
Patient Centered Research: The Audiology Experience
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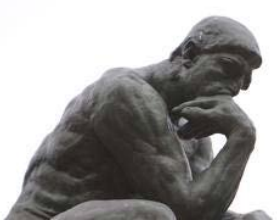
NEMOURS
ALFRED I. duPont HOSPITAL FOR CHILDREN
Thomas Jefferson University

Patient Centered Research?

- Who are we?

- What do we do?



- *A.I. duPont Hospital for Children*
- *The Clinic for Special Children*:
  Collaborating to improve children's lives

Nemours. Alfred I. duPont Hospital for Children

Nemours – a children's health system

- 1936 - Alfred I. duPont American industrialist
- 1940 - Opened as 60-bed hospital for children with orthopedic conditions

Nemours. Alfred I. duPont Hospital for Children

Nemours/Alfred I. duPont Hospital for Children

- 1985 –200-beds
  - full range of pediatric specialties
- Caring for 250,000 children annually in:
  - Delaware Valley
  - Florida
- 2012 - Nemours Children's Hospital to open in Orlando

Nemours. Alfred I. duPont Hospital for Children

Nemours/Alfred I. duPont Hospital for Children

- Expansion of facilities
  - to open 2014
  - 250 single-bed rooms
  - New, larger ED
  - New PICU
  - 188-space underground parking garage
  - Rooftop helipad
  - Five-story atrium entrance and welcome center

Nemours. Alfred I. duPont Hospital for Children

Department of Otolaryngology

Dr. Robert O'Reilly

Audiology Clinic

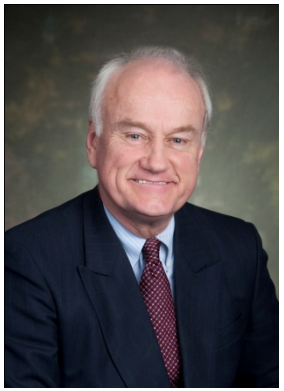
Dr. Yell Inverso

Auditory Physiology and Psychoacoustics Research Laboratory

Dr. Thierry Morlet

Nemours. Alfred I. duPont Hospital for Children

Division of Pediatric Otolaryngology



James Reilly, MD

Steven Cook, MD

Robert O'Reilly, MD

Udayan Shah, MD

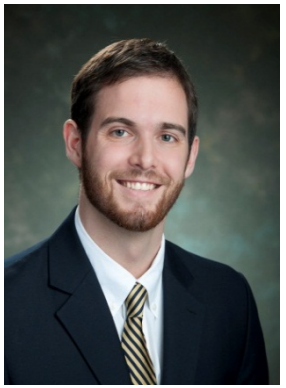
Richard Schmidt, MD

Patrick Barth, MD

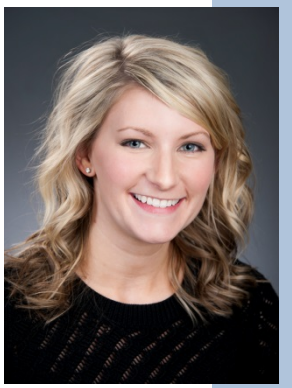
Douglas Johnston, MD

Heather Nardone, MD

Katie Bacik, PA-C



Colin Drake, PA-C



Erin Field, PA-C

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Audiology Clinic

Yell Inverso, PhD

Liesl Looney, Aud

Thomas Jefferson University Dept. of Otolaryngology

Mindy Rabinowitz, MD PGY-4

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Clinical Audiology

Nemours. Alfred I. duPont Hospital for Children

Full-Spectrum Pediatric Audiology Services

- **12 Audiologists, 2 Audiology Assistants, 1 Audiology Doctoral Extern & 3 support staff**
- **Comprehensive Behavioral Hearing Evaluations**
  - Visual Reinforcement Audiometry
  - Conditioned Play Audiometry
  - Standard Behavioral Audiometry
- **Distortion Product and Transient Evoked Otoacoustic Emission Testing**
- **Sedated and un-sedated Auditory Brainstem Response Testing (Diagnostic and Newborn Screening)**
- **Comprehensive Middle Ear Diagnostic Evaluations**

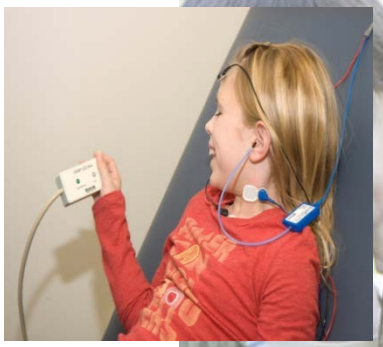
Audiologic Specialty Care

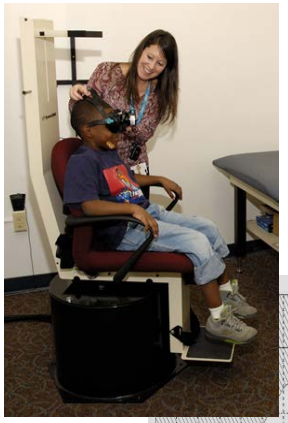
- Cochlear Implant Program
- Central Auditory Processing Disorders (CAPD) Program
- Pediatric Amplification and Assistive Listening Devices Program
- Auditory Neuropathy Spectrum Disorders Program
- Pediatric Vestibular Program

Pediatric Vestibular Program

Vestibular Evoked Myogenic Potential (VEMP)

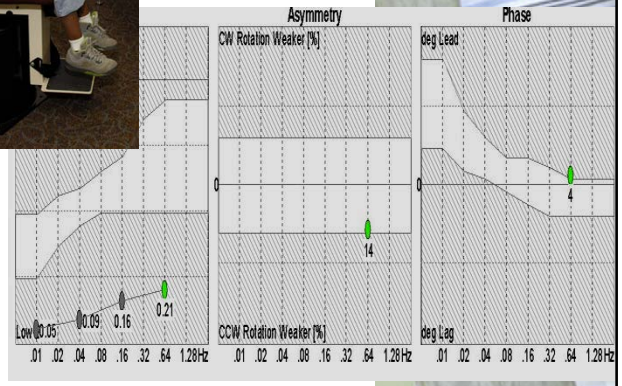
- 500 Hz tone burst (75-95 dB HL air or 66 dB pip bone)
- Tonic SCM contraction = EMG 50-250 microvolts
- 80-100 samples averaged





Rotary Chair Testing (RC)

- 0.01, 0.04,0.16,0.64 Hz at max velocity 50 deg/s
- Gain, Phase, Assymetry



Video Nystagmography Test Battery (VNG)

- IR system to record corneal movement
- Saccades, Pursuit, OPK
- Spontaneous, positional, positioning nystagmus
- Air induced binaural, bithermal, calorics

