The Challenge – Maximizing the value of four different genetic studies of diabetes or diabetic complications

- FIND - Family Investigation of Nephropathy and Diabetes
- GoKinD - Genetics of Kidneys in Diabetes
- EDIC - Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications Study (EDIC)
- Type 1 Diabetes Genetics Consortium

FIND
Family Investigation of Nephropathy and Diabetes (FIND)

The Family Investigation of Nephropathy and Diabetes (FIND) Study

Objectives

- To utilize state-of-the-art genetic technology to identify genes for Diabetic Nephropathy
  - A linkage study using diabetic relative pairs concordant or discordant for diabetic nephropathy. All probands have biopsy-proved nephropathy and/or overt proteinuria (or ESRD)
  - MALD, which uses markers with different allele frequency distributions in two founding populations of an admixed population as a tool for genome-wide mapping of susceptibility loci for both diabetic and non-diabetic kidney disease.

FIND
Family Investigation of Nephropathy and Diabetes (FIND)

Number of Participants

Family study – recruitment completed

	Families	Individuals
African American	399	1169
American Indian	264	1144
European American	222	706
Mexican American	561	2258
Other Hispanic American	11	29
Other	5	18
Total Recruited	1462	5314

MALD study – recruitment to end in fall 2006

Mexican-Americans - 841 cases, 452 hypernormal controls

African-Americans - 278 diabetic nephropathy diads and triads, 478 non-diabetics diads and triads, 77 hypernormal controls

GoKinD
Genetics of Kidneys in Diabetes Study

OVERALL GOALS

The overall goal of the GoKinD ("Genetics of Kidneys in Diabetes") study is to establish a repository of DNA and clinical information from a large number of unrelated patients with type 1 diabetes in order to facilitate studies into the genetic basis of diabetic nephropathy.

All probands (and cases) have overt proteinuria or ESRD.

Enrollment (July, 2005)

	TOTAL
Case Trio Probands:	271/600
Case Singletons:	674/500
Total Cases:	945/1100
Control Trio Probands:	324/500
Control Singletons:	620/500
Total Controls:	944/1000
Total Probands:	1889/2100

DNA and associated data are now available by application for all subjects
See www.gokind.org

GoKinD
Genetics of Kidneys in Diabetes Study

Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications Study (EDIC)

- The DCCT demonstrated the efficacy of glycemic control for slowing the onset and progression of eye, kidney, and nerve diabetic complications.
- In 1994, 96% of the participants were enrolled in EDIC for regular observational follow-up of metabolic and complications status, using similar methods as in the DCCT.
- The goal of the EDIC Genetics substudy is to collect DNA, cells, serum and plasma on all available parents and at least one non-diabetic sib and measure diabetic complications on diabetic siblings

Current collection (as of 2005)

- 1,419 DCCT/EDIC probands
- 2,960 relatives of DCCT/EDIC probands
  - 806 mothers
  - 582 fathers
  - 1,572 siblings
    - Of which 140 have diabetes and complications measured
- 4,379 individuals in total

Type 1 Diabetes Genetics Consortium

The goal of the Type 1 Diabetes Genetics Consortium is to organize international efforts to identify genes that determine an individual's risk of type 1 diabetes, and to establish a renewable source of DNA on 2500 families with at least two type 1 diabetic children, one non-diabetic child and two parents.

