

Advances in Diagnosis and Treatment of NF1



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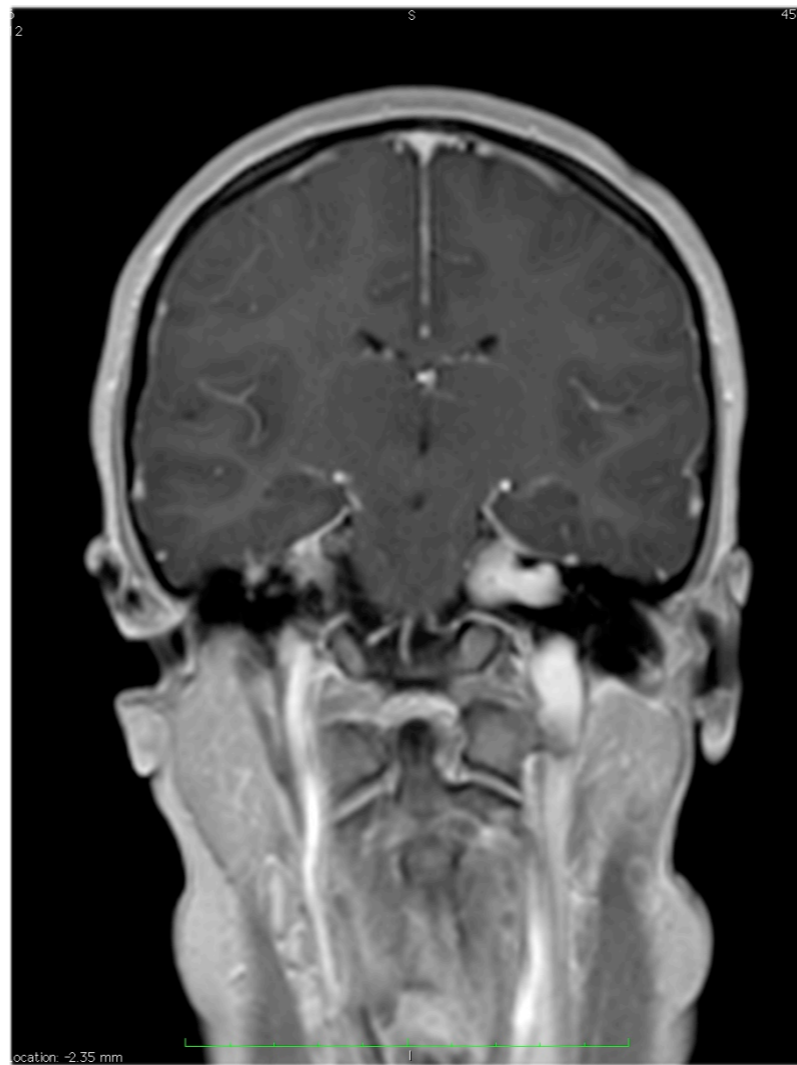
The Neurofibromatoses



NF1



CHROMOSOME 17



NF2



SCHWANNOMATOSIS

NF1 Diagnostic Criteria

- Cafe-au-lait macules (≥ 6 , 5 mm prepuberty, 15 mm post-puberty)
- Skin fold freckles
- Neurofibromas (≥ 2 or one plexiform)
- Iris Lisch nodules (≥ 2)
- Optic glioma
- Skeletal dysplasia (tibial or orbital)
- Affected first-degree relative

Pigmentary Signs

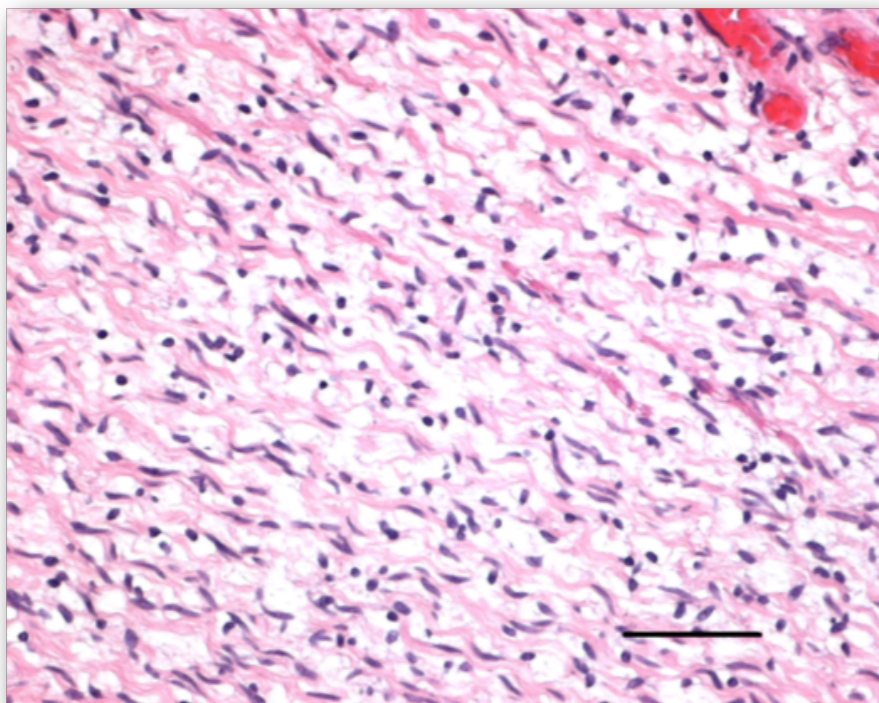
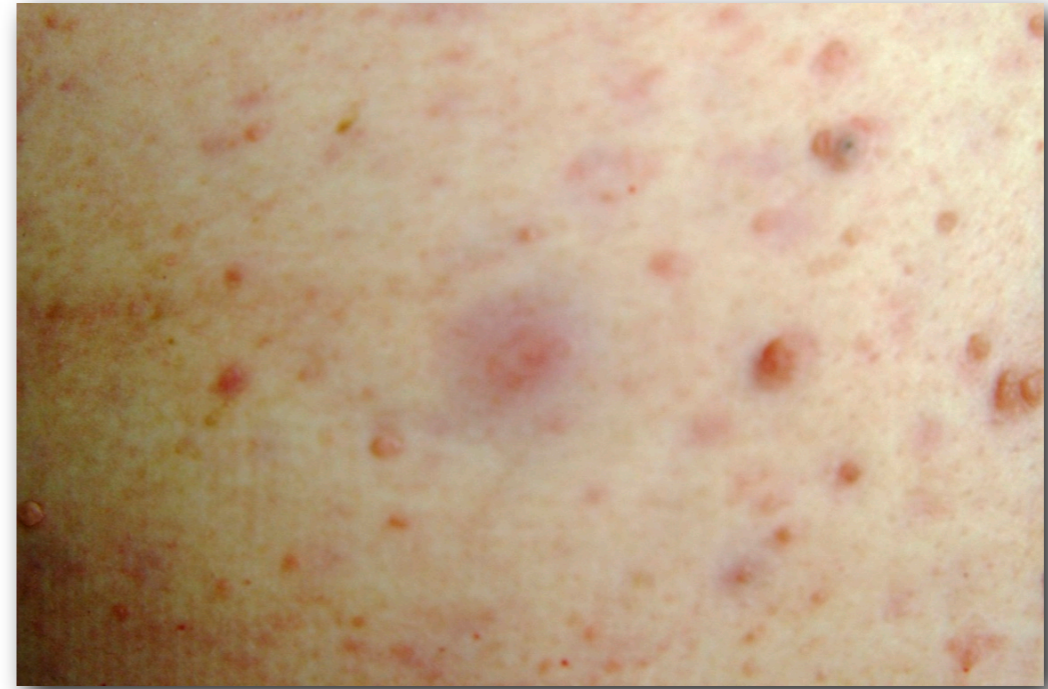
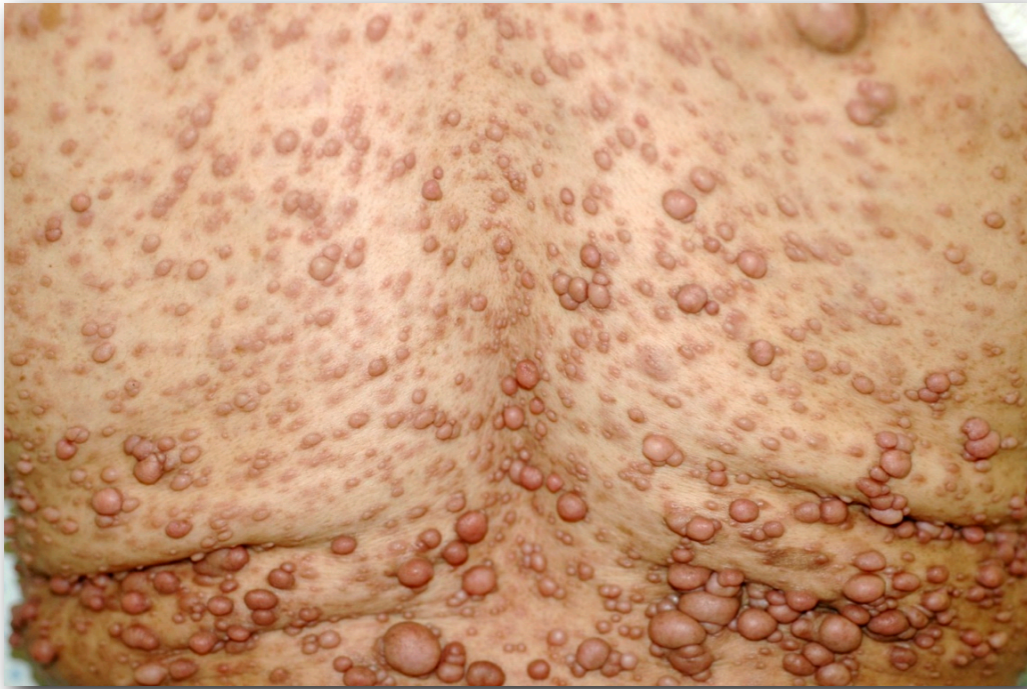


