

Genetics and the Future Health Care System

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THE MICHAEL J.

FOX

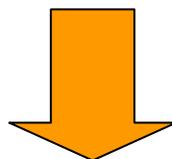
FOUNDATION FOR

PARKINSON'S

RESEARCH

MJFF was founded in 2000 with clear objectives

DRIVE THE BEST PARKINSON'S RESEARCH



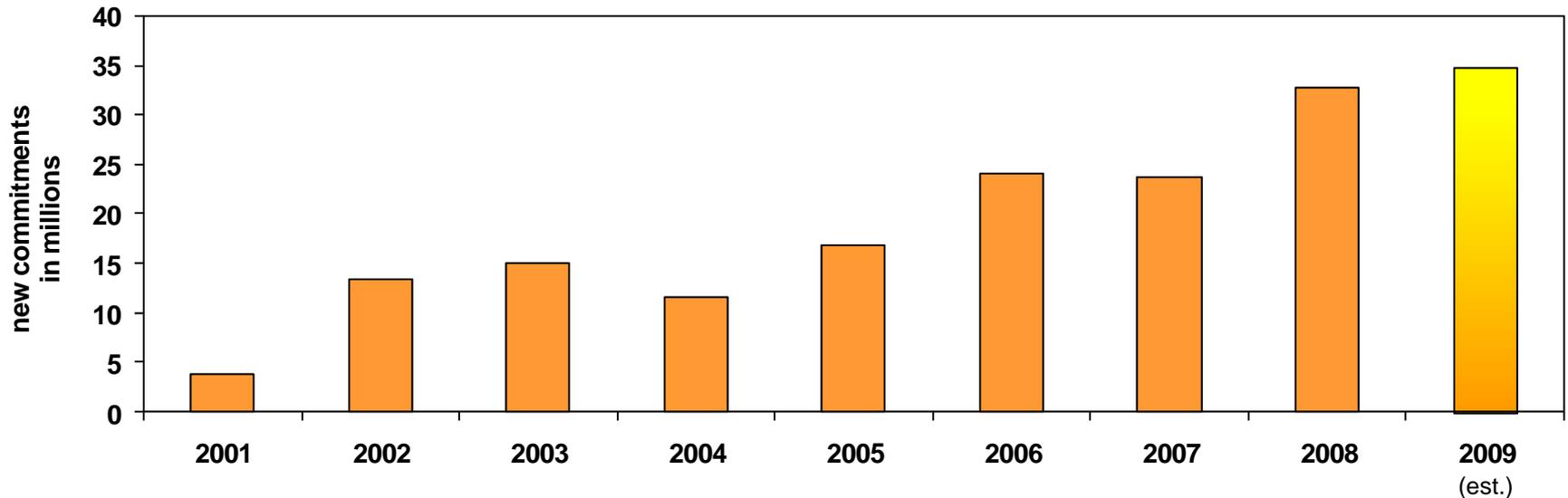
DISCOVER IMPROVED THERAPIES AND A CURE

Unlike many patient-driven nonprofits, we are exclusively focused on driving research and do not engage in other patient-related activities like education, doctor referrals, or support groups

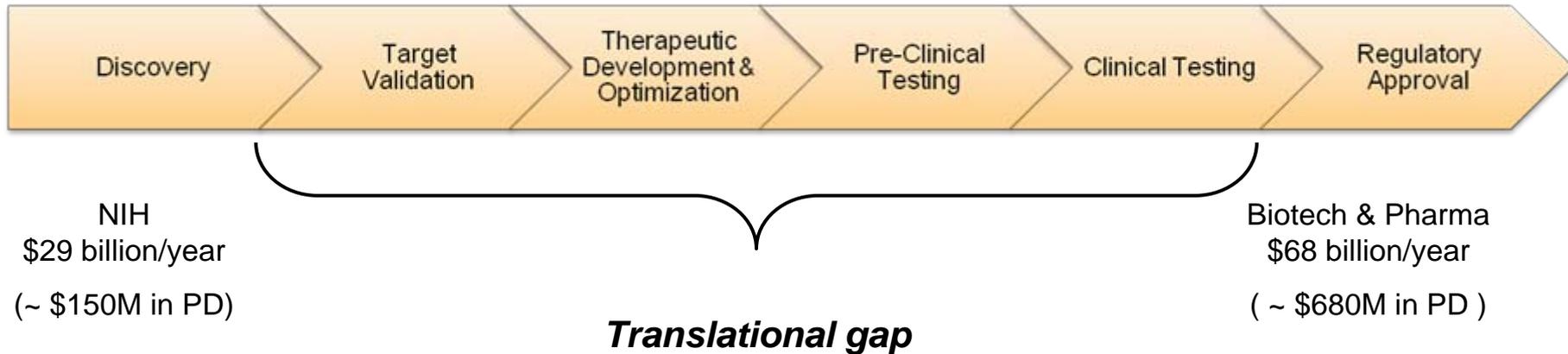
Today, MJFF is the largest private PD funder in the world

