Per quanto concerne i moderatori, relatori, formatori, tutor, docenti è richiesta dall'Accordo Stato-Regioni vigente apposita dichiarazione esplicita dell'interessato, di trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali relativi agli ultimi due anni dalla data dell'evento.
La documentazione deve essere disponibile presso il Provider e conservata per almeno 5 anni.

Dichiarazione sul Conflitto di Interessi

Il sottoscritto_____DAVIDE VECCHIO_____ in qualità di:

☐ moderatore X docente ☐ relatore
☐ tutor

dell'evento "INDIVIDUAZIONE DEI DISTURBI DEL NEUROSVILUPPO 0-3 ANNI"

da tenersi per conto di **Biomedia srl Provider n. 148,**

ai sensi dell'Accordo Stato-Regione in materia di formazione continua nel settore "Salute" (Formazione ECM) vigente,

Dichiara

X che negli ultimi due anni NON ha avuto rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

☐ che negli ultimi due anni ha avuto rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario (indicare quali):

_____ _____
_____ _____
_____ _____
_____ _____

Le basi genetiche dei disordini neuroevolutivi: panoramica su quadri sindromici o geneticamente determinati

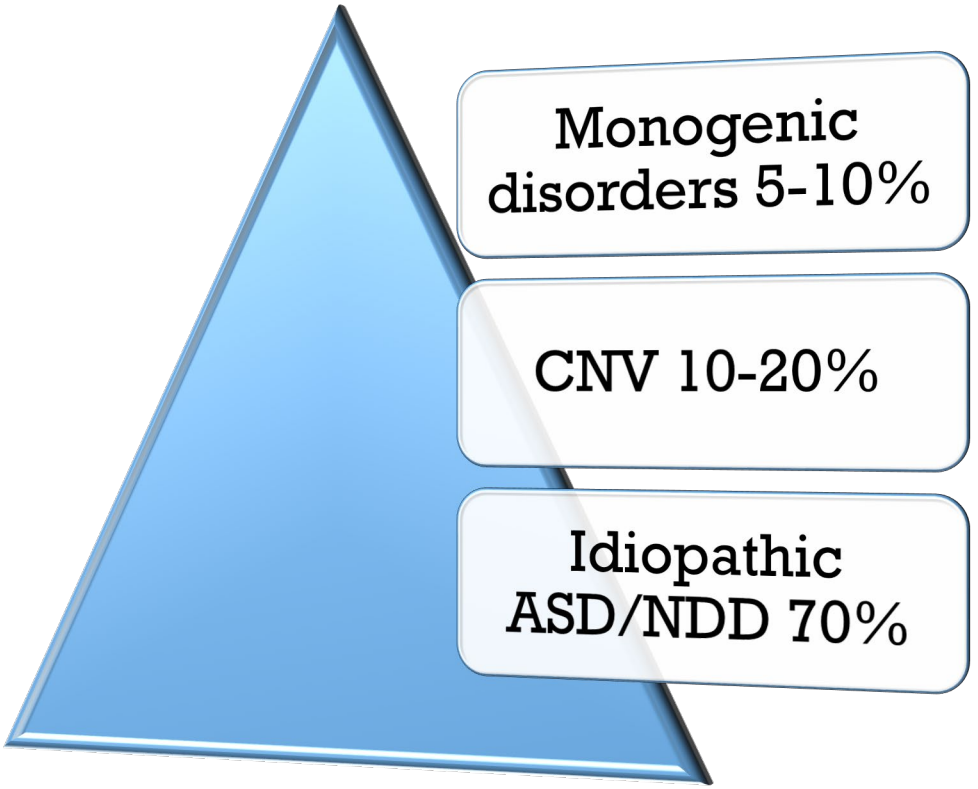
Davide Vecchio

Consigliere junior Società Italiana di Pediatria

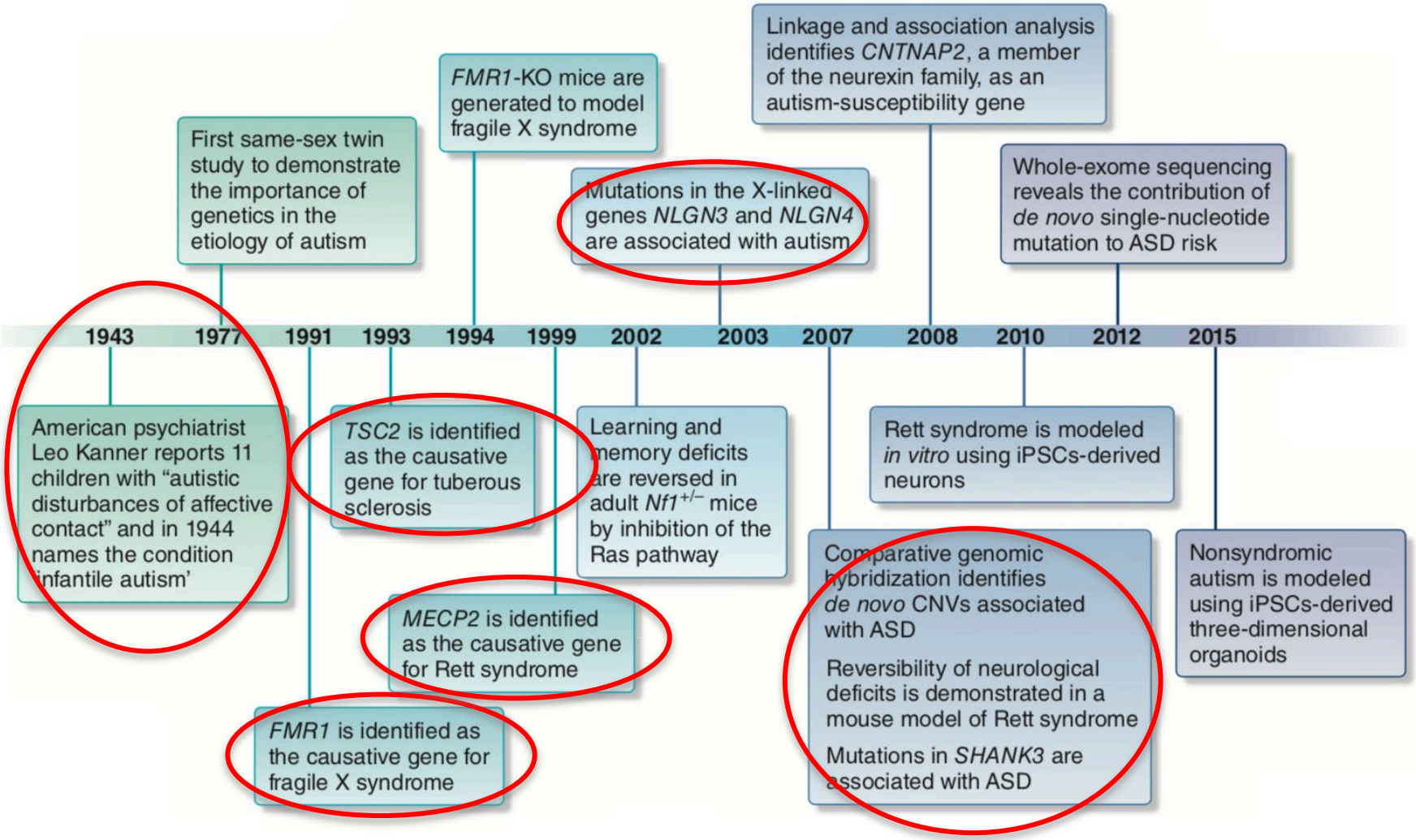
The Genetics of Autism & Neurodevelopmental Disorders

The term "**neurodevelopmental disorders**" is clinically defined in psychiatry as "*a group of conditions with onset in the developmental period… characterized by developmental deficits that produce impairments of personal, social, academic, or occupational functioning*" [**DSM-5**].

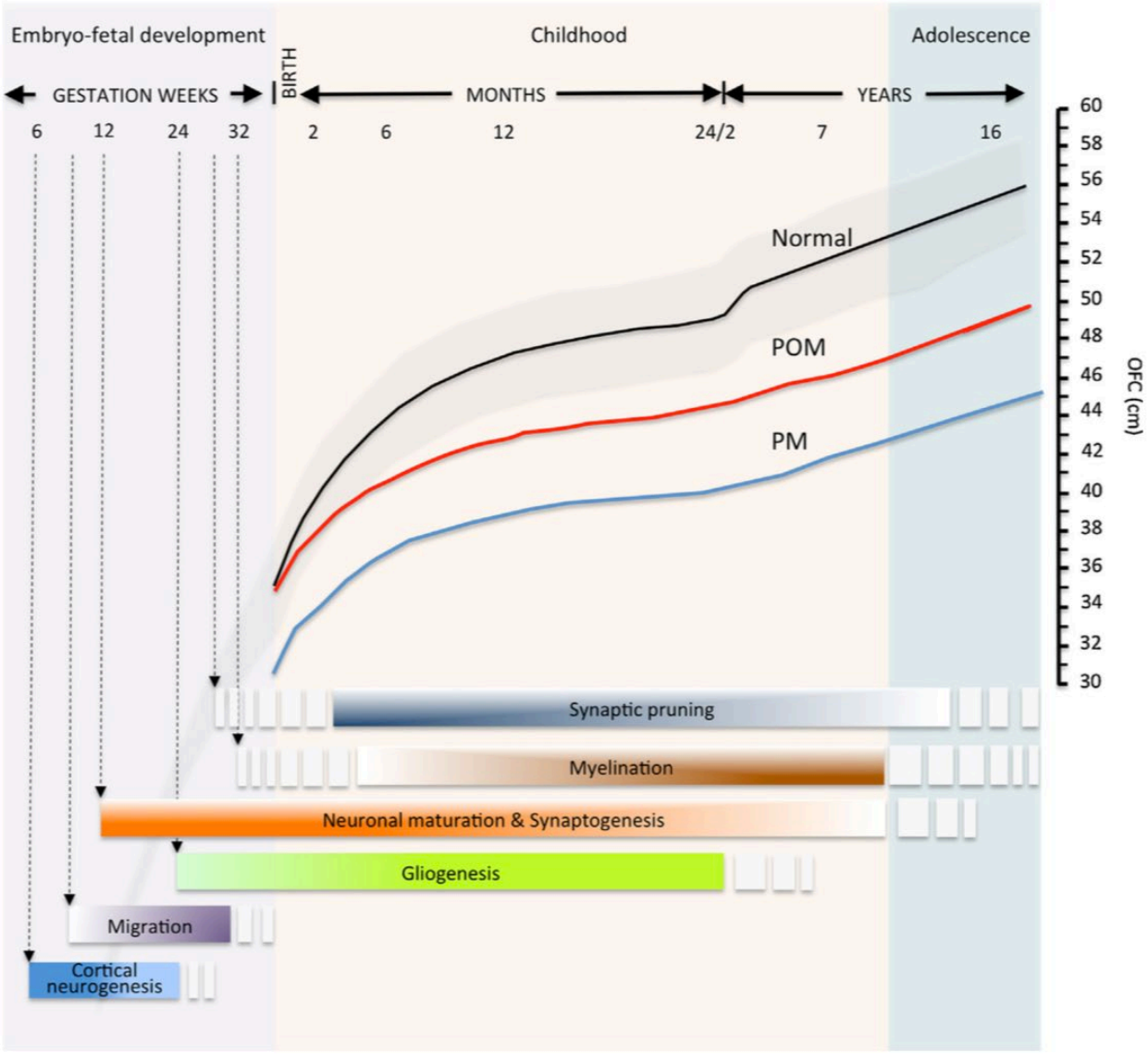
This term encompasses the clinical categories of intellectual disability (ID), developmental delay (DD), autism spectrum disorders (ASD), attention-deficit hyperactivity disorder (ADHD), speech and language disorders, specific learning disorders, tic disorders and others.



