Cri du chat 101

July 2019
Portland, Oregon

- Dennis J. Campbell, PhD @ University of South Alabama
- AmySue Reilly, PhD @ Auburn University

Background- Rare Genetic Disorder

- Cri du chat Syndrome initially Identified in 1963
- French for "Cry of the Cat" Syndrome

- Definition of Cri-du-Chat Syndrome

  a unique combination of *both*

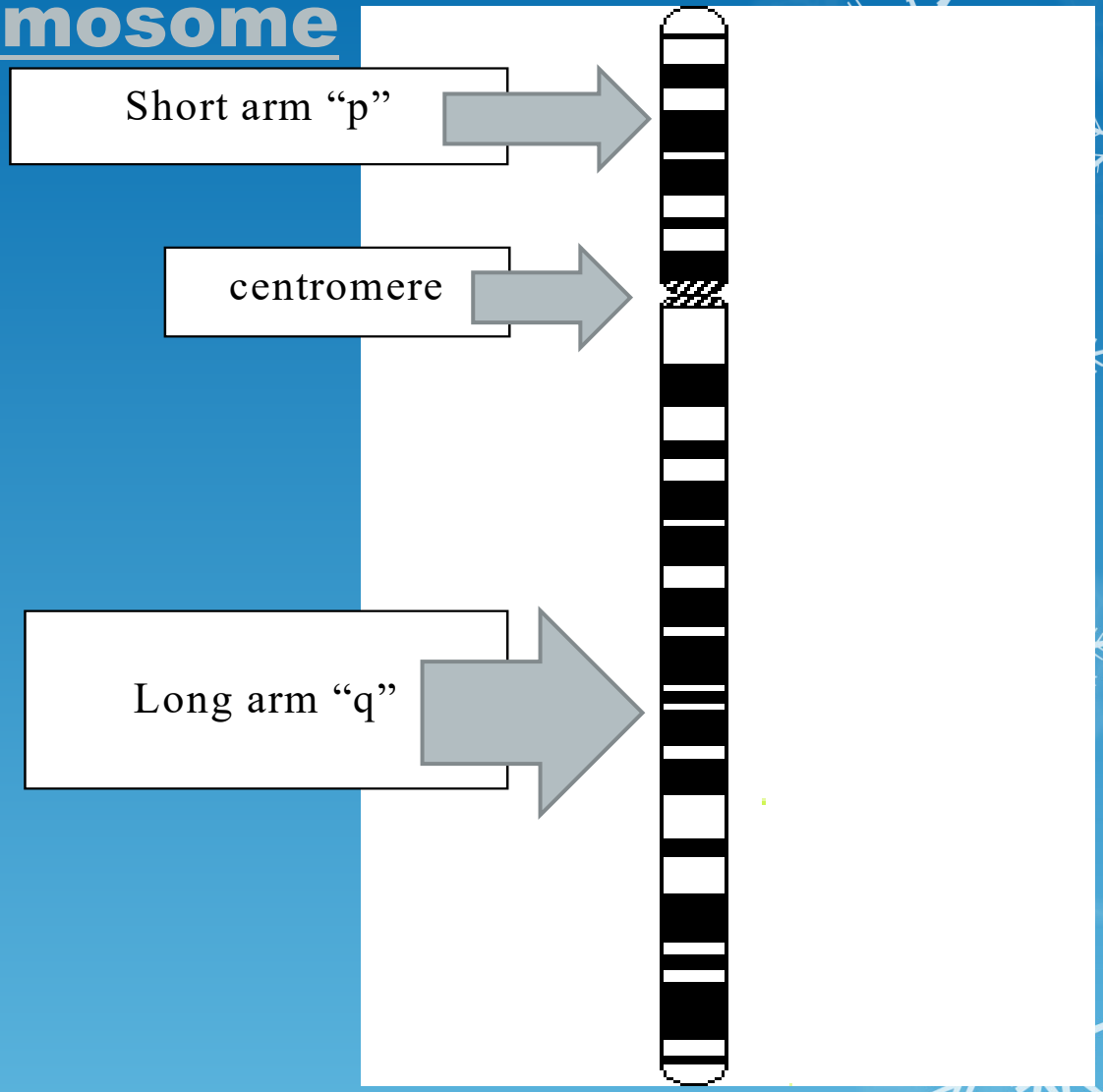
  physical and mental characteristics

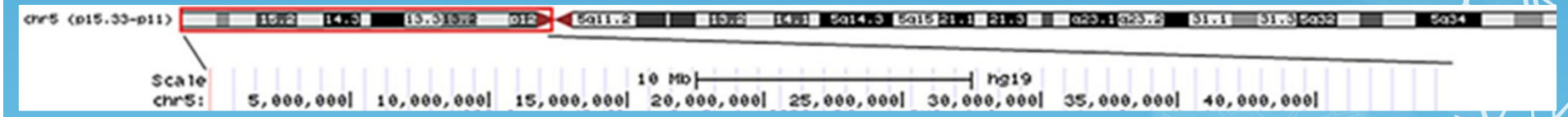
  caused by a loss of genetic material on

