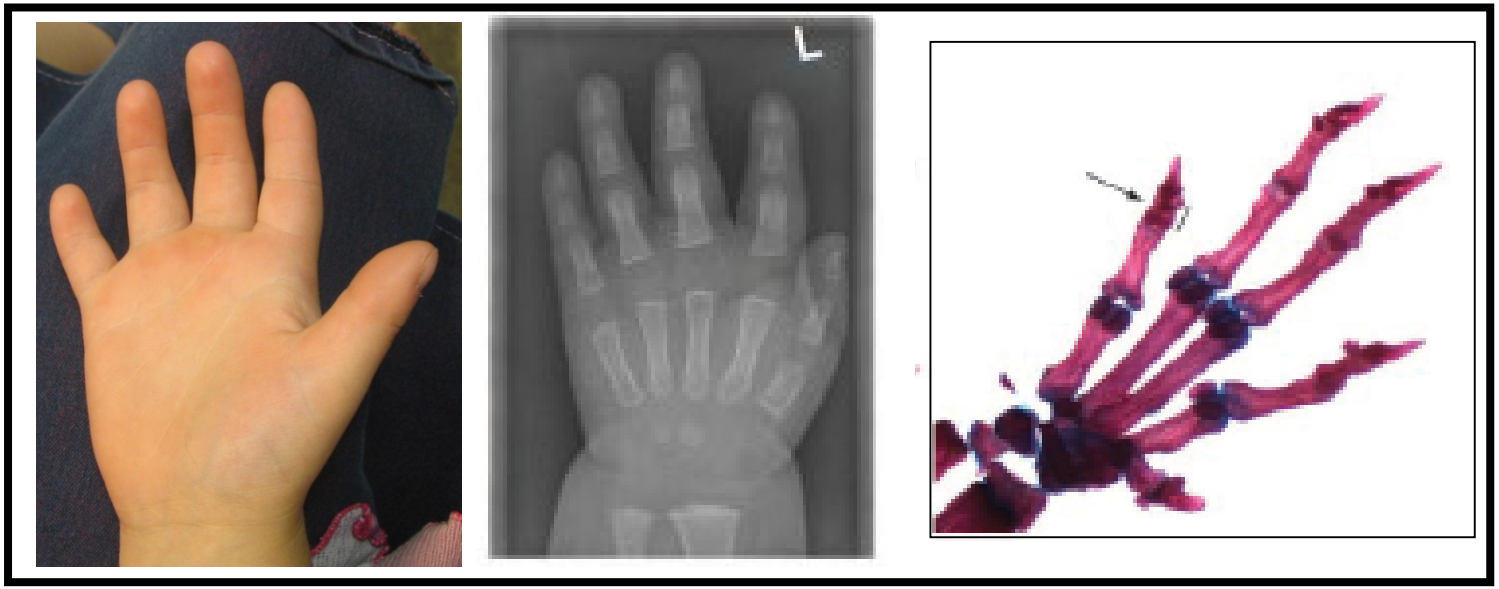

Délétion 13q31.3 et syndrome de Feingold : rôle des microRNAs

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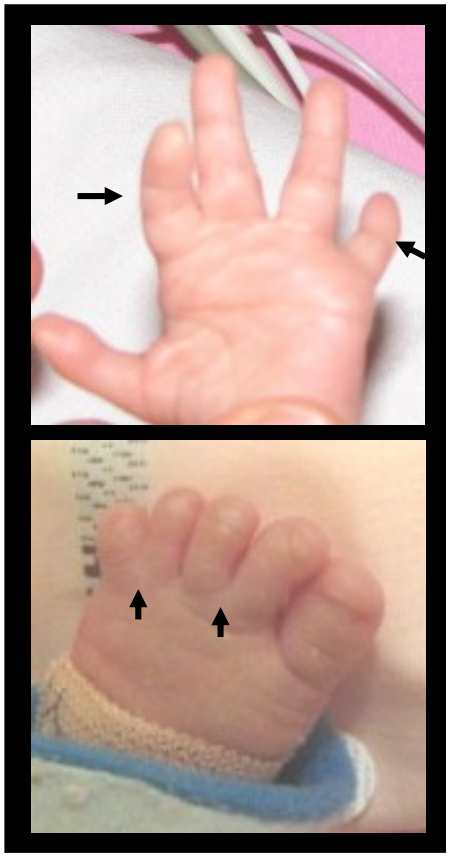
Feingold Syndrome (ODED, MIM164280)



MYCN loss-of-function

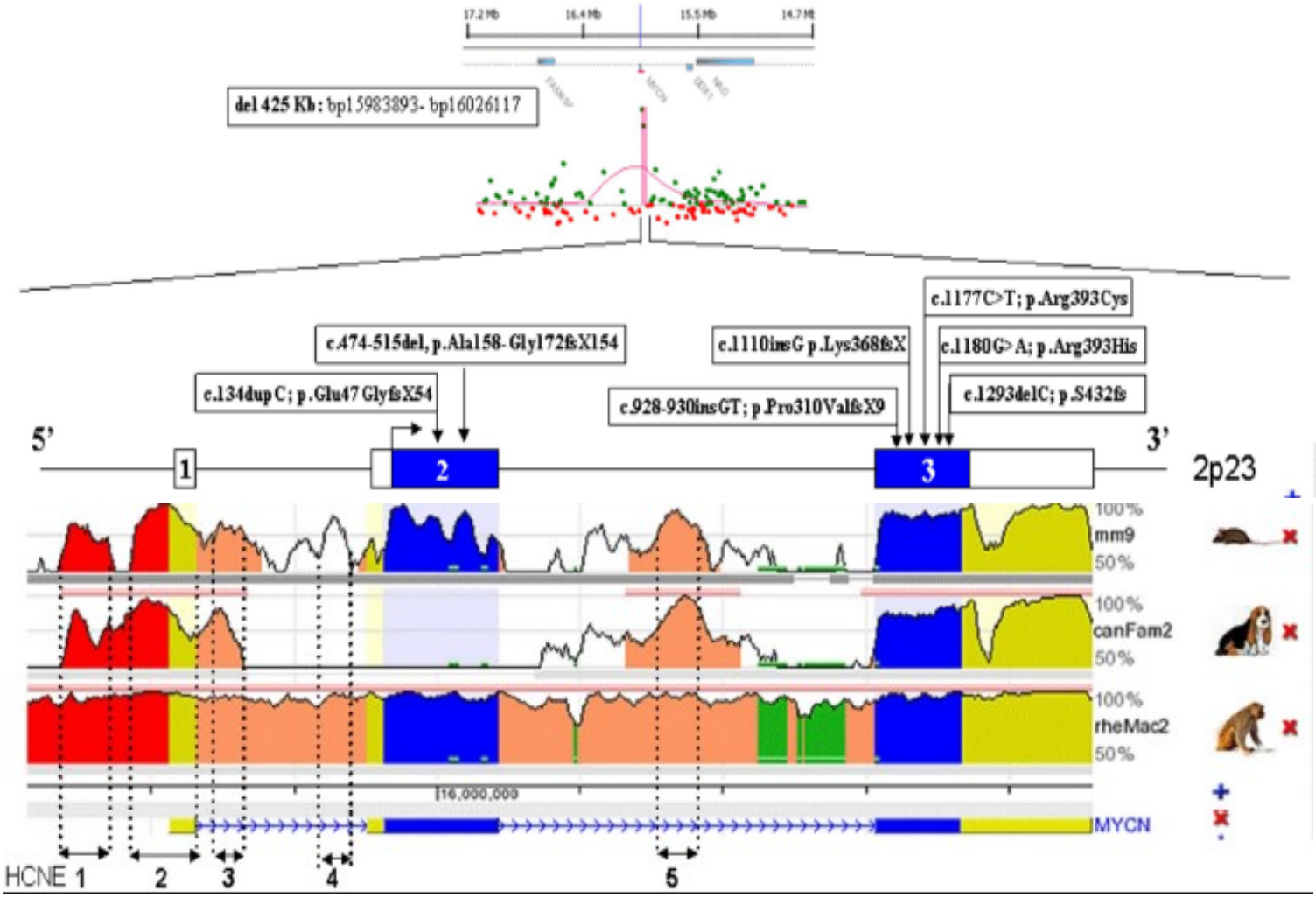
OFC <p10	89
Stature <p10	60
Mild MR	51
Short palpebral fissures	73
Micrognathia	32
Brachymesophalangy	100
Toe syndactyly	97
2/3 only	23
4/5 only	25
2/3+4/5	51
Thumb hypoplasia	17
Gastrointestinal atresia	55
OA	32
DA	31
JA	3
AA	2
Multiple	12
Renal	18
Cardiac	15
PDA	12
Other	10
Deafness	10