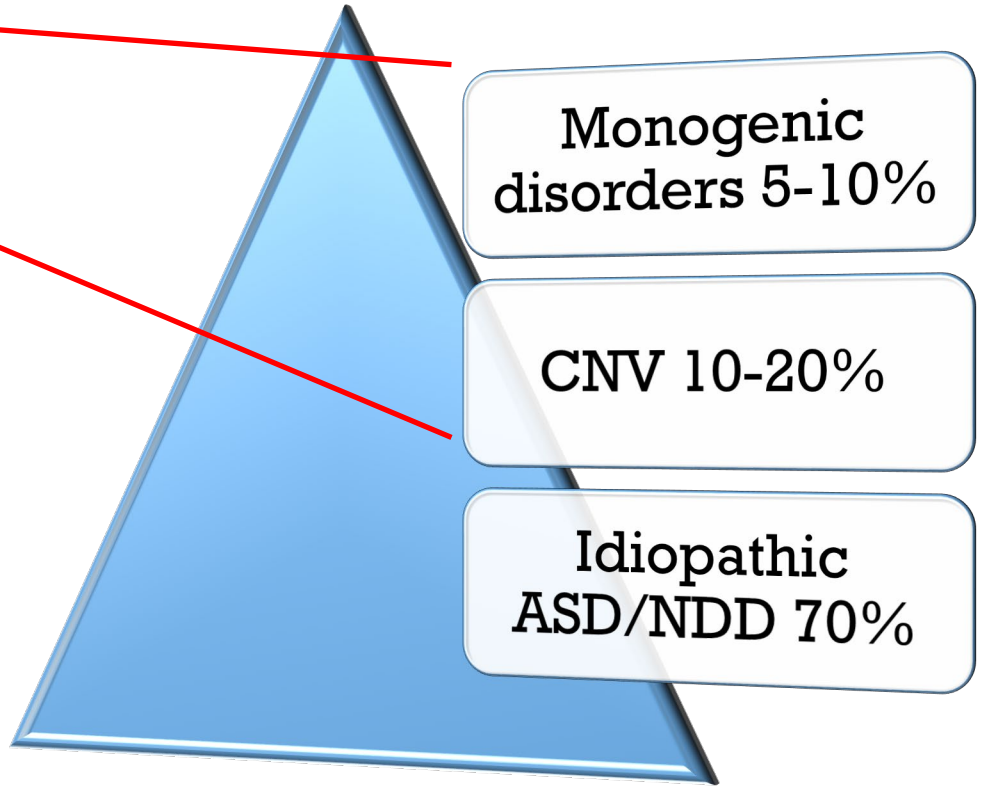
Timeline of key discoveries in the history of NDD research



Autism & Neurodevelopmental Disorders

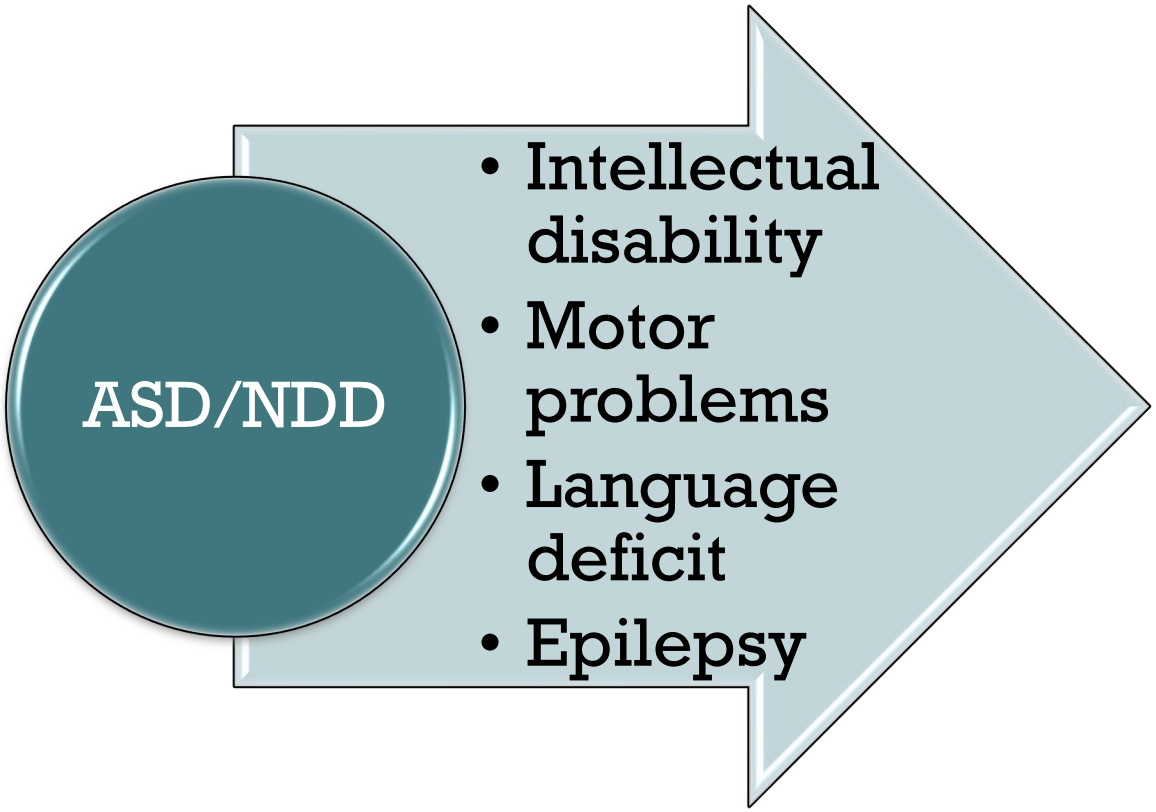


The Genetics of Autism & Neurodevelopmental Disorders



Diagnostic Challanges

Comorbidities

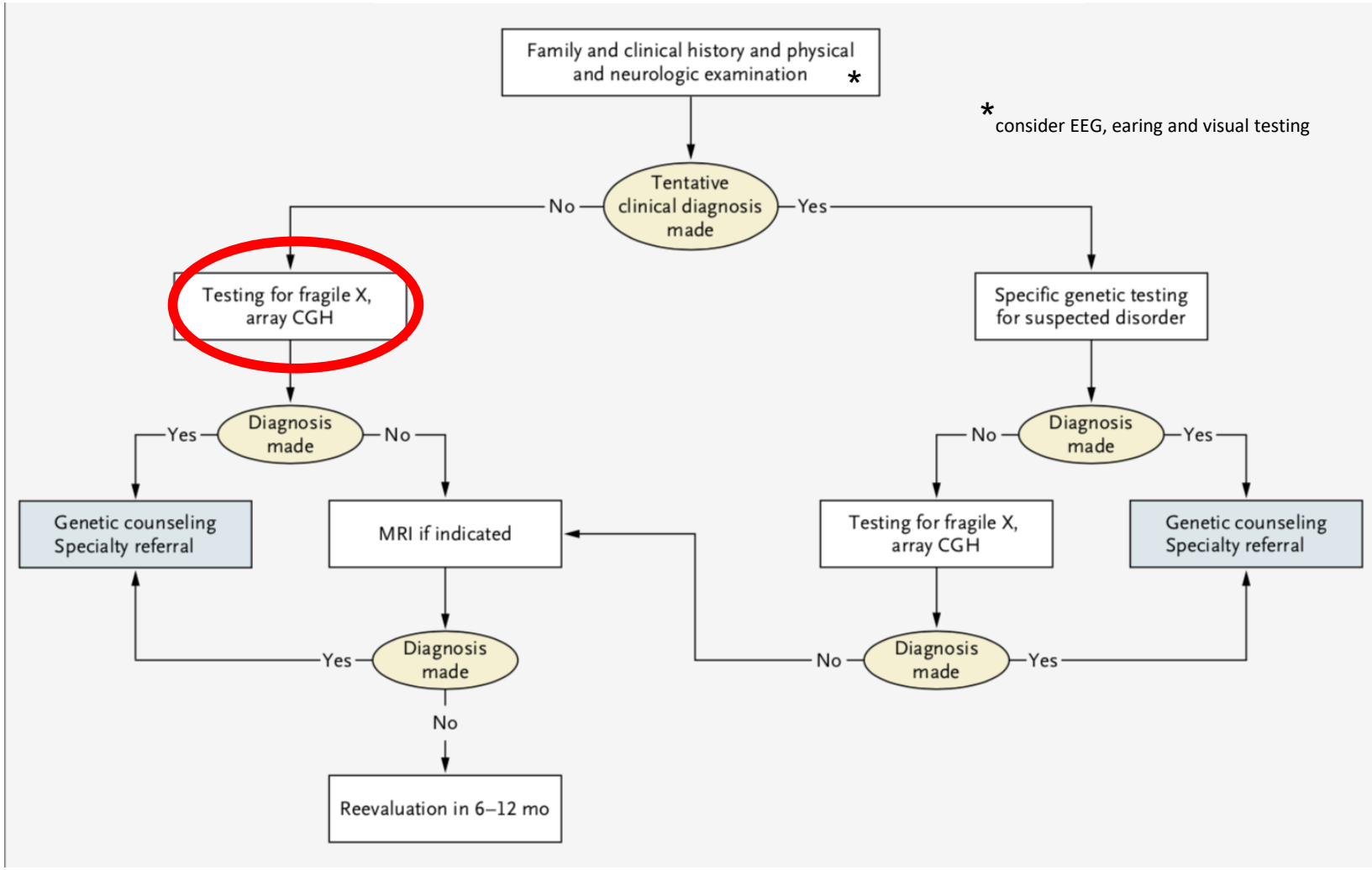


Combining its two Greek roots, *syndrome* means basically "running together". So when diagnosing a condition or disease, look for a group of symptoms existing together.

The NEW ENGLAND JOURNAL of MEDICINE

Genomics, Intellectual Disability, and Autism

Heather C. Mefford, M.D., Ph.D., Mark L. Batshaw, M.D., and Eric P. Hoffman, Ph.D.



Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions

G. Bradley Schaefer, MD[1] and Nancy J. Mendelsohn, MD[2]; for the Professional Practice and Guidelines Committee

First tier

- Three-generation family history with pedigree analysis
- Initial evaluation to identify known syndromes or associated conditions
  - Examination with special attention to dysmorphic features
  - If specific syndromic diagnosis is suspected, proceed with targeted testing
- * If appropriate clinical indicators present, perform metabolic and/or mitochondrial testing (alternatively, consider a referral to a metabolic specialist)
- Chromosomal microarray: oligonucleotide array-comparative genomic hybridization or single-nucleotide polymorphism array
- DNA testing for fragile X (to be performed routinely for male patients only)[a]

Table 3 Clinical symptoms that prompt metabolic or mitochondrial testing in persons with ASDs

Acid/base or electrolyte disturbances *
Anemia with an elevated mean corpuscular volume
Cyclic vomiting
Dermatologic changes: alopecia, hypertrichosis, and pigmented skin eruptions
Developmental regression associated with illness or fever
Gastrointestinal dysfunction, gastroparesis
Hypotonia/dystonia
Lactic acidosis *
Lethargy *
Multisystem involvement, especially cardiac, hepatic, or renal (physical and/or laboratory evidence)
Neurodegeneration outside of the typical ASD speech loss at 18–24 months *
Poor growth, microcephaly
Seizures

ASD, autism spectrum disorder.

ACMG PRACTICE GUIDELINES | Genetics inMedicine

Modified from: Moeschler, John B., and Michael Shevell. "Comprehensive evaluation of the child with intellectual disability or global developmental delays." Pediatrics 134.3 (2014): e903-e918.
AND
Miller, David T., et al. "Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies." The American Journal of Human Genetics 86.5 (2010): 749-764

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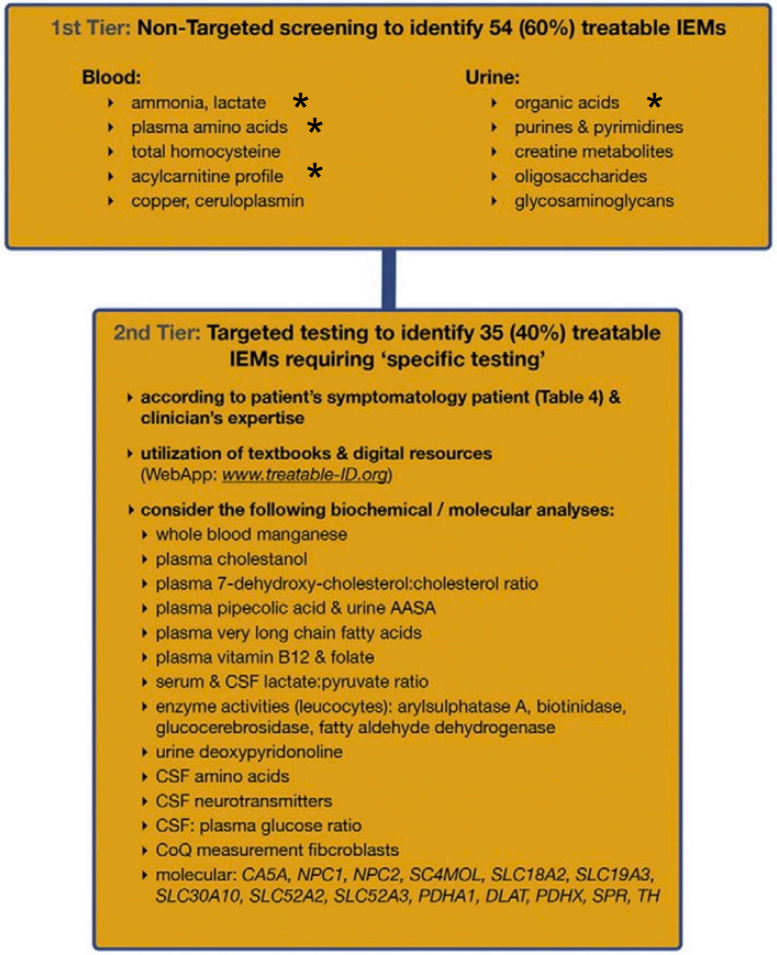
Chromosomal microarray: oligonucleotide array-comparative genomic hybridization or single-nucleotide polymorphism array

DNA testing for fragile X (to be performed routinely for male patients only)[a]