  the short arm of the 5th chromosome

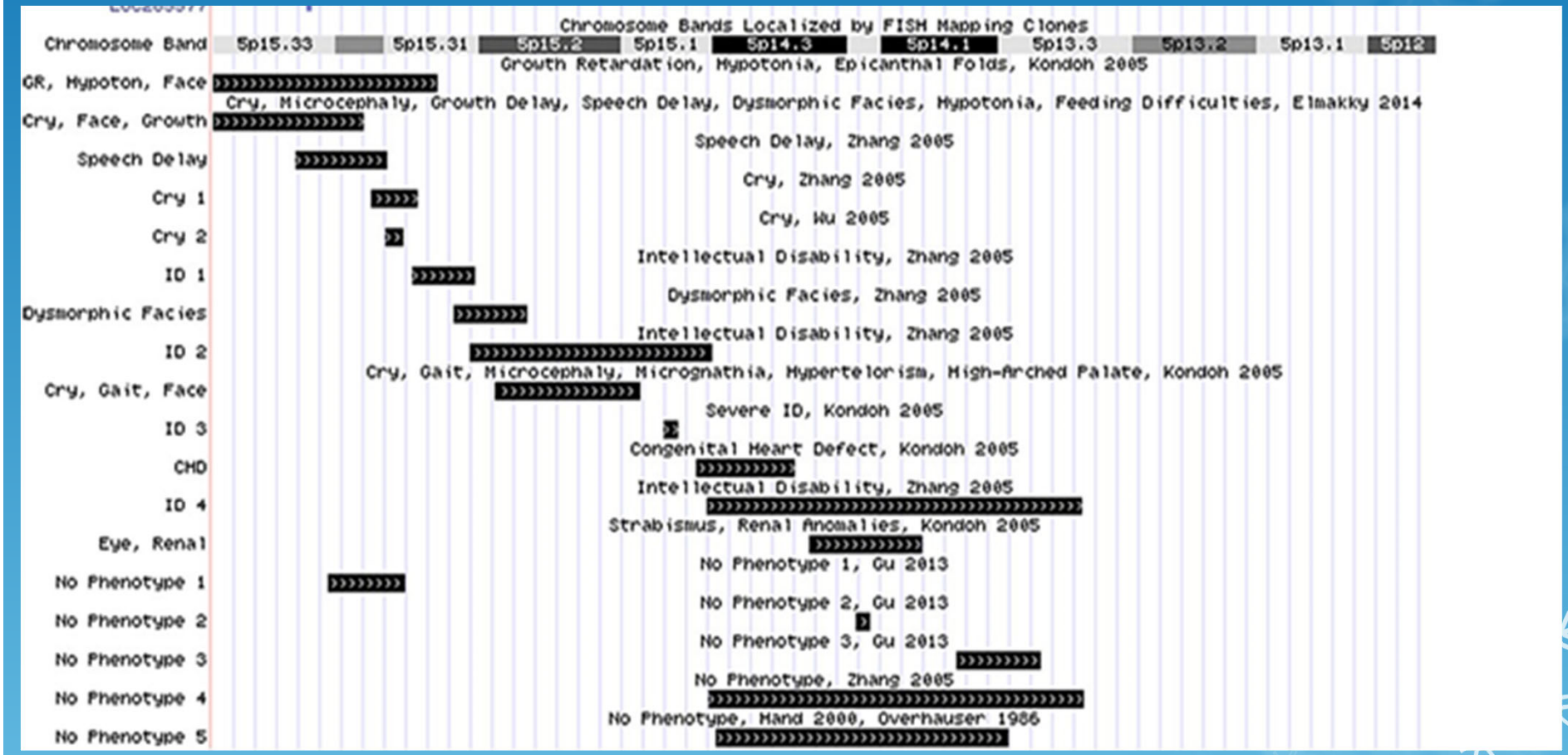
- Five P - is the most commonly used term
  - Prevalence rate approx. 1 in 35,000
  - Most common deletion syndrome

Typical 5th Chromosome





5p deletion research location summary



Adapted from: Nguyen JM,Qualmann KJ, Okashah R, Reilly A, Alexeyev MF, Campbell DJ. 2015. 5p deletions: Current knowledge and future directions. Am J Med Genet Part C Semin Med Genet 9999:1–15.

