

Waarom is de ene Noonan-patient de andere niet?

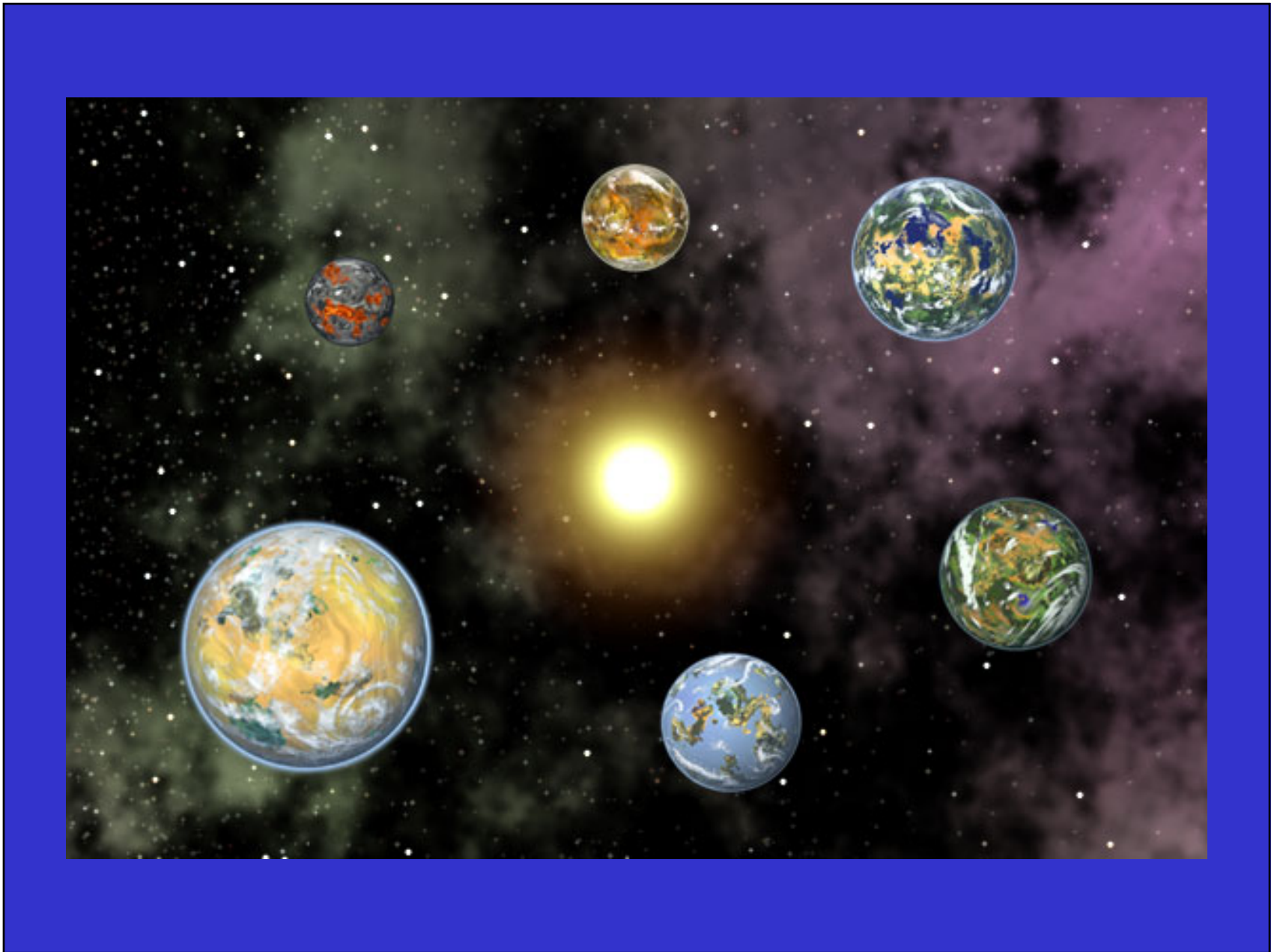
Marjolijn Jongmans

22-11-2003

NS scoring system

Van der Burgt et al. Am J Med Genet 53:187-191 (1994)

Finding	A = major	B = minor
1 Facial	Typical face	Suggestive face
2 Cardiac	PVS and/or typical ECG	Other defect
3 Height	<P3	<P10
4 Chest wall	Pectus car./exc. 2	Broad thorax 3
5 Family history	First degree relative definite NS	First degree relative suggestive NS
6 Other	All 3 (males): MR, cryptorchidism, lymphatic dysplasia	One of MR, cryptorchidism, lymphatic dysplasia