- bHLH-LZ transcription factor
- Amplification in 20% of neuroblastomas
- Poor prognostic factor

van Bokhoven et al. ***Nat Genet*** 2005;
Marcelis et al. ***Hum Mut*** 2008

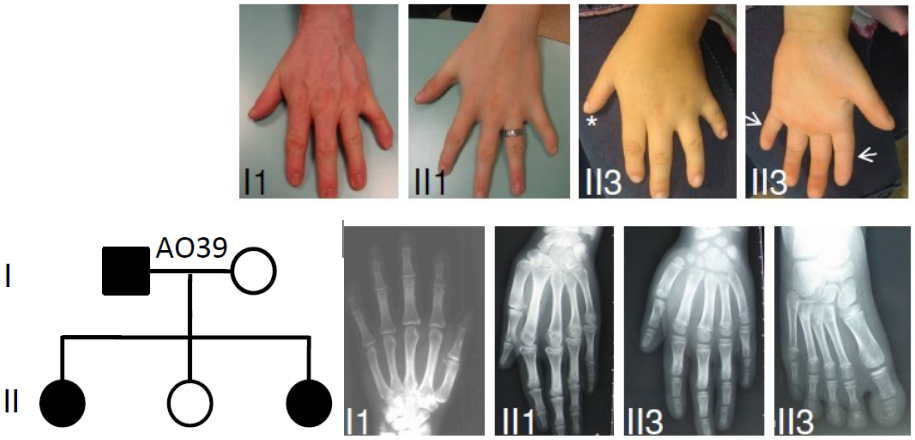
Genetic Heterogeneity in Feingold Syndrome?

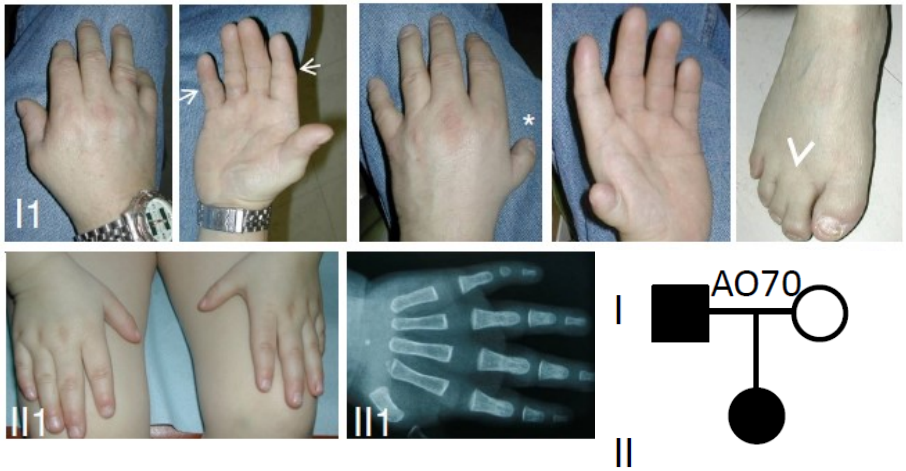
- Cohort of 17 FS index cases
- MYCN mutation/deletion: 8/17 cases

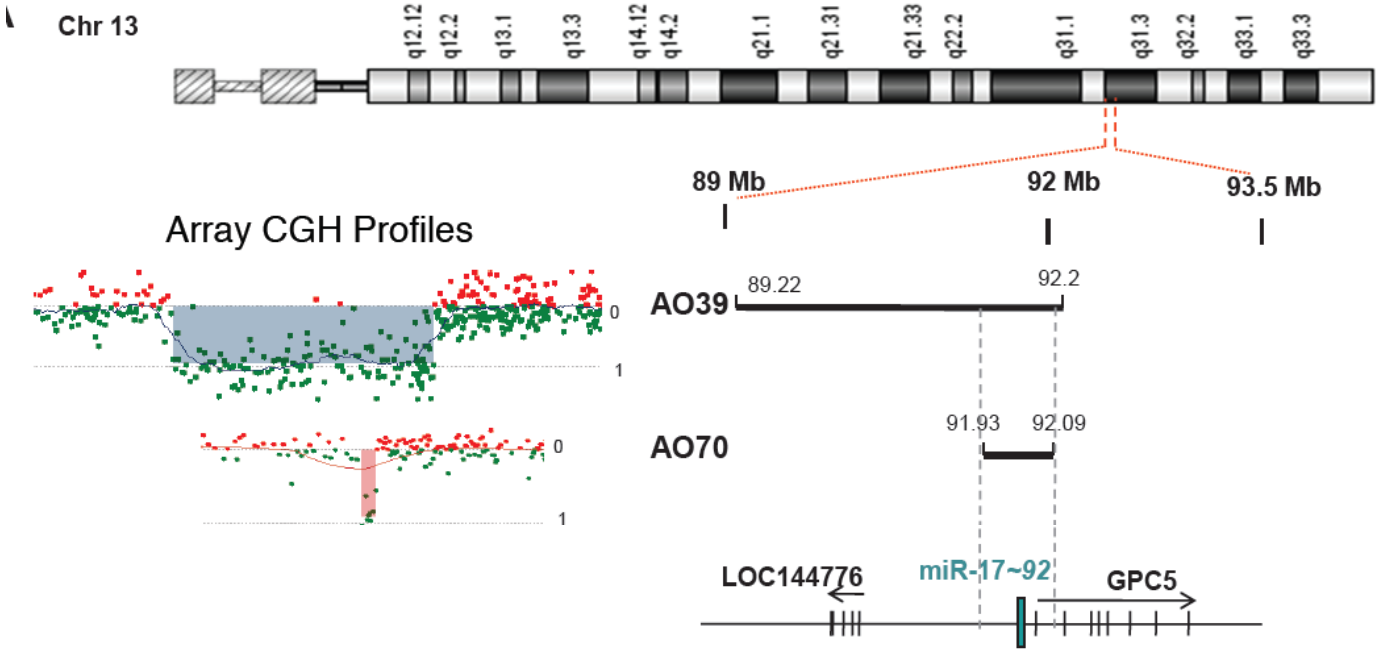


Cognet et al. ***EJHG*** 2011

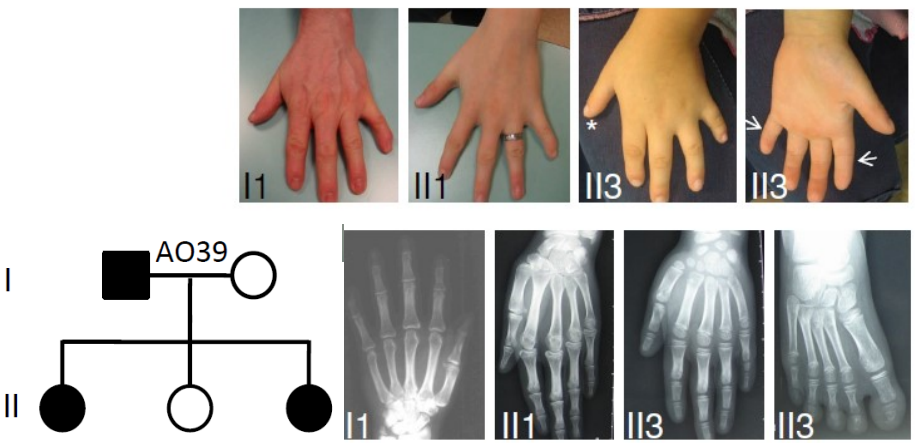
Array-CGH in 10 index cases with Feingold syndrome