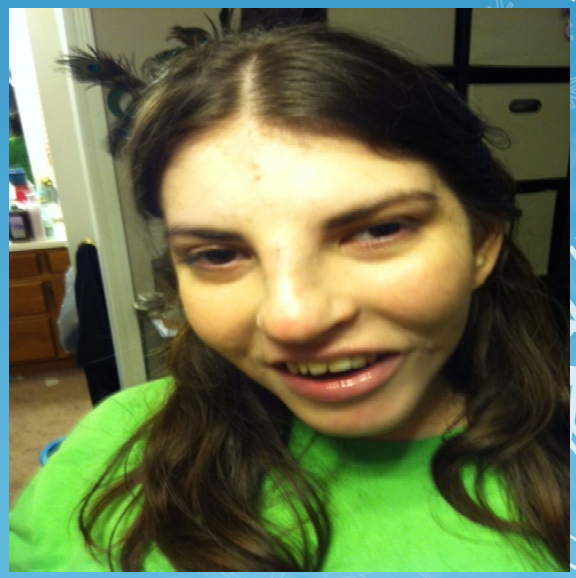
Locus	Cytogenetic location	Gene symbol	Locus	Cytogenetic location	Gene symbol
Haploinsufficiency			Conditional Haploinsufficiency		
1,253,281–1,295,177	5p15.33	*TERT*	1,392,790-1,445,428	5p15.33	SLC6A3
9,035,137–9,546,232	5p15.31	*SEMA5A*	19,473,139-20,575,971	5p14.3	CDH18
10,353,750–10,440,499	5p15.2	*MARCH6*	21,750,869-22,853,730	5p14.3	CDH12
10,971,951–11,904,154	5p15.2	*CTNND2*	24,487,208-24,645,084	5p14.2-p14.1	CDH10
32,710,283–32,791,829	5p13.3	*NPR3*	26,880,708-27,038,688	5p14.1	CDH9
			31,193,761-31,329,252	5p13.3	CDH6

Haploinsufficiency gene product is not sufficient for cell to function normally.

Medical Overview

Genotype/phenotype

- **Smaller deletions tend better development**
- **Tendency for smaller deletions to have less developmental issues**
- **Language acquisition seems to be better**
- ***Less* physiological characteristics**
- ***Amy's deletion***
  - **46, XX, del(5) (p14.1-pter)**
  - Locus of her deletion is
  - Somewhere between
  - 24,487,208–24,645,084



Development

- Median age
  - Walk independently 3 years (range 15 months to 7 years)
  - Sitting up at 14 months,
  - Walking alone at 43 months,
  - Dressing at 78 months, and
  - Toilet-training at 90 months.
- Speech and Language
  - About 50% develop some speech
  - But able to communicate needs through sign language or other types of communication, I.E tablets

Development

- Vision 46% have ophthalmologic findings
  - myopia (15%),
  - strabismus (45-53%),
  - cataracts (2%),
  - optic nerve abnormalities (5-19%)
- Hearing
  - 15% of children had tympanostomy tubes
  - 8.4% had hearing loss
  - Over stimulation to sounds, smells, anticipation of events (hyperacusis), seen in 70-80% of children

TWO PREVALENT BEHAVIORS *REPORTED BY PARENTS*

Reported by over 45% of the parent participants

- Behaviors that show **impulsivity and attention problems**
  - short attention span (60.1%)
  - low frustration tolerance (53.1%)
  - hyperactivity (45.5%).

2 PREVALENT BEHAVIORS *REPORTED BY PARENTS*

2. Contains **self-stimulating behaviors**

— hand sucking (53.1%)

— head banging (49.7%)

— skin picking (49%).