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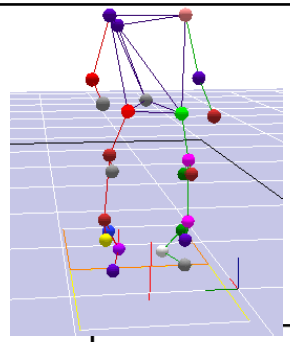
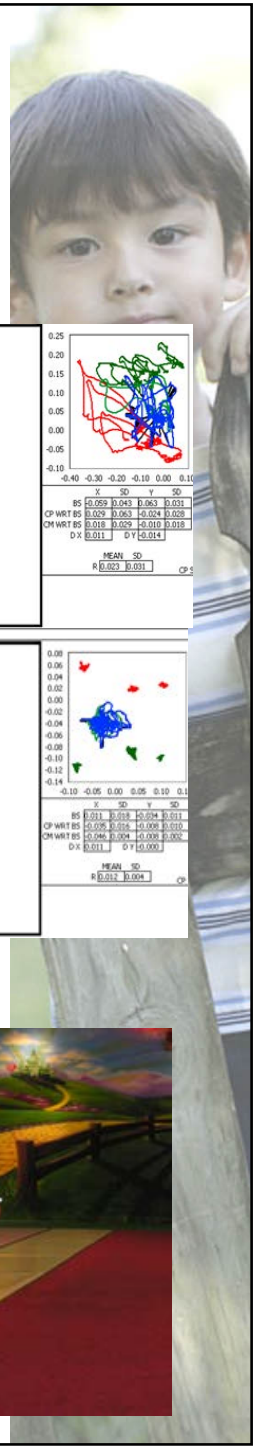
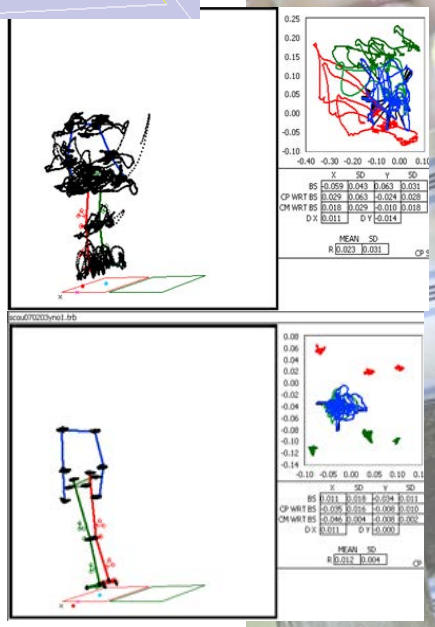
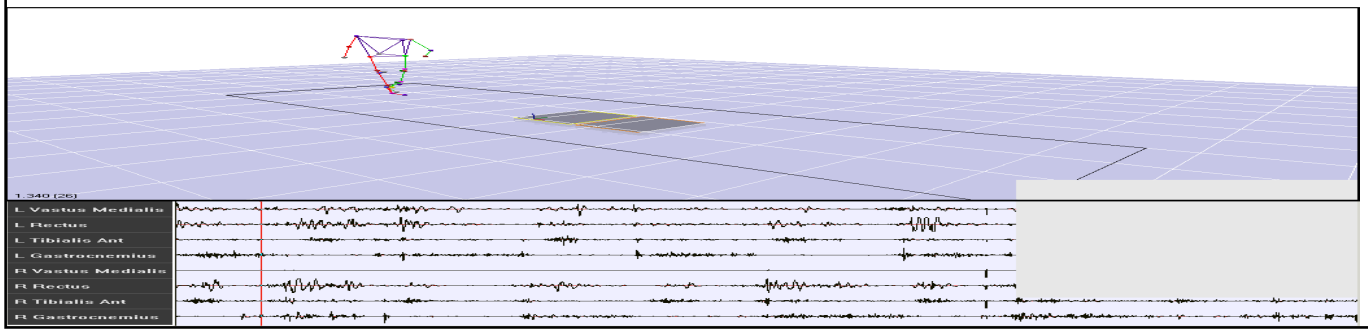
Pediatric Vestibular Program

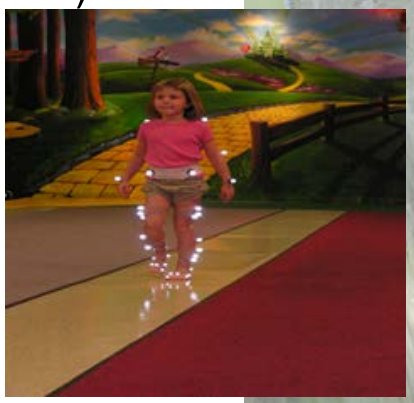
- **Computerized Dynamic Posturography (CDP)**
  - Limits of stability using 8 standard trials
  - Reaction time, movement velocity, endpoint excursion, max excursion,directional control
- **Gross Motor Development**
  - Peabody Developmental Scale (<4 yrs)
  - Bruininks-Ostresky Test Motor Proficiency
- **Full Gait Analysis**
  - Dynamic balance kinetics and kinematics
  - Position / movement CM walking straight line (60 Hz data collection)
    - Self selected speed for 9 meters



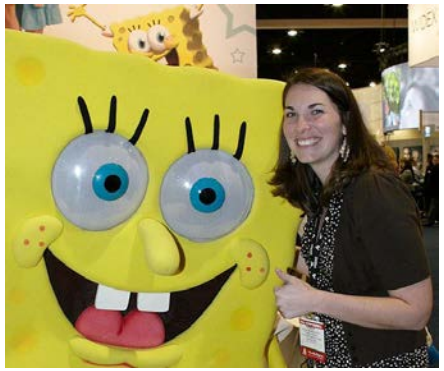








Auditory Physiology and Psychoacoustics Research Laboratory



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Thematic

- **Development of Efferent Auditory Pathways: Cortical control of the auditory periphery**
- **Speech processing at the cortical level (Quiet and noise)**
- **Auditory and Vestibular impairment**
  - Otoacoustic Emissions
  - Suppression of Otoacoustic Emissions
  - Evoked Potentials:
    - Auditory Brainstem Responses
    - Middle Latencies
    - Cortical Potentials (Speech/noise)

Specific Studies

- **Auditory Processing Disorders and Specific Language Impairment:**
  - Efferent function and Hemispheric specialization
- **Friedreich Ataxia**
  - Auditory, Speech and Vestibular functions
- **Rett Syndrome**
  - Auditory function
- **Late Onset Hearing Loss**
- **Vestibular Compensation**
- **Inner Ear Malformation**
- **Noise Induced Hearing Loss**
- **Auditory Neuropathy Spectrum Disorder**
- **….**

Defining Community Needs

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Collaborate to Improve Patient Care

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“Start With a Healthy Child”

Create a Medical Home

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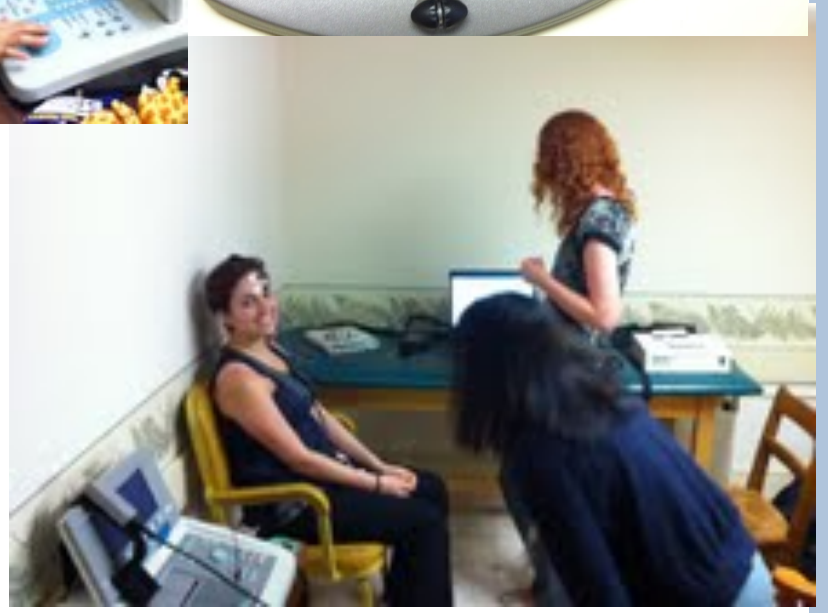
Build Clinical Services



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Link Services to Research

Translate Research into Practice

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Translate Research into Practice: Otosclerosis

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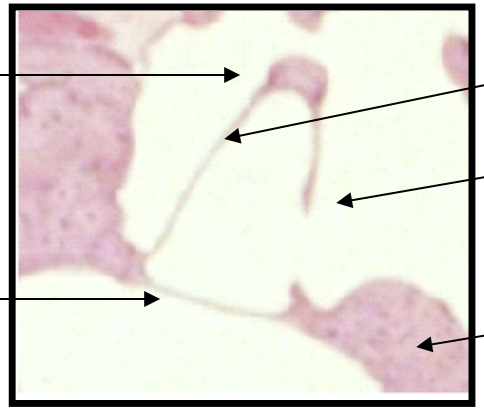
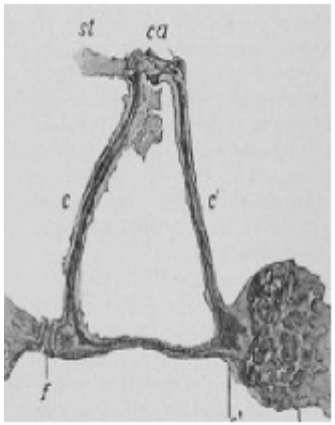
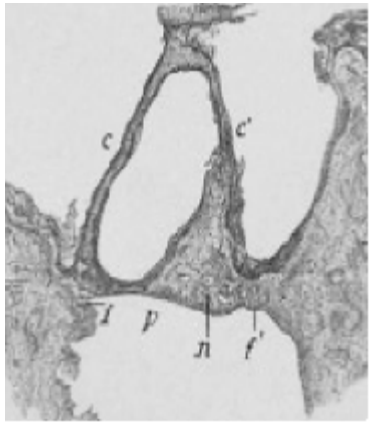
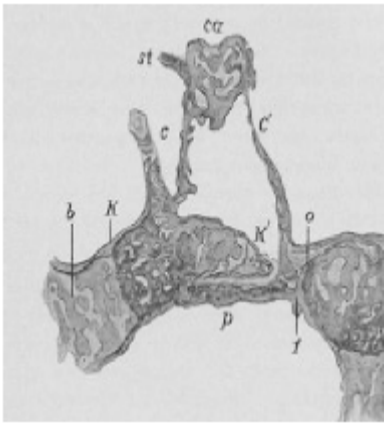
Normal