café-au-lait spots

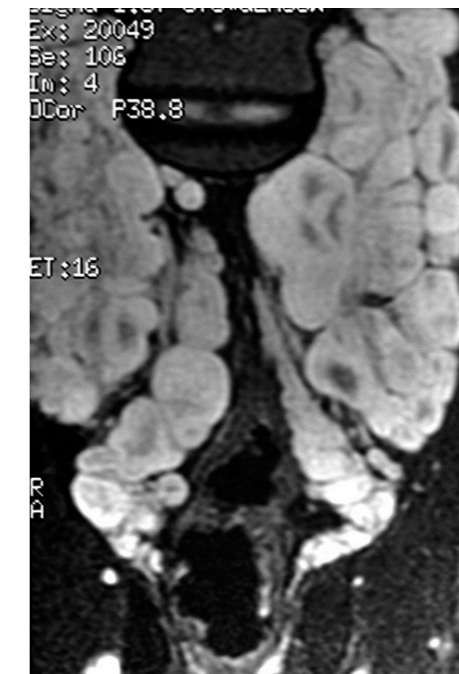
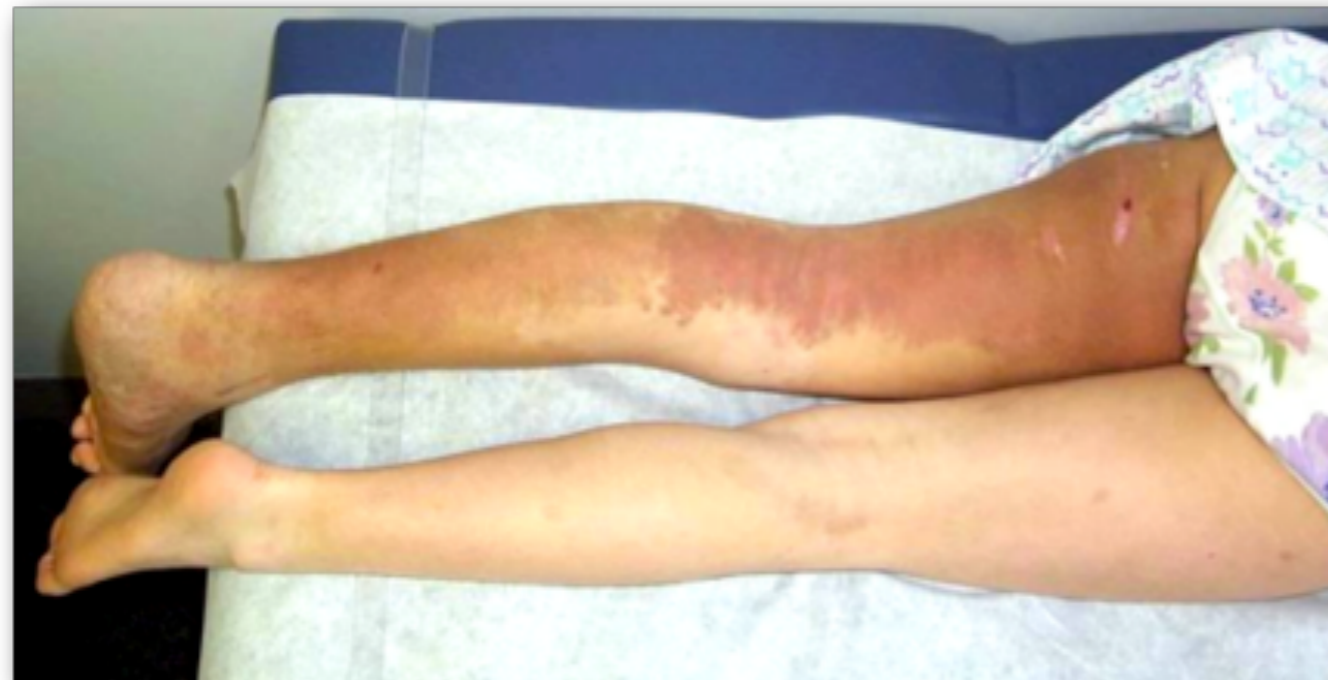


skin fold freckles

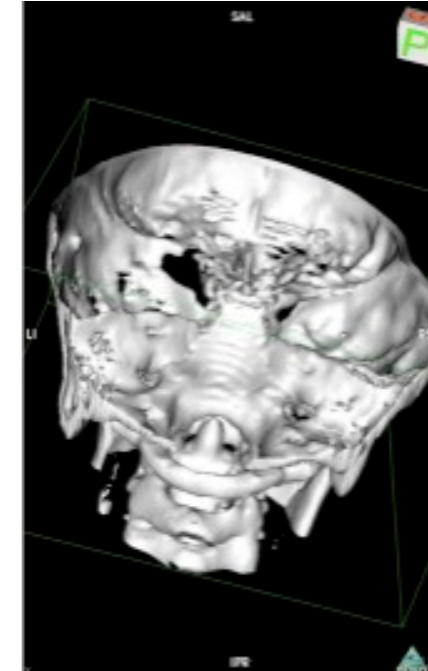
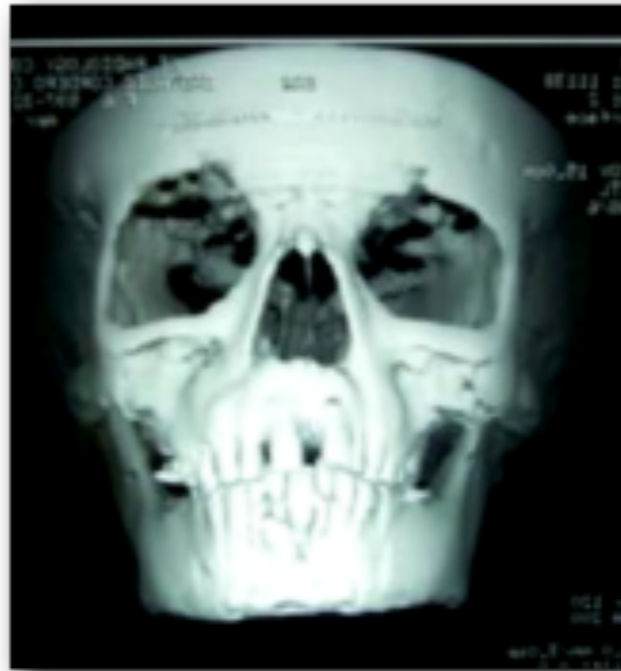
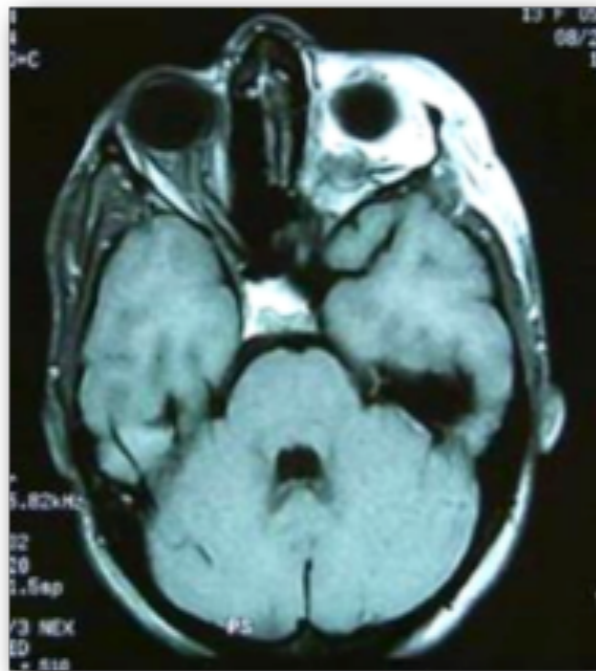
Neurofibromas