Inhoud

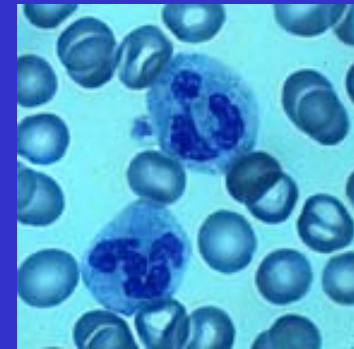
- DNA-onderzoek
- Noonan-gen en -eiwit
- Kenmerken van het Noonan-syndroom
- Genotype / fenotype
- Mijn onderzoek



DNA-onderzoek



Bloed



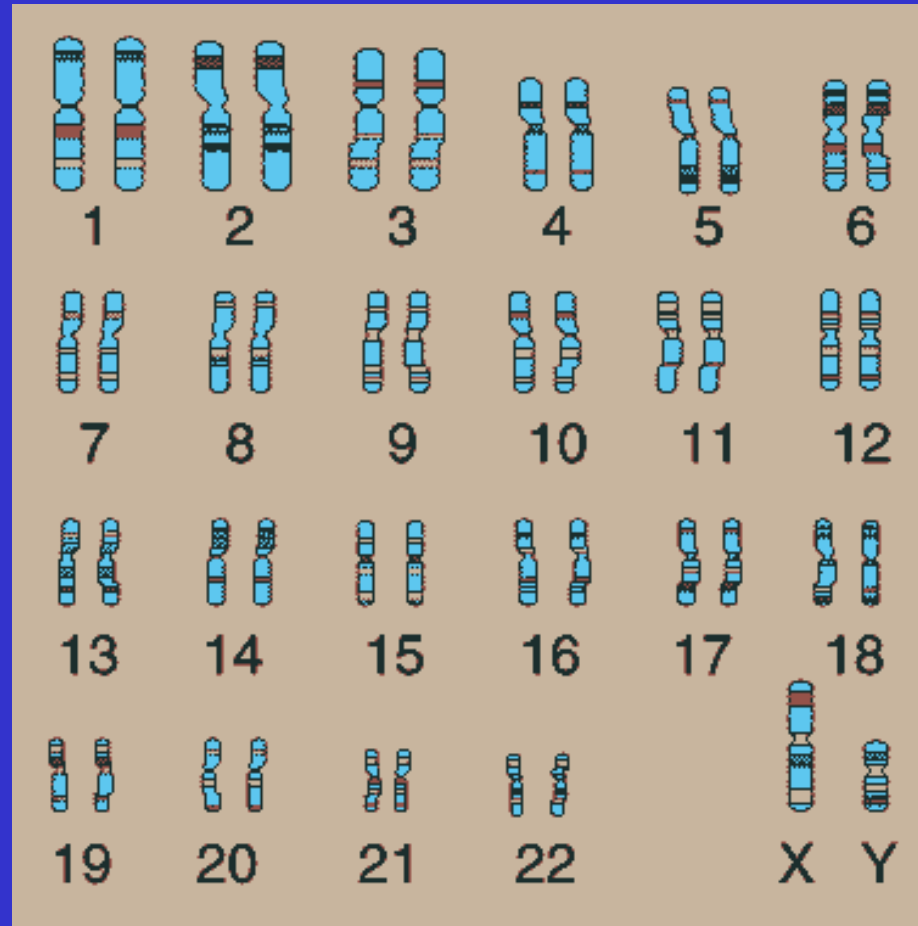
Cellen



Chromosomen

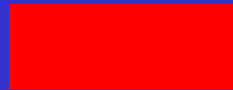
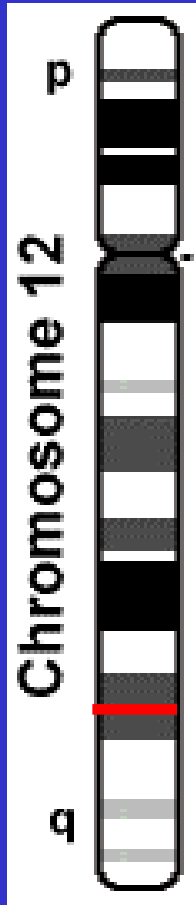