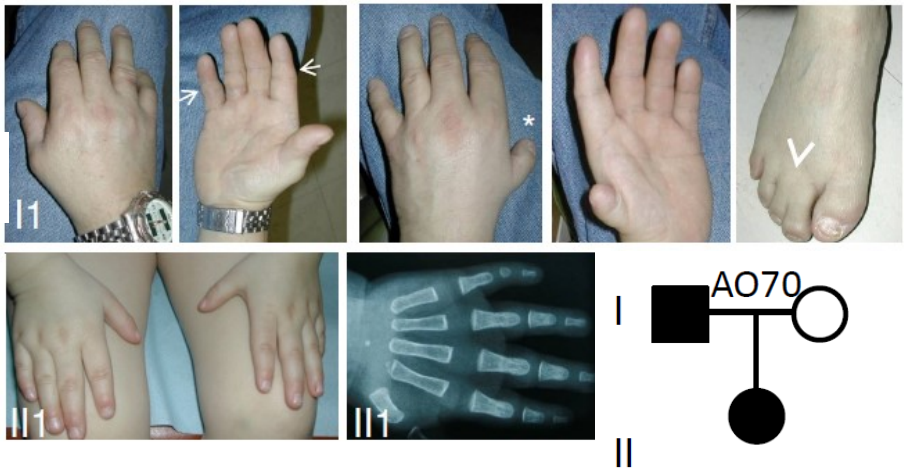


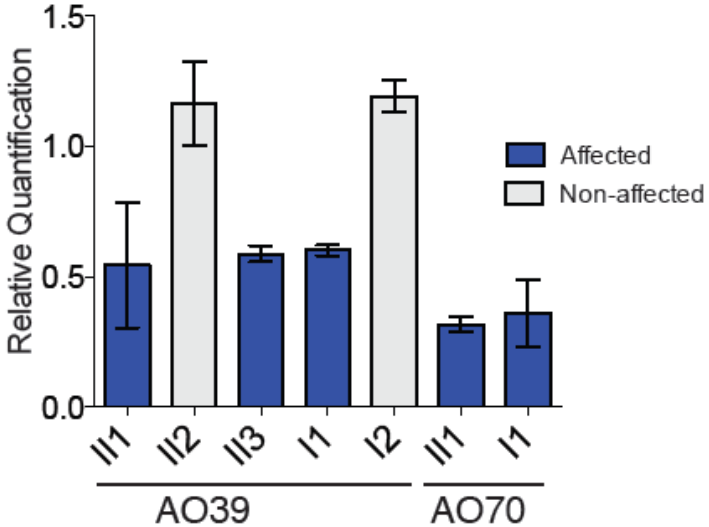


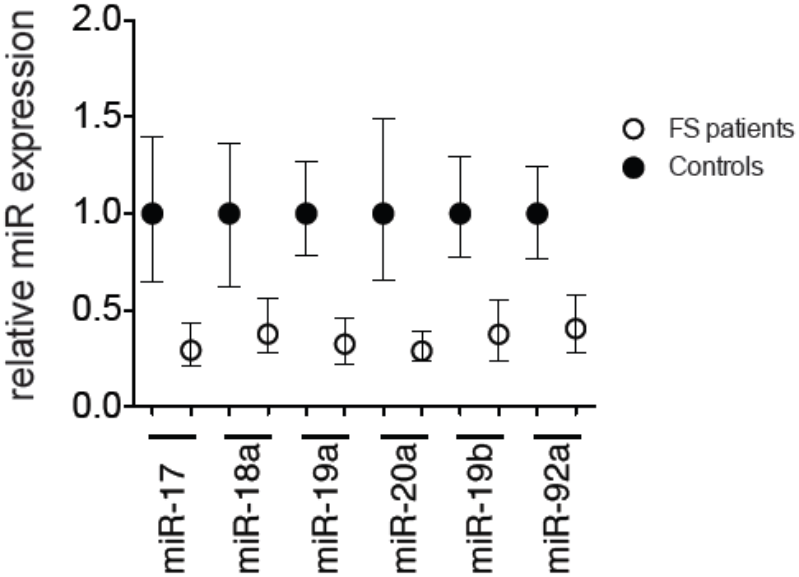


miR-17~92 Expression

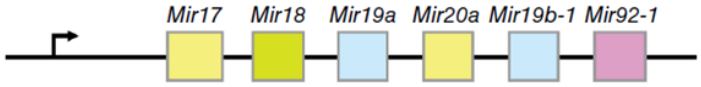




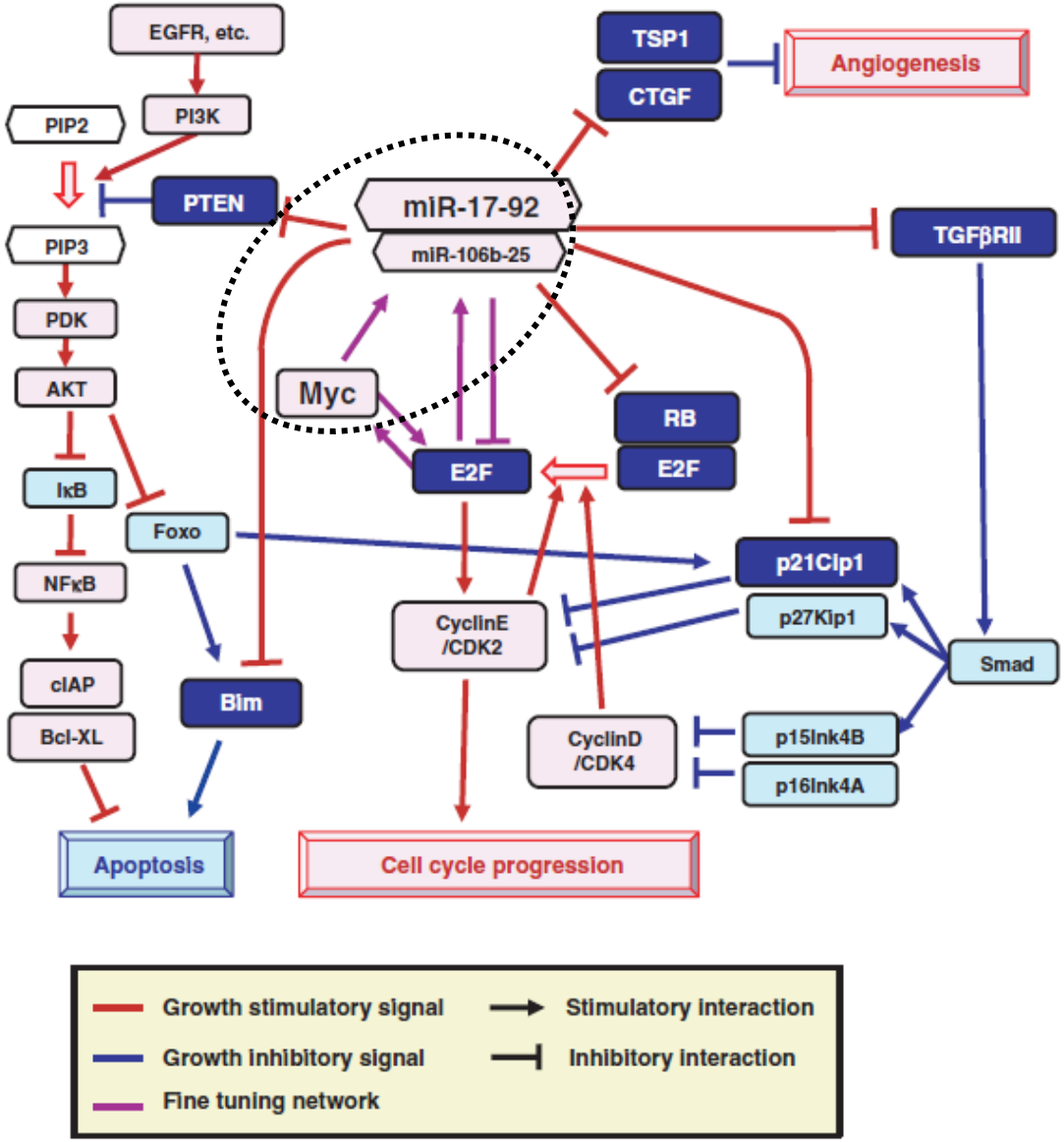




No *miR-17~92* or *GPC5* mutation in the remaining cases



miR-17	CAAAGUGCUUACAGUGCAGGUAGU
miR-20a	UAAAGUGCUUAUAGUGCAGGUAG
miR-18	UAAGGUGCAUCUAGUGCAGAUA
miR-19a	UGUGCAAAUCUAUGCAAAACUGA
miR-19b-1	UGUGCAAAUCCAUGCAAAACUGA
miR-92-1	UAUUGCACUUGUCCCGGCCUG

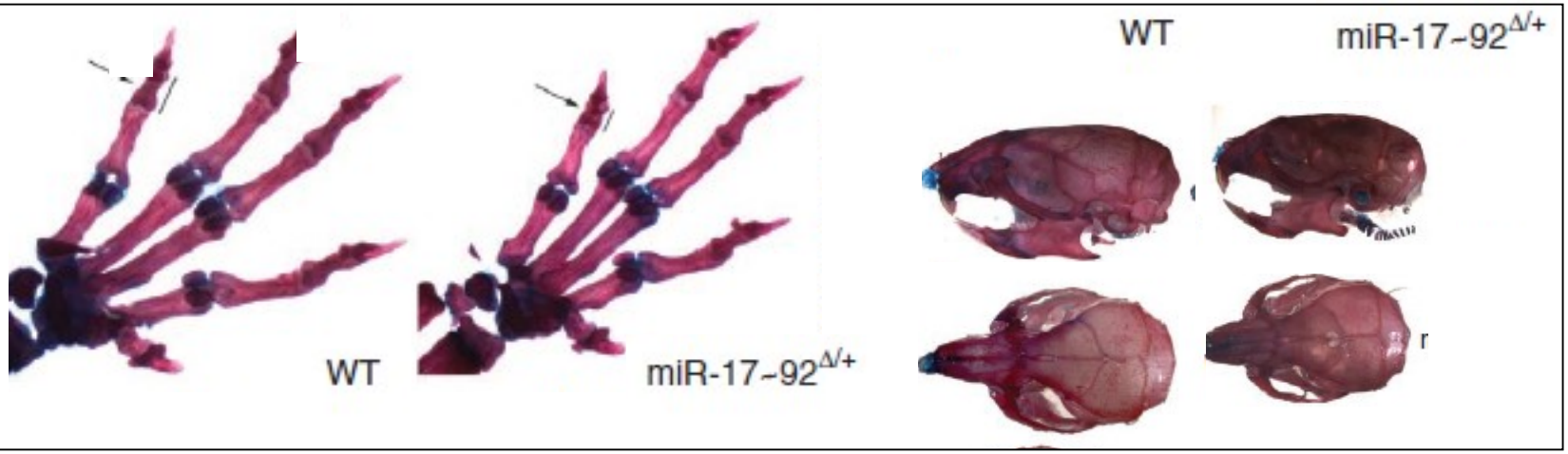