Plexiform Neurofibroma



Orbital Plexiform Neurofibroma

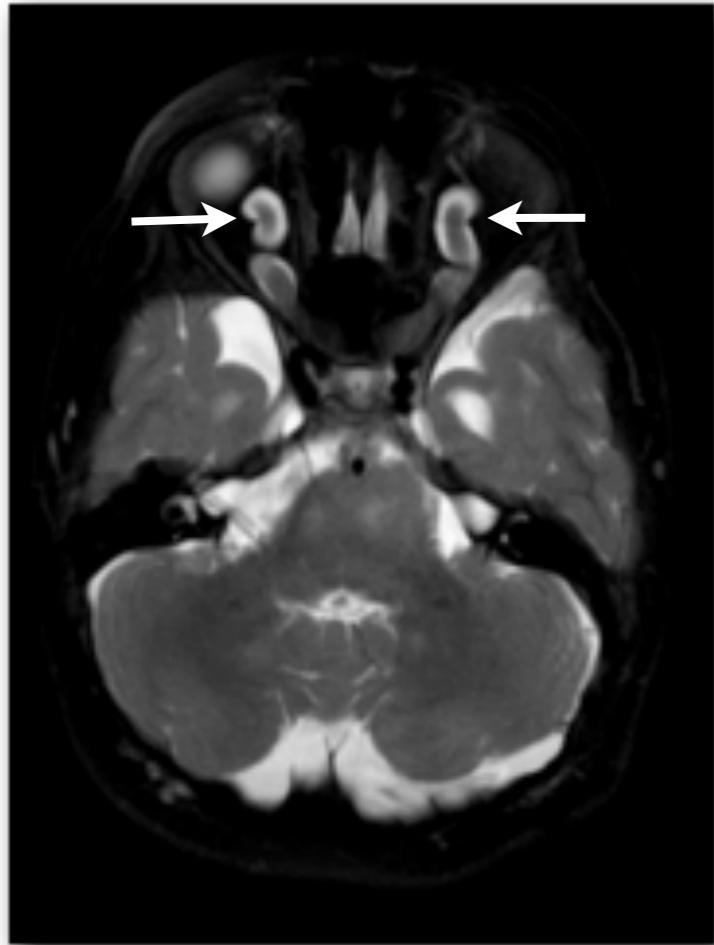


Lisch Nodules

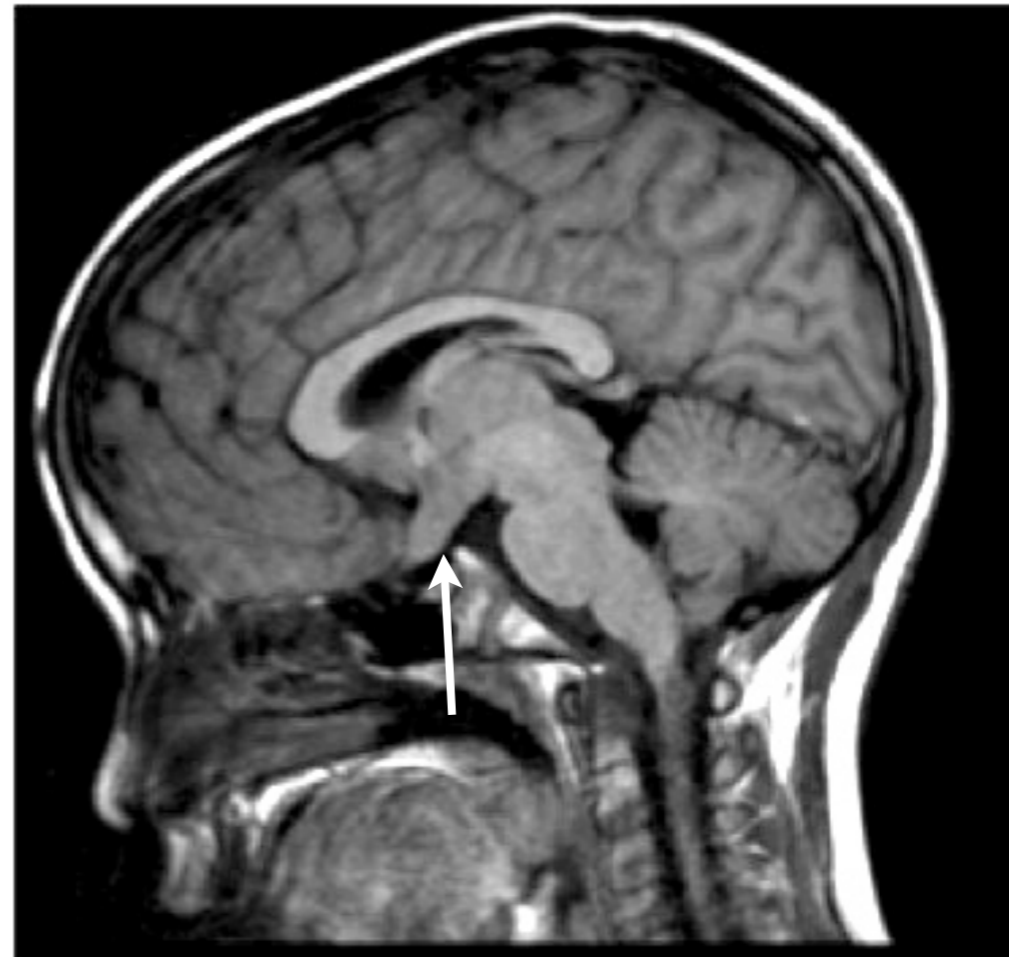
- appear after age 6 years
- melanocytic hamartomas
- no effect on vision
- require slit lamp