Otosclerosis







Fixation disturbs transmission of sound waves through middle ear ossicles, resulting in a CHL

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Thys, Van Den Bogaert, Iliadou, et. al., 2007

http://www.politzersociety.org/content.php?conid=685

http://www.biophysics.uwa.edu.au/auditory/mid_ear4.html

Epidemiology

Prevalence

Caucasians	Tunisians	Asians/Blacks/Native Americans
0.3-0.4%	0.4-0.8%	~0%

Age of Onset

- 3rd decade (late teens – 6th decade)

Gender

- Female:Male= 2:1 (Clinical Otosclerosis)

Laterality

- 70–80 % bilateral

Ealy, Smith. 2009

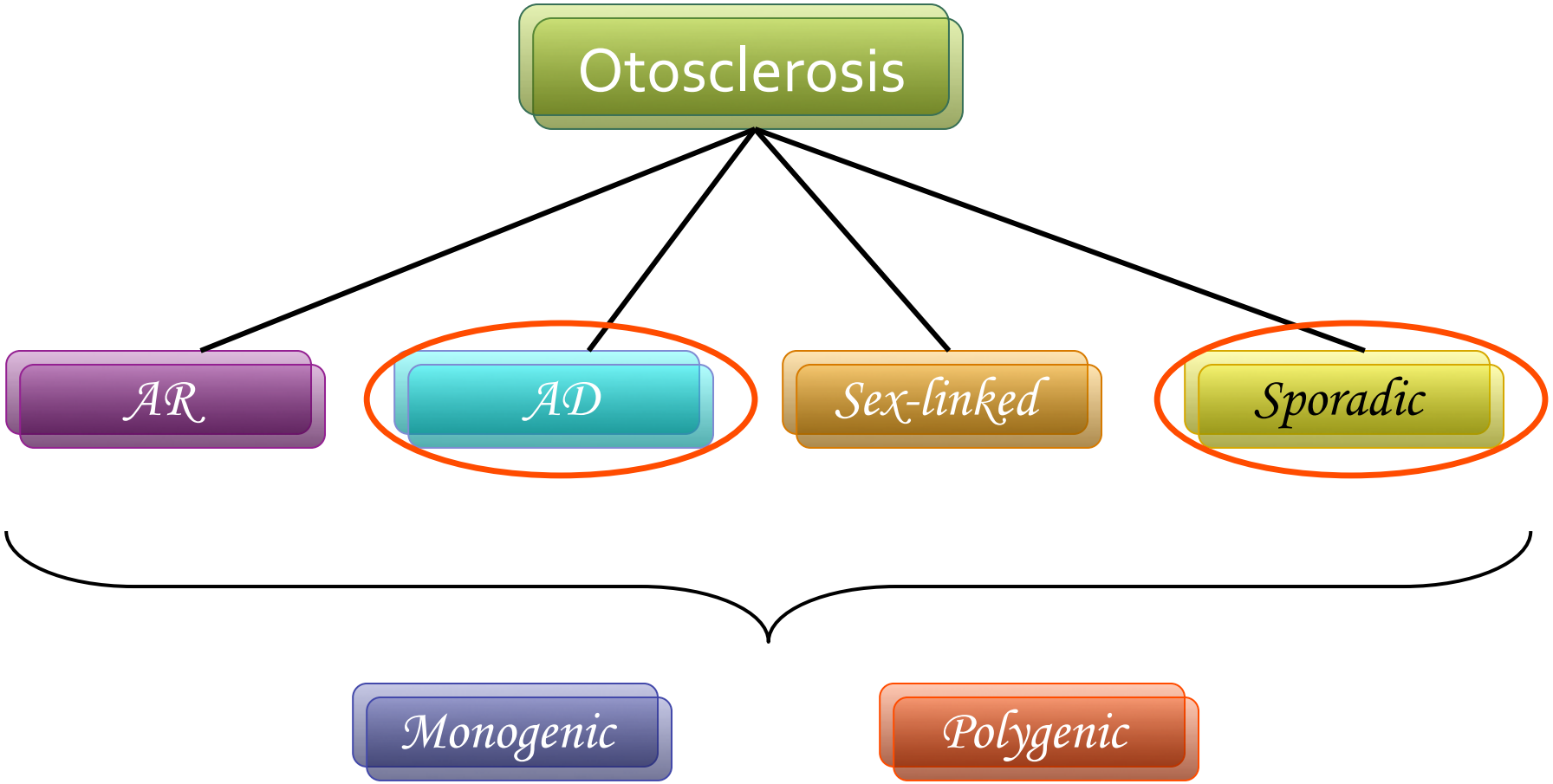
Thys, Van Camp. 2009

Markous, Goudakos. 2009

Csomor, Sziklai, Karosi. 2012

Moumoulidis, Axon, Baguley, 2007

Modes of Inheritance



Markous, Goudakos. 2009

Saeed, Briggs, Lobo, et.al. 2007

Modes of Inheritance

Otosclerosis

Monogenic

Believed to occur rarely in otosclerosis

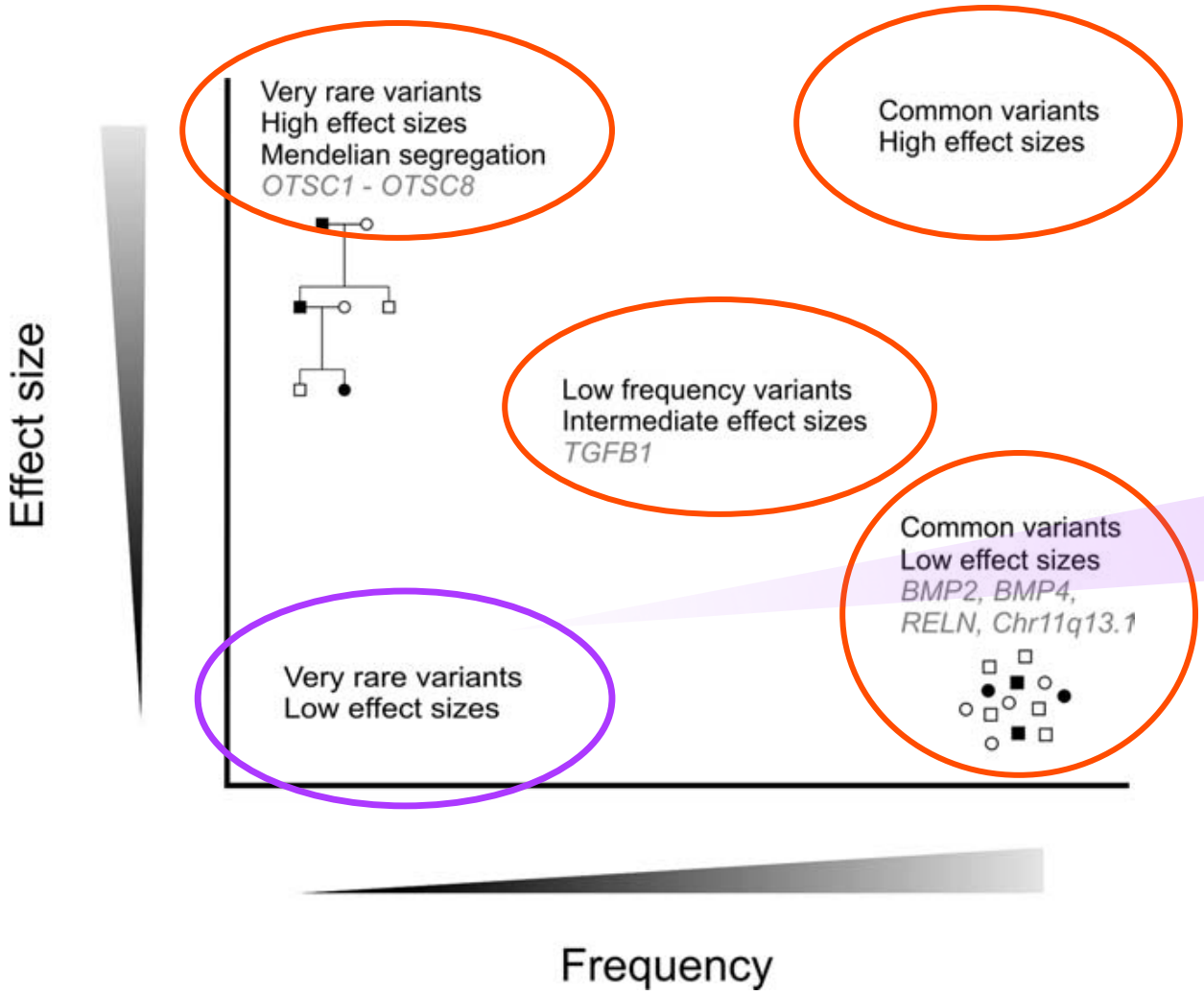
Polygenic

Likely a genetically heterogenous disease

Ealy, Chen, Ryu, et.al. 2008

Schrauwen, Van Camp. 2010

Challenges to Genetic Analysis



1. Diagnosis is presumptive

2. Pedigree construction difficult

   -<u>AD family</u>:

   Ideal for linkage

   analysis = 10 meioses

   →diff to find

3. Incomplete penetrance & variable expression

Schrauwen, Van Camp. 2010

Saeed, Briggs, Lobo, et.al. 2007

Otosclerosis

- 3 Generations of affected family
- Audiometrics, Op-notes, Genetic analysis

Translate Research into Practice: SLITRK6

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SLITRK6

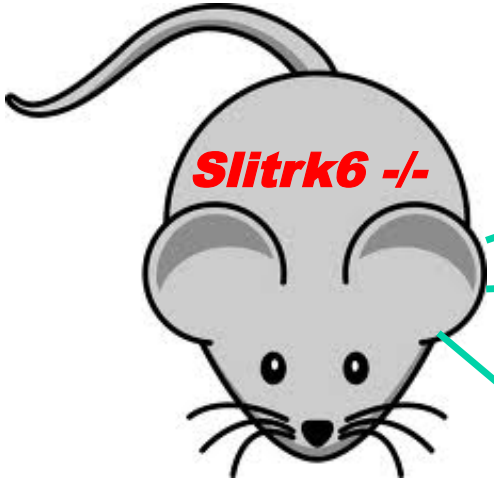
SLITRK Family of Proteins control:

- Neurite outgrowth
- Synaptic development

SLITRK6 play role in survival and innervation:

- Auditory System
- Vestib apparatus
- Retina

Mouse model: SLITRK6



Organ of Corti normal

↓ Cochlear innervation density

- Development:
  - Sensory neurons
  - Spiral & vestibular ganglia die

Affected mice

- ↓ Wave I ABR
- ↓ Auditory startle
- ↓ Vertical VOR gain
- ↓ Locomotor activity
- Mid-Frequency hearing loss

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http://free.clipartof.com/details/57-Free-Cartoon-Gray-Field-Mouse-Clipart-Illustration

F&M Clinic for Special Children | Nemours. Alfred I. duPont Hospital for Children | Jefferson.

Methods

Patients

- 9 subjects
- Endogamous Amish Community
- Age 0.3-36.8 years (mean: 15.3 ± 13.9)

Genetic Testing

- SNP genotype & mapping
  - GeneChip Mapping 10K Assay Kit
  - All Pts homozygous for novel nonsense variant of SLITRK6

Auditory/ Vestibular

- Tympanometry
- MEMR
- DPOAE
- ABR
- PTA, SDS, SRT
- VEMP

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F&M Clinic for Special Children | Nemours. Alfred I. duPont Hospital for Children | Jefferson.

Results

- VEMPS present in 3 of 4 ears tested

		MEMR		DPOAE		CM (duration in ms)		Waves	
Subject ID	Age (years)	*Left*	*Right*	*Left*	*Right*	*Left*	*Right*	*Left*	*Right*
1	0.3	*nt*	*nt*	*nt*	*nt*	+ (1.0)	+ (3.0)	-	-
2	1.5	*nt*	*nt*	-	-	+ (2.0)	+ (2.0)	I	I, II
3	5.6	100 dB/4 kHz	-	-	-	+ (5.0)	+ (5.0)	I	I
4	6.2	100 dB/4 kHz	-	-	-	+ (2.5)	+ (2.5)	I	I
5	11.9	100 dB/4 kHz	100 dB/4 kHz	-	-	+ (3.0)	+ (2.0)	I, V*	I
6	13.9	-	-	-	-	+ (3.0)	+ (2.5)	I	I
7	29.1	-	-	*nt*	*nt*	-	+ (0.5)	-	-
8	32.3	-	-	-	-	-	-	-	-
9	36.8	-	-	-	-	-	-	-	-

*No latency/intensity shift. Abbreviations: CM, cochlear microphonic; DPOAE, distortion product otoacoustic emission; MEMR, ipsilateral middle ear muscle reflex; *nt*, not tested; "-", absent response.

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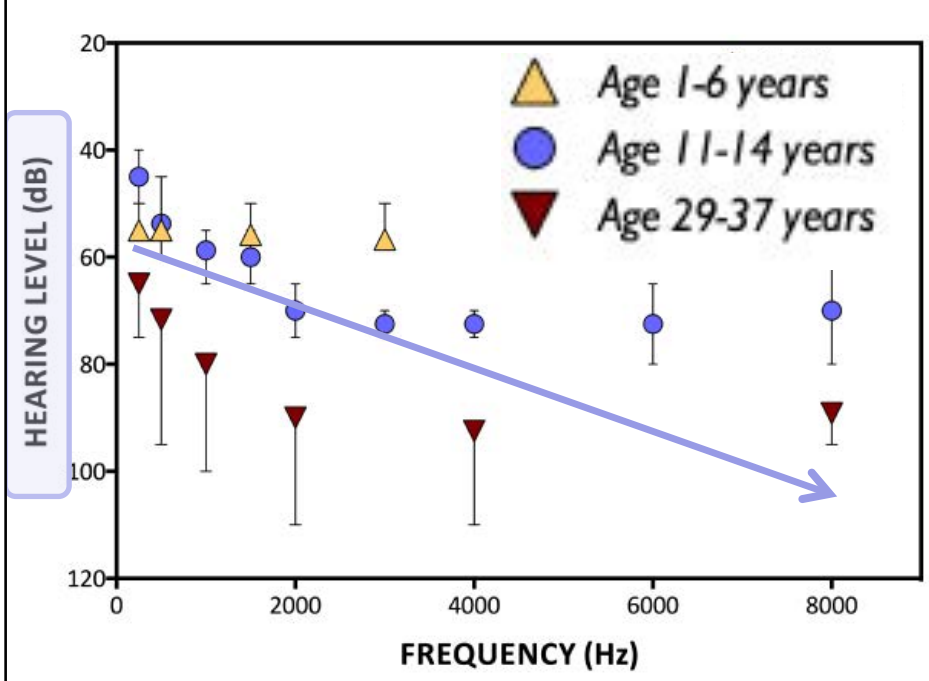
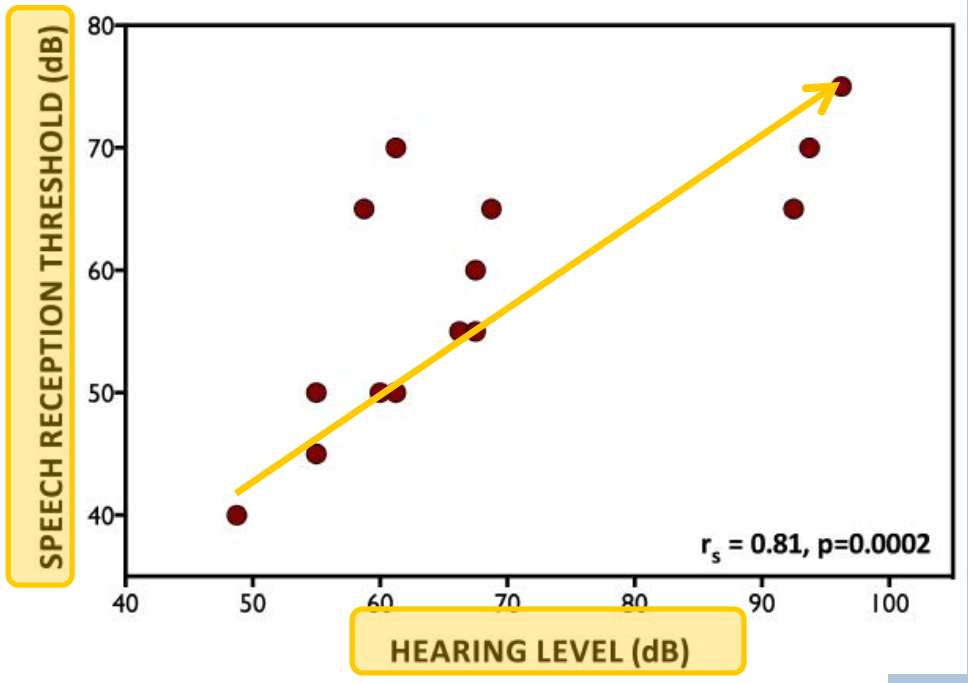
F&M Clinic for Special Children Nemours. Alfred I. duPont Hospital for Children Jefferson.

