Genomics and Epigenetics of Common Variable Immune Deficiency & REcurrent SinoPulmonary Infections (CVID & RESPI)

Harry W Schroeder Jr MD PhD, PI
Professor of Medicine, Microbiology and Genetics
Director, UAB Program in Immunology
University of Alabama at Birmingham

Elizabeth E Brown PhD MPH, Co-PI
Associate Professor of Public Health
University of Alabama at Birmingham
A Typical History

• High School - Catches every cold
• College – Repeated Sinusitis & Bronchitis
  – First Sinus Surgery
• First Job – First Pneumonia
• Depression, Chronic Fatigue, Always Sick
• Develops hypo- or hyperthyroidism
• Pneumonia #3, Sinus Surgery #5, or Cushingoid due to Steroid Therapy
CVID is a Multi Organ and System Disease

Immune deficiency in CVID

- Decreased B cells
- Blunted /absent antibody titers
- Reduced Ig Levels

75% of patients develop chronic pulmonary structural complications

- Recurrent infection
- Tissue damage
- GI complications
- Increase gastric cancer and
- Non Hodgkin lymphoma (1.5-7%)
CVID is a Multi Organ and System Disease

- 20% of CVID patients have some form of autoimmunity
- Cytopenias are more common presenting disorder in children than adults
- Pernicious anemia
- Autoimmune neutropenia
- Graves disease
- Hypothyroidism
- Evans syndrome
- SLE
- RA

Spectrum of Antibody Deficiency

- IgA Deficiency
  1/500

- CVID
  1/50,000

- IgG Subclass Deficiency
  1/5,000

- IgG Deficiency
  1/10,000

- IgM Deficiency

- RESPI
  1/10,000

- SPAD
  ?
• 4,000,000 people in the catchment area
• Most European-Americans a product of two waves of emigration
  ▪ (Scottish Borders to Appalachian Piedmont, then to Alabama)
• 3rd most stable population in the US
Pathogenesis of CVID/RESPI

**RESPI**

**class I**

- HLA -B Allele

**class II**

- HLA -DR Allele

**CVID**

- HLA -B Allele

- HLA -DR Allele

Schroeder, HW
A Wide and Deep Analysis
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