Osada and Takahashi. ***Cancer Sci*** 2010

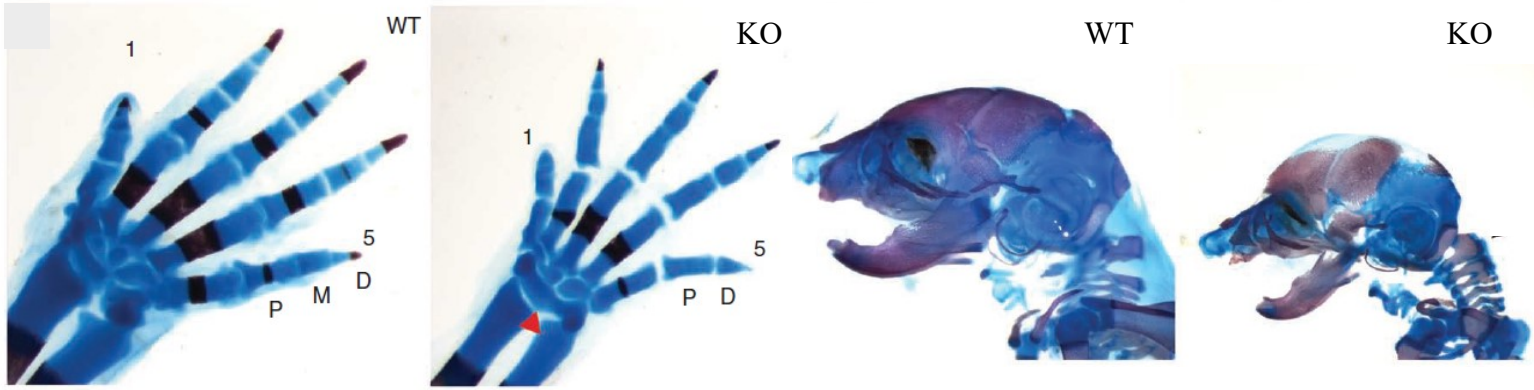
Mice Models

	Mycn $^{\Delta/\Delta}$	miR-17~92$^{\Delta/\Delta}$	*Mycn* $^{9a/9a\ **}$, Mycn$^{Lneo/Plox}$
Small from	E10.5	E13.5	E12.5
Lethal at	E11.5	P0	P0
Brain	small, abnl	small, nl	small, nl
Limbs	poor dev	abnormal patterning	ND
Lung	no branching	nl branching	reduced branching
Heart	VSD	VSD, DORV	nl
Gut	no midgut derivatives	nl	nl
Kidney	disorganised	nl	nl
Other		vertebral fusion	vertebral fusion reduced spleen