Enrollment

- ASPs 1541
- Minority Trios 41

DNA and data soon available
see www.t1dgc.org

RFA-DK-06-005

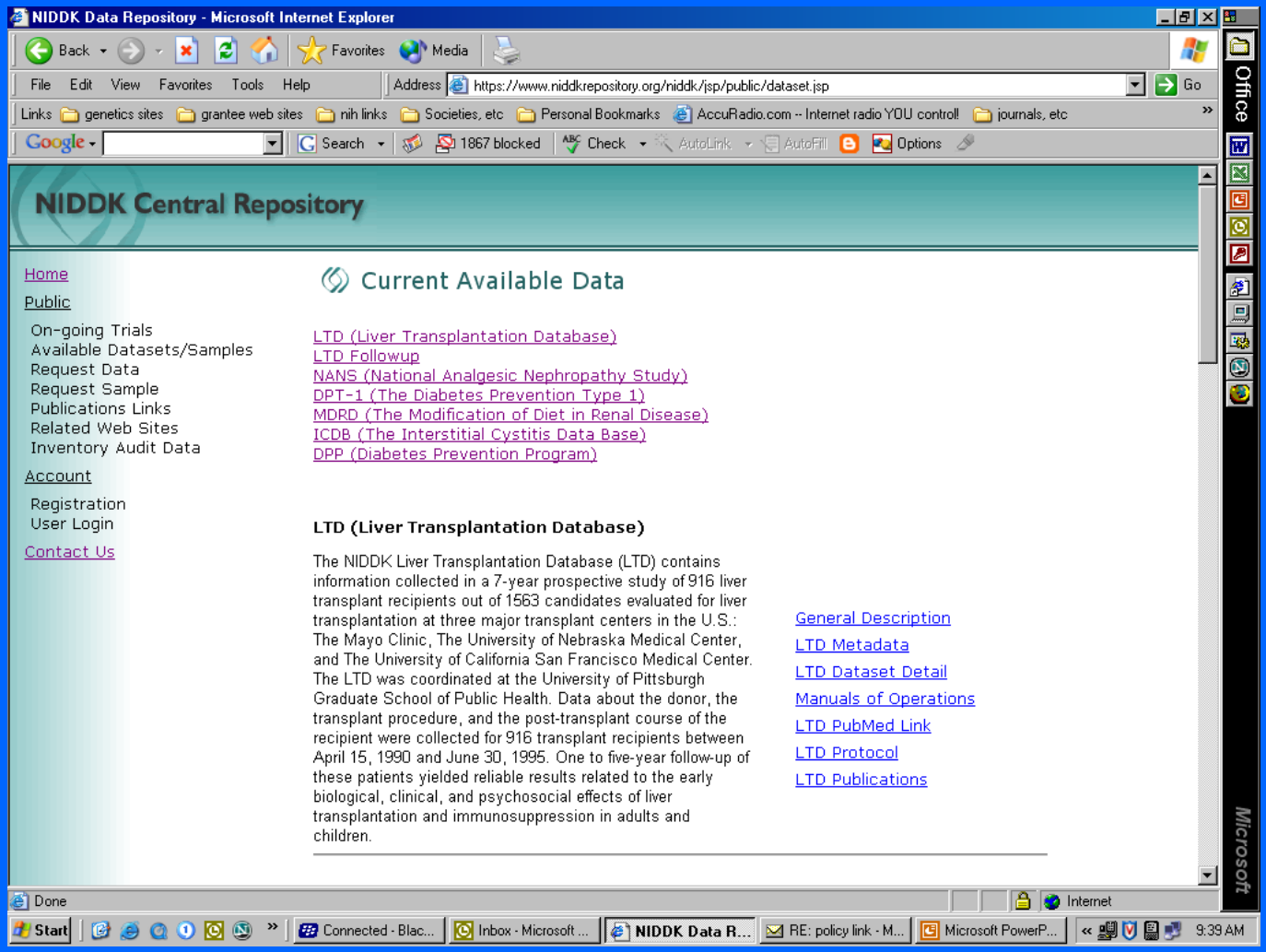
High-Density Genotyping of Diabetes and Diabetic Complications Sample Collections

- Will support high-density genotyping of the EDIC and GoKIND collections.
- Genotyping data will be stored in an NIDDK repository and shared with the research community one year after it is generated.
- The participating Institutes (NIDDK, NHLBI, NIAID) will award up to $3.0 million for the first year and $2M for each of 2 additional years.
- Genotyping costs are NOT included. Genotyping will be funded separately through direct NIDDK contracts
- Applications have already been received.
- Next year, a similar RFA will support genotyping of all 4 studies

Challenges in receiving and repositing data

1. Need expertise in acquiring massive amounts of SNP genotype data
2. Need system to link SNP data to associated genomic data
3. Need way to link seamlessly to phenotypic databases that are complex and often have many versions
4. Need to actively maintain phenotypic databases to assist investigators unfamiliar with the datasets
5. Need to facilitate cross-study comparisons

The NIDDK Central Database Repository will house the phenotypic data to be shared



Challenges with data heterogeneity

	Study (variable #s)			
	FIND	GOKIND	T1DGC	EDIC
Lab Test				
AutoAb GAD65	18, 24, 25		206 to 210	
AutoAb IA-2			211 to 215	
Genotyped	9			
HbA1C (%)	27	28,35		(yes)
Serum creatinine (mg/dL)	28	38, 43, 44, 45, 24, 36, 37, 38		yes
BUN (mg/dL)	29			
Urine total protein (mg/dL)	30, 38			
Urine albumin (Medstar-mg/L and Steffes mg/dL)	31, 39	yes (0 to 3 times)		
Urine creatinine (mg/dL)	32, 40	yes (0 to 3 times)		yes
Glucose (mg/dL)	33			
Albumin/creatinine	35, 41	21 (0 to 3 times)		yes
Urine protein/creatinine	36, 42			
Kidney biopsy	83, 84, 169 to 182			
Biopsy				
ACR/AER		31, 32, 33		
AER		yes (RASS)		(yes)
lipid cholesterol		25, 36		(yes)
lipid HDL		26, 37		(yes)
lipid LDL				(yes)
LDL/HDL				(yes)
Hyperlipidemia				(yes)
Serum cystatin		27, 39		yes
GFR	34			yes
GFR1 (MDRD; (ml/min/1.73m2))		yes		
GFR2 (Cockcroft-Gault)		yes		
GFR3 (1/serum creatinine)		yes		
Trigylcerides				yes

Summary

Even when projects are studying the same phenotype, it may be difficult to compare subjects from different studies

The requirements for storing SNP data are different from those for storing phenotypic data

The complexity of phenotypic data may be a barrier for phenotype non-specialists