ACMG PRACTICE GUIDELINES | Genetics inMedicine

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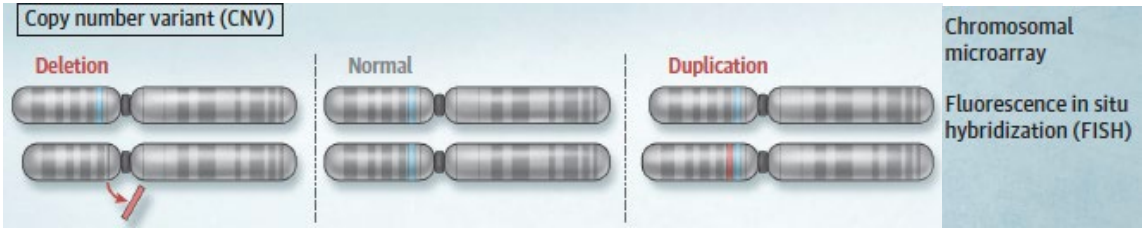
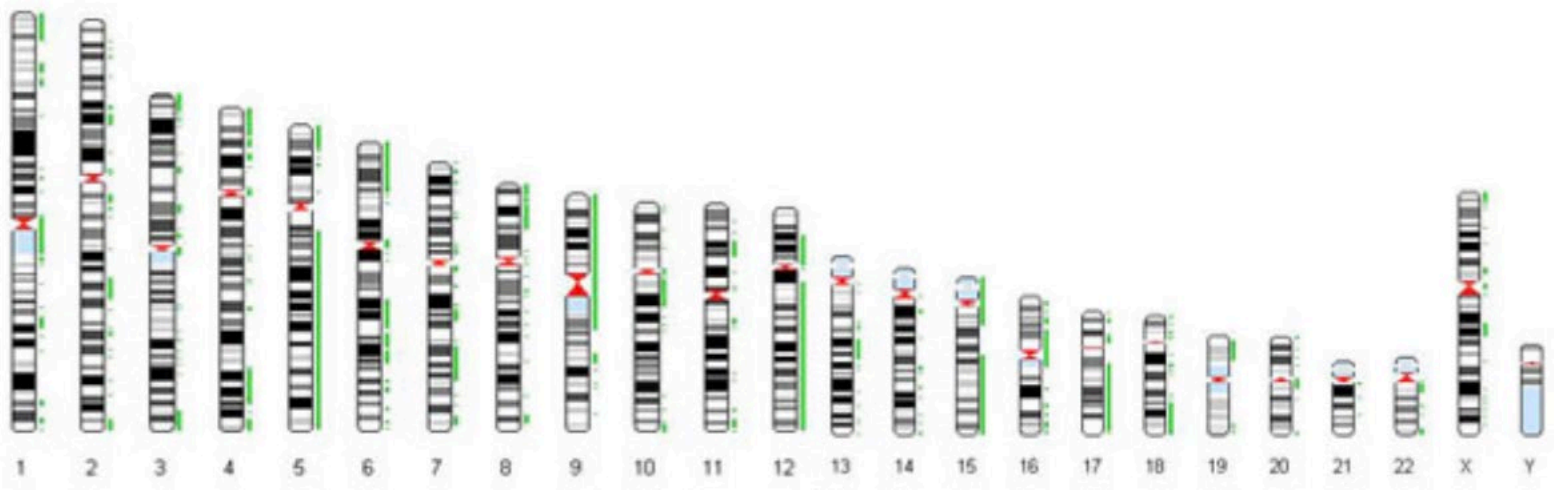
Miller, David T., et al. "Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies." The American Journal of Human Genetics 86.5 (2010): 749-764

CNVs





Statistics

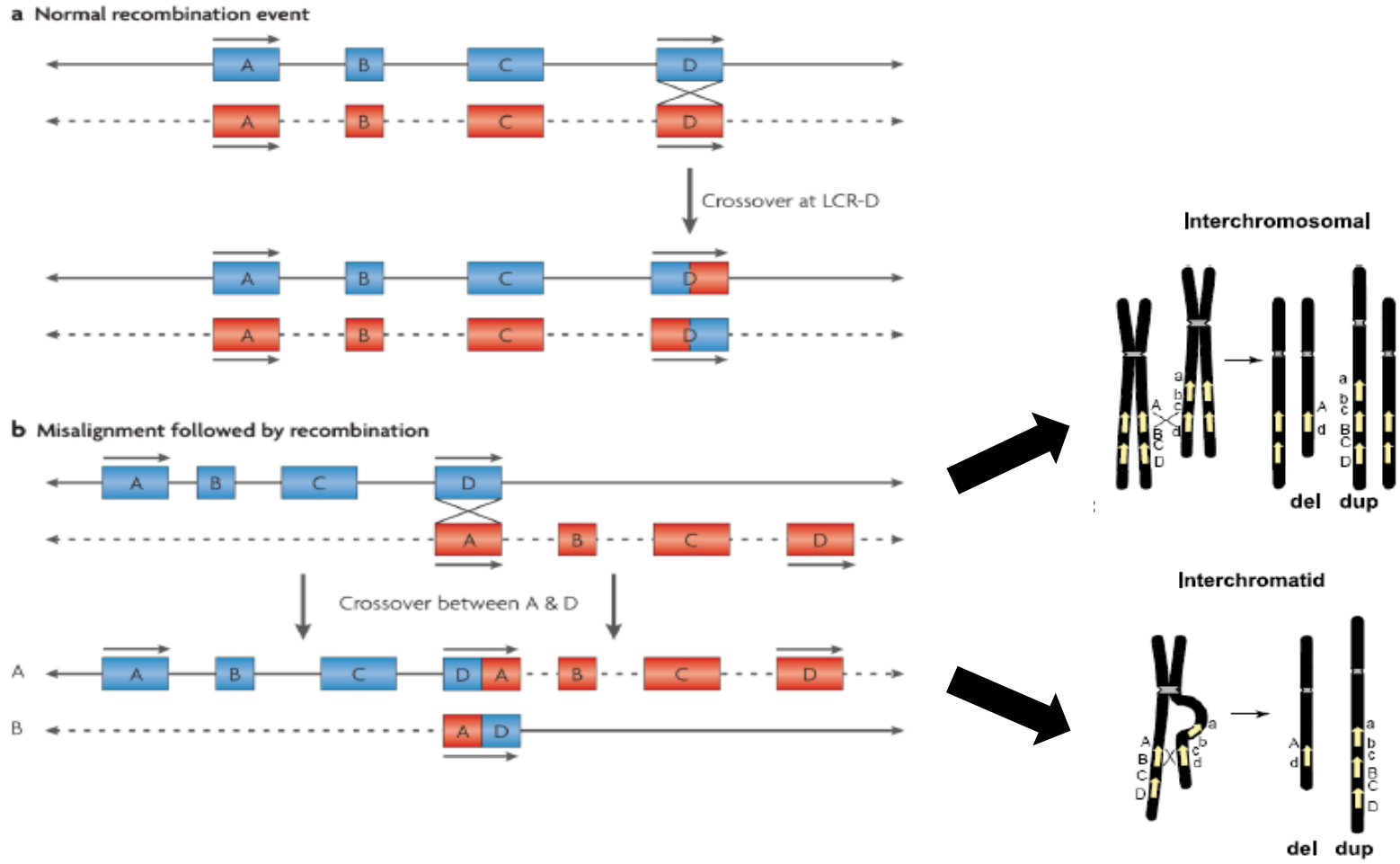
# of annotated reports: 583 # of CNV loci: 2274 Last update: September, 2018 AutDB

Originally defined as ≥ 1 kbp in length; the definition has been extended to include differences ≥ 50 bp in length

Published in final edited form as:
Nat Rev Genet. 2007 November ; 8(11): 869–883. doi:10.1038/nrg2136.

From microscopes to microarrays: dissecting recurrent chromosomal rearrangements

Beverly S. Emanuel and **Sulagna C. Saitta**



CNVs

CNVs often arise mechanistically as a result of elevated mutation rates in regions flanked by segmental duplications (long DNA sequences with > 90% sequence similarity that exist in multiple locations across the genome) due to unequal crossing over between the repeats during meiotic recombination

DECIPHER GRCh38 About Browse DDD (UK) Search DECIPHER Help Join Log in

Mapping the clinical genome

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Projects affiliated to DECIPHER can deposit and

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Log in to access your patient data

Public health information (CDC) | Research information (NIH) | SARS-CoV-2 data (NCBI) | Prevention and treatment information (HHS)

ClinVar
ClinVar aggregates information about genomic variation and its relationship to human health.

UNIVERSITY OF CALIFORNIA SANTA CRUZ Genomics Institute UCSC **Genome Browser**

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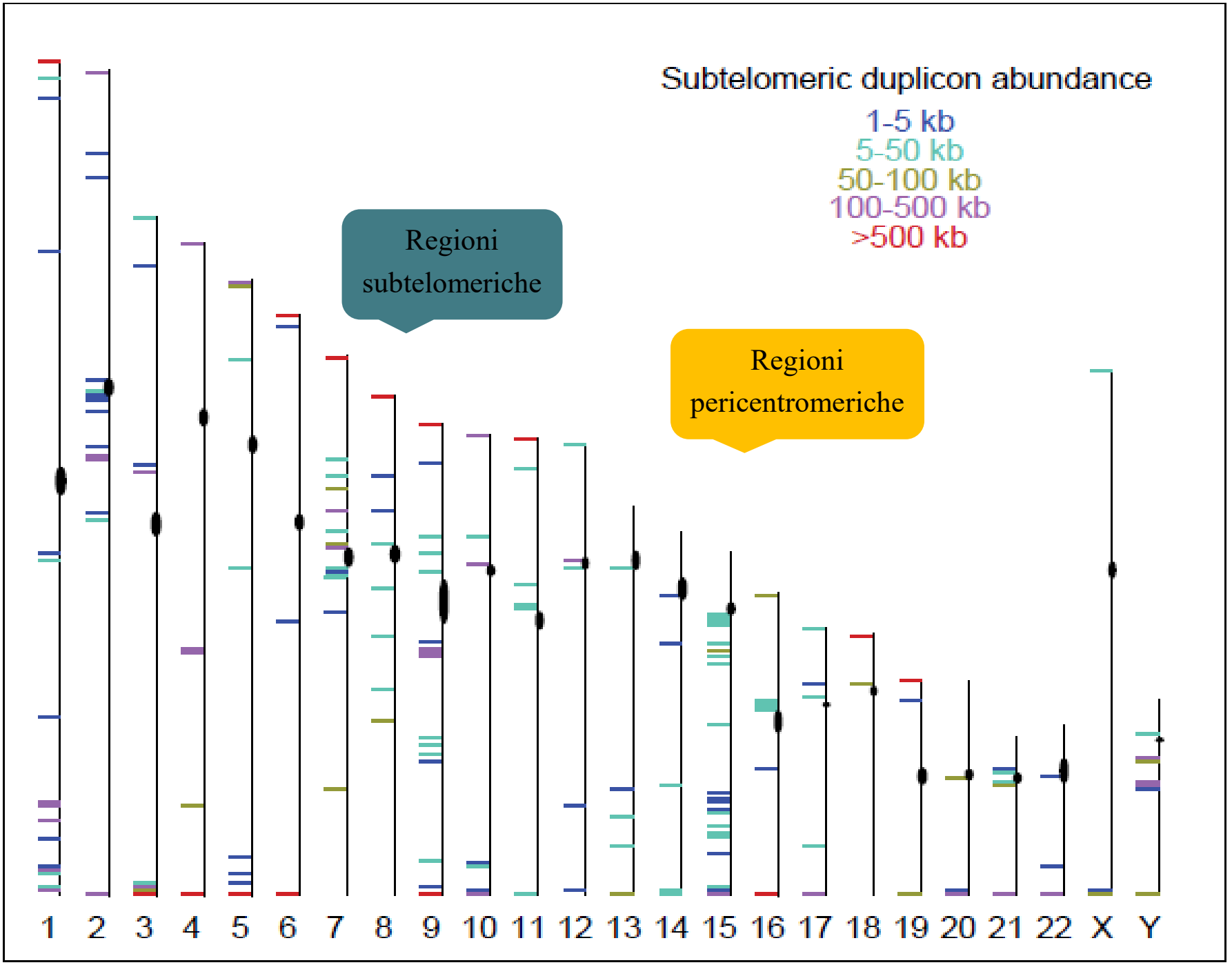
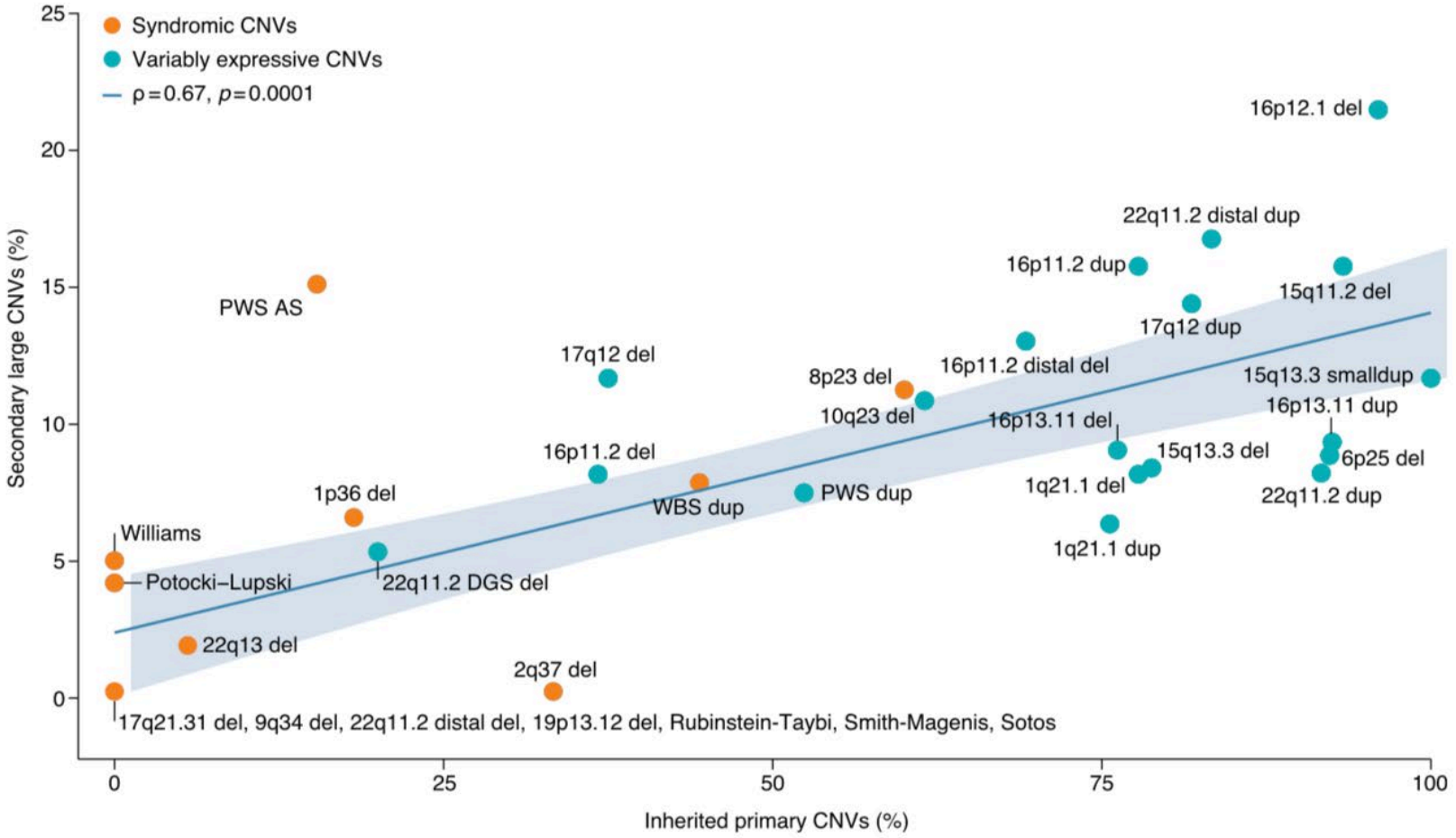
Our tools