Optic Glioma

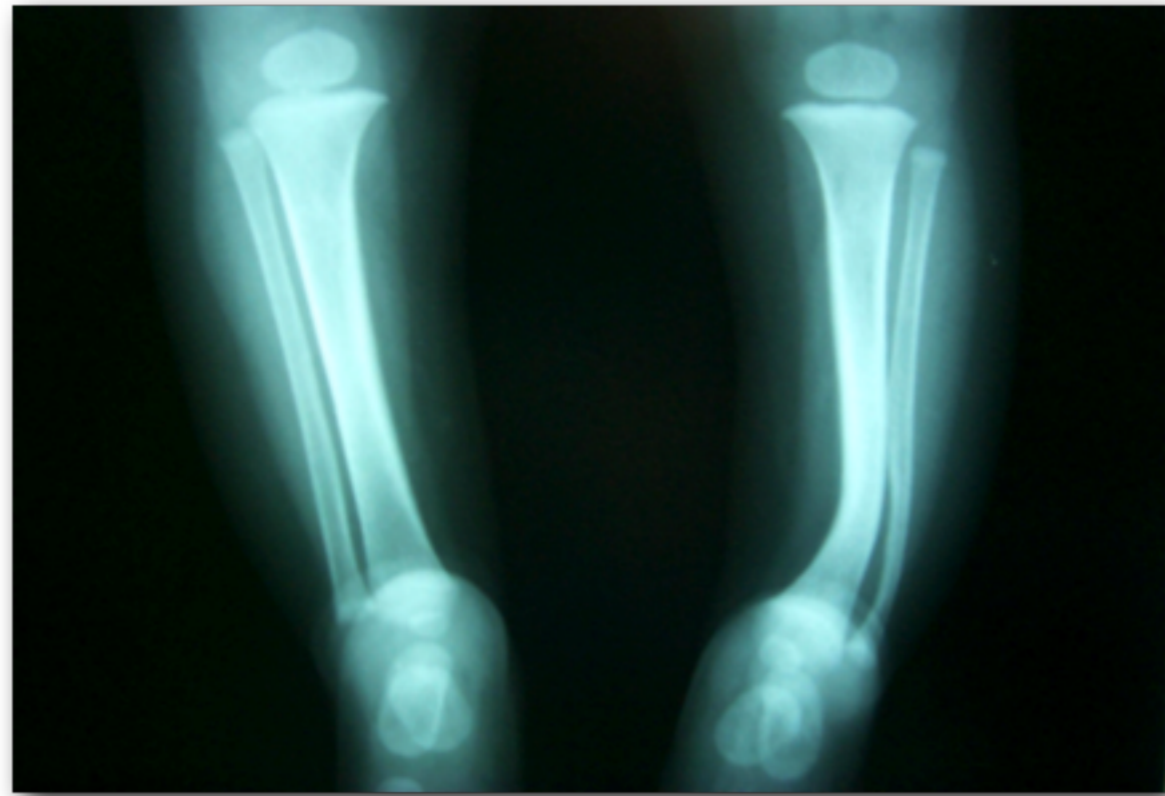


orbital

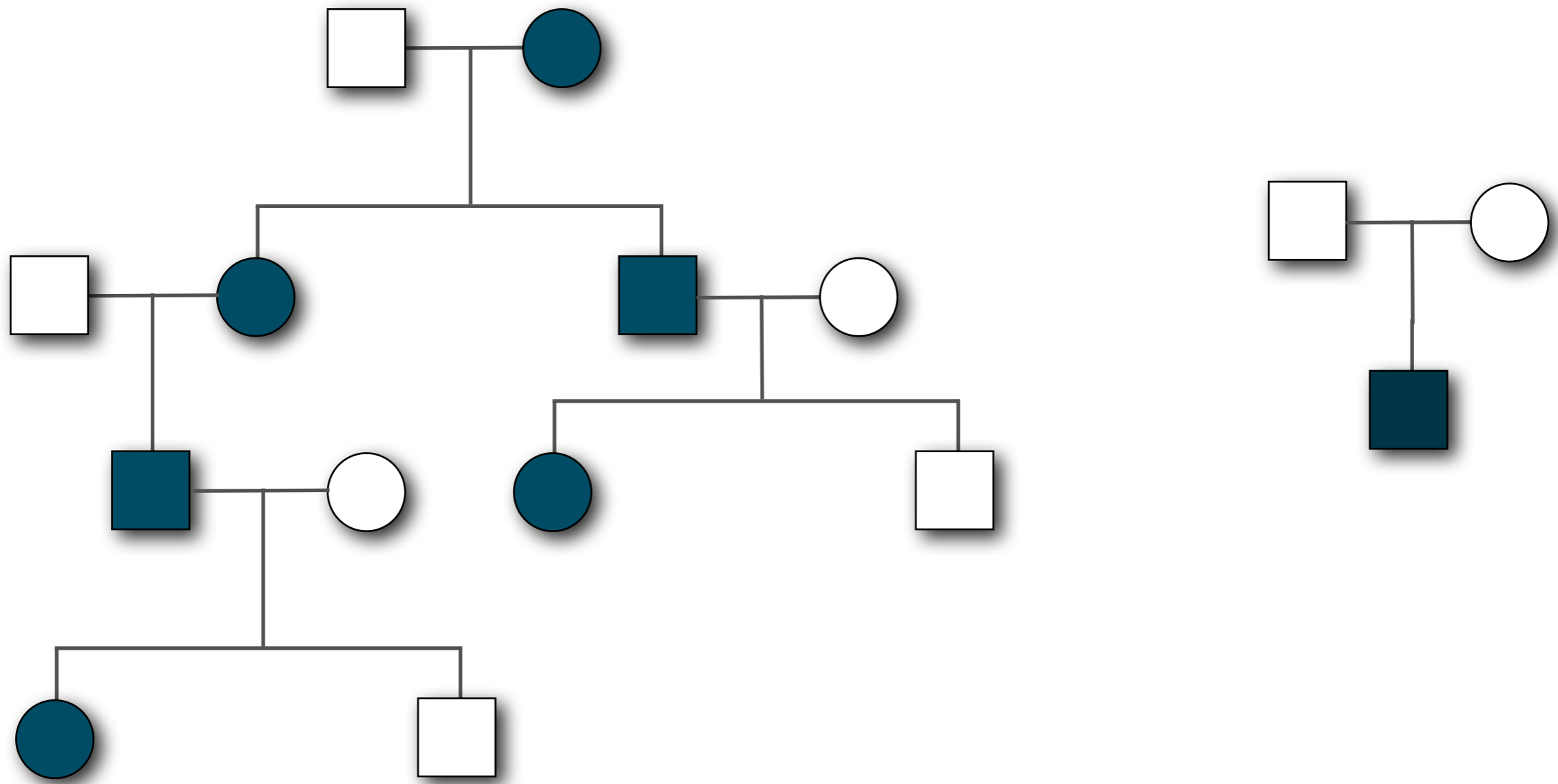


chiasm

Skeletal Dysplasia

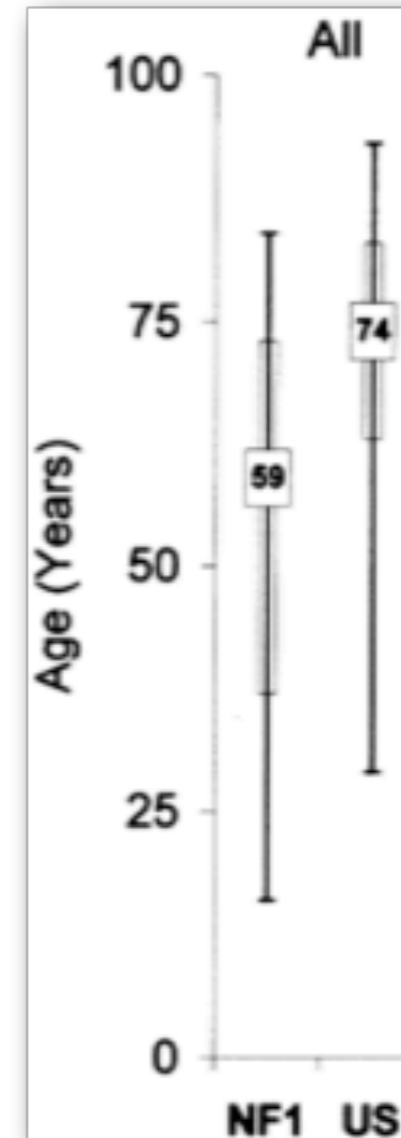


Genetic Transmission

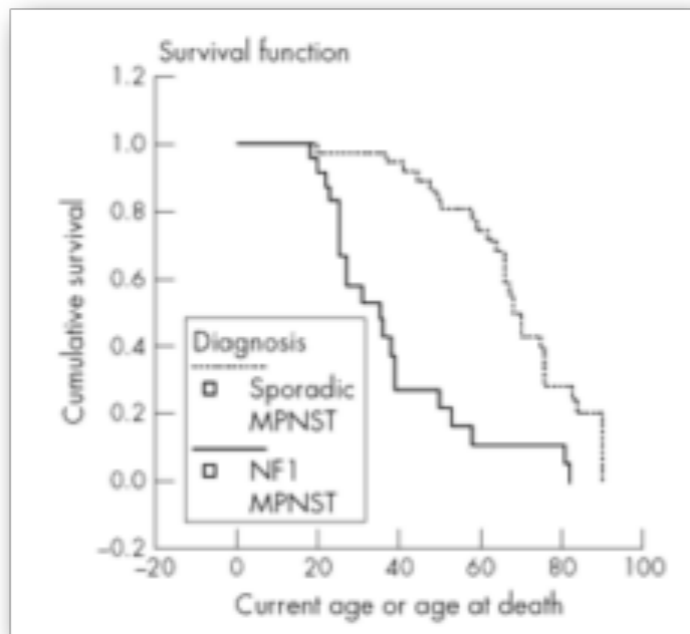
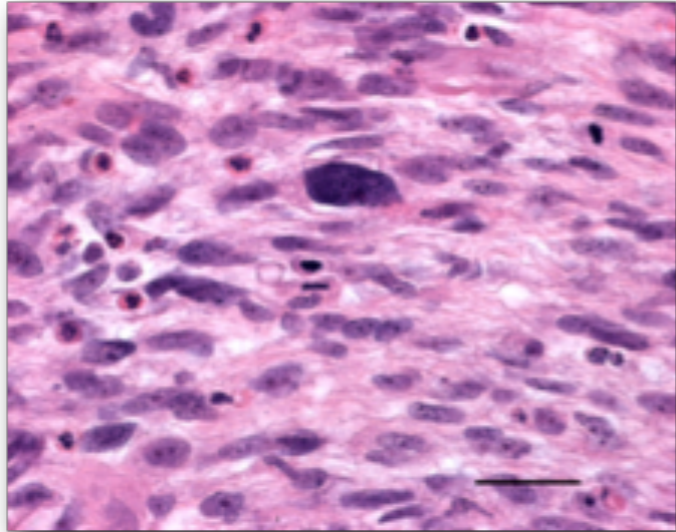