Adult mice



E18.5 mice



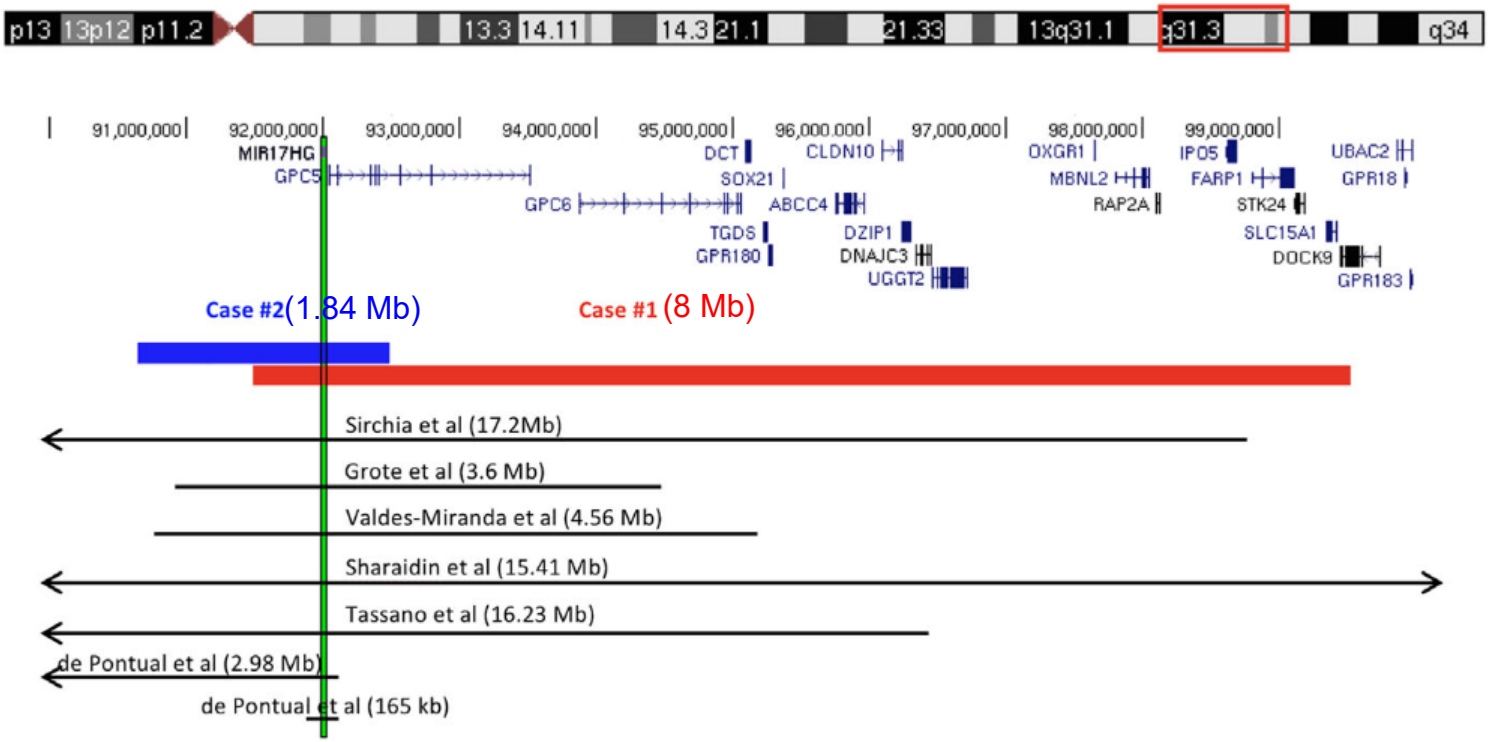


FIGURE 3 Schematic representation of the deletions identified in Patients 1 and 2 and the genes in the region (only those with OMIM phenotype are included), above the deletions reported in the literature. The vertical bar shows the location of *MIR17HG* [Color figure can be viewed at wileyonlinelibrary.com]

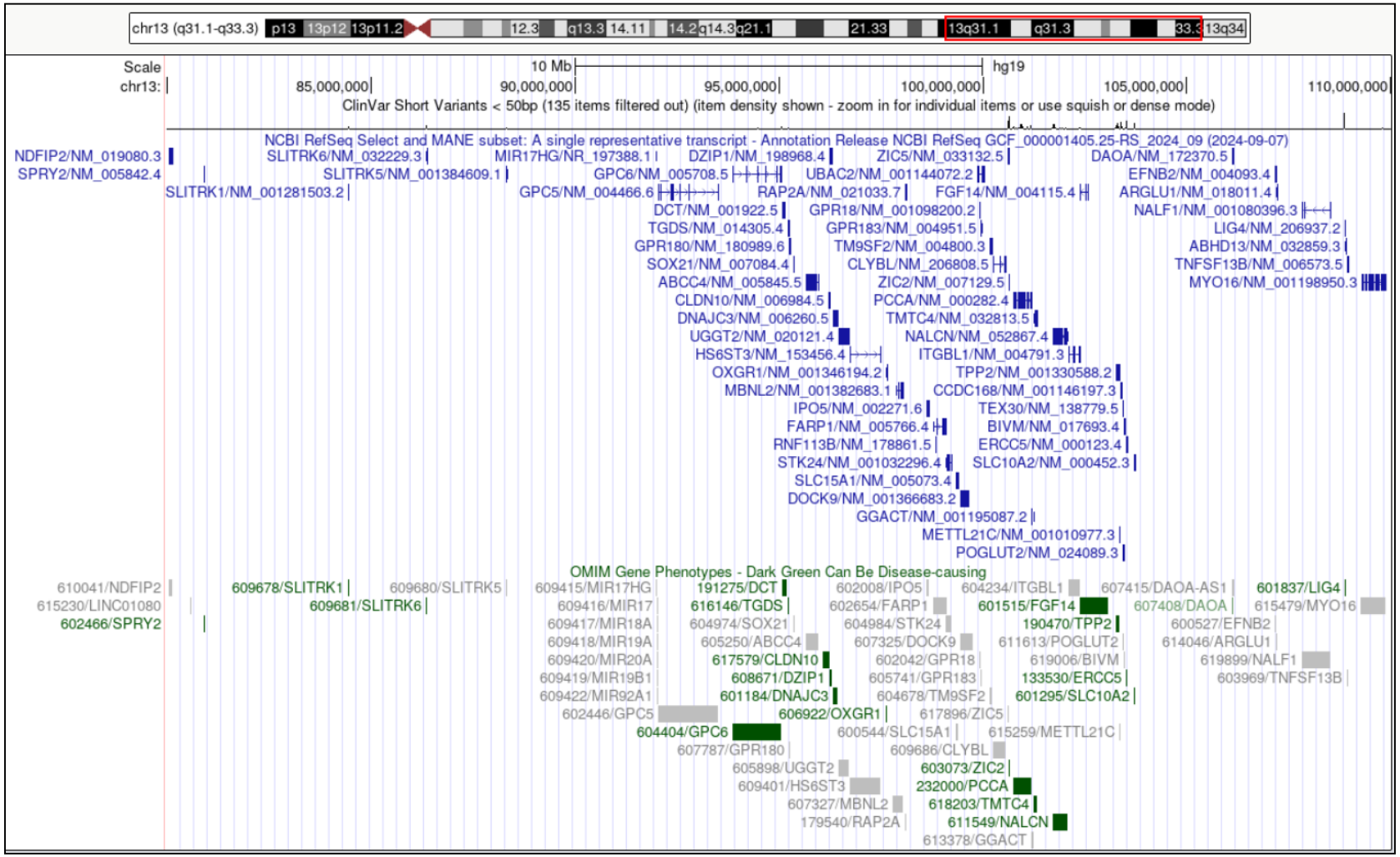
Muriello et al. ***Am J Med Genet*** 2019