- **Genome Browser**
  interactively visualize genomic data
- **Coronavirus Data**
  view SARS-CoV-2 genome and COVID-19-related datasets
- **BLAT**


Subtelomeric duplicon abundance
1-5 kb
5-50 kb
50-100 kb
100-500 kb
>500 kb
Regioni subtelomeriche
Regioni pericentromeriche
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y

Recurrent de novo mutations in neurodevelopmental disorders: properties and clinical implications

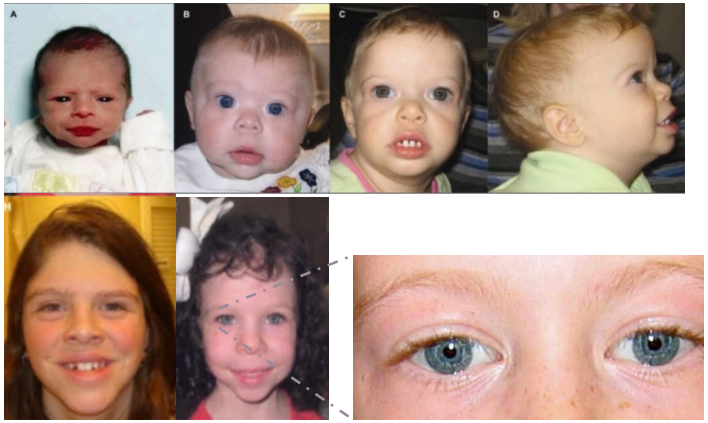
Amy B. Wilfert[1†], Arvis Sulovari[1†], Tychele N. Turner[1], Bradley P. Coe[1] and Evan E. Eichler[1,2*]

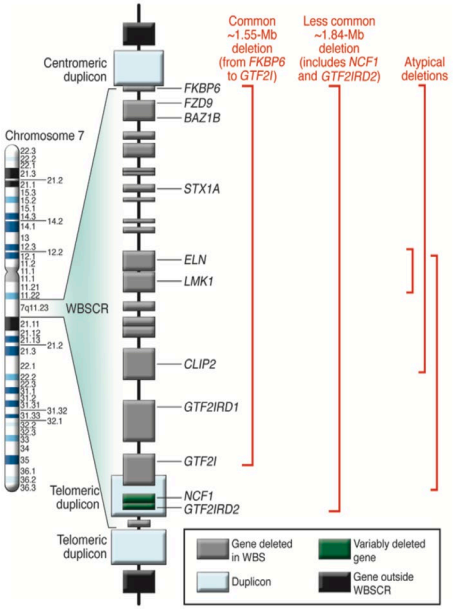


Wilfert *et al. Genome Medicine* (2017) 9:101
DOI 10.1186/s13073-017-0498-x

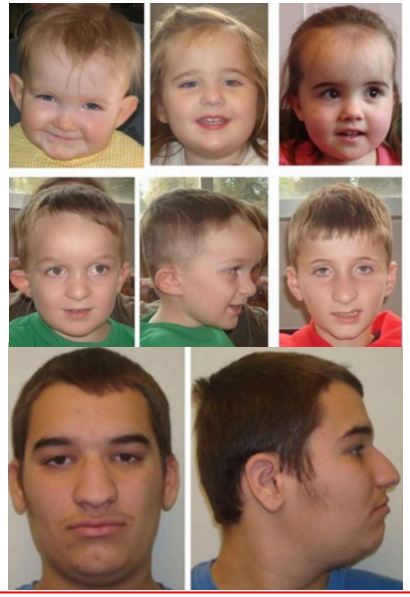
The 7q11.23 region

del 7q11.23
Williams–Beuren Syndrome
[OMIM 94050]





7q11.23 Duplication Syndrome
[OMIM 609757]

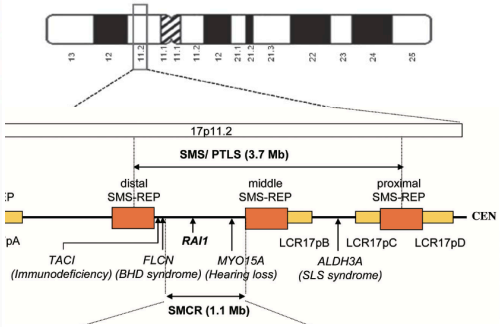


Clinical Features of the Disorder		
Most Common Congenital Heart Disease	**Distinguishing Facial Features**	**Additional Features**
Supravalvar aortic stenosis	• Stellate/lacy iris • Periorbital fullness • Wide mouth • Loss of cupid's bow of the upper lip • Full lower lip • Large earlobes	• Hypercalcemia • Hoarse voice • Overly friendly personality

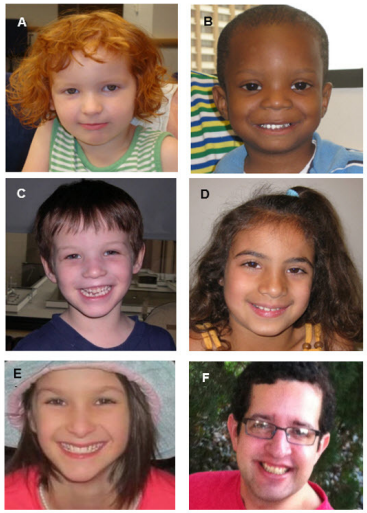
- ❖ Dilation of the ascending aorta in 46%
- ❖ ~~Hypotonia~~
- ❖ Childhood apraxia of speech and/or dysarthria and phonologic disorders;
- ❖ Social anxiety disorder [social phobia]), selective mutism
- ❖ Attention deficit hyperactivity disorder (ADHD)
- ❖ Oppositional disorders, physical aggression, and autism spectrum disorders (ASD)

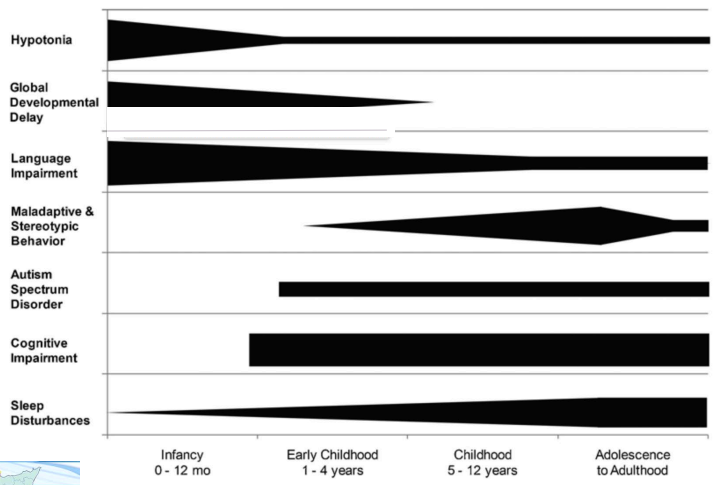
The 17p11.2 region

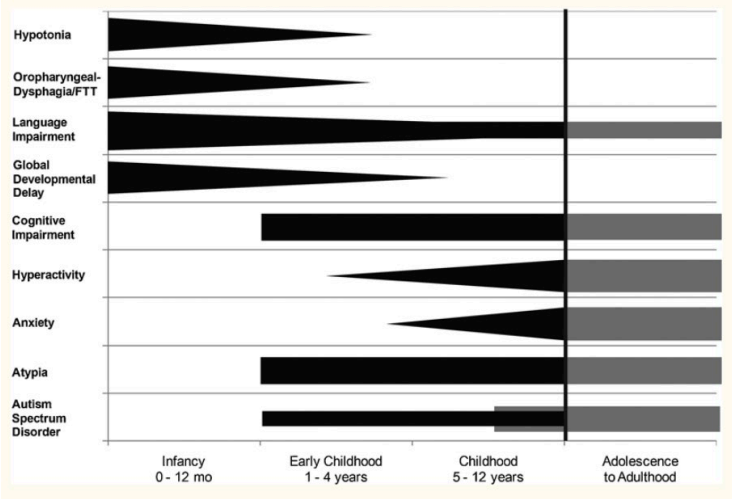
del 17p11.2
Smith-Magenis Syndrome
[OMIM 182290]



dup 17p11.2
Potocki-Lupski Syndrome
[OMIM 610883]







The 17p11.2 region neuro-phenotype

del 17p11.2
Smith-Magenis Syndrome
[OMIM 182290]

NEUROLOGIC
Central Nervous System
- Speech delay
- **Intellectual disability (IQ 20-78)**
- **Sleep disturbance**
- **Structural brain abnormalities**

Peripheral Nervous System
- Peripheral neuropathy
- **Decreased pain sensitivity**

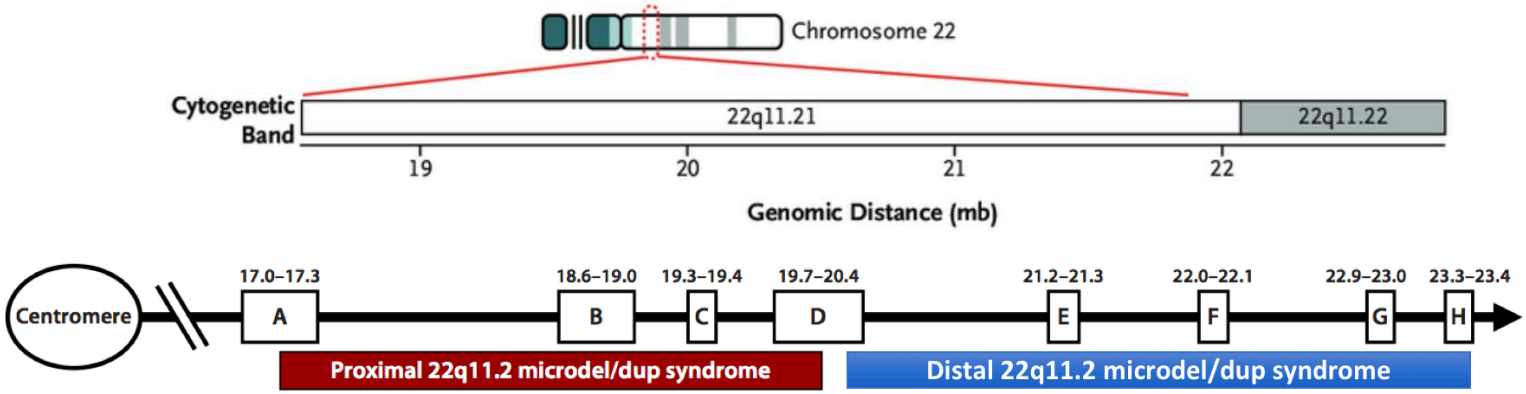
Behavioral Psychiatric Manifestations
- Hyperactivity
- Polyembolokoilamania (insertion of foreign bodies into body orifices)
- Behavioral problems
- **Self-destructive behavior**
- Onychotillomania (pulling out nails)
- Wrist-biting
- Head-banging

dup 17p11.2
Potocki-Lupski Syndrome
[OMIM 610883]

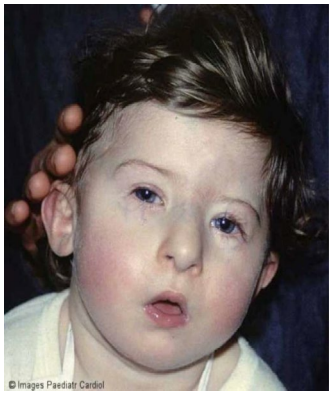
NEUROLOGIC
Central Nervous System
- **Developmental delay**
- **Intellectual disability, mild**
- Hypotonia
- Speech delay
- EEG abnormalities
- No overt seizures
- Delayed myelination
- Hypoplastic corpus callosum

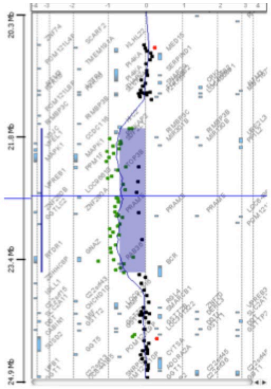
Behavioral Psychiatric Manifestations
- **Autistic features**
- Attention-deficit disorder
- Hyperactivity

The 22q11.2 region



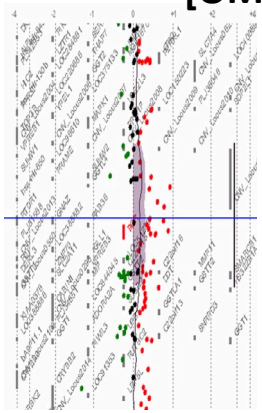
DiGeorge Syndrome [OMIM 192430]