Chromosomen





Chromosoom 12

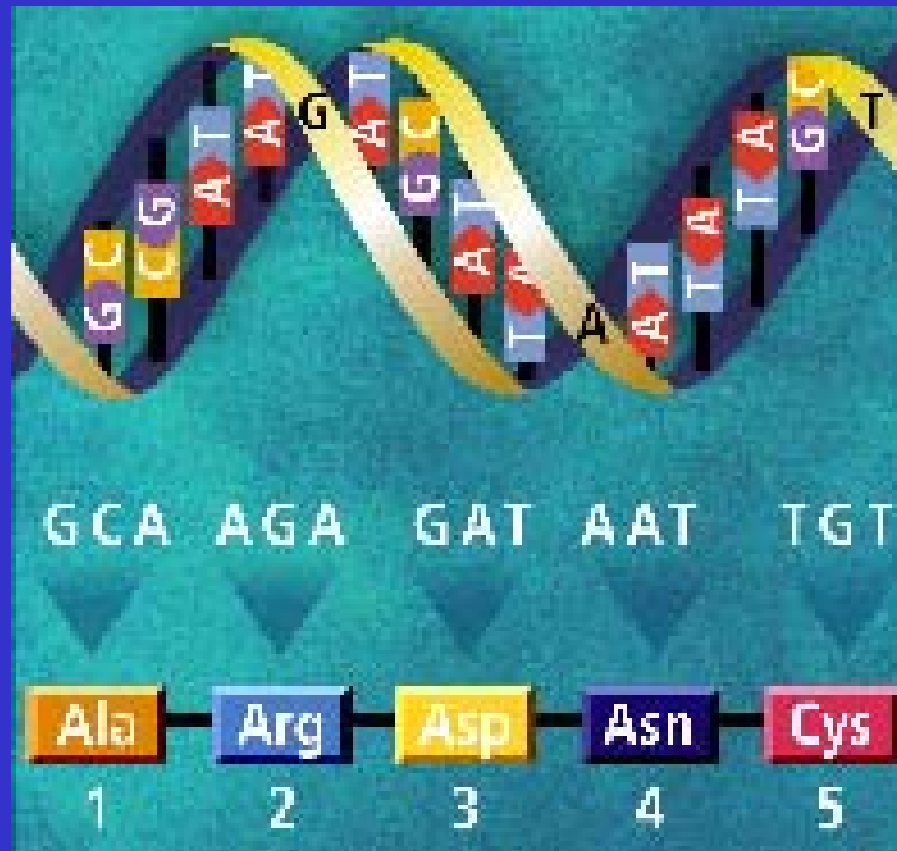


DNA

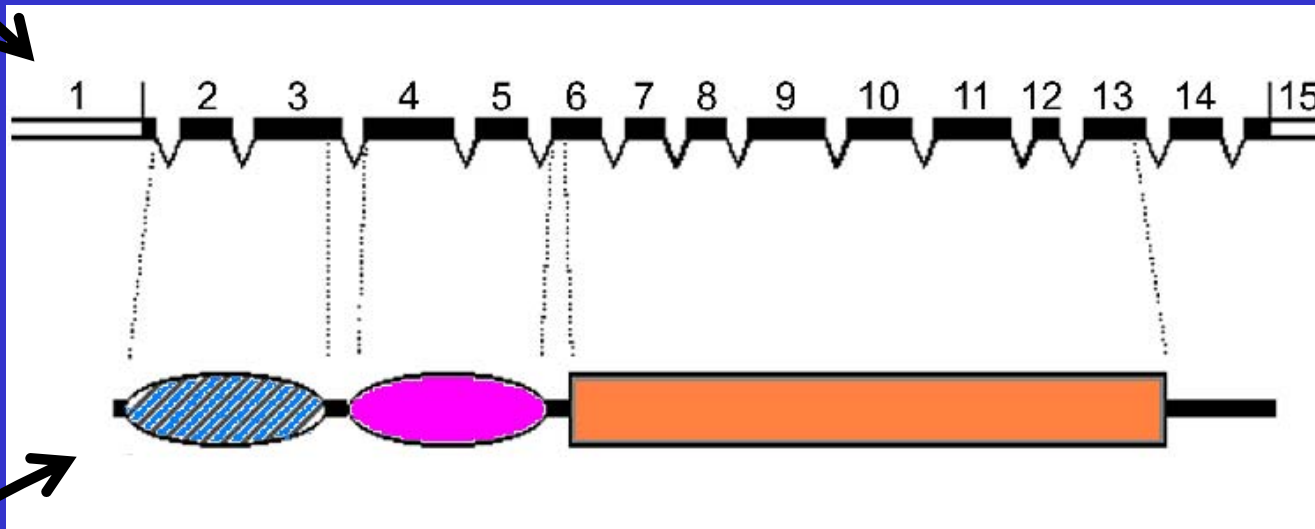
Noonan - gen



DNA



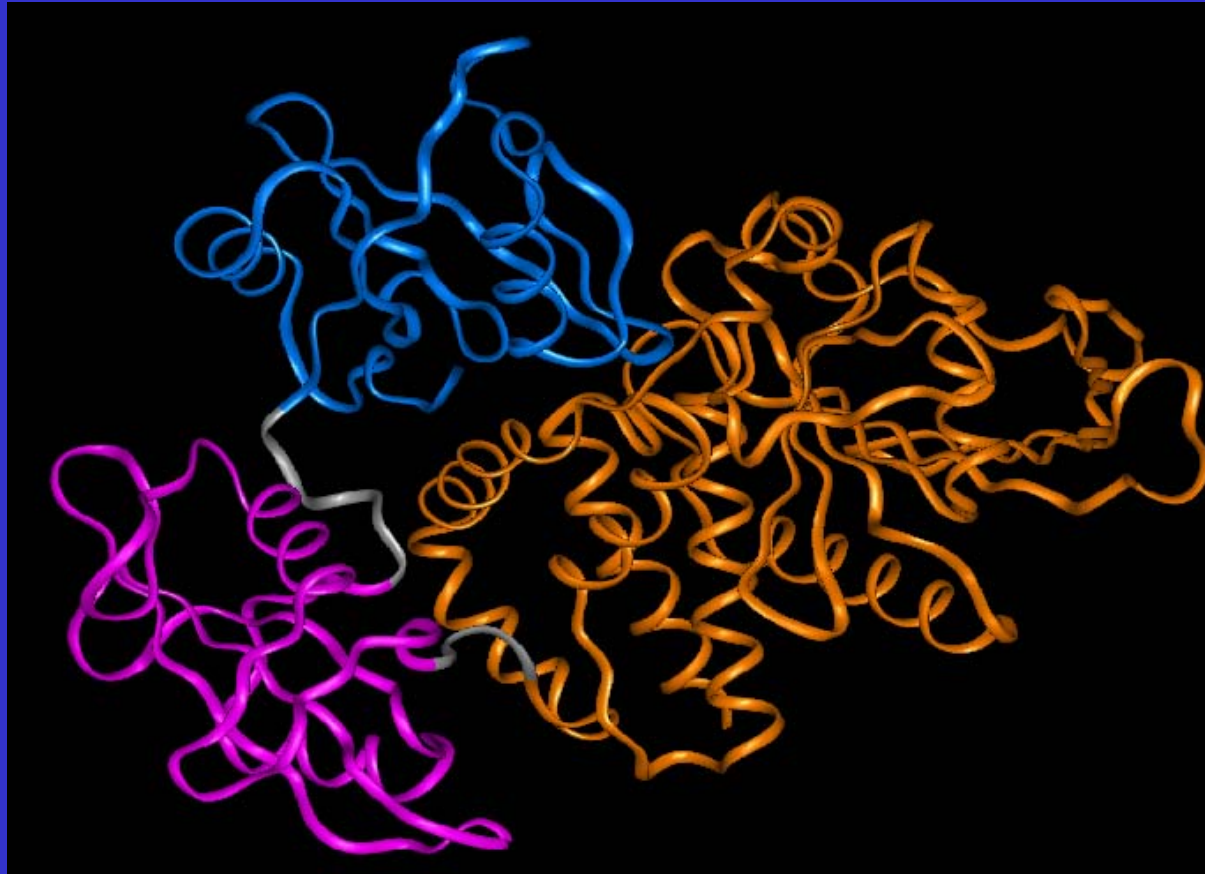
Noonan - gen



Noonan - eiwit



Noonan - eiwit

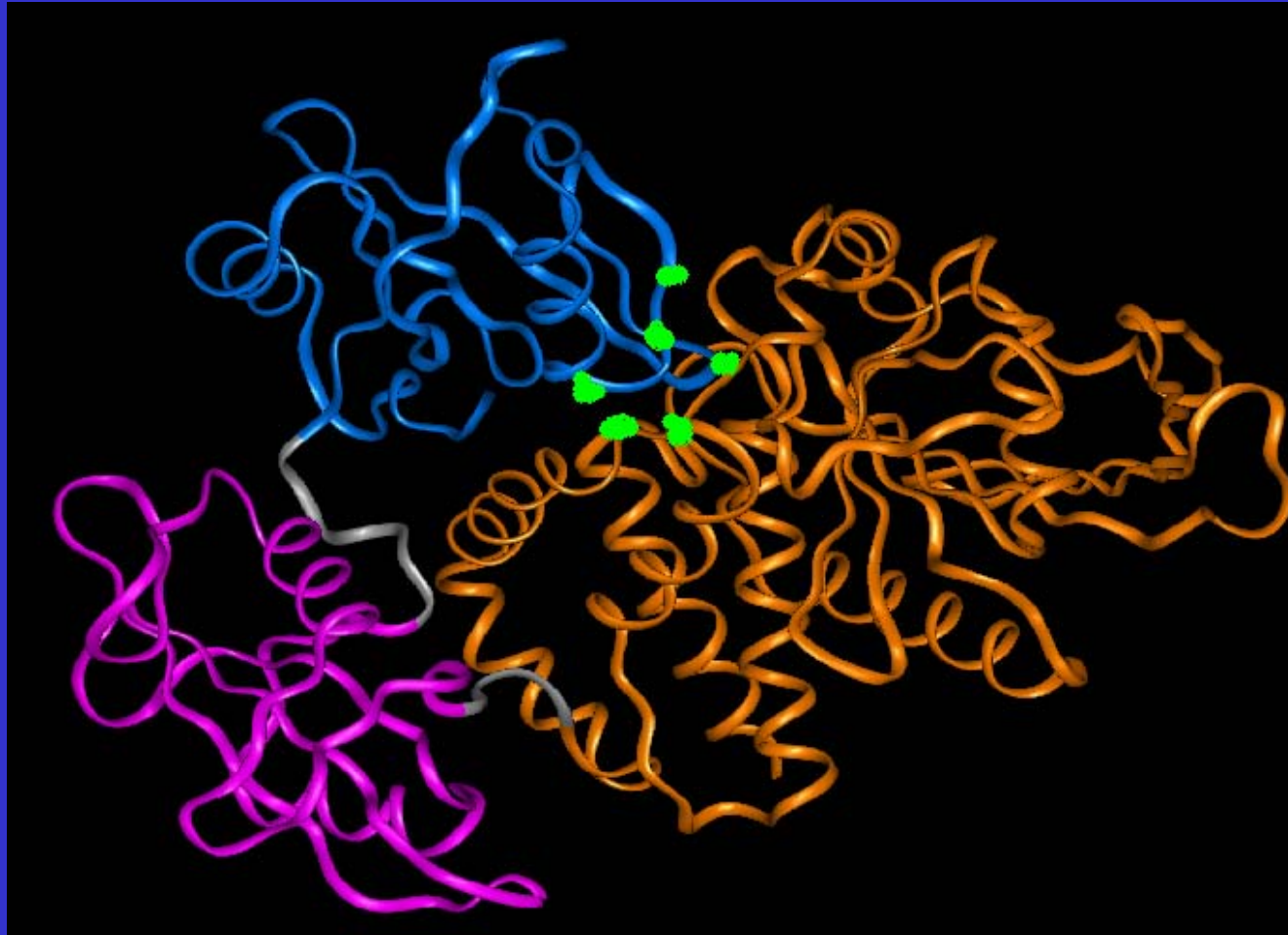




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 CTG TTG ACA AGA GGA GTT GAT GGC AGT TTT TTG GCA AGG CCT AGT AAA AGT AAC CCT
 GGA GAC TTC ACA CTT TCC GTT AGA AGA AAT GGA GCT GTC ACC CAC ATC AAG ATT CAG
 AAC ACT GGT GAT TAC TAT GAC CTG TAT GGA GGG GAG AAA TTT GCC ACT TTG GCT GAG