Life Expectancy

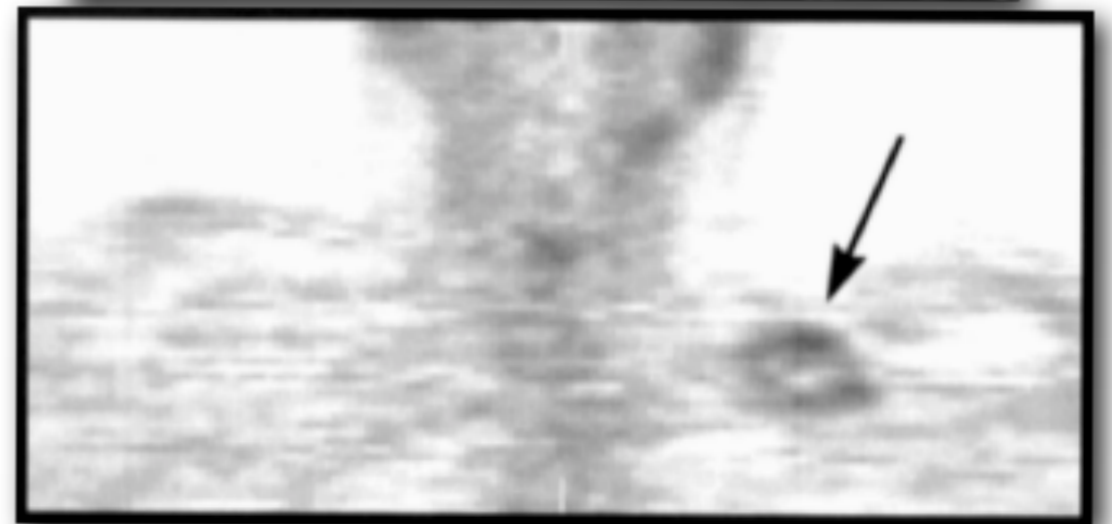
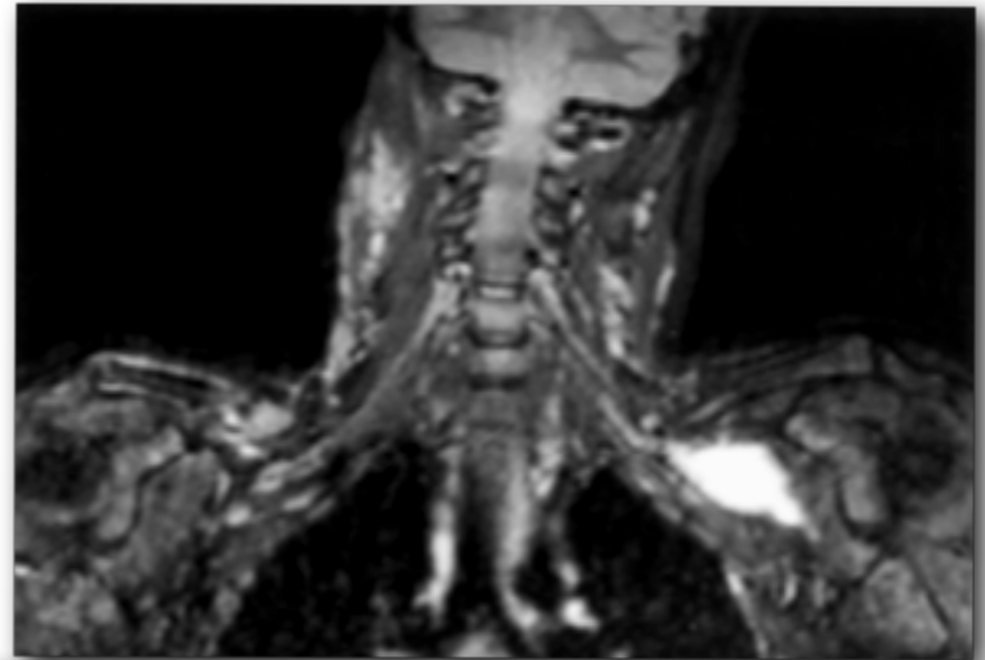
- Malignancy
 - MPNST
- Vascular dysplasia
 - renal artery stenosis
 - moya moya
 - dissection



MPNST

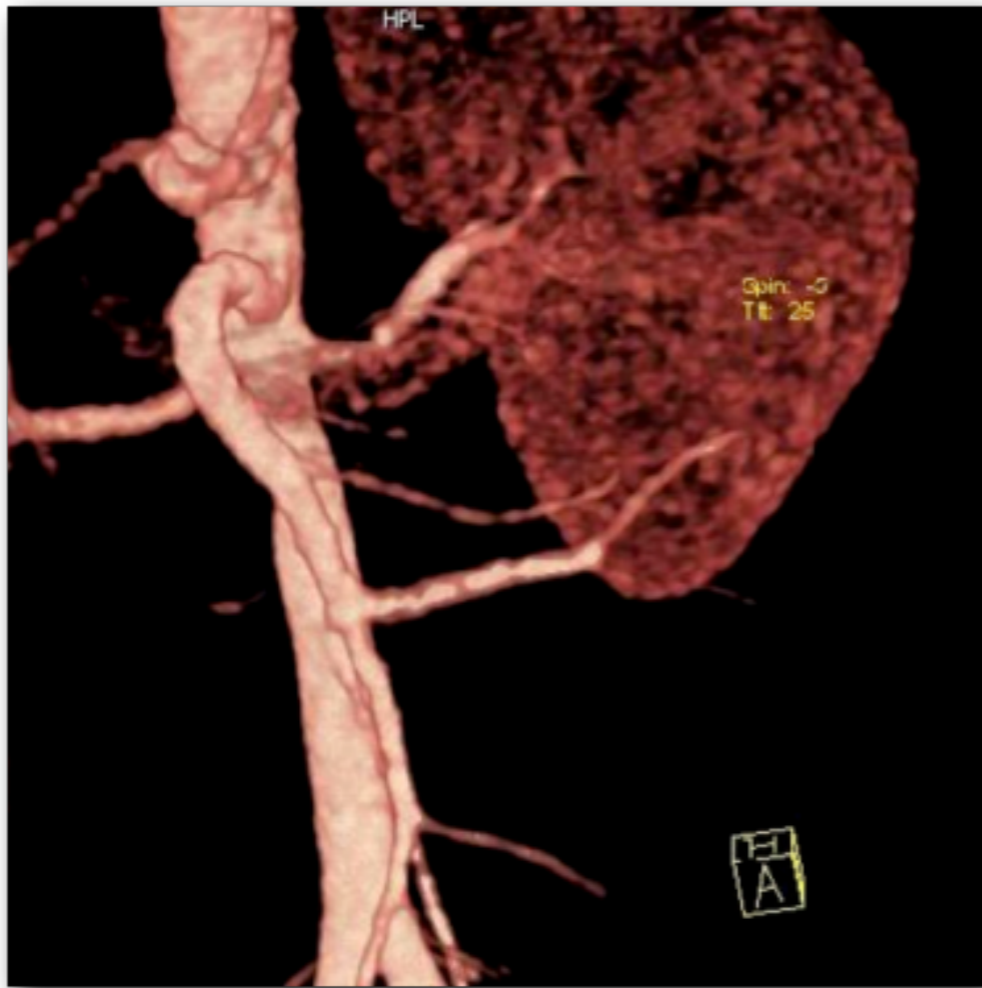


Evans et al., J. Med. Genet. 2002; 39:311.

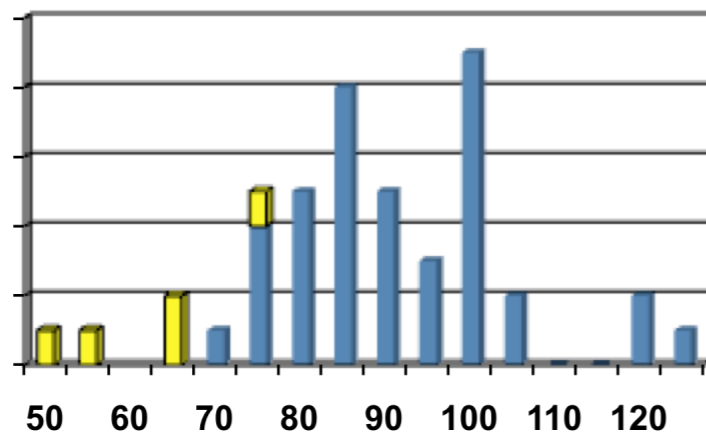


Ferner R et al. *J Neurol Neurosurg Psychiatry* 2000;68:353-357)

Vascular Dysplasia



Neurocognitive Dysfunction



North et al., Neurology 44:878, 1994.



Natural History



- plexiform neurofibroma
- tibial dysplasia

- optic glioma
- Lisch nodules
- learning disability
- hypertension
- short stature
- macrocephaly

