Rare Diseases Clinical Research Center in Urea Cycle Disorders

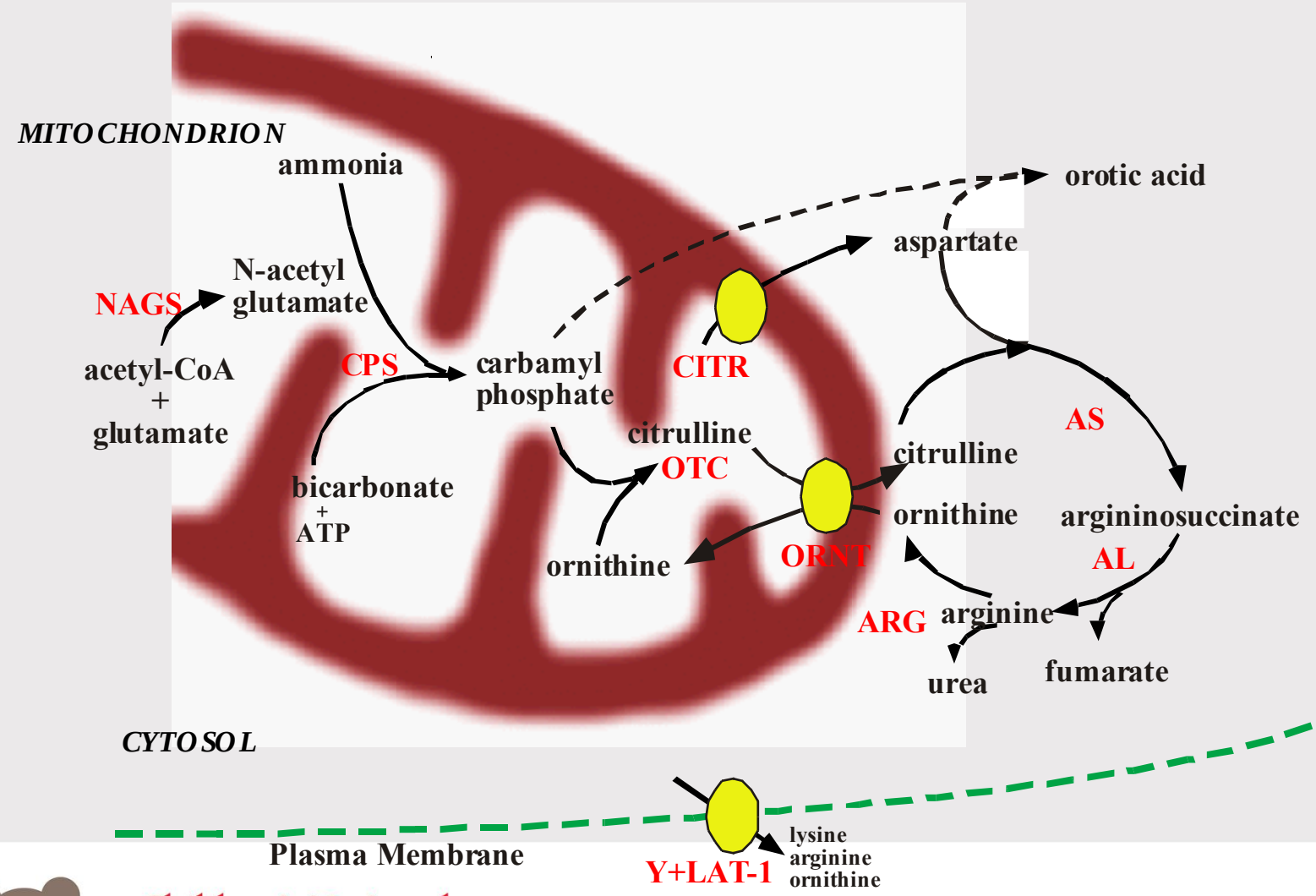
April 17, 2013

Mark L. Batshaw, M.D.
Physician-in-Chief and
Chief Academic Officer, CNMC
Chairman of Pediatrics and
Associate Dean for Academic Affairs,
GW