 TTG GTC CAG TAT TAC ATG GAA CAT CAC GGG CAA TTA AAA GAG AAG AAT GGA GAT GTC
 ATT GAG CTT AAA TAT CCT CTG AAC TGT GCA GAT CCT ACC TCT GAA AGG TGG TTT CAT
 GGA CAT CTC TCT GGG AAA GAA GCA GAG AAA TTA TTA ACT GAA AAA GGA AAA CAT GGT
 AGT TTT CTT GTA CGA GAG AGC CAG AGC CAC CCT GGA GAT TTT GTT CTT TCT GTG CGC
 ACT GGT GAT GAC AAA GGG GAG AGC AAT GAC GGC AAG TCT AAA GTG ACC CAT GTT ATG
 ATT CGC TGT CAG GAA CTG AAA TAC GAC GTT GGT GGA GGA GAA CGG TTT GAT TCT TTG
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 CTA CAA CTC AAG CAG CCC CTT AAC ACG ACT CGT ATA AAT GCT GCT GAA ATA GAA AGC
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 GAG GGT CAA AGG CAA GAA AAC AAA AAC AAA AAT AGA TAT AAA AAC ATC CTG CCC TTT
 GAT CAT ACC AGG GTT G C CTA CAC GAT GGT GAT CCC AAT GAG CCT GTT TCA GAT TAC
 ATC AAT GCA AAT ATC ATG C C T GAA TTT GAA ACC AAG TGC AAC AAT TCA AAG CCC
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 CGG ATG GTG TTC CAA GAA AAC TCC CGA GTG ATT GTC ATG ACA ACG AAA GAA GTG GAG
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 GAA CTT AAA CTT TCA AAG GTT GGA CAA GGG AAT ACG GAG AGA ACG GTC TGG CAA TAC