Reported Behaviors	N Reported	% Reported
Short attention span	86	60.1%
Low frustration tolerance	76	53.1%
Hand sucking	76	53.1%
Head banging	71	49.7%
Skin pinching/picking	70	49.0%
Hyperactive	65	45.5%
Aggressive toward others	45	31.5%
Grinding teeth	45	31.5%
Repeating behaviors or perseveration	44	30.8%
Rocking	39	27.3%
Poor eye contact	39	27.3%
Anxious/shy around others	32	22.4%
Repeating sound/words/phrases	28	19.6%


SUPER HERO

Cri-du-Chat Characteristics

GROWTH

- As infants & toddlers, have an overall slower growth rate sometimes viewed as “failure to thrive”
- Heads can be in the microcephaly-range
- Have low-low-low hypotonia yet not as low as “floppy baby syndrome”

Communication

- Is the ***most prevalent*** functional challenge.
  - About half of the children develop some verbal language.
  - Early use of sign language is effective.
  - Receptive language development substantially exceeds expressive skills.

Facial Features

- Round facies
- Hypertelorism
- Epicanthal folds
- Downslanting palpebral fissures
- Broad nasal bridge
- Low-set ears
- Preauricular tags
- Downturned corners of mouth
- Short neck
- Micrognathia
- Dental malocclusion

GROWTH AND DEVELOPMENT

- **Hearing** about 15% had tubes
- **Over stimulation** to sounds, smells, **anticipation of events** `
  - **"Hyperacusis"** occurs in 70 to 80%
- **Vision** 46% have ophthalmic findings
  - Myopia 15%
  - Strabismus 45 to 53%
  - Optic nerve abnormalities 5 to 19%
- Advanced **social & self-help skills** compared to other **developmental areas.**
- **Balance and motor planning** difficulties.

- **Caregivers guide**
- 144 respondents
- 88 female (61%) 56 male (39%)
- Average Age 19
- 84% de novo deletions 14% unbalanced

- **Family History**
- 297 respondents 175 females (59%)122 males (41%)
- Average Age 12
- 91% Deletions 7% Unbalance 1% Mosiacism (1%) other

Family History Data

Trait	Number	Percentage
Cat cry	287	95%
Constipation	217	72%
Drooling past age one	200	67%
Feeding difficulties	248	82%
Recurrent cold hands and feet	175	58%
Small head	247	82%
Poor muscle tone	248	82%

Studies
Assessment of children Ages 3 to 18

Traditional assessments often **fail to show abilities** for these children

Individual assessment score of **two *or* more standard deviations below the mean** becomes unreliable and often masks or fails to demonstrate abilities.

We **ignored** the **ceiling** in **assessment instruments**

To **document skills present** that would *not* be reported if the instrument was used in a standardized manner.

Range of splinter skills was from 1 to 34 with an average of 10.7 skills per participant.

Participants ***ages ranged*** from 35 months to 18 years.

Average age was 8 years 9 months.

Behavior and Social Development

- ***Typically***, children with CDCS have:
  - Friendly, happy disposition
  - Affectionate
  - Enjoy social interaction
  - Short attention span
  - Self stimulating behaviors

CDC and "Autistic like tendencies"

- A coined phrase
- Difference with CDCS are:
  - Cognitive abilities to manipulate the environment and those in the environment
  - Selective hearing and selective interactions
  - More like kids with ID

Research Studies

- (1999) Children w Cri-du-Chat w Prelinguistic developmental patterns & its interpretation during interaction.
- (2000) Addressing domains' developmental patters in infants and toddlers Cri-du-Chat & their families.
- (2003 to 2006) Assessment of all areas related to Communicative Abilities of Individual with Cri-Du-Chat w 70 evaluation.
- (2007 to present on-going) Continual on-going compiling of Family History Database for The Five P Minus International Society

Selected studies and articles

- Campbell, D. J., Carlin, M.E., Justen, J. III, & Baird, S. M.; (2004) *Cri-du-chat Syndrome: A Topical Overview.* Journal of the 5P Minus Society 1 1-7.
- Campbell, D. & Reilly, A. (2016). Accurate (TRUE) Present Level of Performance by Documenting Splinter Skills. In Proceedings of Society for Information Technology & Teacher Education International Conference 2016 (pp. 2765-2770). Chesapeake, VA: Association for the Advancement of Computing in Education (AACE).
- Campbell, D., Reilly, A.S., & Henley, J.G. (2008). *Comparison of Assessment Results of Children with Low Incidence Disabilities.* Education and Training in Developmental Disabilities 43 (2) 217-225
- Nguyen J.M.,Qualmann K.J., Okashah R., Reilly A., Alexeyev M.F., Campbell D.J. (2015). 5p deletions: Current knowledge and future directions. American Journal of Medical Genetics Part C Seminar in Medical Genetics 169C:224–238.
- P.C. Mainardi et al. The natural history of Cri du Chat Syndrome. A report from the Italian Register European Journal of Medical Genetics 49 (2006) 363–383