TABLE 1 Comparison of reported patients with Feingold syndrome type 2

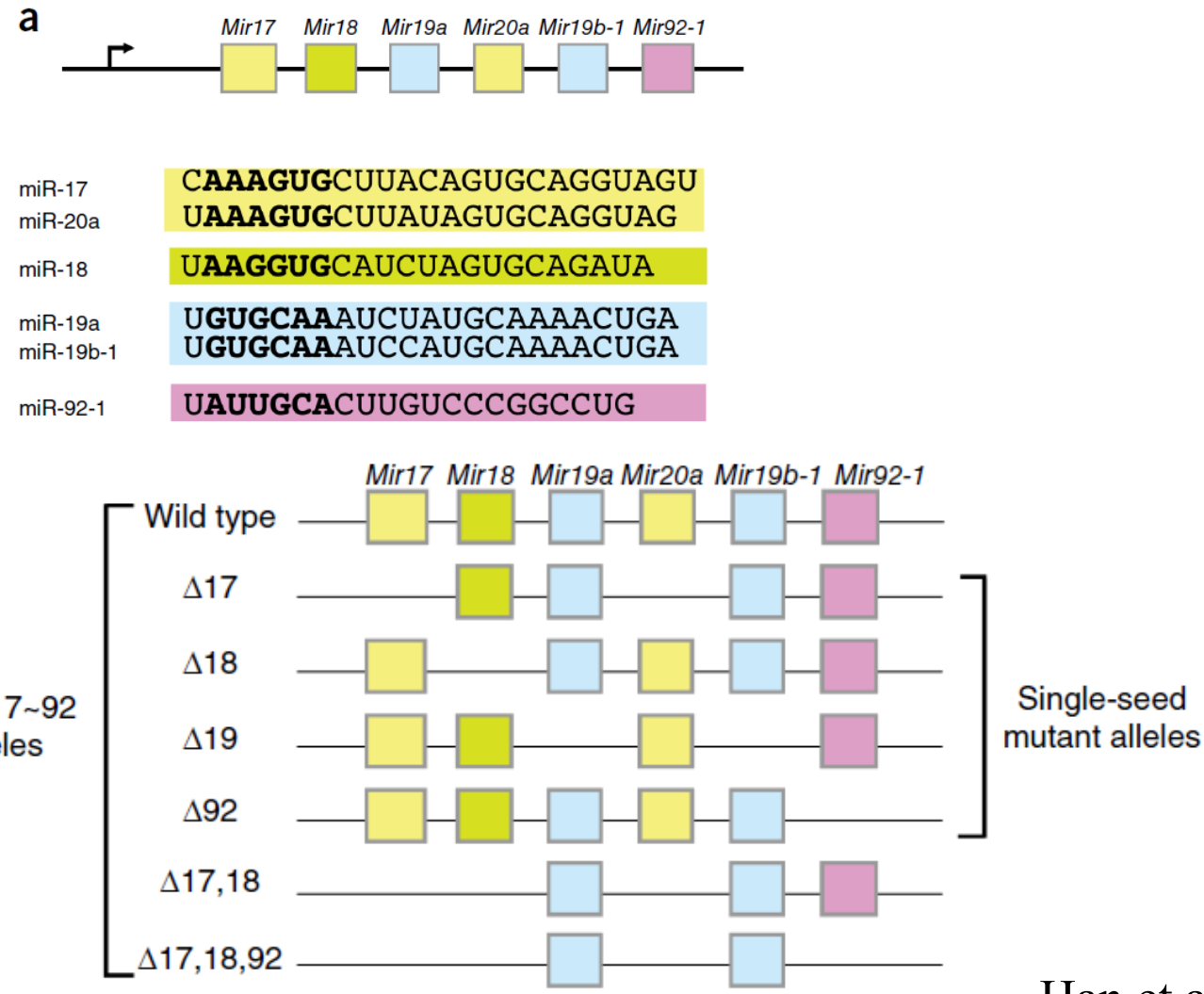
Features	Present study	Muriello et al., 2019	Sirchia et al., 2017	Grote et al., 2015	De Pontual et al., 2011	Sharaidin et al., 2013	Tassano et al., 2013	Valdes-Miranda et al., 2014	Low et al., 2015	Ganjavi et al., 2014	DECIPHER cases
Number of patients	1	3	1	1	5	1	1	1	1	1	6
Deletion size	4.8 Mb	1.84 Mb–8 Mb	17.2 Mb	3.6 Mb	165 kb–2.98 Mb	15.41 Mb	16.23 Mb	4.56 Mb	3 Mb	7.4 Mb	180 kb-5.28 Mb
Gender	Female	3 Male	Female	Male	3 Female, 2 Male	Female	Female	Female	Male	Female	3 Female, 2 Male, 1 NR
Microcephaly	Y	2/3	Y	N	5/5	Y	Y	Y	Y	Y	4/6 (2 NR)
DD/ID/LD	Y	3/3	Y	Y	5/5	Y	Y	N	Y	Y	4/6 (2 NR)
Skeletal features											
Short stature	Y	2/3	Y	Y	3/5(1 NR)	Y	Y	Y	Y	Y	3/6 (3 NR)
Brachymesophalangy	Y	3/3	Y	Y	5/5	Y	Y	Y	Y	Y	5/6 (1 NR)
5th finger clinodactyly	Y	3/3	Y	Y	5 NR	Y	Y	Y	Y	Y	2/6 (4 NR)
Thumbs anomalies	Left thumb polysyndactyly[a]	0/3	NR	N	3/5	N	N	N	N	N	1/6 (5 NR)
Toes anomalies	Brachydactyly, first toe, bilateral	Syndactyly, 2/3	Brachydactyly	Syndactyly, 8/16 (3 NR)	Syndactyly 5/5	N	N	N	N	Syndactyly	Syndactyly, 3/6 (3 NR)
Cardiac anomalies	N	2/3	N	Y	0/5	NR	NR	Y	Y	NR	1/6 (5 NR)
Gastrointestinal atresia	N	0/3	N	N	0/5	N	N	N	N	N	0/6
Hearing loss	N	0/3	N	Y	5 NR	NR	NR	Y	NR	NR	6 NR

Abbreviations: DD, developmental delay; ID, intellectual disability; LD, learning disability.
[a]Wassel's classification type IV; NR, not reported.