 CAC TTT CGG ACC TGG CCG GAC CAC GGC GTG CCC AGC GAC CCT GGG GGC GTG CTG
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 CTT ATT GAC ATC ATC AGA GAG AAA GGT GTT GAC TGC GAT ATT GAC GTT CCC AAA ACC
 ATC CAG ATG GTG CGG TCT CAG AGG TCA GGG ATG GTC CAG ACA GAA GCA CAG TAC CGA
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 GAC CAG ACG AGT GGA GAT CAG AGC CCT CTC CCG CCT TGT ACT CCA ACG CCA CCC TGT
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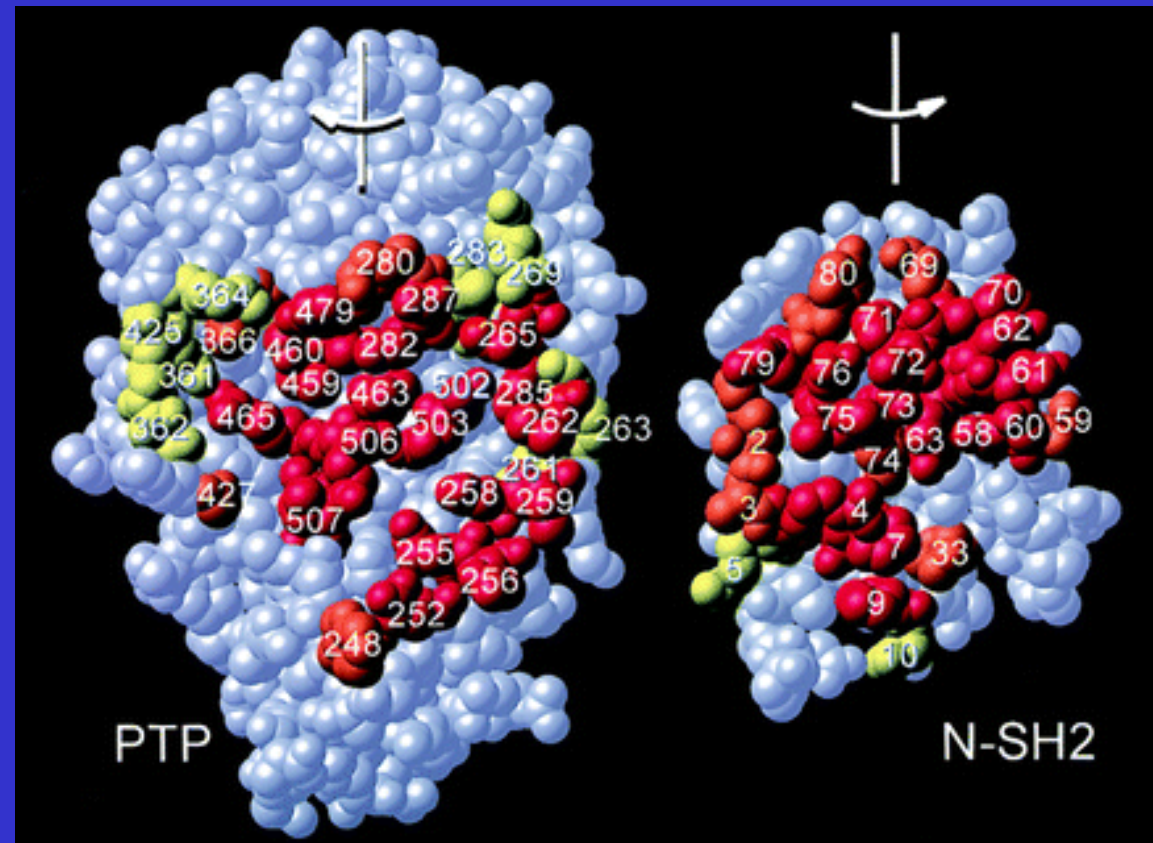