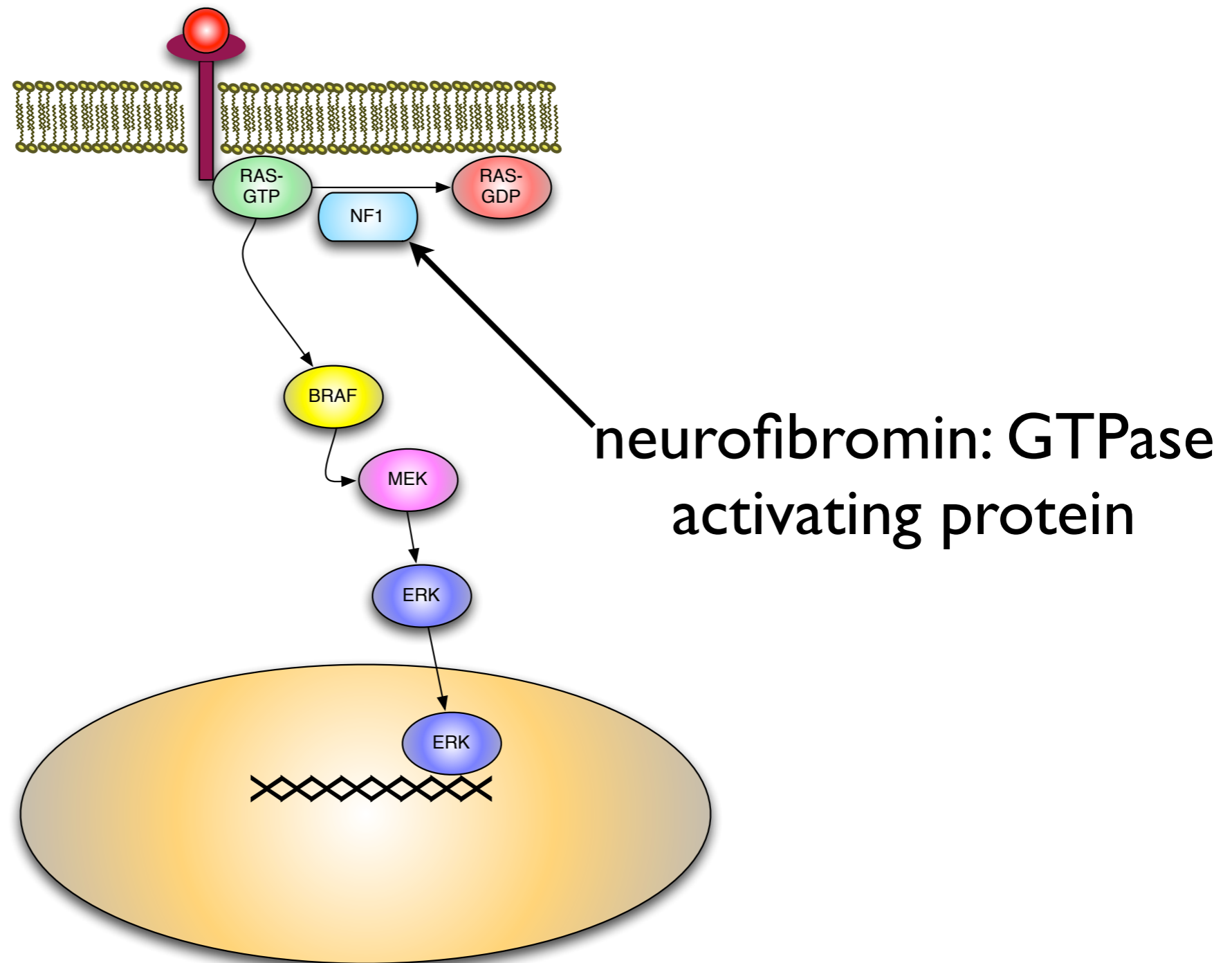
- neurofibromas
- MPNST
- scoliosis

- neurofibromas
- MPNST
- genetic risk

Follow-up

Physical Exam	Referrals	Testing
<ul style="list-style-type: none">• Change in neurofibromas• Growth• Blood pressure• Neurological exam	<ul style="list-style-type: none">• Ophthalmology• Development	<ul style="list-style-type: none">• As indicated

NF1 Gene

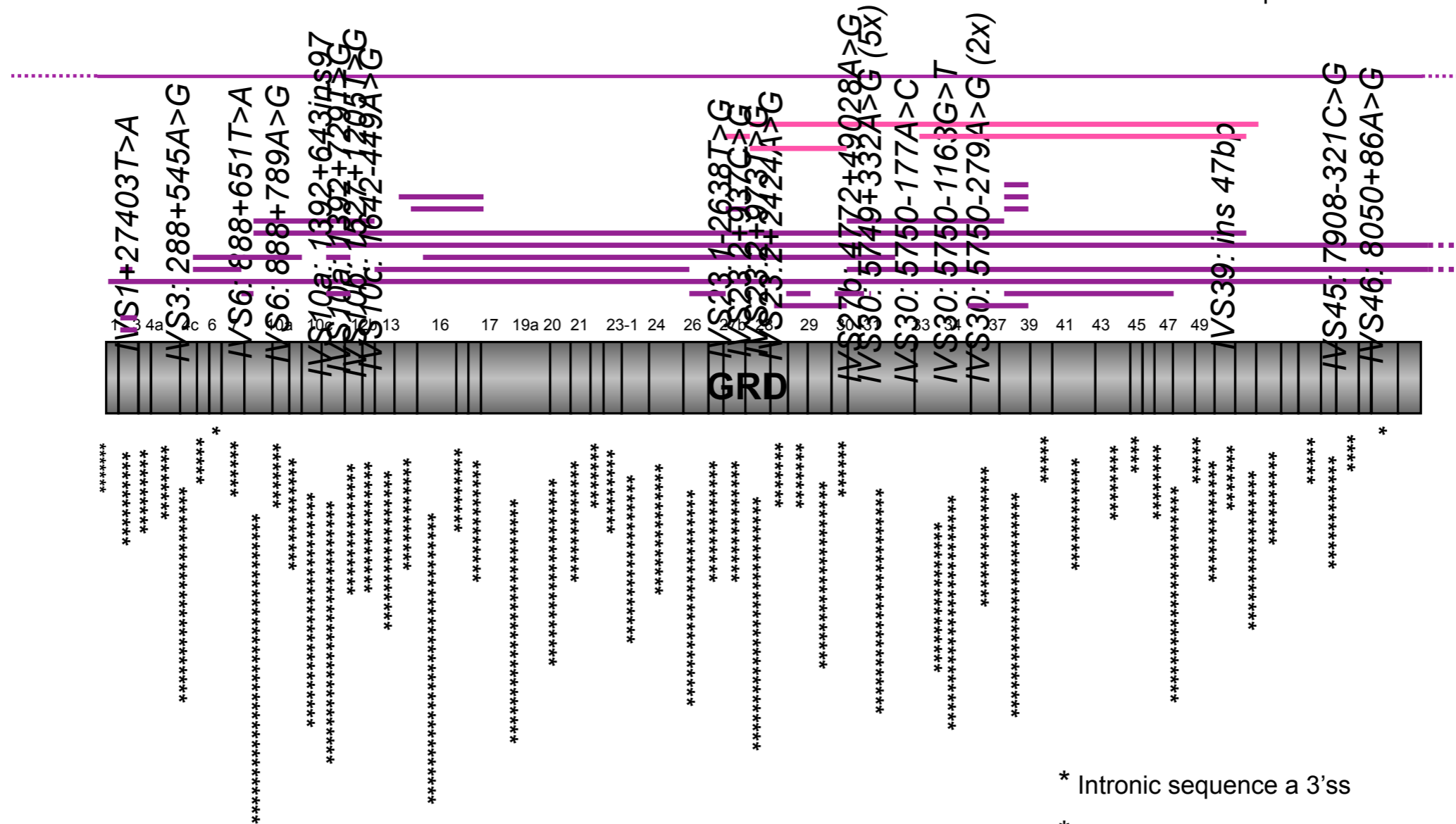


NF1 Mutations

Translocation: n=1
 Total gene deletions: n=72

~5% total gene del; ~2-3% 1-multi exon del; ~2% deep intronic splice mutation;
 ~28% splice mutation (exon/ -borders ±30nt); ~48% nonsense/frameshift (~50:50);
 ~13% missense