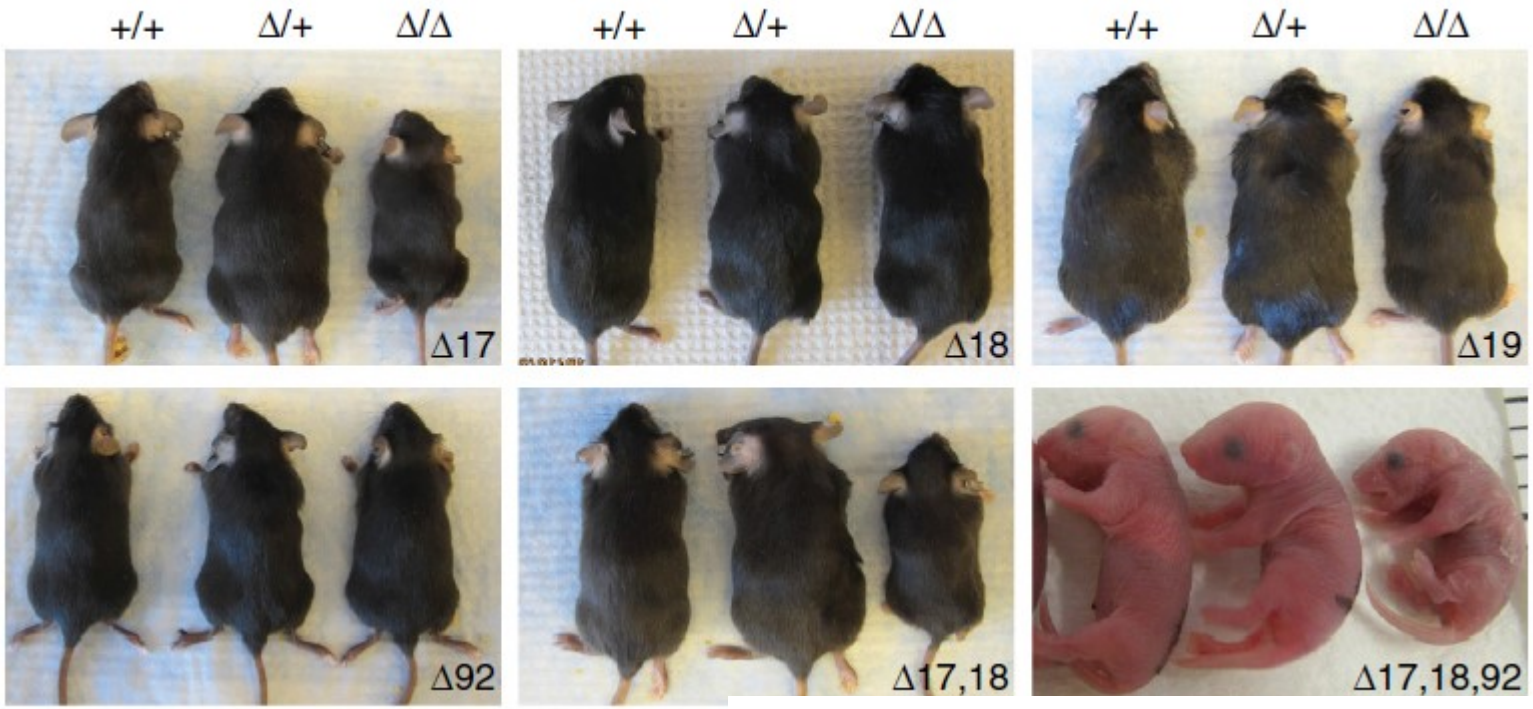
Lei et al. ***Am J Med Genet*** 2021


chr13 (q31.1-q33.3)
p13
13p12
13p11.2
12.3
q13.3
14.11
14.2
q14.3
q21.1
21.33
13q31.1
q31.3
33.3
13q34
Scale
10 Mb
hg19
chr13:
85,000,000
90,000,000
95,000,000
100,000,000
105,000,000
110,000,000
ClinVar Short Variants < 50bp (135 items filtered out) (item density shown - zoom in for individual items or use squish or dense mode)
NCBI RefSeq Select and MANE subset: A single representative transcript - Annotation Release NCBI RefSeq GCF_000001405.25-RS_2024_09 (2024-09-07)
NDFIP2/NM_019080.3
SPRY2/NM_005842.4
SLITRK6/NM_032229.3
SLITRK5/NM_001384609.1
SLITRK1/NM_001281503.2
MIR17HG/NR_197388.1
DZIP1/NM_198968.4
GPC6/NM_005708.5
GPC5/NM_004466.6
ZIC5/NM_033132.5
UBAC2/NM_001144072.2
RAP2A/NM_021033.7
FGF14/NM_004115.4
DAOA/NM_172370.5
EFNB2/NM_004093.4
ARGLU1/NM_018011.4
NALF1/NM_001080396.3
DCT/NM_001922.5
GPR18/NM_001098200.2
TGDS/NM_014305.4
GPR183/NM_004951.5
LIG4/NM_206937.2
GPR180/NM_180989.6
TM9SF2/NM_004800.3
ABHD13/NM_032859.3
SOX21/NM_007084.4
CLYBL/NM_206808.5
TNFSF13B/NM_006573.5
ABCC4/NM_005845.5
ZIC2/NM_007129.5
MYO16/NM_001198950.3
CLDN10/NM_006984.5
PCCA/NM_000282.4
DNAJC3/NM_006260.5
TMTC4/NM_032813.5
UGGT2/NM_020121.4
NALCN/NM_052867.4
HS6ST3/NM_153456.4
ITGBL1/NM_004791.3
OXGR1/NM_001346194.2
TPP2/NM_001330588.2
MBNL2/NM_001382683.1
CCDC168/NM_001146197.3
IPO5/NM_002271.6
TEX30/NM_138779.5
FARP1/NM_005766.4
BIVM/NM_017693.4
RNF113B/NM_178861.5
ERCC5/NM_000123.4
STK24/NM_001032296.4
SLC10A2/NM_000452.3
SLC15A1/NM_005073.4
DOCK9/NM_001366683.2
GGACT/NM_001195087.2
METTL21C/NM_001010977.3
POGLUT2/NM_024089.3
OMIM Gene Phenotypes - Dark Green Can Be Disease-causing
610041/NDFIP2
615230/LINC01080
602466/SPRY2
609678/SLITRK1
609681/SLITRK6
609680/SLITRK5
609415/MIR17HG
609416/MIR17
609417/MIR18A
609418/MIR19A
609420/MIR20A
609419/MIR19B1
609422/MIR92A1
602446/GPC5
191275/DCT
616146/TGDS
604974/SOX21
605250/ABCC4
617579/CLDN10
608671/DZIP1
601184/DNAJC3
606922/OXGR1
604404/GPC6
607787/GPR180
605898/UGGT2
609401/HS6ST3
607327/MBNL2
179540/RAP2A
602008/IPO5
602654/FARP1
604984/STK24
607325/DOCK9
602042/GPR18
605741/GPR183
604678/TM9SF2
600544/SLC15A1
609686/CLYBL
603073/ZIC2
232000/PCCA
618203/TMTC4
611549/NALCN
613378/GGACT
604234/ITGBL1
601515/FGF14
190470/TPP2
611613/POGLUT2
617896/ZIC5
601295/SLC10A2
615259/METTL21C
607415/DAOA-AS1
607408/DAOA
601837/LIG4
615479/MYO16
600527/EFNB2
614046/ARGLU1
619006/BIVM
619899/NALF1
603969/TNFSF13B

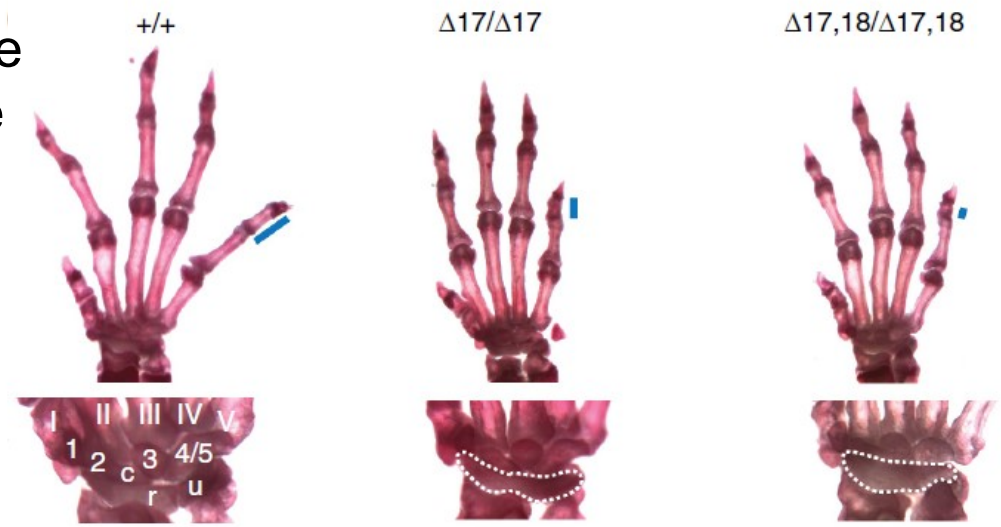
An allelic series of miR-17~92–mutant mice uncovers functional specialization and cooperation among members of a microRNA polycistron