RARE DISEASES CLINICAL RESEARCH NETWORK

Children's National Medical Center

The Urea Cycle



Children's National Medical Center

8 UCD Studied by the UCDC

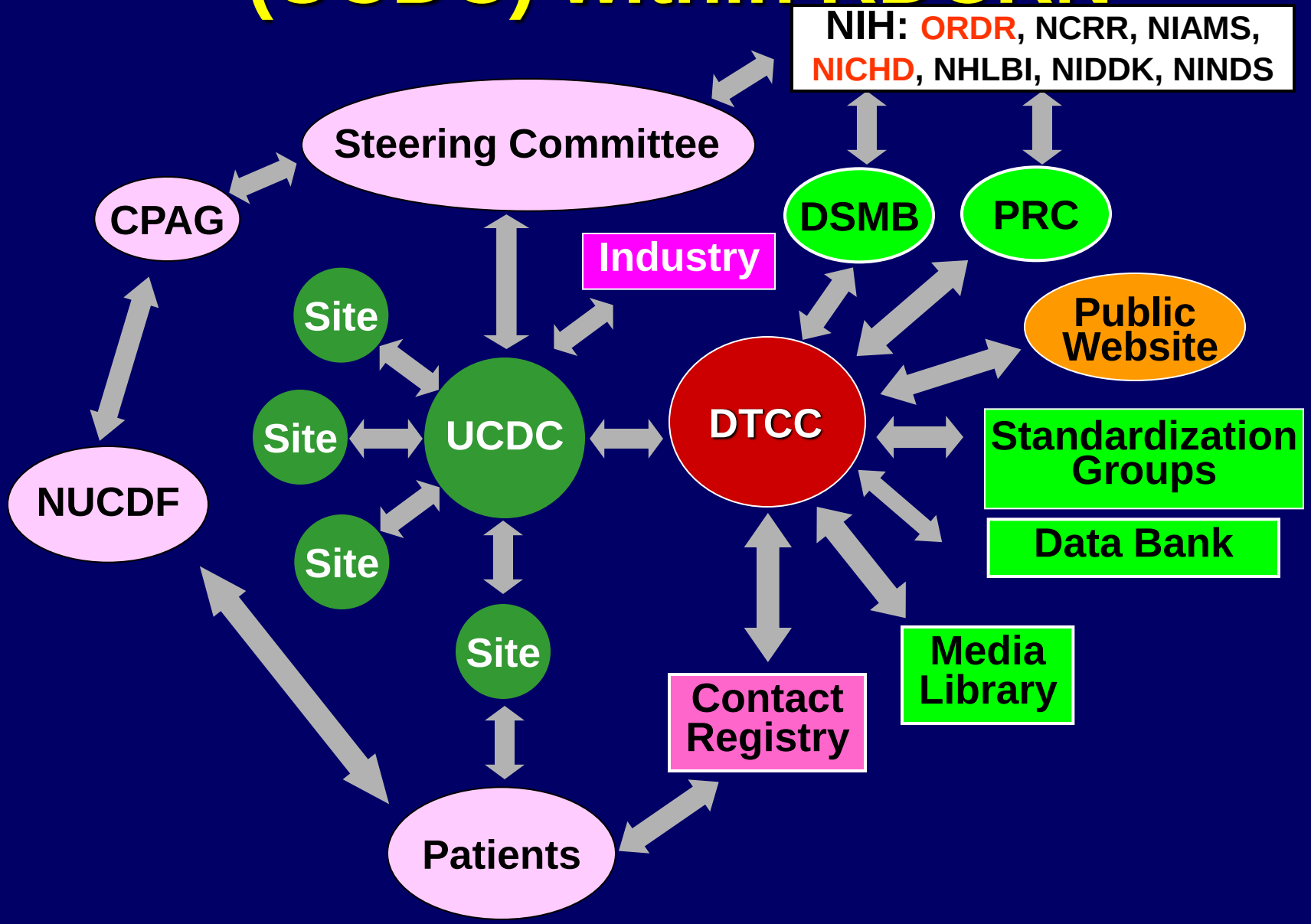
- N-acetylglutamate synthase (unknown)
- Carbamyl phosphate synthetase I (1:62,000)
- Ornithine transcarbamylase (1:14,000)
- Argininosuccinate synthetase (citrullinemia, 1:57,000)
- Argininosuccinate lyase (argininosuccinic aciduria, 1:70,000)
- Arginase (hyperargininemia, 1:350,000)
- Ornithine carrier (HHH, unknown)
- Aspartate/glutamate carrier (citrullinemia type II, unknown)