Noonan - eiwit



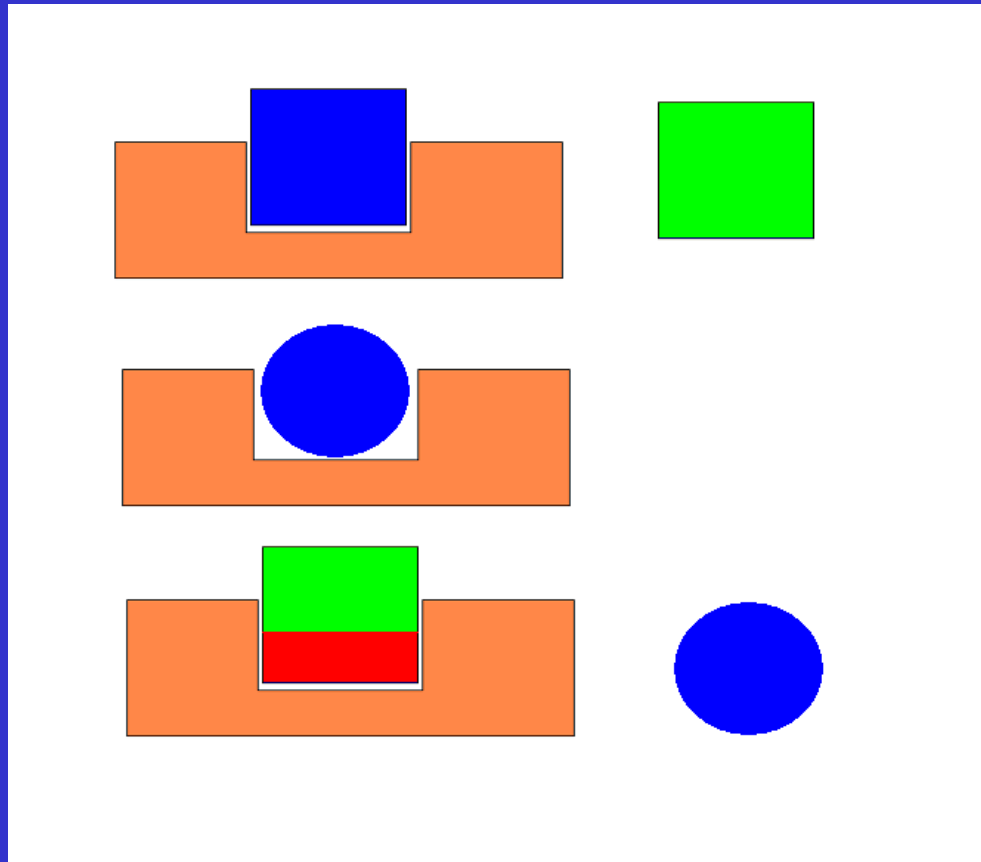


Een kijkje in het Noonan-eiwit





Gevolg van foutjes in het Noonan-eiwit



**Het eiwit
werkt te
hard!!**

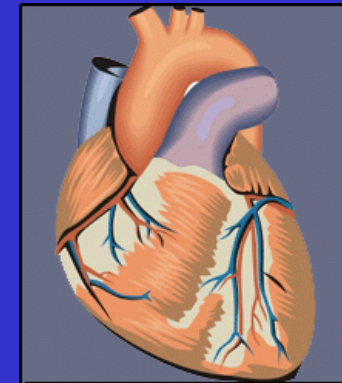


Veel werk voor het Noonan- eiwit.....



Kenmerken van het Noonan-syndroom

- Kenmerkend gezichtje
- Klein
- Vernauwing van de longslagader
- Slechte eters
- Afwijkende borst



Kenmerken van het Noonan-syndroom

- Moeite met leren
- Snel blauwe plekken
- Niet indalen van de testikels



Vertoont iemand met het Noonan-syndroom al deze kenmerken?



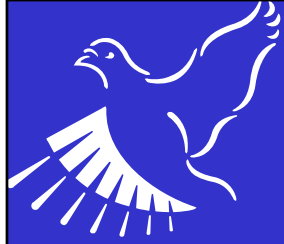
Genotype / Fenotype

Genotype:



Fenotype:





Zelfde genotype.....



zelfde fenotype!



Zelfde genotype.....



**Niet helemaal hetzelfde
fenotype!**

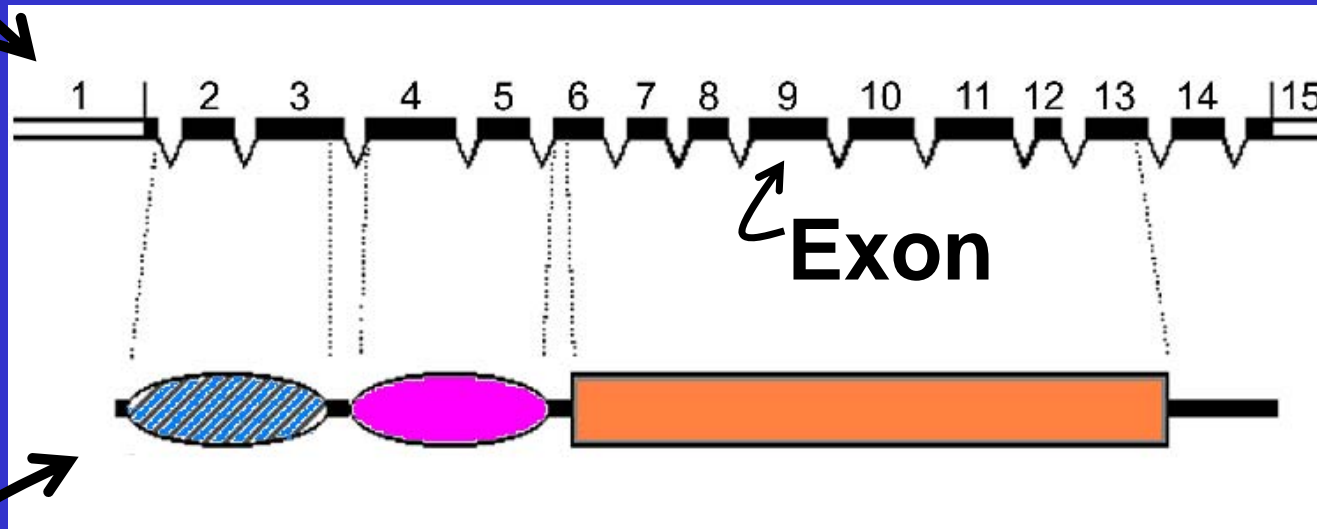


Verschillend genotype.....