(NF1: 1-1500)
 April 2007

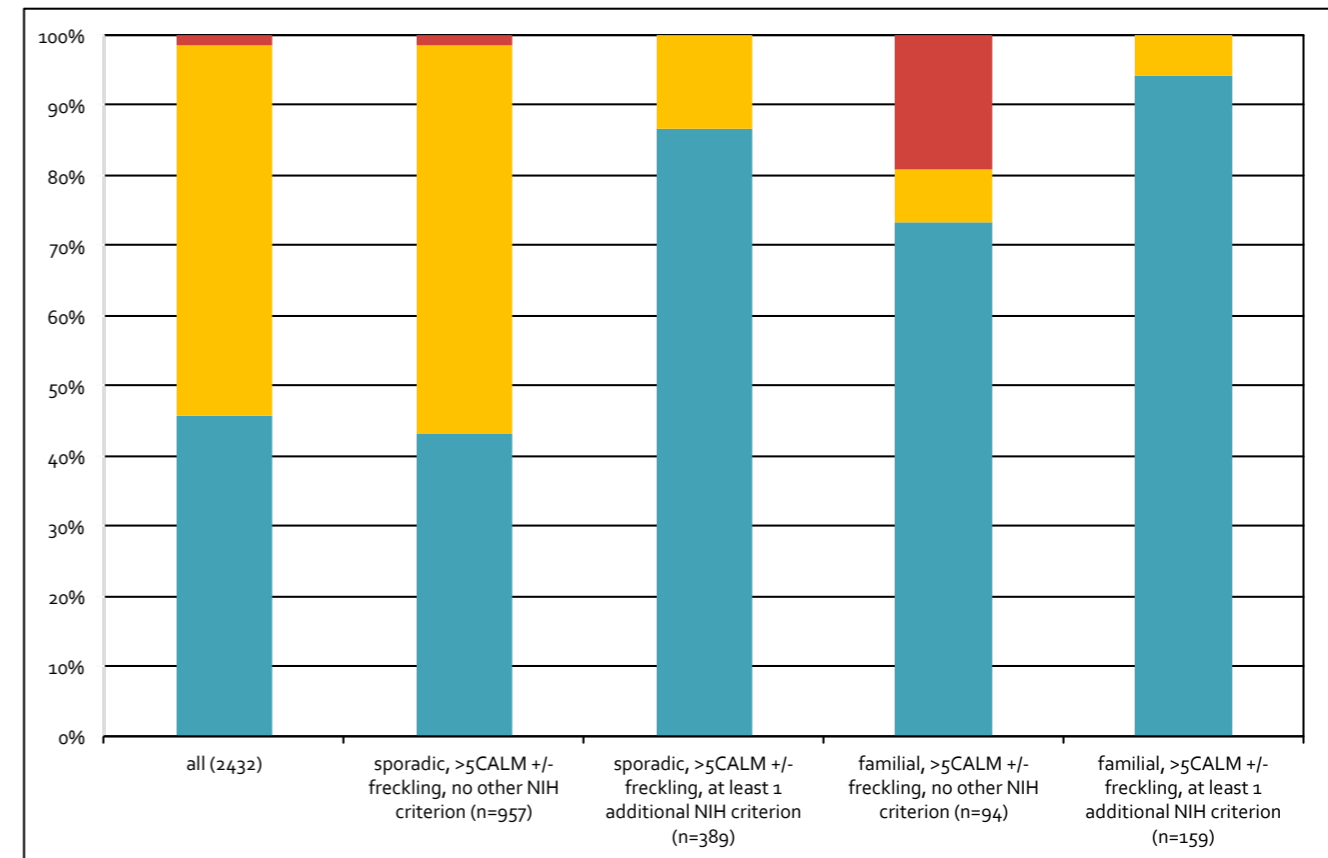


- * Intronic sequence a 3'ss
- * Exonic sequence
- * Intronic sequence a 5'ss

Indications for Genetic Testing

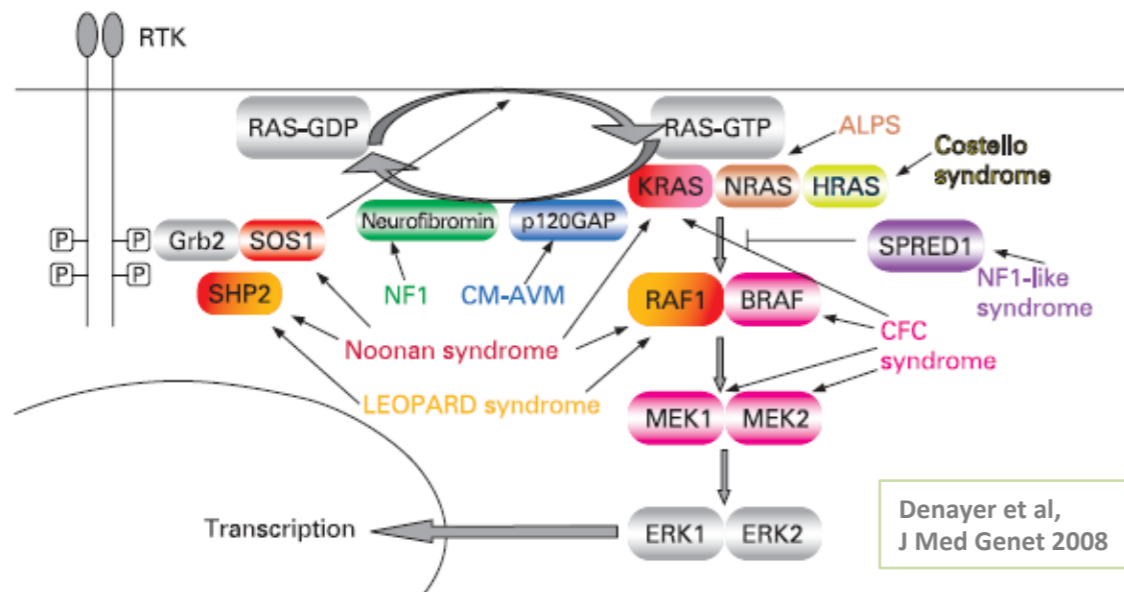
- Child with multiple cafe-au-lait spots
- Relative of affected individual
- Unusual presentation
- Prenatal diagnosis

Legius Syndrome



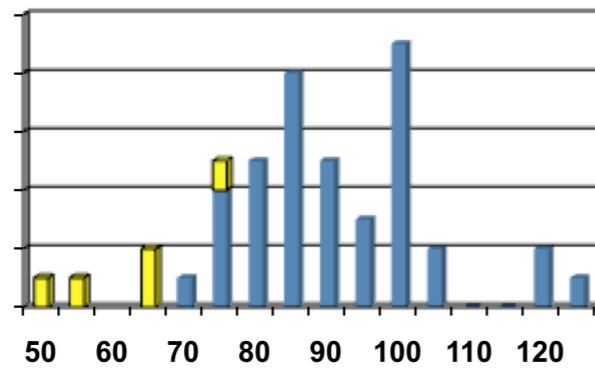
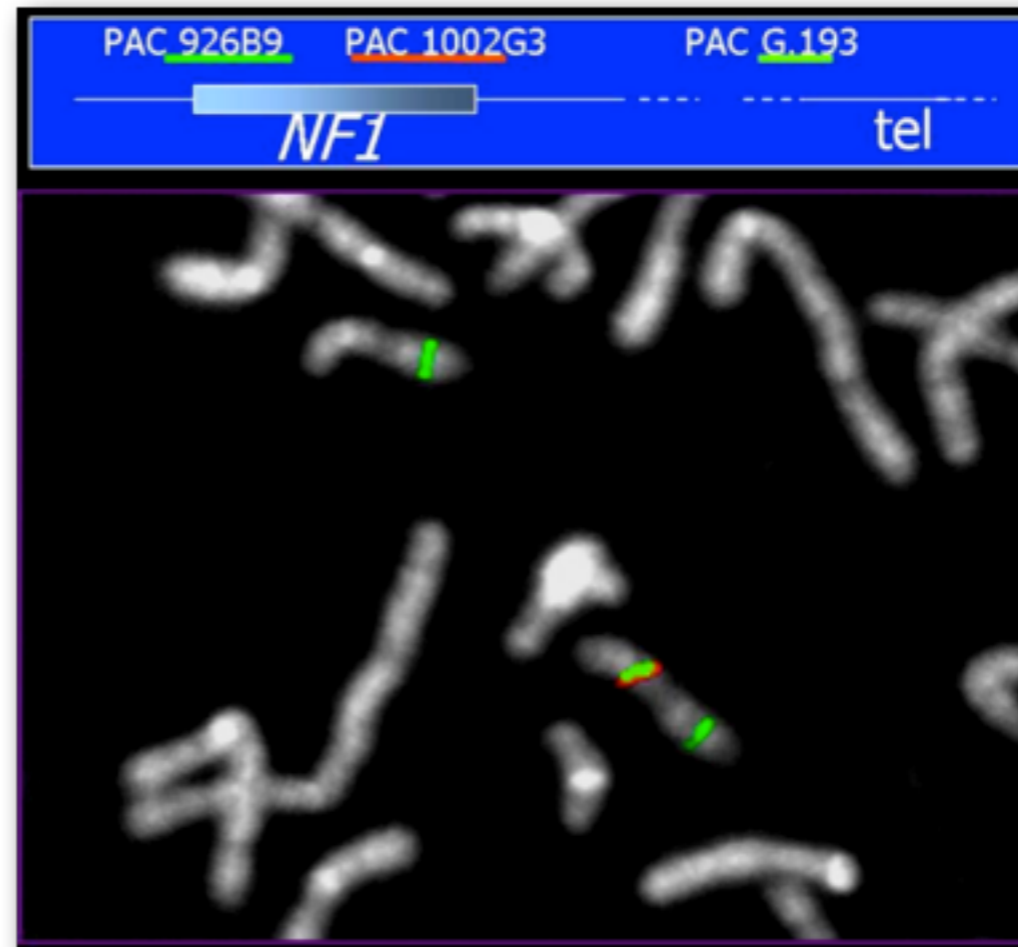
■ NF1
 ■ No NF1/SPRED1
 ■ SPRED1