Results

Audiologic Testing (Audiogram)





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Conclusions

Speech & Language Development

- Speech perception impaired out of proportion to pure tone threshold
- OHC dysfunction & auditory dys-synchrony
  - Youth: Develop speech/language
  - Adult: Good lip reading
- 2 oldest subjects
  - Hearing aid users
  - Limited benefit
- No cochlear implants used
  - Possible benefit?

Translate Research into Practice

The Laryngoscope

A homozygous nonsense mutation of SLITRK6 is associated with an autosomal recessive auditory neuropathy

Journal:	*The Laryngoscope*
Manuscript ID:	lscope-13-0484.R1
Wiley - Manuscript type:	Original Reports
Date Submitted by the Author:	04-Apr-2013
Complete List of Authors:	Morlet, Thierry; duPont Hospital for Children, Auditory Physiology and Psychoacoustics Research Laboratory Rabinowitz, Mindy; Thomas Jefferson University, Otolaryngology- Head and Neck Surgery Looney, Liesl; duPont Hospital for Children, Audiology Riegner, Tammy; duPont Hospital for Children, Audiology Greenwood, L.; duPont Hospital for Children, Audiology Sherman, Eric; Franklin and Marshall College, Biology and Biological Foundations of Behavior Program; Swarthmore College, Biology Achilly, Nathan; Franklin and Marshall College, Biology and Biological Foundations of Behavior Program Zhu, Anni; Franklin and Marshall College, Biology and Biological Foundations of Behavior Program Yoo, Estelle; duPont Hospital for Children, Otolaryngology-Head and Neck Surgery O'Reilly, Robert; duPont Hospital for Children, Otolaryngology-Head and Neck Surgery; Thomas Jefferson University Hospital, Otolaryngology-Head and Neck Surgery; Thomas Jefferson University Hospital, Pediatrics Jinks, Robert; Franklin and Marshall College, Biology and Biological Foundations of Behavior Program Puffenberger, Erik; Franklin and Marshall College, Biology and Biological Foundations of Behavior Program; Clinic for Special Children, Heaps, Adam; Clinic for Special Children, Morton, Holmes; Franklin and Marshall College, Biology and Biological Foundations of Behavior Program; Clinic for Special Children, ; Lancaster General Hospital, Strauss, Kevin; Franklin and Marshall College, Biology and Biological Foundations of Behavior Program; Clinic for Special Children, ; Lancaster General Hospital,
Keywords - Combo:	Molecular Biology, Central auditory processing < Otology, Molecular biology < Otology, Hearing loss < Pediatric otology < Pediatrics

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Translate Research into Practice: GM3 Synthase Deficiency