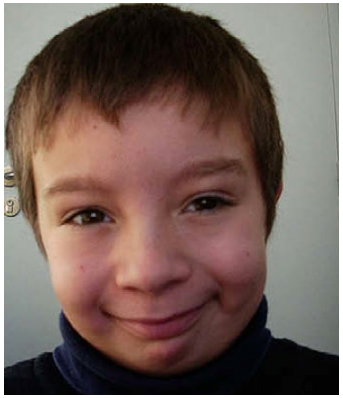




cleft palate/
velopharyngeal insufficiency, cardiac anomalies, hypoplasia of the thymus, hypoparatiroidsm, global developmental delay,
intellectual disability, ASD

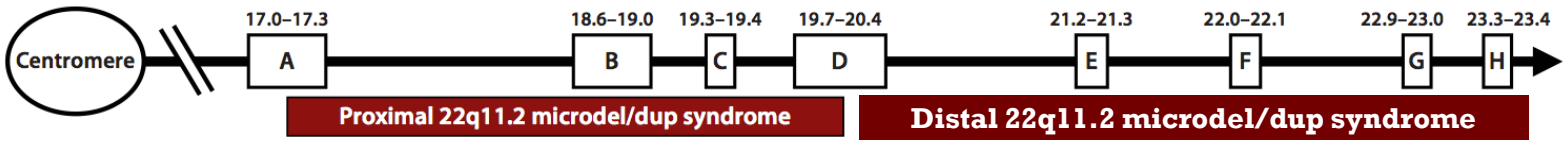
22q11.2 proximal microduplication Syndrome [OMIM 608363]



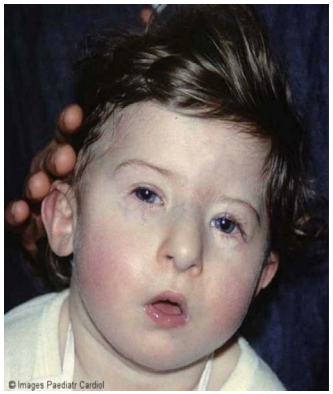


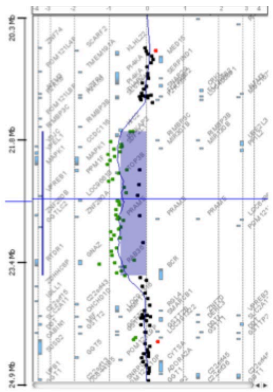
intellectual disability/learning disability, delayed psychomotor development, growth retardation, and muscular hypotonia, epilepsy, ASD

The 22q11.2 region

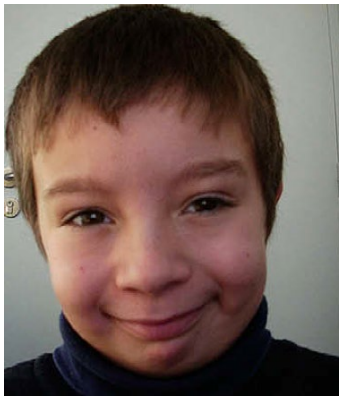


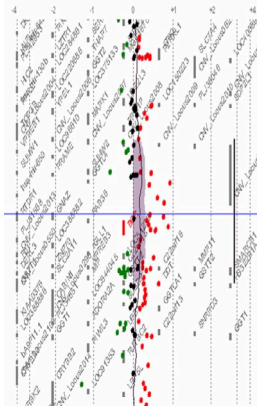
DiGeorge Syndrome
[OMIM 192430]

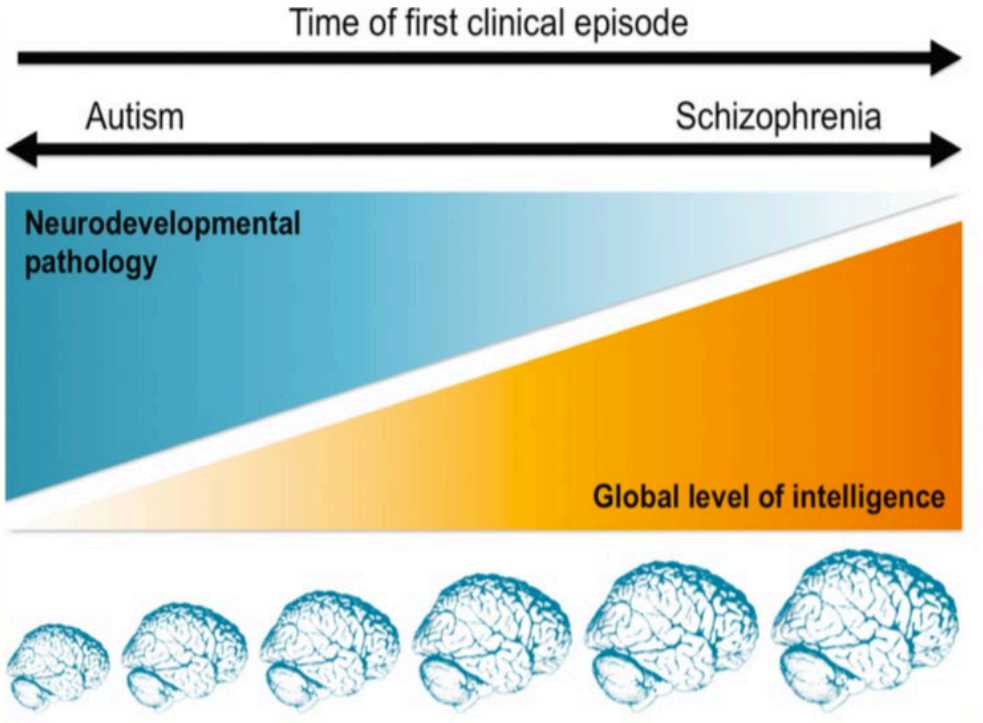




22q11.2 proximal microduplication Syndrome
[OMIM 608363]



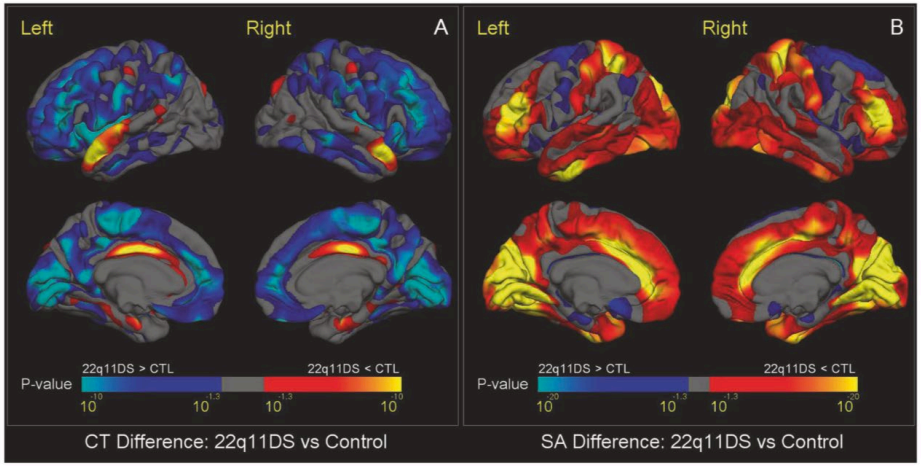


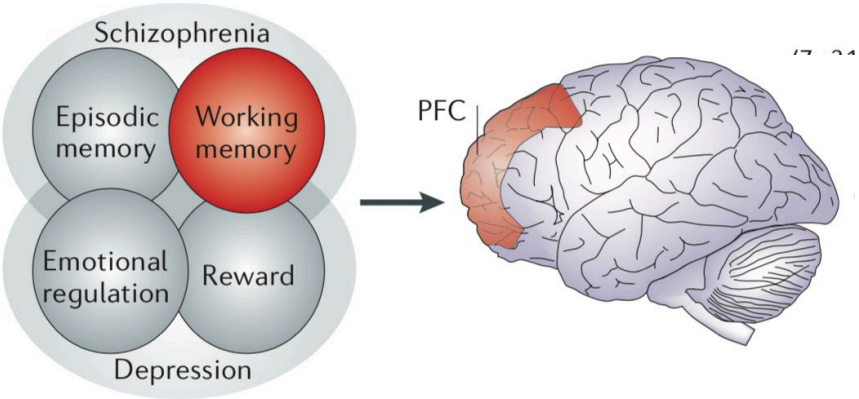


Aggernæs, B. (2018). *European Journal of Neuroscience*, *47*(6), 515-533.

Large-scale mapping of cortical alterations in 22q11.2 deletion syndrome: Convergence with idiopathic psychosis and effects of deletion size

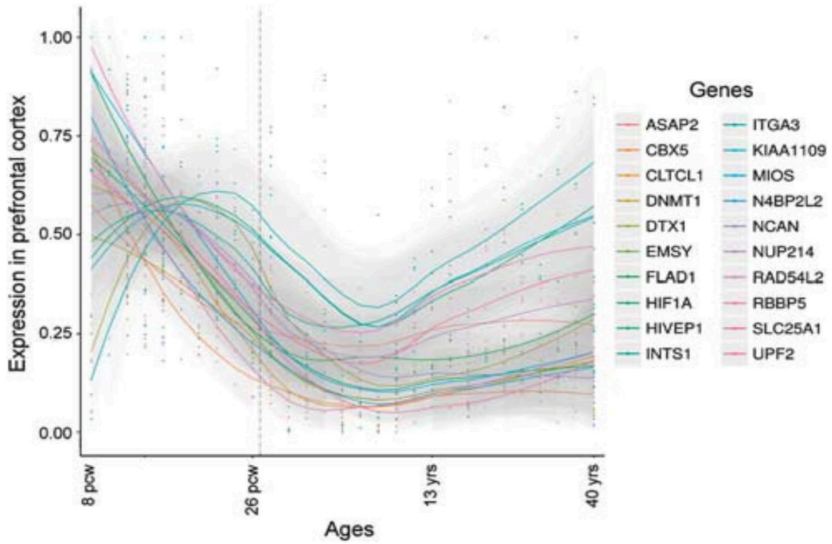
ENIGMA 22q11.2

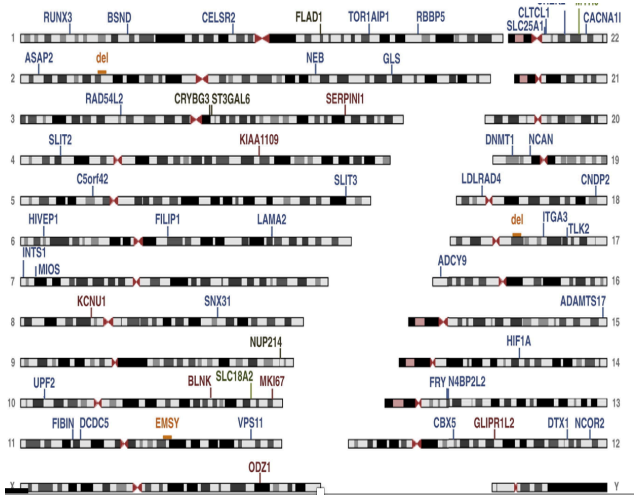




Sun, D., (2018). *Molecular psychiatry*.

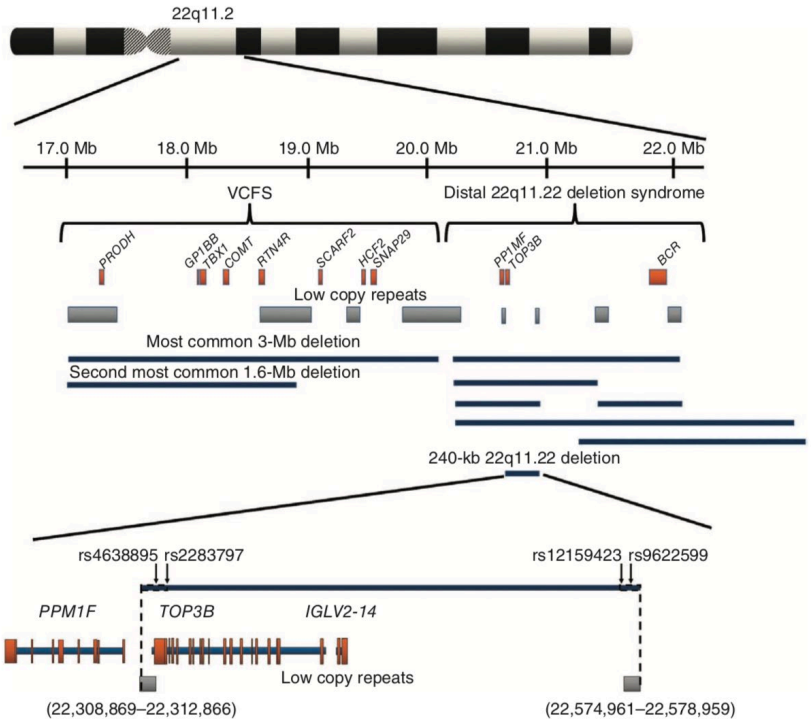
Spatial and temporal mapping of de novo mutations in schizophrenia to a fetal prefrontal cortical network.

