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CMT 4C in Norway
prevalence and clinical characteristics

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Classification of CMT

Disease Name	Pathology	Mode of Inheritance	Proportion of all CMT
CMT1	Myelinopathy	AD	40%-50%
CMT2	Axonopathy	AD	10%-15%
AR-CMT2	Axonopathy	AR	Rare
CMT4	Myelinopathy	AR	Rare
CMTX	Axonopathy with secondary myelin changes	XLD	10%-15%
Intermediate form	Combination of myelinopathy and axonopathy	AD	Rare

Charcot-Marie-Tooth Hereditary Neuropathy Overview, Gene review, 2015

Background

- 2012: two patients with probable CMT 1, not genetically confirmed
  - clinically typical CMT (distal sensorimotoric neuropathy and foot deformity)
  - Onset in early childhood
  - Severe scoliosis
  - Demyelination on neurophysiological examination
  - One sister affected, but else no other family member affected

Background

- Could it be a recessiv demyelinating CMT – CMT 4?
- Scoliosis and early onset typical for CMT 4C (mutations in the *SH3TC2* gene)
- *Sanger sequencing of the SH3TC2* gene revealed a homozygous mutation in both patients
- Expanded testing of patients with demyelinating CMT without genetic diagnoses revealed new cases

Study of CMT 4C in Norway

- Prevalence and mutation spectrum - *SH3TC2*-gene
  - Diagnostic biobanks:
    - Dept. of Medical Genetics University Hospital of North Norway
    - Dept. of Medical Genetics, Hospital of Telemark

- Natural history and phenotypical characteristics
  - Questionnaires
  - Medical records from hospitals

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Charcot–Marie–Tooth disease type 4C in Norway: Clinical characteristics, mutation spectrum and minimum prevalence

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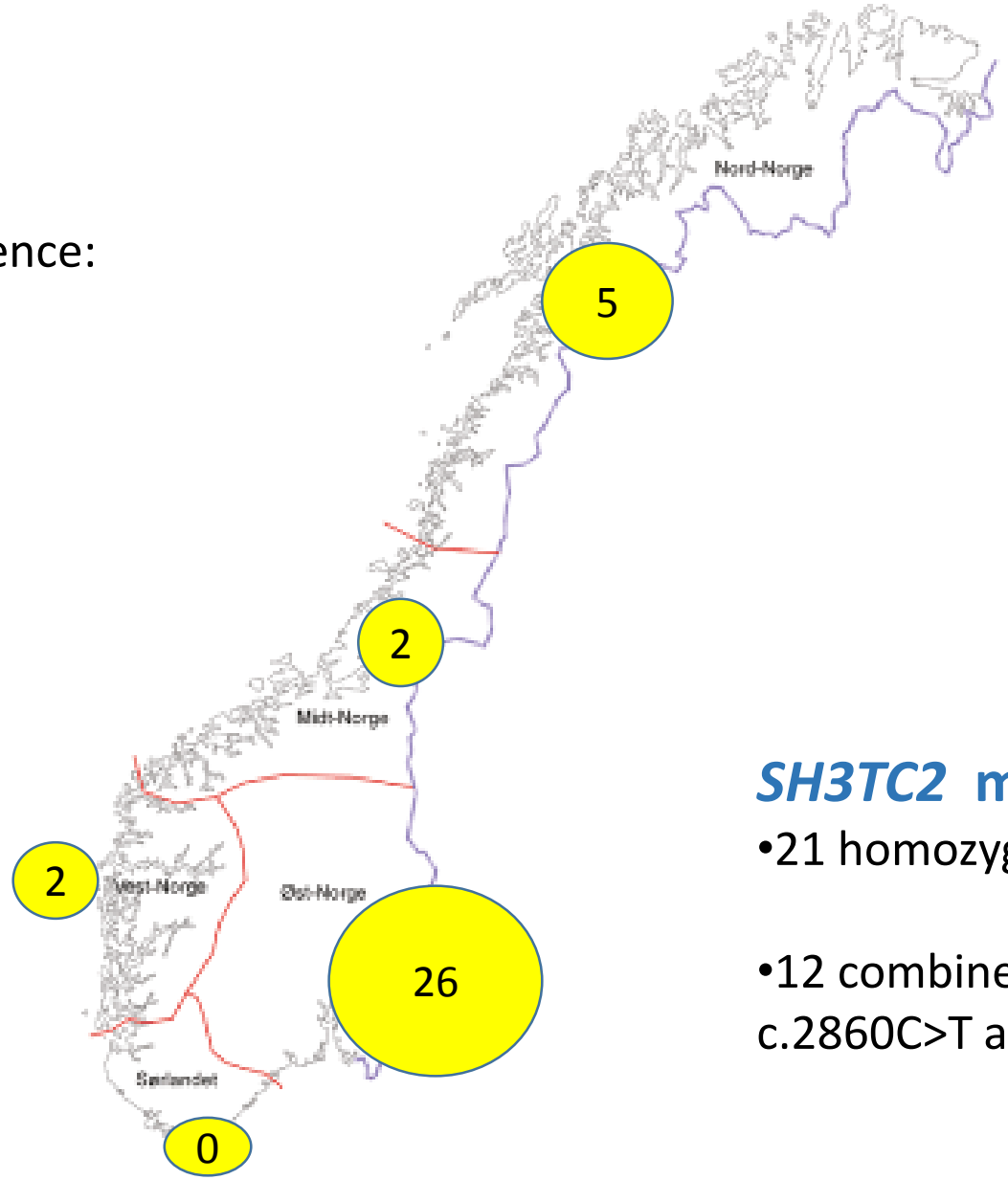
Prevalence