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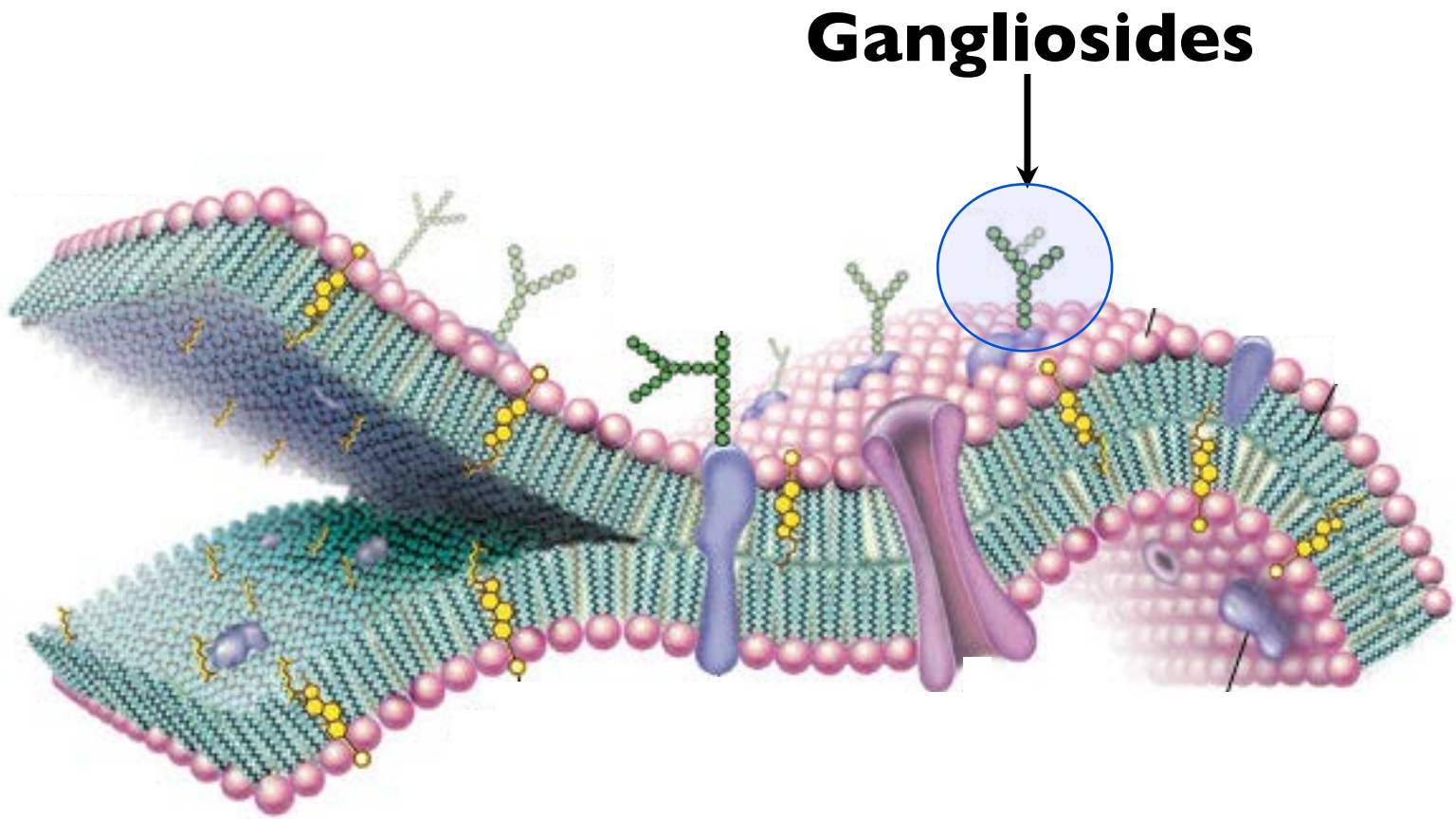
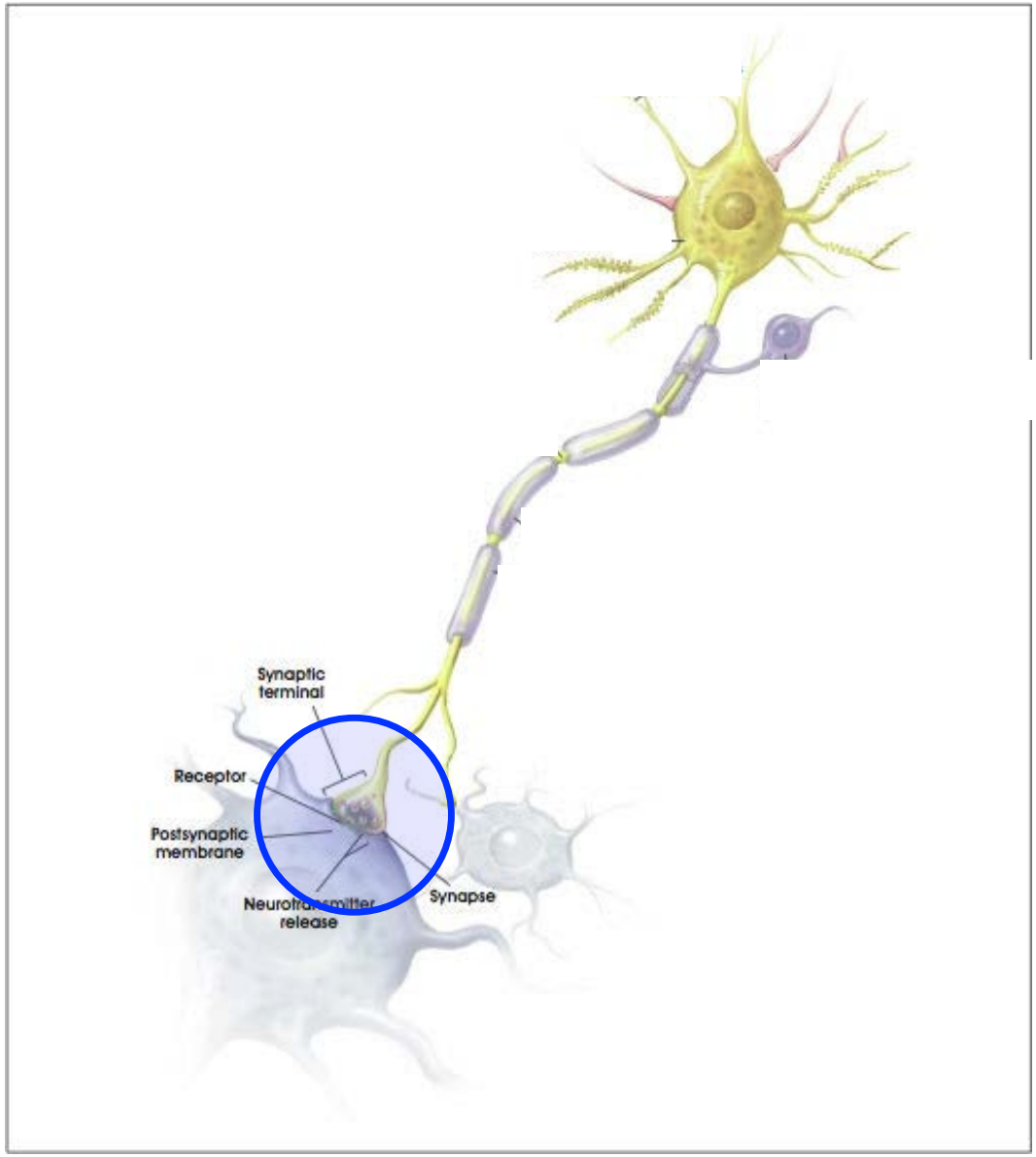
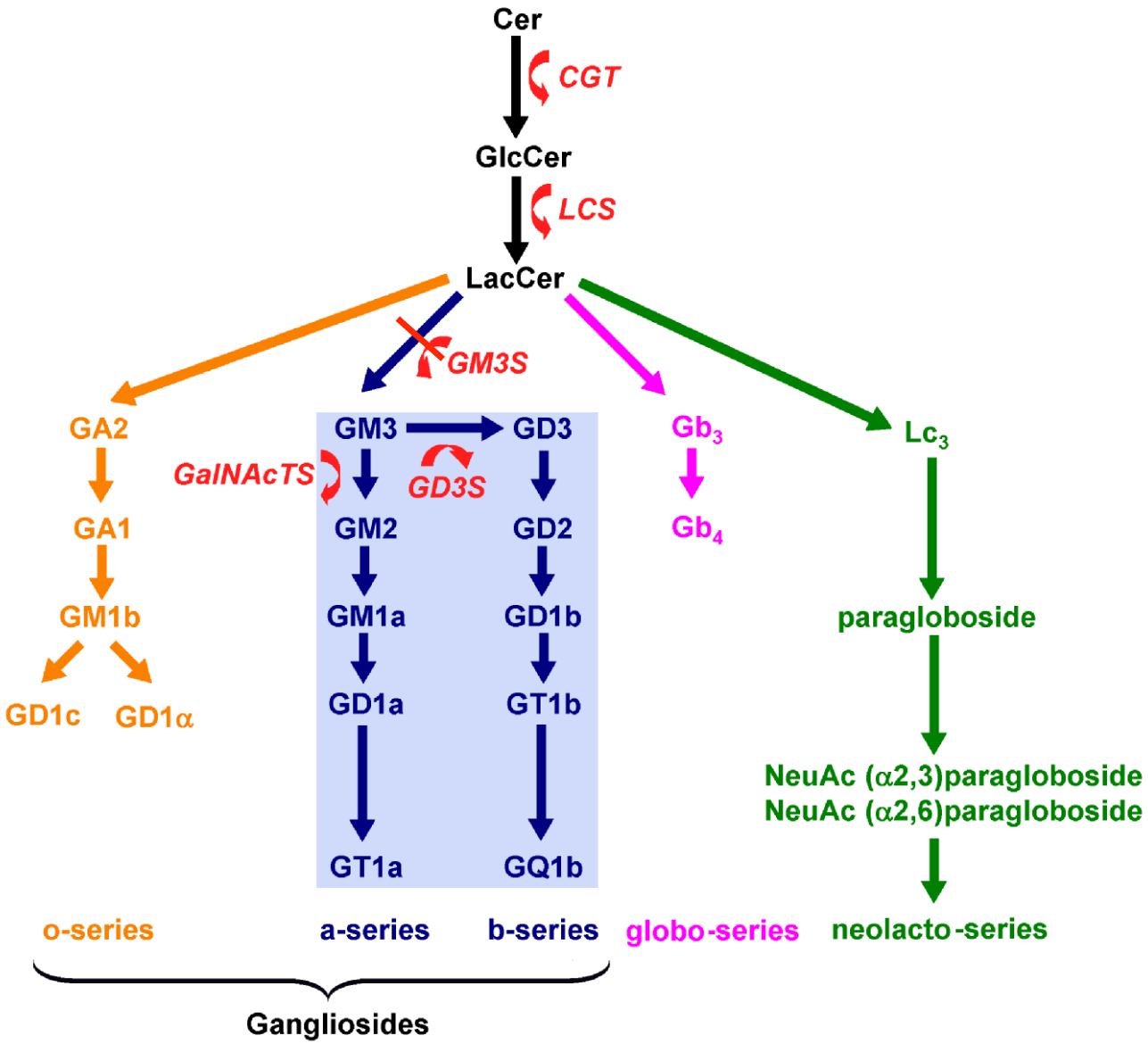
What is the Defect in GM3 Disease?

Where are Gangliosides Found in the Brain?

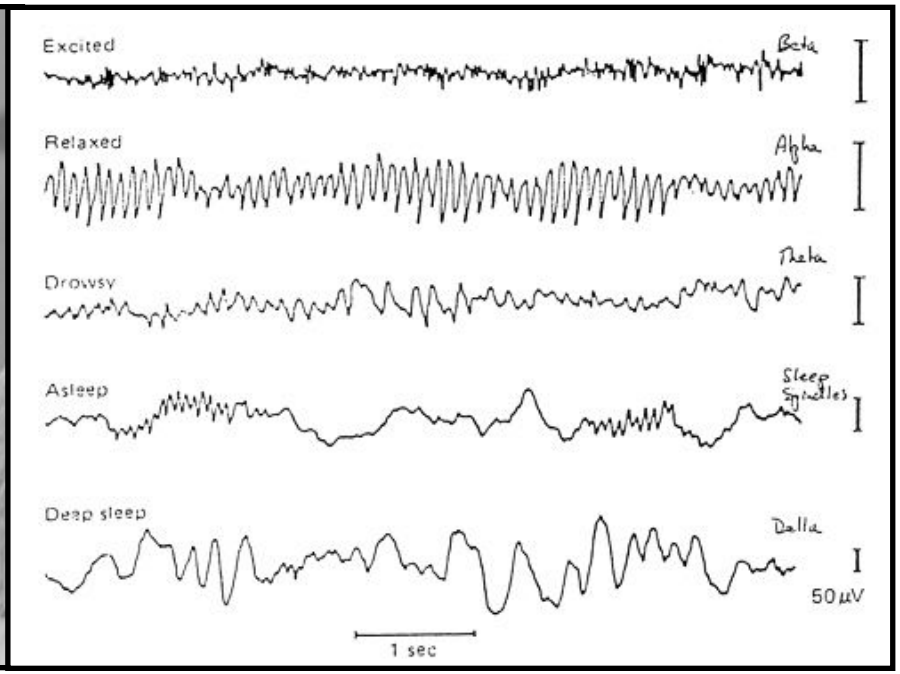


Where are Gangliosides Found in the Brain?