Messiaen et al, JAMA 302: 2111; 2009



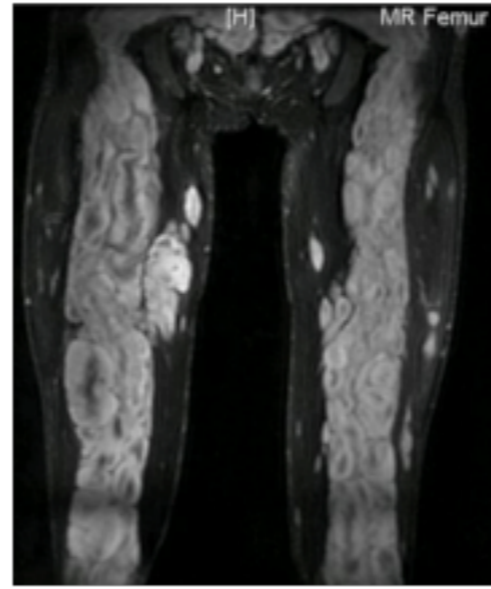
Denayer et al, J Med Genet 2008

NF1 Deletions



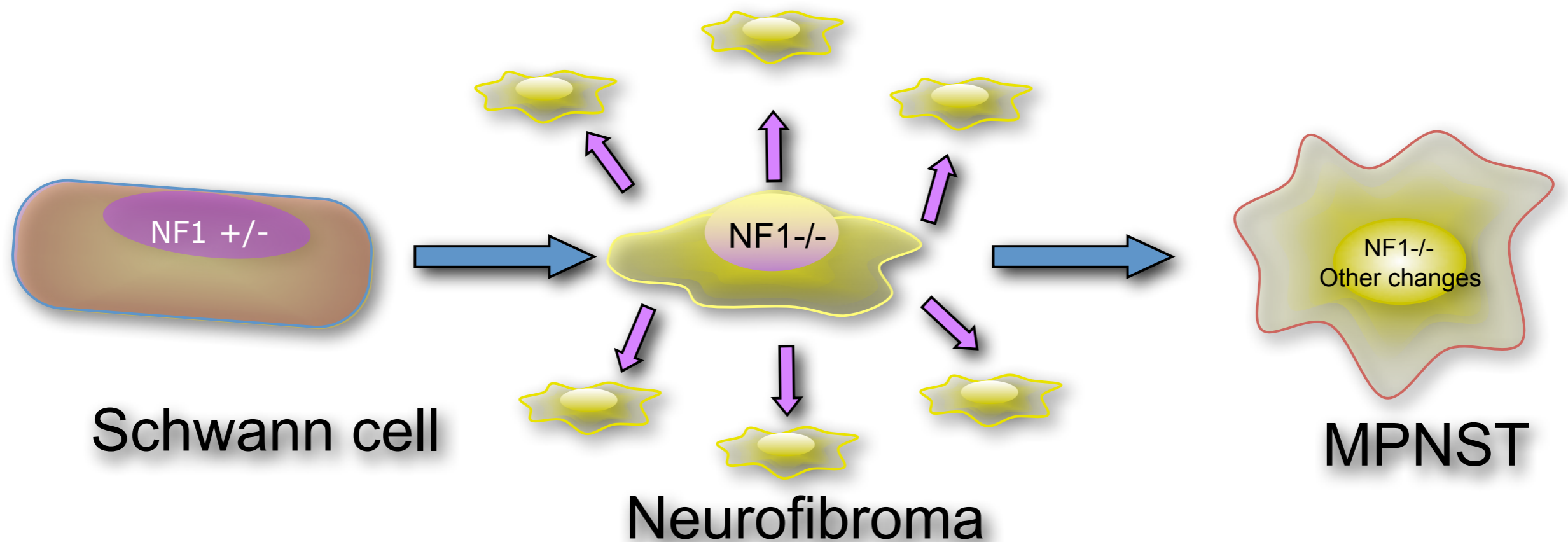
North et al., Neurology 44:878, 1994.

“Spinal NF”

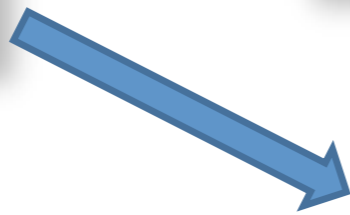
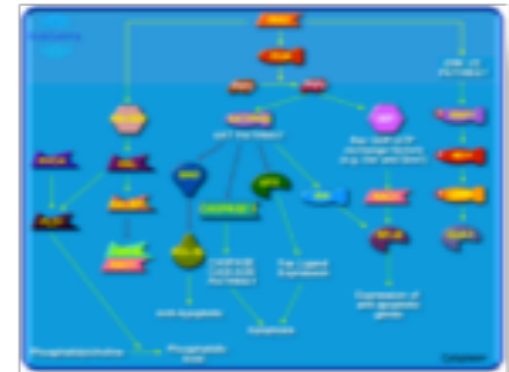


predominantly missense and splicing mutations

Pathogenesis of Neurofibromas



Drug Discovery



NF Consortium



Clinical Trials

Plexiform
Neurofibroma

Learning
Disability

Low-grade
Glioma

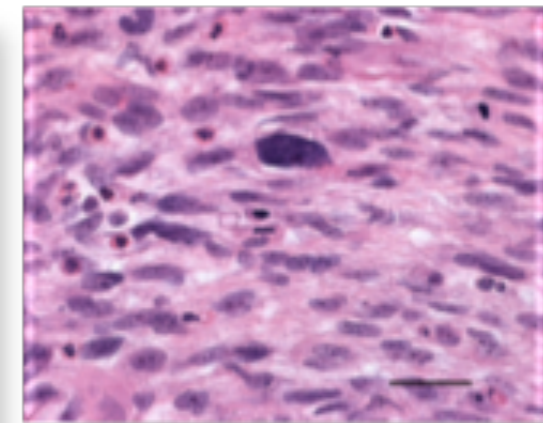
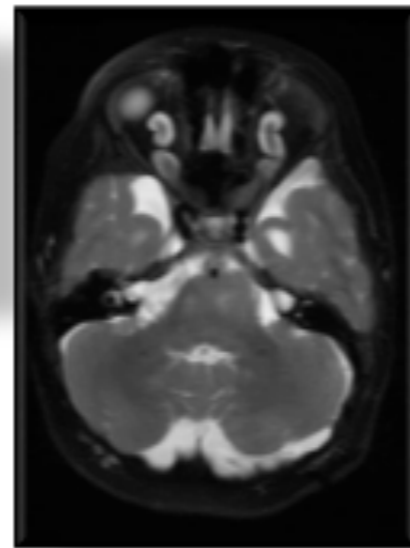
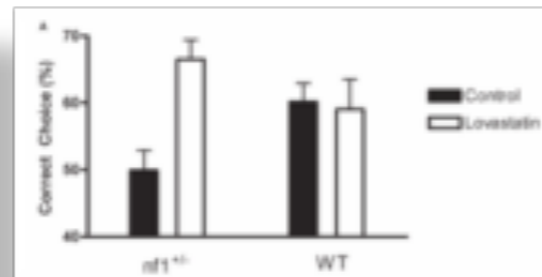
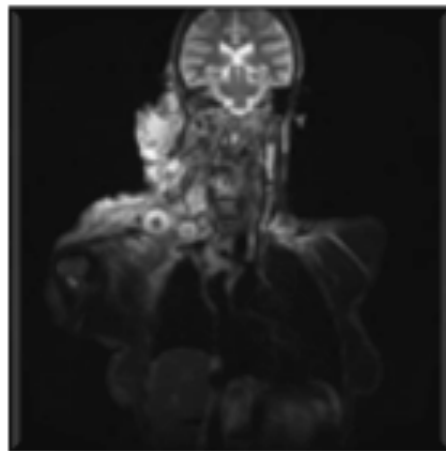
Malignant Peripheral
Nerve Sheath Tumor

STOPN

STARS

RAD001

MPNST



Patient Education

about this site | site map
enhanced glossary

In Their Own Words

Megan | Andres | Syrel | Miguel



understanding NF1 A medical resource about Neurofibromatosis 1 for parents, patients, and providers



Identifying	Explaining	Managing	Supporting	Consultation Video
<ul style="list-style-type: none">•What is NF1?•How do I know if I have it?•How is it diagnosed?	<ul style="list-style-type: none">•What causes NF1?•What can I expect?•What are we learning about it?	<ul style="list-style-type: none">•What are my medical options?•Are other resources and tools available?	<ul style="list-style-type: none">•How do I care for and support my child?•How do I talk about NF1?	<p>Parents Abby and Paul speak with an expert about their daughter Hannah's NF1.</p> <p>You will need QuickTime 5 to view the video resources in this site.</p>

A resource from the Harvard Medical School Center for Neurofibromatosis and Allied Disorders. Development of this Web site was made possible by funds from the Massachusetts Department of Public Health.



credits | copyright | comments

Produced by: 

Acknowledgements

- Radiology
 - Tina Young Poussaint
 - Diego Jaramillo
 - Eva Dombi
 - Stuart Royal
- Dermatology
 - Amy Theos
 - Kevin Boyd
- Genetics
 - Ludwine Messiaen
- Pathology
 - Steve Carroll
 - NF Consortium
 - Karen Cole-Plourde
 - Alan Cantor
- Support
 - US Army CDMRP
 - NINDS