2016: 35 patients in Norway

Population minimum prevalence:
6,7/mill. = about 1/150.000



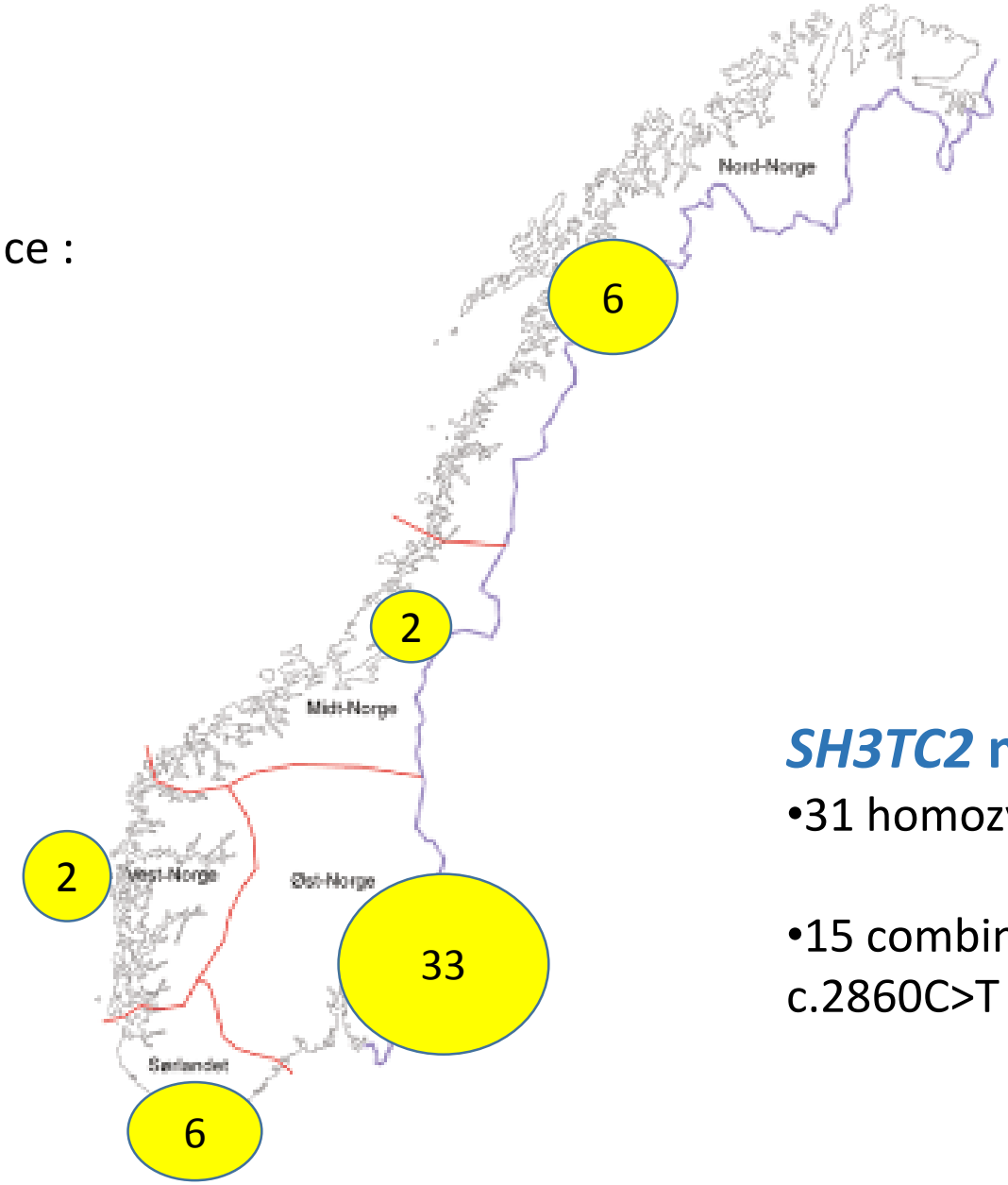
SH3TC2 mutations

- 21 homozygous c.2860C>T
- 12 combined heterozygous with c.2860C>T as one of the mutations

Prevalence

2019: 49 patients in Norway

Population minimum prevalence :
9.2/mill. = about 1/100.000



SH3TC2 mutations

- 31 homozygous c.2860C>T

- 15 combined heterozygous with c.2860C>T as one of the mutations

Clinical characteristics of CMT4C in Norway

Medical consent from 21/35 patients (60 %)

Mean age: 37 years (19-60 yrs)

Disease duration 31 years (8-56 yrs)

- Early onset: median 4 years (0-14yrs)
- Symptoms at onset: 95 % lower limb weakness

Clinical characteristics of CMT4C in Norway

- Onset walking: median 17 months
- Foot deformity: 100 %
  - 42 % surgery for foot deformity
- Walking capacity
  - 1/3 No problems walking
  - 1/3 In need of a weelchair outdoor

Clinical characteristics of CMT4C in Norway

- Proximal paresis in 50 %
- Sensory ataxia or balance problems in 80 %
- Upper limb affektion in 100 %

Clinical characteristics of CMT4C in Norway

- Scoliosis: 80 %, median onset 11 years

- Scoliosis treatment:
  - Corset: 8 (42 %)
  - Surgery: 4 (21 %)

Clinical characteristics of CMT4C in Norway

- Cranial nerve affection in half of the patients:
  - **Hearing impairment**
  - **Facial nerve paresis**
  - Ptosis/ophtalmoplegia/nystagmus
  - Dysphagia
- Neuropathic pain: 50 %

When to suspect CMT 4C?

Demyelinating CMT with suspected recessive inheritance and

-Early onset
-Scoliosis
-Sensory ataxia/impaired balance
-Cranial nerve involvement
-Proximal muscle weakness