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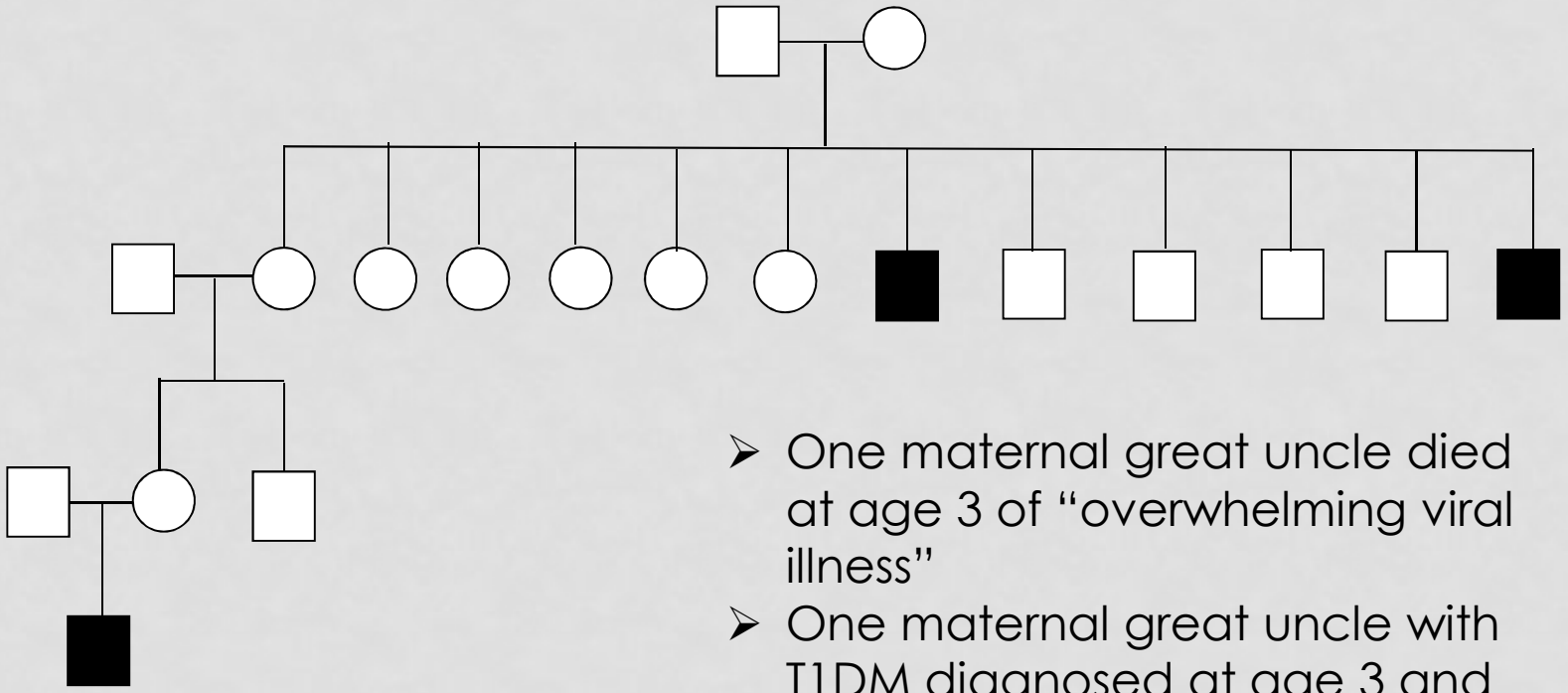
- Hospitalized at age 2 (2010)
  -Fever, Rash, Arthralgias, and Nausea/vomiting
- Admitted with DKA, HbA1c-11.3 and diagnosed with T1DM
- Infectious and rheumatologic workup negative
- Ab u/s—borderline hepatosplenomegaly

- Developmental delay
  -Never crawled
  -Walked at 25 months
- Muscle biopsy (2012)
  -perivascular and endomysial mononuclear infiltrates
  -immunohistochemical staining with patchy MHC-I upregulation, increased CD4+ staining and endomysial cellularity
  -1 necrotic and 1 regenerating fiber
- Prednisone trial (2012) stopped due to side effects and no benefit after 6 weeks

- No other autoimmune disease
- Growth
  - Weight
    Age 3—90th percentile
    Age 8—25th percentile
  - Height
    Age 3—50th percentile
    Age 8—25th percentile
- Hospitalizations
  -Twice for GI illness/dehydration

FAMILY HISTORY



- One maternal great uncle died at age 3 of "overwhelming viral illness"
- One maternal great uncle with T1DM diagnosed at age 3 and oral cancer (non-smoker/drinker) now age 52

- **Clinical whole exome sequencing (GeneDx) sent for unexplained inflammatory myositis**

WHOLE EXOME SEQUENCING

- Variant of unclear clinical significance in *FOXP3* gene
  - -p.K332E hemizygous variant inherited from mother
  - -missense variant located in forkhead/DNA binding domain

Lysine (amide)

Glutamic Acid (acidic)

Unable to obtain maternal great-uncle's FoxP3 gene sequencing

DO WE CARE?

- Further history
  - -dry skin since birth and frequent episodes of atopic derm
  - -loose, non-bloody stool since birth
    - -never had solid bowel movement
    - -EGD normal, colonoscopy deferred
- Workup
  - -RUQ u/s mild hepatomegaly
  - -IgG-578 (608-1572)
  - -IgM-30 (52-352)
  - -IgE-1154
  - -S pneumo titers protective 18/18 serotypes (5 non-linear dilutions)
  - -Absolute eosinophil count-600
  - -T-reg flow
    - -high normal percentage of FOXP3+ CD4+ T-cells (7.3%, normal 3.5-8%)
    - -substantial proportion of FOXP3+ CD4+ T-cells are CD25-negative (5.8%)
  - -T-reg functional testing
    - -pending at Dr. Torgerson's lab

TREATMENT

- Summary
  - -p.K332E variant in *FOXP3*
  - -T1DM, inflammatory myositis, dermatitis, chronic loose stools
  - -Mild hepatomegaly
  - -Ab Eos-600, IgE-1154
  - -High normal percentage of FOXP3+CD4+ T-reg with substantial percentage CD25 negative

Consistent with clinically significant variant and hypomorphic IPEX

- Hematology
  - -following in background, no BMT now
- Attempting to sequence maternal great-uncle's *FOXP3* gene
- Started rapamycin at 1 mg (0.04 mg/kg/day)
  - -will treatment help with myositis?
    - -baseline objective neuro testing done
  - -will treatment prevent more autoimmune disease?
- Currently rapamycin 4 mg/day (0.16 mg/kg/day)
  - Trough 7 mcg/L (goal 5-10 mcg/L)