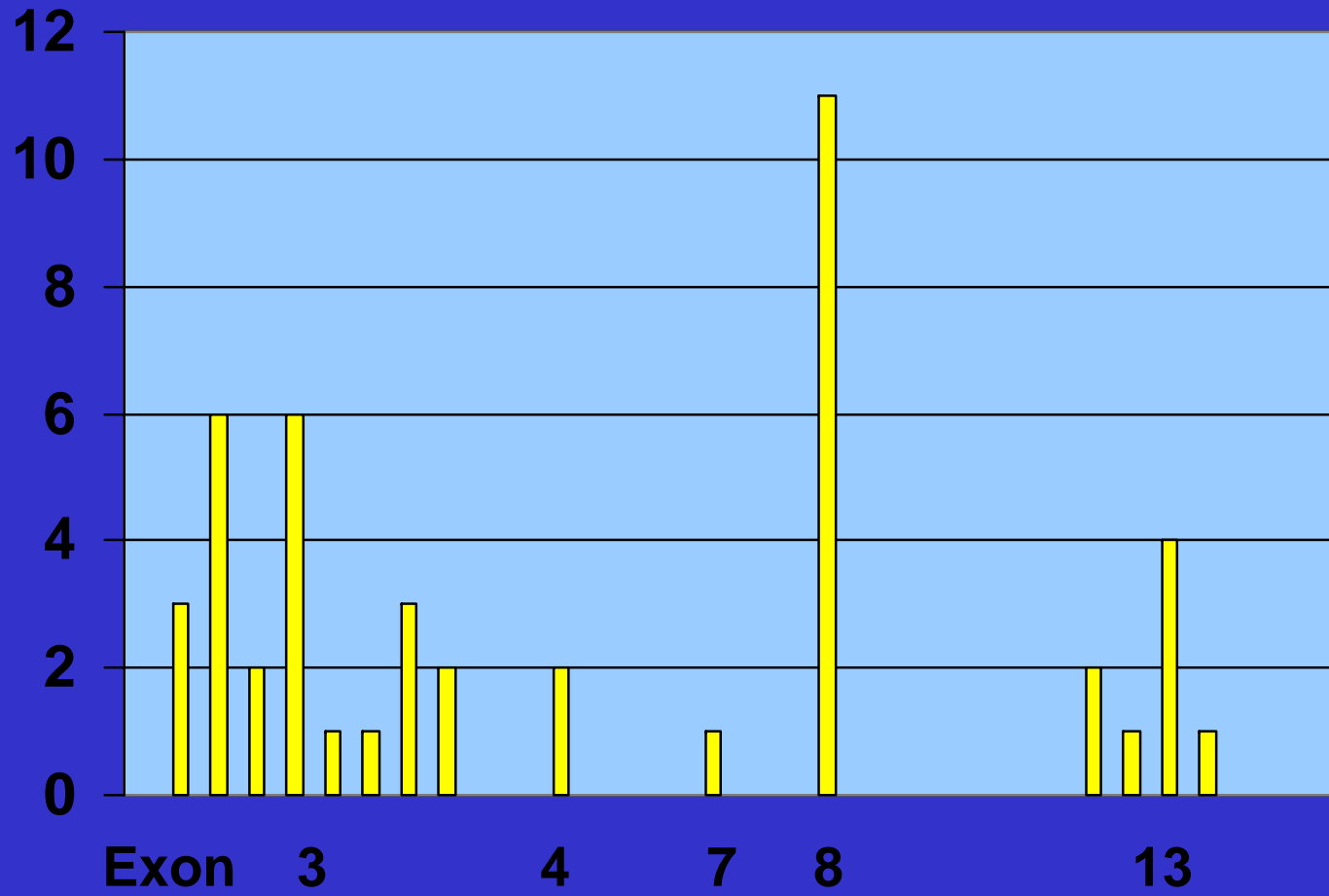


**Toch een beetje hetzelfde
fenotype!**

Noonan - gen



Noonan - eiwit

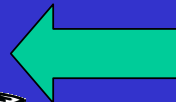
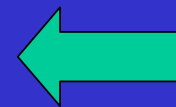
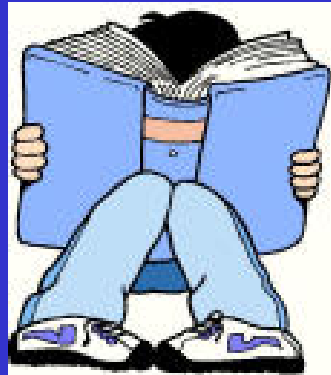


Genotype-phenotype correlation in patients with Noonan-syndrome and a mutation in PTPN11



Marjolijn Jongmans

Onderzoek doen



Kenmerken	Exon	→	3	8	13
↓			(26)	(12)	(8)
Typisch gezicht			92	92	75
Klein			77	83	25
Vernauwing van de longslagader			69	58	75
Slechte eters			65	50	88
Afwijkende borst			54	50	25
Moeite met leren			62	33	50
Snel blauwe plekken			65	75	50
Testikels			94	100	71