Han et al. ***Nature Genet*** 2015

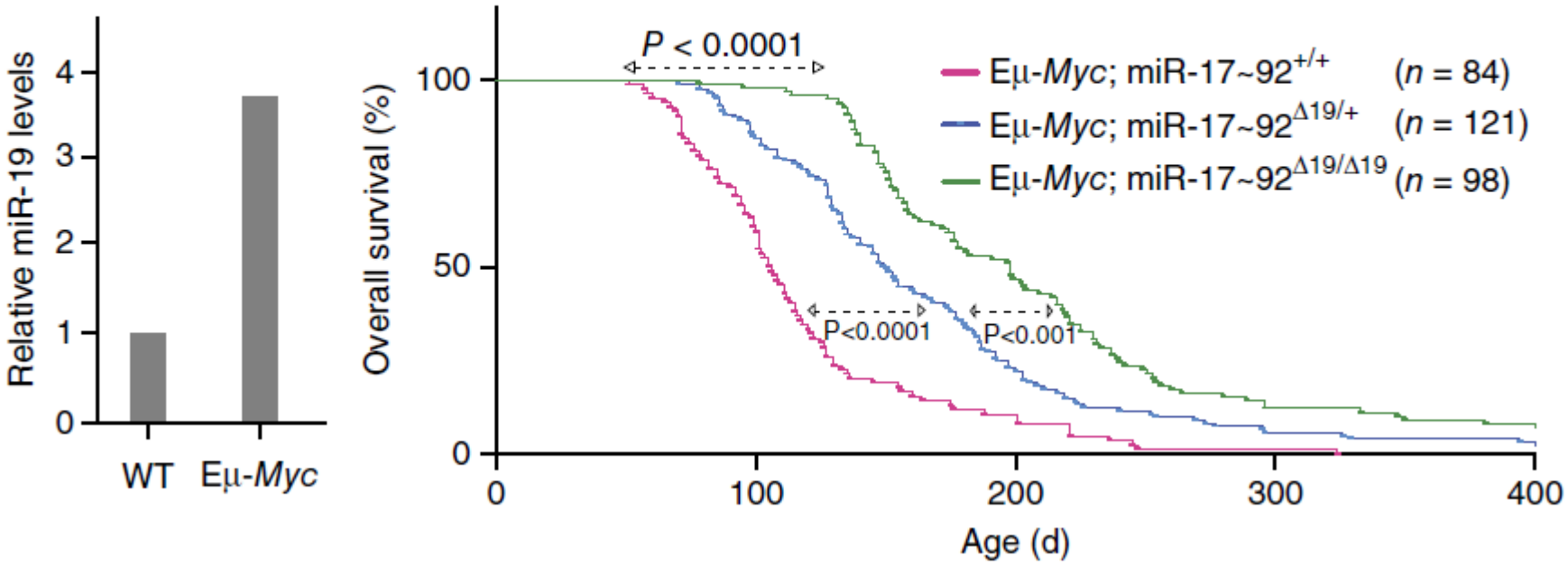


Rôle de miR17 dans la croissance
Et le développement du squelette



Han et al. ***Nature Genet*** 2015

miR-19-deficient mice are resistant to MyC-driven tumorigenesis



Han et al. ***Nature Genet*** 2015

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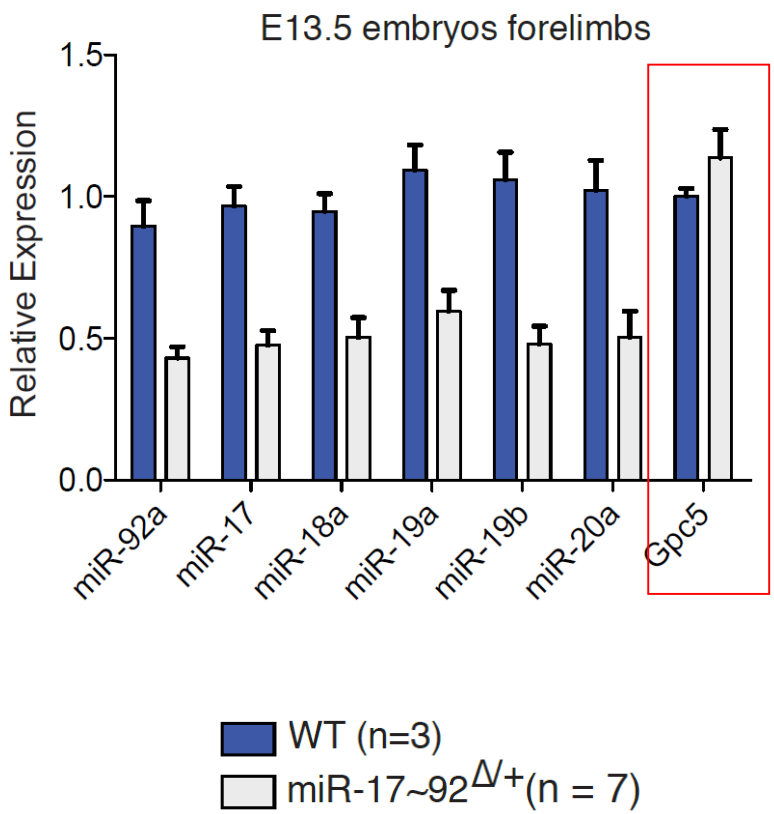
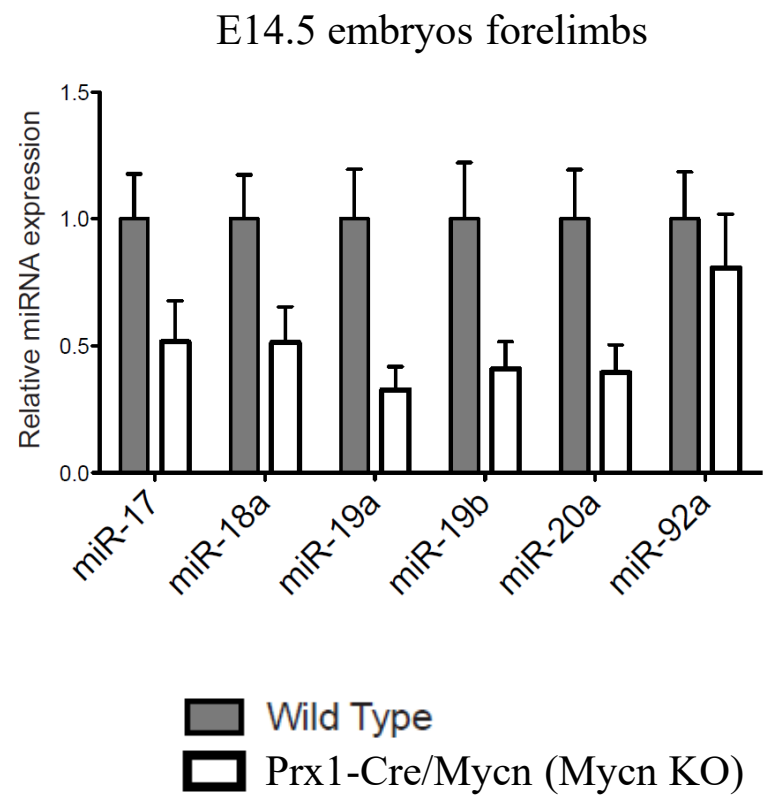
Mature miRs and GPC5 Expression





Ota et al. ***Development*** 2007