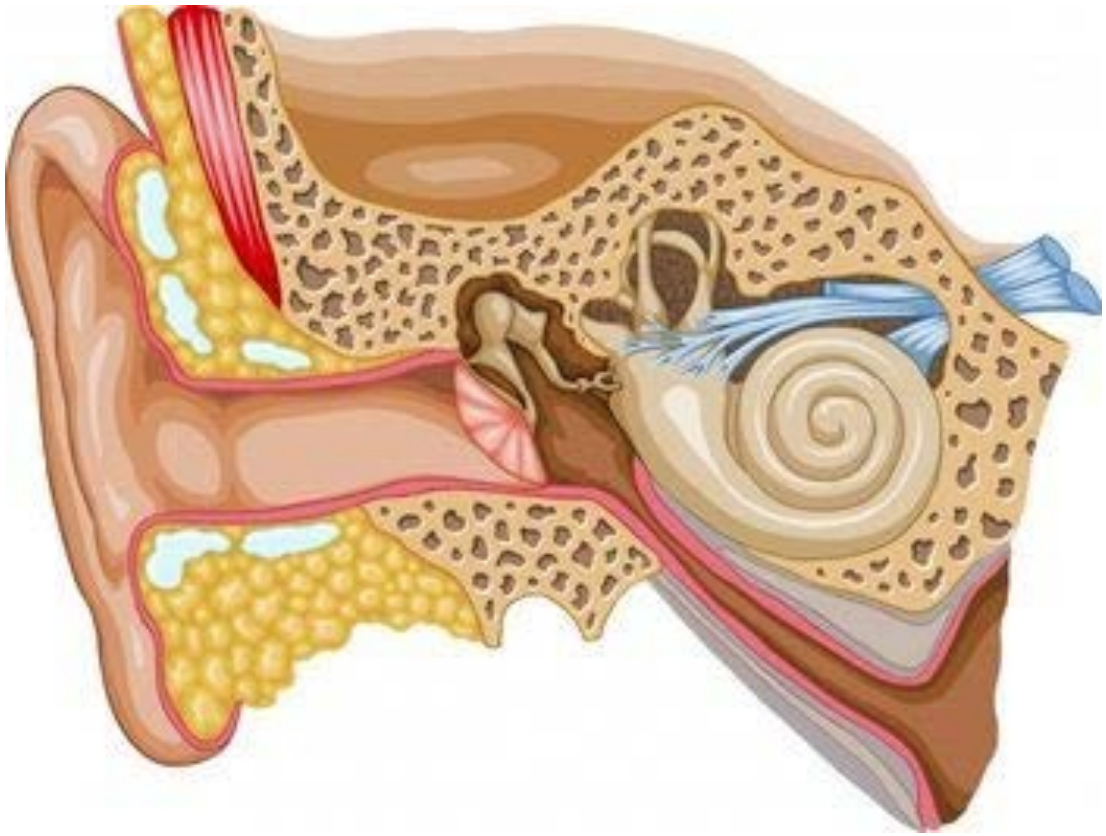



Cer
CGT
GlcCer
LCS
LacCer
GM3S
GA2
GA1
GM1b
GD1c
GD1α
GalNAcTS
GM3
GD3S
GD3
GM2
GD2
GM1a
GD1b
GD1a
GT1b
GT1a
GQ1b
Gb3
Gb4
Lc3
paragloboside
NeuAc (α2,3)paragloboside
NeuAc (α2,6)paragloboside
o-series
a-series
b-series
globo-series
neolacto-series
Gangliosides