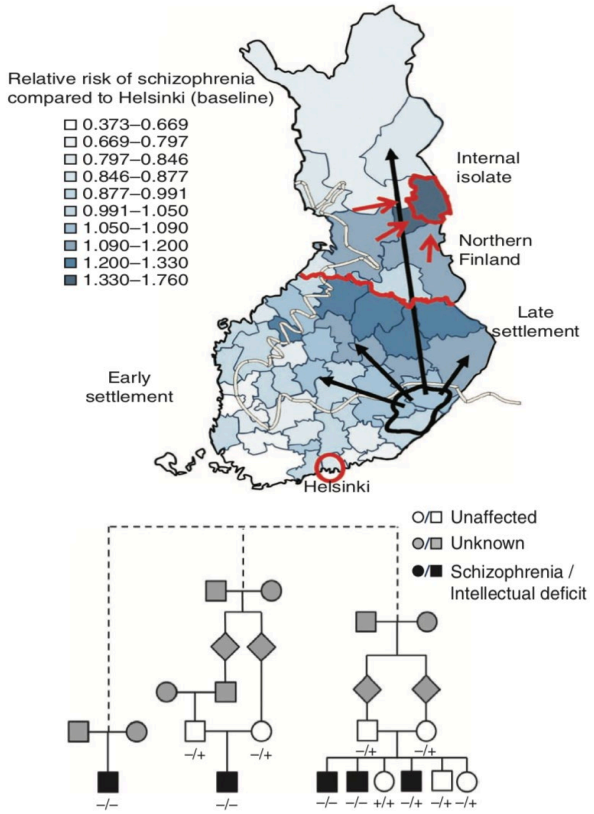




Gulsuner, S., et al. (2013). *Cell*, *154*(3), 518-529.

Deletion of TOP3β, a component of FMRP-containing mRNPs, contributes to neurodevelopmental disorders





Haploinsufficiency: intellectual disability
Nullisomy: intellectual disability + schizophrenia

Stoll, Georg, et al.
Nature neuroscience 16.9 (2013): 1228.

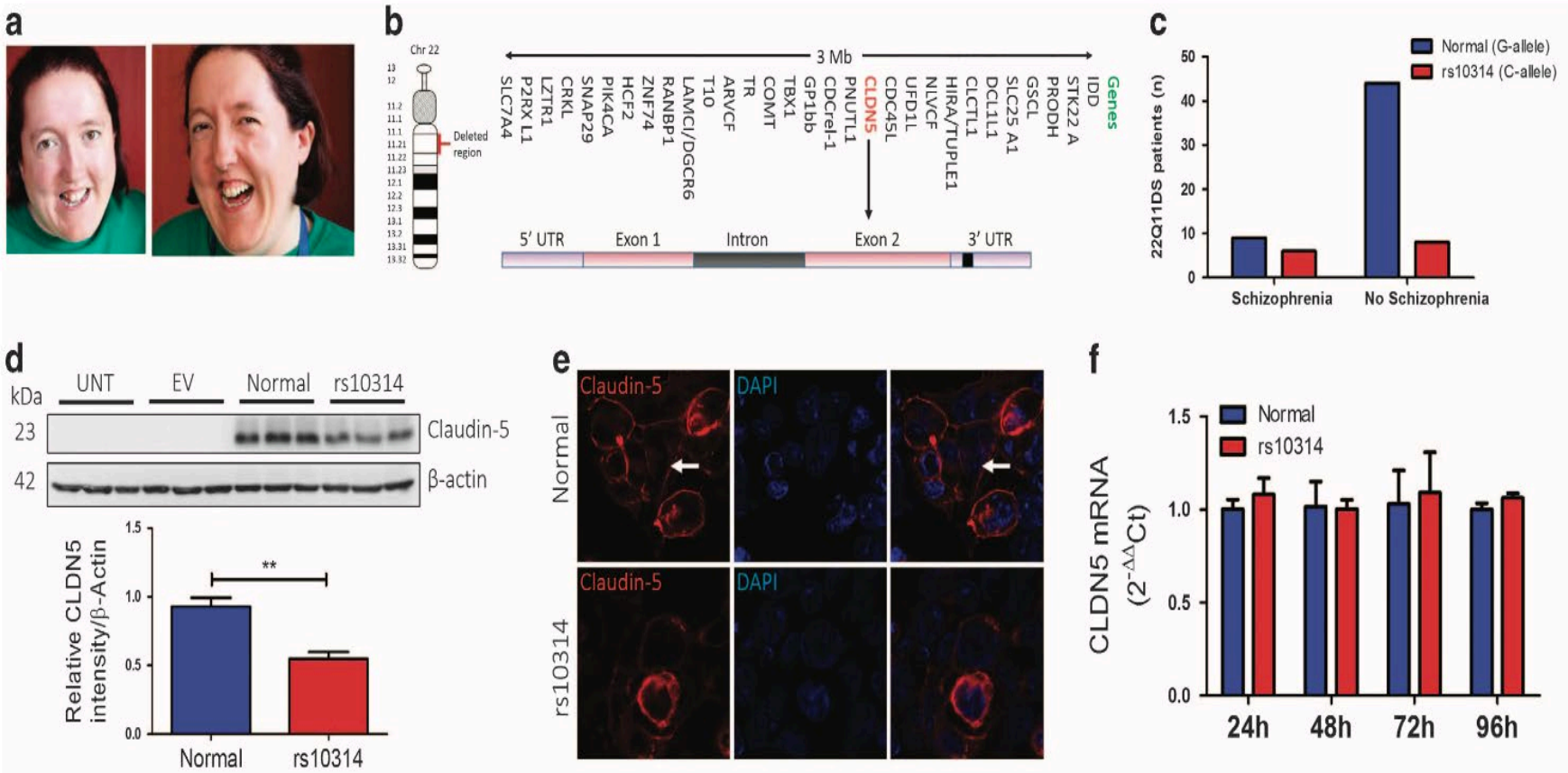
OPEN

Molecular Psychiatry (2017) 00, 1–11

www.nature.com/mp

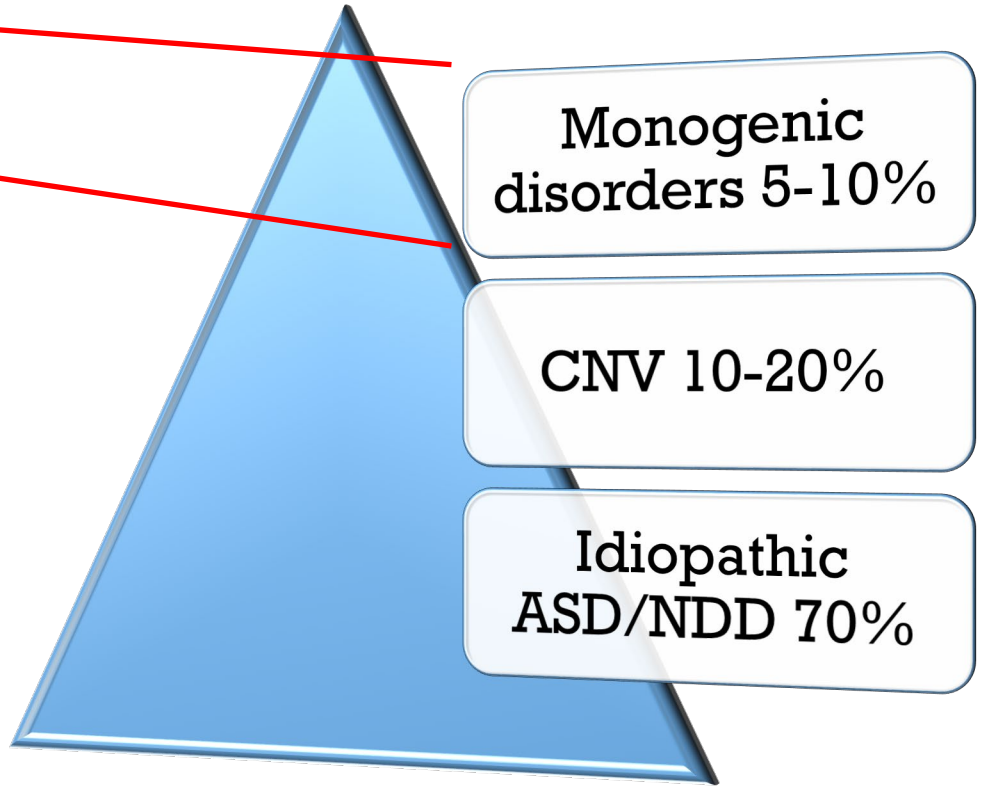
ORIGINAL ARTICLE

Dose-dependent expression of claudin-5 is a modifying factor in schizophrenia

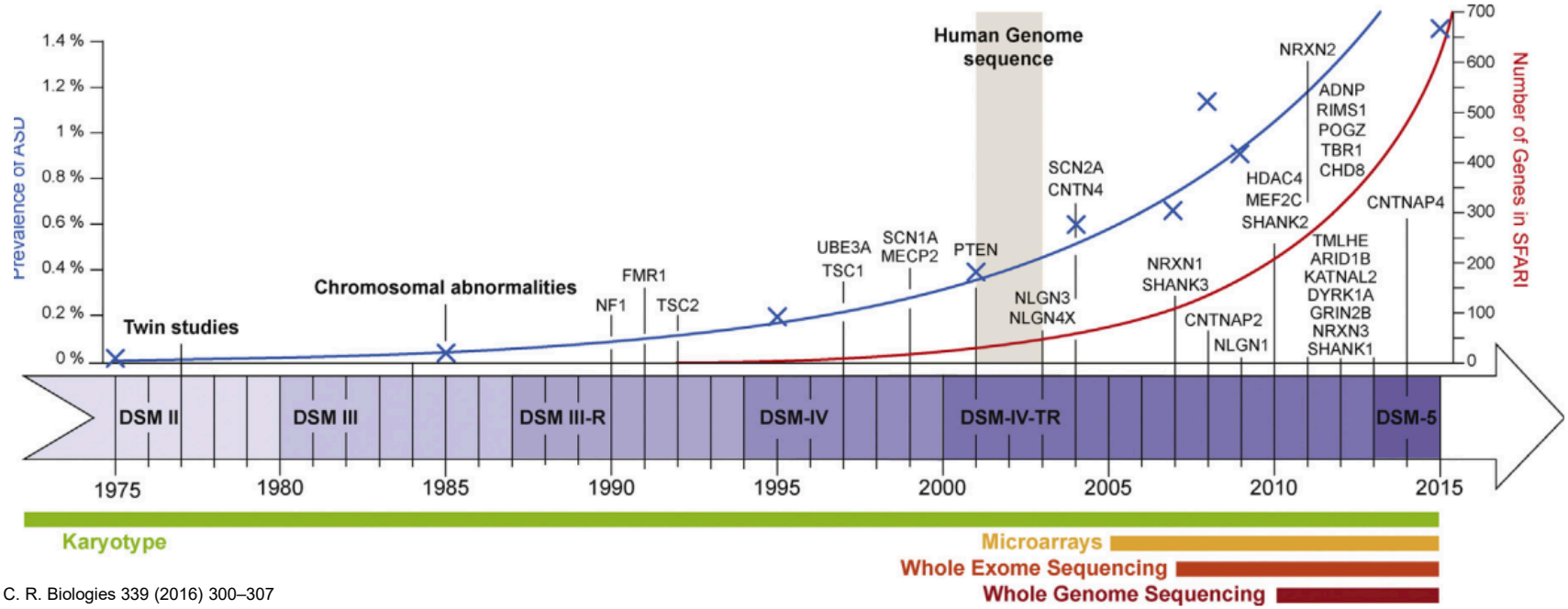


Greene, C., et al. "Dose-dependent expression of claudin-5 is a modifying factor in schizophrenia." Molecular psychiatry (20

The Genetics of Autism & Neurodevelopmental Disorders



Monogenic Disorders & Non Syndromic Autisms



C. R. Biologies 339 (2016) 300–307

Affected gene (OMIM)	Chromosomal locus	Protein name	Gene function	Clinical phenotype	Inheritance	Prevalence among individuals with autism
NLGN3 (300336)	Xq13.1	Neuroligin-3 precursor	Neuroligins function as ligands for the neurexin family of cell-surface receptors	Autism, Asperger syndrome, PDD-NOS	X-linked	<1%
NLGN4 (300427)	Xp22.33	Neuroligin-4, X-linked precursor	Same as *NLGN3*	Autism, Asperger syndrome, X-linked mental retardation, PDD-NOS	X-linked	<1%
SHANK3 (606230)	22q13.3	SH3 and multiple ankyrin repeat domains protein 3	Encodes a scaffolding protein found in the PSD complex of excitatory synapses,where it binds directly to neuroligins	Autism with severe language and social deficits	Unknown	1.1%
NRXN1 (600565)	2p16.3	Neurexin-1α precursor	Neurexins functionin the vertebrate nervous system as cell adhesion molecules and receptors	Autism with seizures, facialdysmorphism mild to severe spokenlanguage deficits	Unknown	<1%
MeCP2 (300005)	Xq28	Methyl-CpG-binding protein 2	A transcriptional repressor that binds to methylated CpG dinucleotides generally located at gene promoters and recruits HDAC1 and other proteins involved in chromatin repression	Autism, learning disability, Angelman syndrome phenotype, preserved speech variant of Rett syndrome	X-linked	0.8–1.3% of the female ASD population
HOXA1 (142955)	7p15.3	Homeobox protein Hox-A1	Transcription factor essential to the development of head and neck structures, including hindbrain, ear, and occipital and hyoid bones	Autism spectrum disorder susceptibility	Autosomal recessive	Very rare
PTEN (601728)	10q23.31	Phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase	A tumour-suppressor gene influencing G1 cell cycle arrest and apoptosis. In the central nervous system, *PTEN* inactivation results in excessive dendritic and axonal growth with increased numbers of synapses	ASD with macrocephaly has been consistently found in approximately 20% of individuals with autism recruited in independent samples	Unknown	4.7%