Goals of Rare Diseases Clinical Research Network

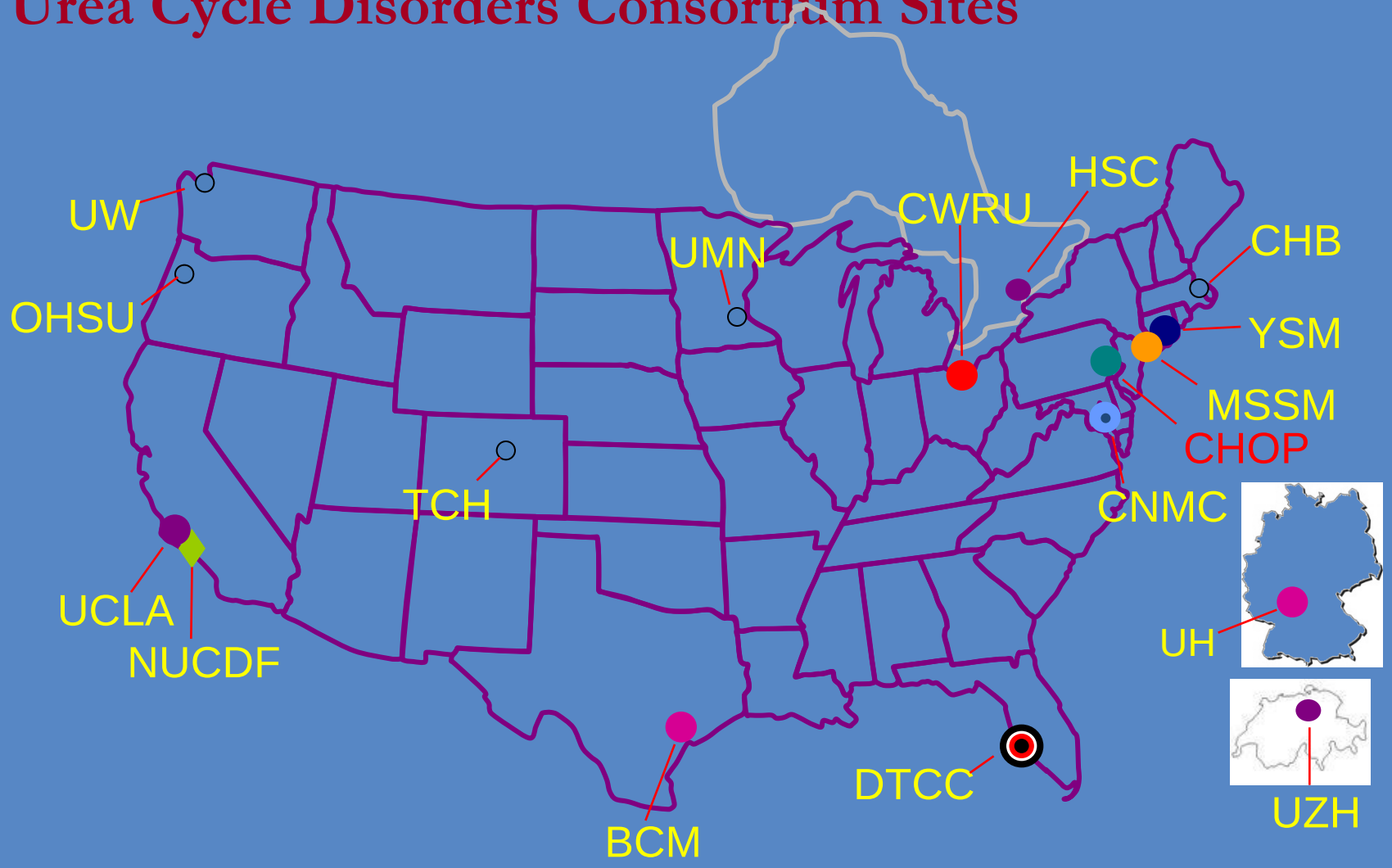
- Collaborative clinical research in rare diseases
  - longitudinal studies
  - clinical studies (phase 1 and 2 trials, pilot projects)
- Training of clinical investigators in rare disease research
- Centralized data repository and data sharing for rare diseases
- Improve quality of diagnostic and clinical practice

Children's National Medical Center

Urea Cycle Disorder Consortium (UCDC) within RDCRN



Urea Cycle Disorders Consortium Sites



Children's National Medical Center

Recruitment of UCD Patients

- UCDC Sites
- National Urea Cycle Disorders Foundation (NUCDF)
- Contact Registry
- Society of Inherited Metabolic Diseases (SIMD)
- State Newborn Screening Programs

Children's National Medical Center

Relationships with Advocacy, Industry, NBS

- National Urea Cycle Disorders Foundation (NUCDF)
- Four pharmaceutical companies developing novel interventions for UCD (drugs and biologics)
- Newborn Screening Programs: a study to evaluate the impact and cost/benefit of newborn screening for UCD

UCDC Lessons Learned

- The more sites, the more recruitments and diversity
- Think through protocols carefully so they are doable
- Interdisciplinary collaboration with colleagues is essential
- Large research networks develop slowly
- Networks improve care by clinical pathway development and adherence
- National networks attract attention to rare disorders

Children's National Medical Center

Barriers to Mission

- **Insufficient funding to accommodate all interested sites**
- **Lack of centralized IRB to approve studies in all sites**
- **Difficult process of protocol amendment**
- **Inability of sites to contact patients after they have registered**
- **Lack of data standardization for rare diseases**

Children's National Medical Center

Funding-Partners and Collaborators

- **NIH and FDA**
- **Collaborations with patient advocacy groups are essential**
- **Important role of major individual patient donors-philanthropy often follows NIH as gold standard**
- **Industry involvement and IP opportunities help funding**
- **Industry becomes interested when there are well characterized, relatively large enrolled populations from diverse ethnic groups**

Children's National Medical Center