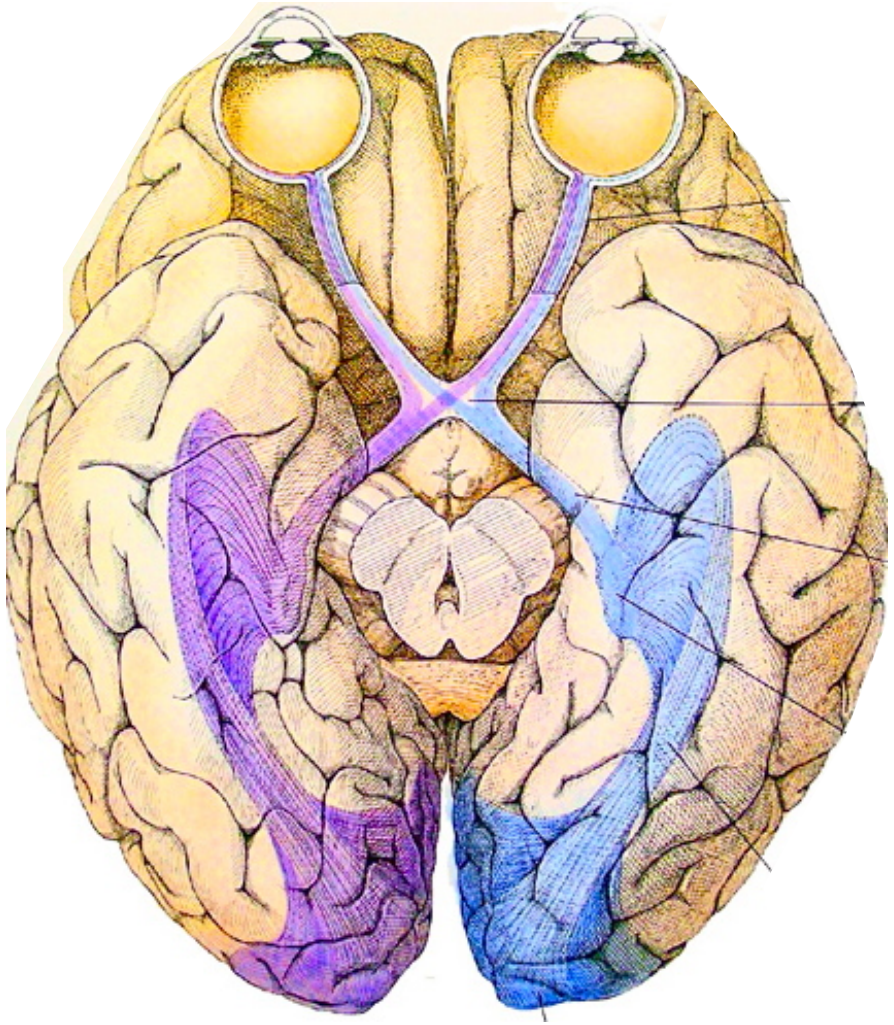
Seizures

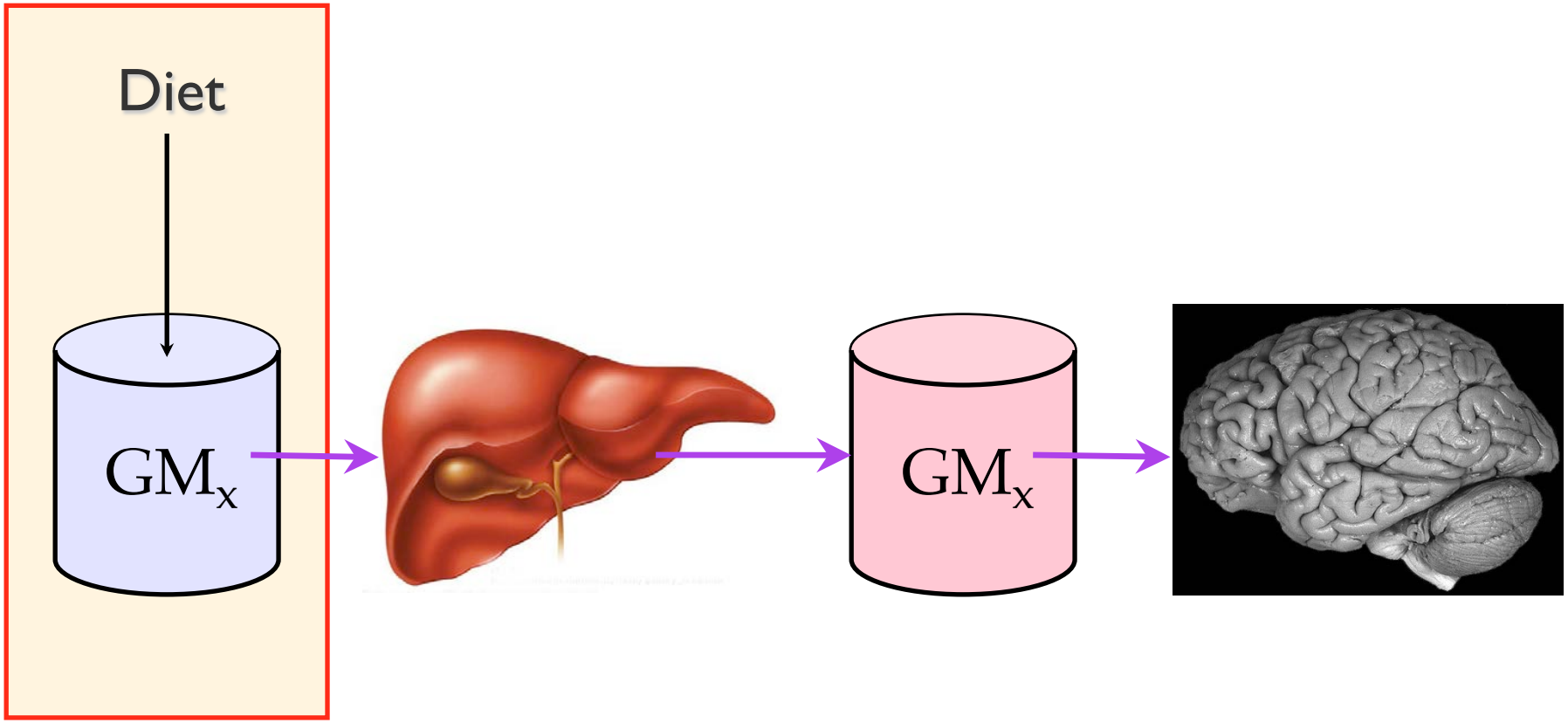

Excited
Beta
Relaxed
Alpha
Drowsy
Theta
Asleep
Sleep Spindles
Deep sleep
Delta
50 μV
1 sec

Hearing



Vision

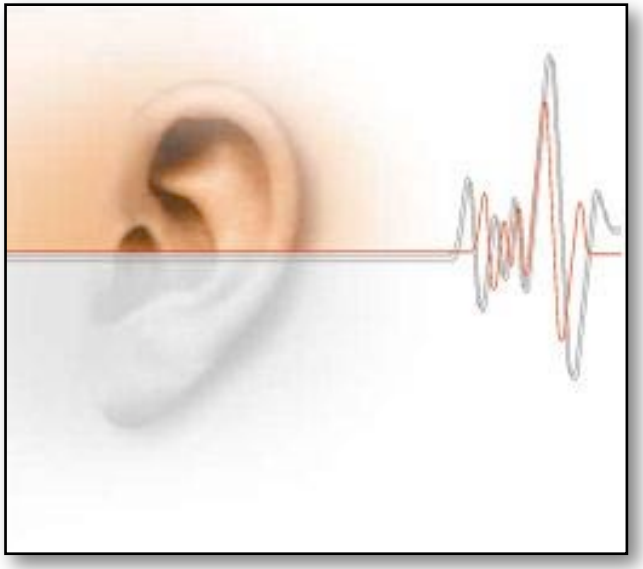



Diet
GM_x
GM_x

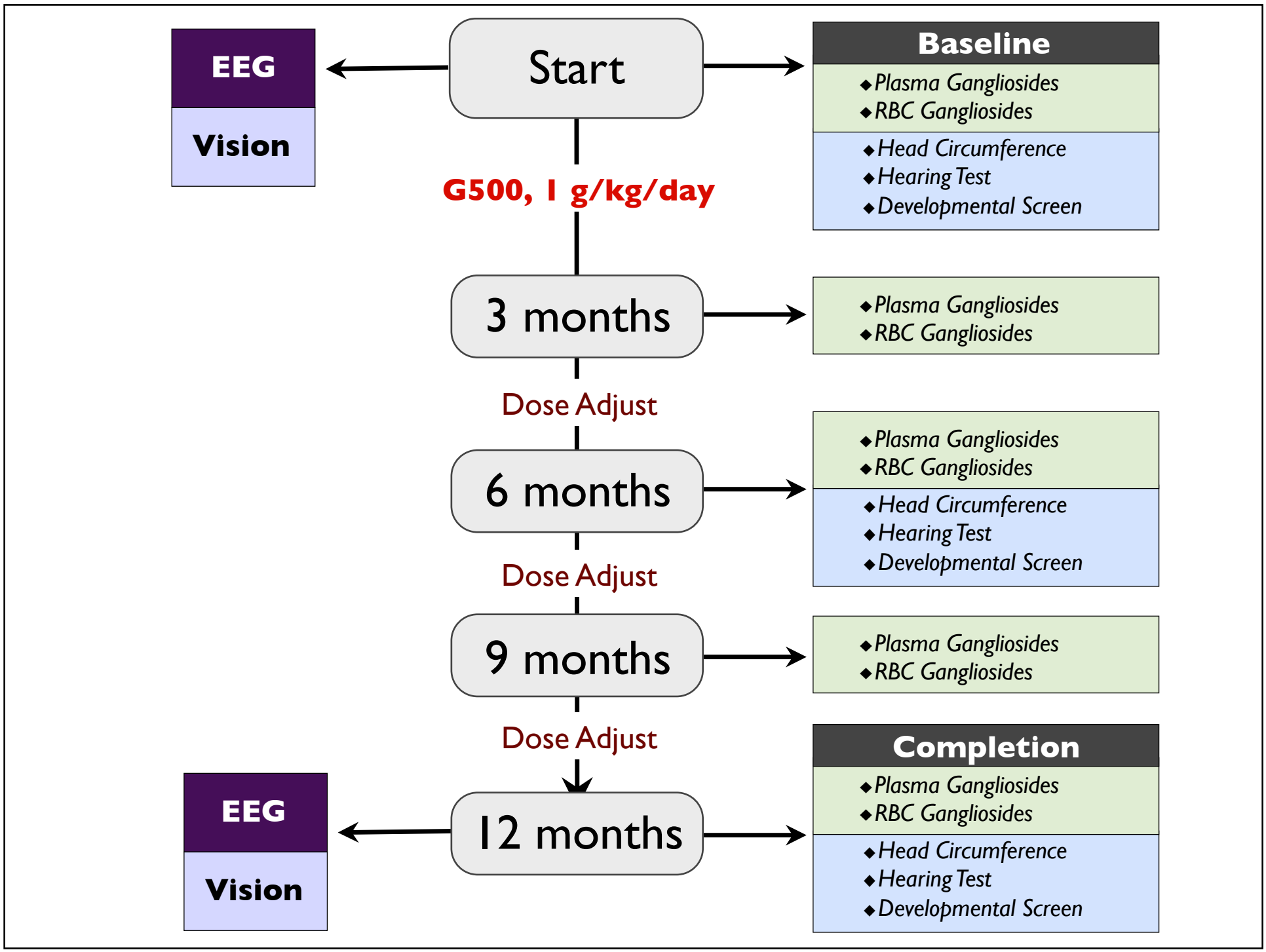
Measuring Effects

Brain Growth

Hearing



Vision


EEG
Vision
Start
Baseline
Plasma Gangliosides
RBC Gangliosides
Head Circumference
Hearing Test
Developmental Screen
G500, 1 g/kg/day
3 months
Plasma Gangliosides
RBC Gangliosides
Dose Adjust
6 months
Plasma Gangliosides
RBC Gangliosides
Head Circumference
Hearing Test
Developmental Screen
Dose Adjust
9 months
Plasma Gangliosides
RBC Gangliosides
Dose Adjust
12 months
Completion
Plasma Gangliosides
RBC Gangliosides
Head Circumference
Hearing Test
Developmental Screen
EEG
Vision

Monitoring

- Otoacoustic Emissions (cochlear amplifier)
- Auditory Brainstem Responses
- Cortical Responses

- We will also check the status of the external ear and middle ear.
- All tests are non invasive!

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Translate Research into Practice: Bowling-Haught Family Waardenberg's Type SNHL

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Translate Research into Practice: The Difference for One Child

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