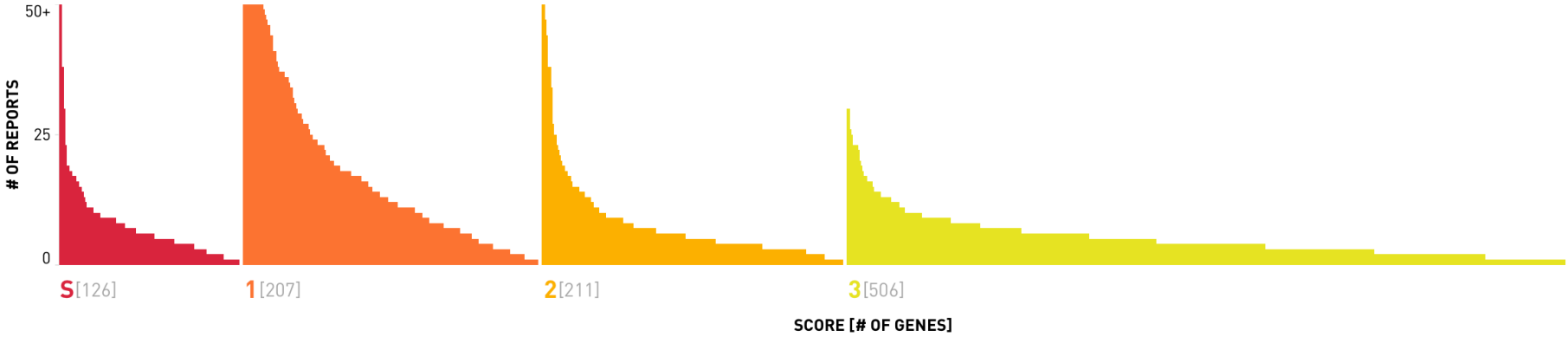
Developmental Medicine & Child Neurology 2010, 52: 130–138

Gene	Chromosomal location	Estimated percentage of individuals with an ASD in whom this variant is identified	ASD penetrance* (rate of ASD in carriers)	Neuropsychiatric pleiotropy‡ (associated neuropsychiatric phenotypes)	Somatic pleiotropy‡ (associated somatic phenotypes)
KATNAL2 (REF. 37)	18q21.1	0.08	Unknown	Unknown	Unknown
POGZ[37]	1q21.3	0.08	Incomplete[164]	ID[164,165], speech delay[164], language delay[164], schizophrenia[61]	Microcephaly[164], obesity[164], impaired vision[164]
TBR1 (REFS 37,166)	2q24.2	0.08	Unknown	ID[167]	Unknown
ADNP[37]	20q13.13	0.10	Complete[118]	ID[118,165], ADHD[118]	Recurrent infections[118], short stature[118], heart defect[118], hypotonia[118], hypermetropia[118], epilepsy[118], hyperlaxity[118]
SYNGAP1 (REF. 37)	6p21.32	0.10	Unknown	ID[168,169]	Epilepsy[168]
GRIN2B[37,166]	12p13.1	0.13	Unknown	ID[170]	Epilepsy[170]
ANK2 (REF. 37)	4q25-q26	0.13	Unknown	None reported	Heart arrhythmia[171]
ARID1B[37]	6q25.3	0.13	Incomplete[172]	ID[172], speech impairment[172,173]	Short stature[174], hypertrichosis[173], cryptorchidism[173], epilepsy[173], vision impairment[173]
SCN2A[37]	2q24.3	0.13	Incomplete[59]	ID[60], schizophrenia[61]	Epilepsy[62], episodic ataxia[62]
DYRK1A[37,166]	21q22.13	0.13	Incomplete[175]	ID[175,176], speech impairment[175,176], ADHD[175], anxiety[175]	Microcephaly[175,176], epilepsy[175,176], vision impairment[175], short stature[175], gastrointestinal symptoms or feeding difficulties[175,176]
CHD8 (REFS 37,166)	14q11.2	0.21	Incomplete[32]	ID[32,177], schizophrenia[177], speech delay[177], sleep problems[32]	Macrocephaly[32,177], gastrointestinal symptoms[32]

Nature Reviews Genetics,2017, *18*(6), 362.

Monogenic Disorders & Non Syndromic Autisms

Score Distribution Click on a score to refine results



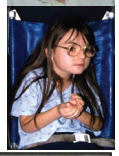
SFARI GENE

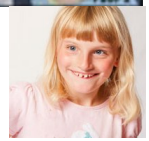
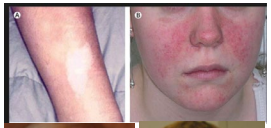
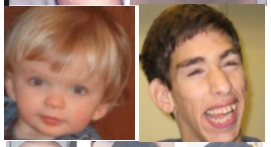
SFARI Gene is an evolving database for the autism research community that is centered on genes implicated in autism susceptibility.

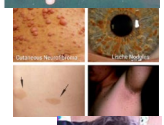
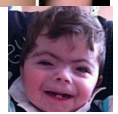
Toggle Gene Score Categories

- Category S (Syndromic)
- Category 1 (High Confidence)
- Category 2 (Strong Candidate)
- Category 3 (Suggestive Evidence)

Monogenic Disorders & Autisms

Syndrome (OMIM number)	Primary gene affected	Estimated autism prevalence	Verbal	ID	Behavior	Motor	Dysmorphic features	Other associated conditions
Fragile X (300624)	*FMR1*	30–60% (males only)[26,36]	Delayed	Moderate	Little social interaction, aversion to touch, poor eye contact	Hyperactivity, stereotypical movements, weakness of connective tissue	Large head, long face, prominent forehead and chin, protruding ears	Developmental delay, abnormal behavior, macroorchidism at puberty
Rett (312750)	*MECP2*	61% (females only)[26]	Limited or absent	Moderate to severe	Expressionless face, lack of eye contact early on, social anxiety	Stereotypical hand movements, progressive scoliosis, ataxia, apraxia	Normal	Regression, microcephaly, hyperventilation, epilepsy
MECP2 duplication (300260)	*MECP2*	>90% (males only)[62,63]	Limited or absent	Severe to profound	Gaze avoidance, limited facial expression, atypical socialization	Hypotonia, progressive spasticity, developmental delay	Brachycephaly, large ears, midface hypoplasia, depressed nasal bridge	Respiratory infections, epilepsy, GI dysfunction, premature death
Angelman (105830)	*UBE3A*	34%[26]	Limited or absent	Severe to profound	Excessive laughter and smiling, decreased eye gaze	Ataxia, hypermotoric behavior, jerky movements, scoliosis, developmental delay	Brachycephaly, wide mouth, protruding tongue, prominent chin	Microcephaly, epilepsy
Tuberous sclerosis complex (191100, 613254)	*TSC1* or *TSC2*	36–50%[26,27]	Absent to normal	Mild to severe in ~50%	ADHD, impulsivity, hyperactivity, social impairment, anxiety	Normal	None	Epilepsy, benign tumors in multiple tissues, lung and kidney dysfunction, cortical tubers
Phelan-McDermid (606232)	*SHANK3*	75%[149]	Absent or delayed	Moderate to profound	Impulsivity, social anxiety, biting, obsessive chewing	Hypotonia, psychomotor delay	Long eyelashes, prominent ears, pointed chin, elongated head, deep-set eyes, dysplastic nails	Epilepsy, kidney dysfunction, cardiac anomalies
Timothy (601005)	*CACNA1C*	60%[150]	Severely delayed	Mild to moderate	Shyness, social avoidance	Developmental delay	Flattened nasal bridge, small teeth, low-set ears, small upper jaw, thin upper lip	Congenital heart malformations, cardiac arrhythmia, syndactyly, weakened immune system, premature death
Neurofibromatosis type 1 (162200)	*NF1*	18%[26]	Delayed	Mild cognitive disabilities	ADHD, social anxiety, depression, aggressive behavior	Hyperactivity, scoliosis, pseudoarthrosis	None	Multiple benign neurofibromas, abnormal skin pigmentation, macrocephaly, epilepsy
Cornelia de Lange	*NIPBL, SMC1A,SMC3, RAD21, HDAC8*		Delayed	Mild to severe	ASD, increased anxiety, selective mutism,	Microcephaly, growth retardation	synophrys, long eyelashes low-set ears, small, upturned nose	

Sindrome dell'X fragile (FXS)

Prevalence approximately 1 in 4,000 males

Head
- Macrocephaly

Face
- Coarse facies, large forehead, long face, prominent jaw, large ears

External Genitalia (Male)
- Macroorchidism

Central Nervous System
- Intellectual disability (moderate to severe in males) & seizures
- Abnormal head movements
- Periventricular heterotopia

Behavioral Psychiatric Manifestations
- Hyperactive behavior & ASD

Classe Genotipica	Nr. di ripetizioni della tripletta nucleotidica
Normale	**5-45**
Gray Zone	**46-60**
Premutazione	**61-199**
Mutazione Completa	**> 200**

Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions

G. Bradley Schaefer, MD[1] and Nancy J. Mendelsohn, MD[2]; for the Professional Practice and Guidelines Committee

First tier

- Three-generation family history with pedigree analysis
- Initial evaluation to identify known syndromes or associated conditions
  - Examination with special attention to dysmorphic features
  - If specific syndromic diagnosis is suspected, proceed with targeted testing
- * If appropriate clinical indicators present, perform metabolic and/or mitochondrial testing (alternatively, consider a referral to a metabolic specialist)
- Chromosomal microarray: oligonucleotide array-comparative genomic hybridization or single-nucleotide polymorphism array
- DNA testing for fragile X (to be performed routinely for male patients only)[a]

Second tier

- *MECP2* sequencing to be performed for all females with ASDs
- *MECP2* duplication testing in males, if phenotype is suggestive
- *PTEN* testing only if the head circumference is >2.5 SD above the mean
- Brain magnetic resonance imaging only in the presence of specific indicators (e.g., microcephaly, regression, seizures, and history of stupor/coma)

ACMG PRACTICE GUIDELINES | Genetics inMedicine

* **Table 3** Clinical symptoms that prompt metabolic or mitochondrial testing in persons with ASDs

Acid/base or electrolyte disturbances
Anemia with an elevated mean corpuscular volume
Cyclic vomiting
Dermatologic changes: alopecia, hypertrichosis, and pigmented skin eruptions
Developmental regression associated with illness or fever
Gastrointestinal dysfunction, gastroparesis
Hypotonia/dystonia
Lactic acidosis
Lethargy
Multisystem involvement, especially cardiac, hepatic, or renal (physical and/or laboratory evidence)
Neurodegeneration outside of the typical ASD speech loss at 18–24 months
Poor growth, microcephaly
Seizures

ASD, autism spectrum disorder.

1st Tier: Non-Targeted screening to identify 54 (60%) treatable IEMs

Blood:
- ammonia, lactate
- plasma amino acids
- total homocysteine
- acylcarnitine profile
- copper, ceruloplasmin

Urine:
- organic acids
- purines & pyrimidines
- creatine metabolites
- oligosaccharides
- glycosaminoglycans

2nd Tier: Targeted testing to identify 35 (40%) treatable IEMs requiring 'specific testing'

- **according to patient's symptomatology patient (Table 4) & clinician's expertise**
- **utilization of textbooks & digital resources** (WebApp: *www.treatable-ID.org*)
- **consider the following biochemical / molecular analyses:**
  - whole blood manganese
  - plasma cholestanol
  - plasma 7-dehydroxy-cholesterol:cholesterol ratio
  - plasma pipecolic acid & urine AASA
  - plasma very long chain fatty acids
  - plasma vitamin B12 & folate
  - serum & CSF lactate:pyruvate ratio
  - enzyme activities (leucocytes): arylsulphatase A, biotinidase, glucocerebrosidase, fatty aldehyde dehydrogenase
  - urine deoxypyridonoline
  - CSF amino acids
  - CSF neurotransmitters
  - CSF: plasma glucose ratio
  - CoQ measurement fibcroblasts
  - molecular: *CA5A, NPC1, NPC2, SC4MOL, SLC18A2, SLC19A3, SLC30A10, SLC52A2, SLC52A3, PDHA1, DLAT, PDHX, SPR, TH*

Modified from: Moeschler, John B., and Michael Shevell. "Comprehensive evaluation of the child with intellectual disability or global developmental delays." Pediatrics 134.3 (2014): e903-e918. AND Miller, David T., et al. "Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies." The American Journal of Human Genetics 86.5 (2010): 749-764

Sindrome di Rett

Colpisce prevalentemente il sesso femminile ed è una delle cause più comuni di deficit cognitivo grave nelle ragazze (decorso severo in epoca di vita prescolare nel sesso maschiile). La prevalenza è stimata in 1/9.000 ragazze di 12 anni e la prevalenza nella popolazione generale è stimata in circa 1/30.000.

