many Rare Diseases are caused by defects/modifications in single genes. Replication of those changes in corresponding genes of an model animal is an effective way to explore the association of the human genetic variation and the rare disease condition.
- Phenotypes of the reconstructed genetic modification may vary in different animal species; hence, various species will be investigated.
- Past progress in making and characterizing genetically-modified animals in several species (ranging from single cell organisms to fish to pig) combined with support for appropriate technologies positions DCM/ORIP in an ideal position to support this activity.

Proposal (2):

The first year cost for this program that would involve other ICs' participation is estimated at $6 – 12M per year for five years duration.

Potential Impact of this Program:

- Infrastructure and research funding to create Animal Model Centers for Rare Human Diseases.
- Centers will make available: Characterized animals, associated biomaterials (*e.g.*, vectors, information), expertise.
- Expand potential to elucidate the nature of rare diseases. Encourage and enable discovery, validation, and preclinical trials of new therapies.

Rhesus monkeys engineered to develop an aggressive form of Huntington's Disease
(at the Yerkes National Primate Research Center and Emory University)

Questions?