MJFF has funded over \$142 million in PD research with an additional \$30-35 million in new commitments planned for 2009

- MJFF revenues come from over 40,000 contributions (mostly from individuals) ranging from \$5 to multi-million dollar donations
- MJFF values efficiency and accountability: 85 cents of every \$1 goes straight to funding research efforts



Our focus is on driving translational research



The gaps in the drug development pipeline guide our actions and priorities

- What are the most promising therapeutic approaches?
- What are the critical next steps and what stands in the way of progress?
- Where can MJFF involvement and leadership uniquely facilitate advancement?
- Ultimately, can MJFF sufficiently de-risk investment for other players?

The power and potential of genetics is clear

- In diseases where cause is unknown, genetics can provide powerful clues about disease pathogenesis
 - While most diseases are not directly linked to a single causal gene (monogenic), increased understanding of risk factor genes and “gene-gene interactions” will inform research directions and ultimately therapeutic development
- Increased understanding of the powerful role genes play in disease is critical to developing new therapeutics
 - Defining targets for novel therapeutics
 - Basis for rational drug discovery and development
 - Better guiding of therapeutic development, clinical trial design and patient care
- Tying genomic variation to variation in clinical phenotypes is a very important piece of the puzzle.
 - Concept that “clinical PD” may be a mix of multiple underlying disease mechanisms
 - Value as diagnostic and prognostic markers

Harnessing the potential of genetics: critical questions

- How can we most efficiently identify the complete genetic map for PD? Standardization, data-sharing and collaboration is critical!
 - Coordination of multiplex PD families and other well-defined cohorts using standard data collection methods
 - Leveraging shared technology resources
- How do we best validate genetic findings?
 - GWA studies have been everywhere, but are frequently underpowered to be conclusive plus the amount of data produced in these studies can be overwhelming
→ how do we interpret the data that technology has enabled us to find?
 - Coordination of large-scale replication efforts based on a priority list of candidate genes is needed
- What do we do with genetic findings once we have them?
 - Rapid generation of shared tools and resources (e.g. animal models, human cell lines, antibodies, etc.)

MJFF supported efforts in PD genetics

- First GWA study (Maraganore et al, 2004) and large-scale validation study (Elbaz et al, 2005)
 - Raw data submitted in 2008 to NHGRI
- Seed funding toward development of the Safra Genetics Consortia
 - 2004 initiative funded 5 collaborative projects exploring genes and gene expression in PD
- Opportunistic funding to support gene discovery and subsequent validation studies
- Increasing focus on priority targets: LRRK2 and SNCA
 - Alpha-synuclein: first ‘causal’ gene associated with PD but also a pathological hallmark in Lewy bodies
 - LRRK2: most prevalent genetic link to PD (mutations seen in estimated 1-2% of all PD cases and up to 40% in certain ethnic groups) and a highly ‘druggable’ enzymatic target

What will the future of PD genetics look like?

- New technologies will accelerate advances (e.g. cheaper/faster whole-genome sequencing)
- Rapidly increased interest in and acceptance of importance of understanding one's genome, driven in part by rise of direct to consumer genetic testing...
 - Our involvement with 23andme: What is it and why are we doing it?
- ...But truly driven more broadly by culture-wide shifts in views about technology and information
 - Again, the internet is inducing seismic changes in how people want to be involved with the world and with each other

As research progress speeds, so will the development of related health care advances

- Advances in screening and diagnostic/prognostic tests will lead to even greater interest in preventative medicine
- As we're seeing in cancer, genetic information will accelerate personalized medicines and more targeted treatments
 - Will we see the elimination of broad disease categories like PD in favor of more specific disease definitions?
- While the day is not far away where one's genome is an integral piece of what they consider with their doctor, much education is required
 - Skepticism exists today about value of this information in an individual's hands, and whether it is responsible for them to have it
 - Acceptance that this will be the new reality and incorporating it into the thinking of medical practitioners is another key to recognizing the value of genetics to improved patient health