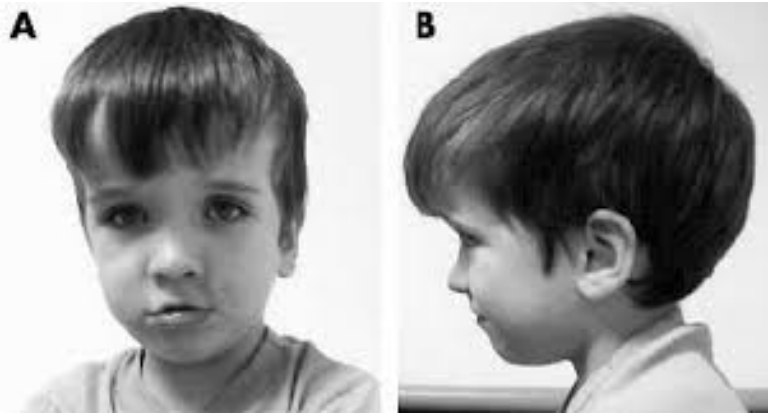
Head
- Normal birth head circumference
- Deceleration of head growth
- Microcephaly

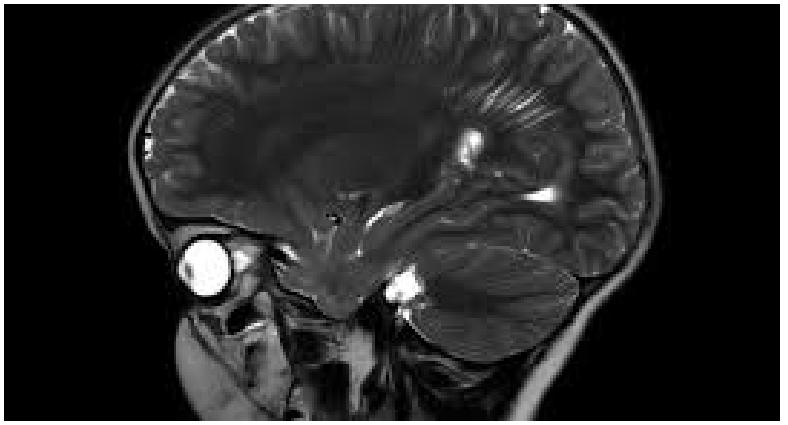
Central Nervous System
- Normal development until 6-18 months
- ID, profound
- Spasticity
- EEG abnormalities
- Seizures
- Reduction or loss of acquired skills
- Cortical atrophy (frontal area)
- ASD & Hand stereotypies

La RTT classica è caratterizzata da sviluppo apparentemente normale nei primi 6-18 mesi di vita e, successivamente, perdita della motricità grossolana e fine già acquisita, perdita della capacità di interagire e socializzare e comparsa di movimenti stereotipati delle mani.

Macrocephaly/autism syndrome

(*PTEN*-related, OMIM 605309)



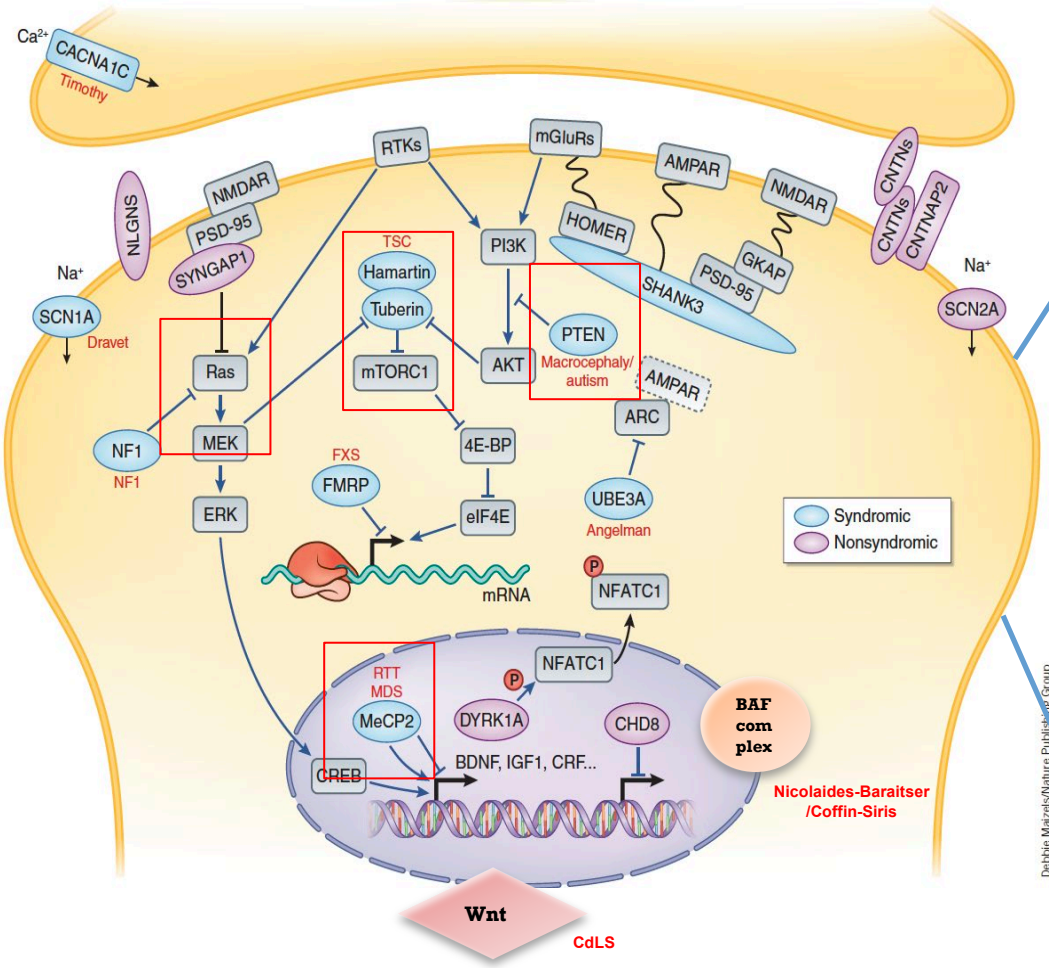


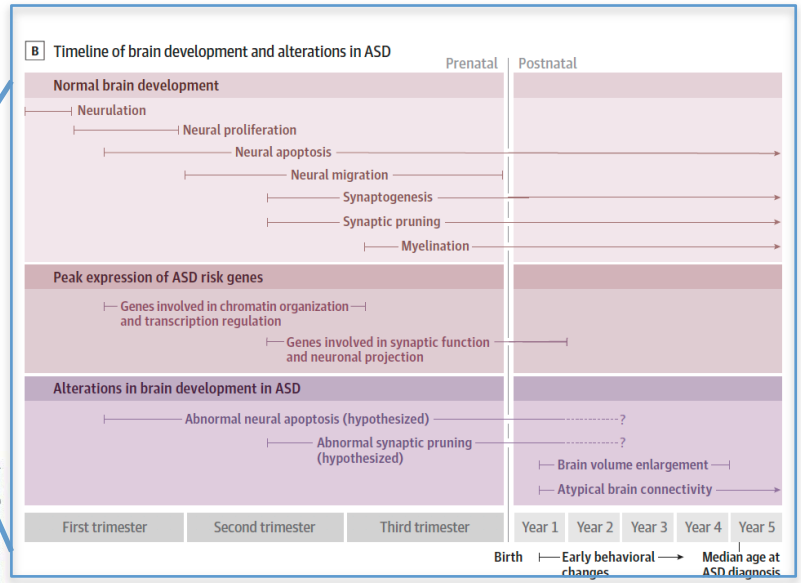
Location	Phenotype	Phenotype MIM number	Inheritance	Phenotype mapping key
10q23.31	{Glioma susceptibility 2}	613028		3
	{Meningioma}	607174	AD	3
	Cowden syndrome 1	158350	AD	3
	Lhermitte-Duclos syndrome	158350	AD	3
	Macrocephaly/autism syndrome	605309	AD	3
	Prostate cancer, somatic	176807		3

Central Nervous System: Developmental delay & ID

Behavioral Psychiatric Manifestations: Autism

Biological pathways associated with ASDs





Debbie Maizels/Nature Publishing Group

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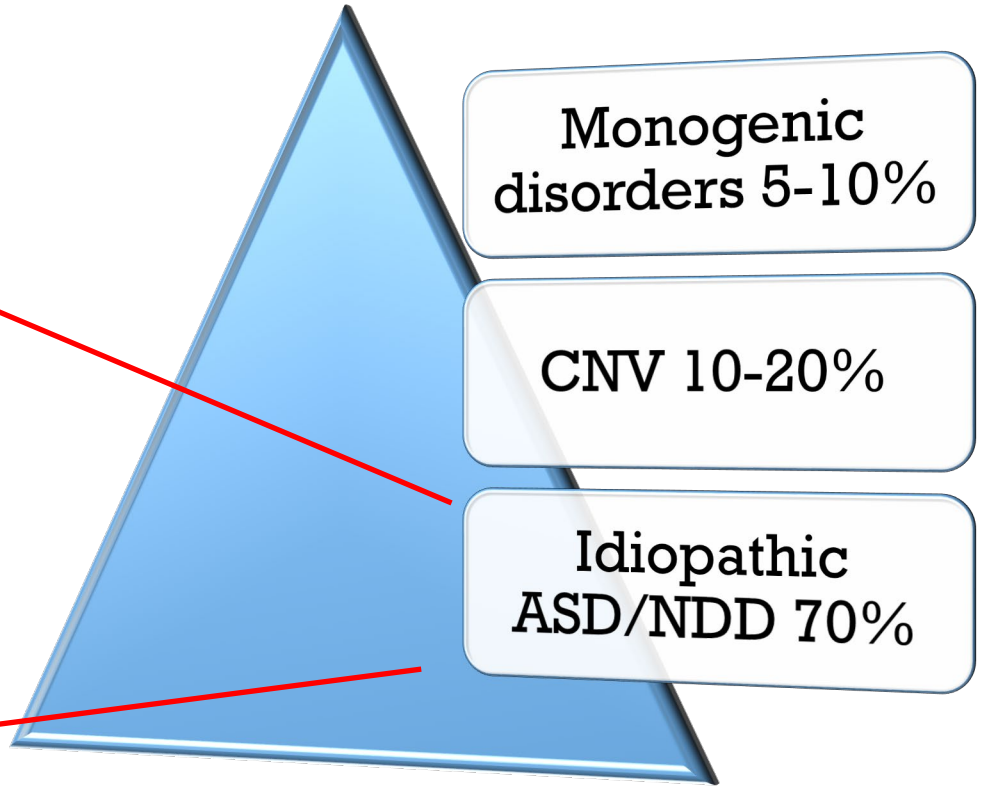
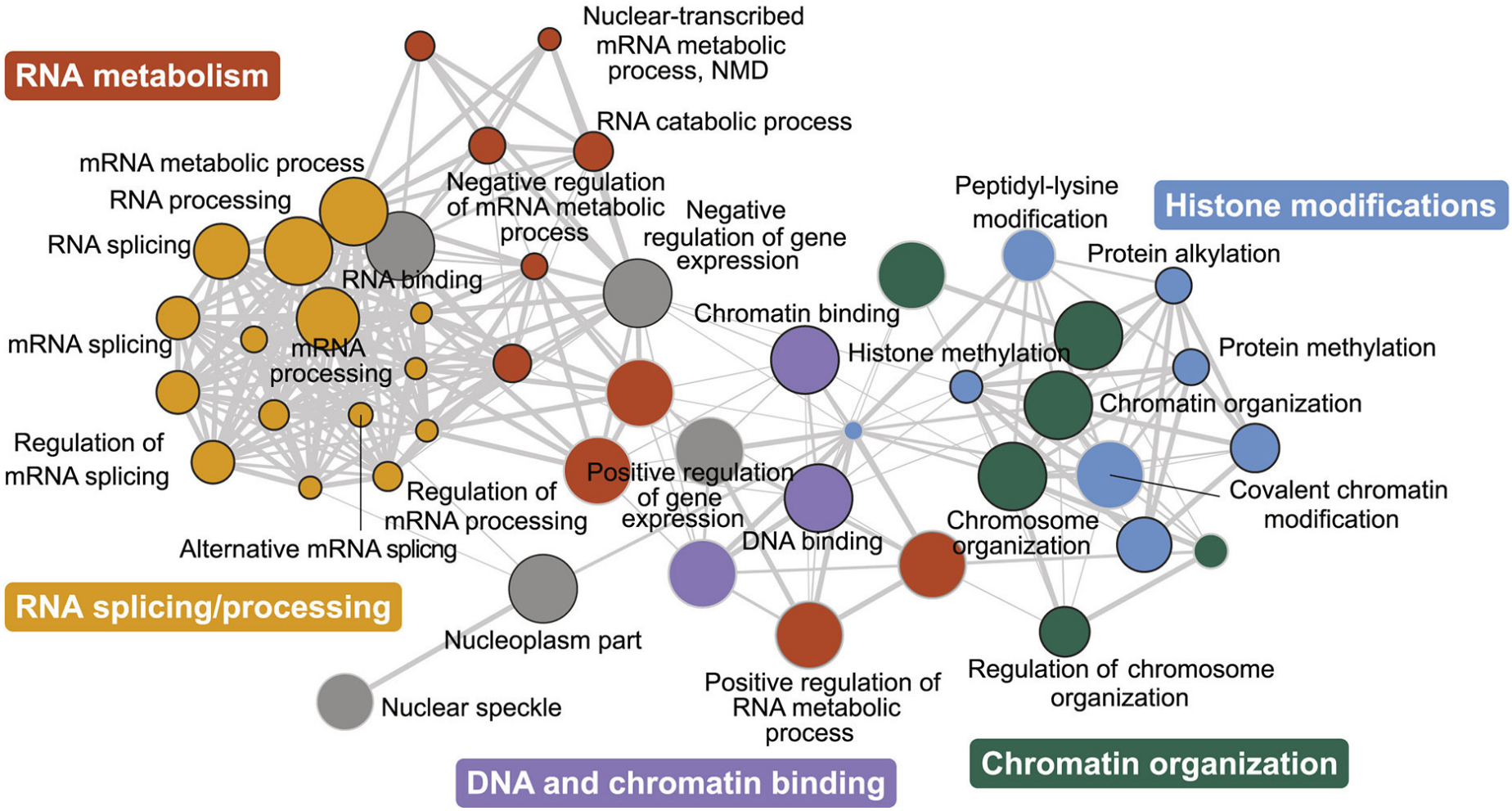
The Genetics of Autism & Neurodevelopmental Disorders



Molecular Cell

Genome-wide CRISPR-Cas9 Interrogation of Splicing Networks Reveals a Mechanism for Recognition of Autism-Misregulated Neuronal Microexons

Unraveling a genetic network linked to Autism



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