Barth Syndrome Foundation
2006 Scientific/Medical & Family Conference

Session:

JEANS TO GENES OVERVIEW: WHAT'S IN YOUR GENES?

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Thursday, July 6

- **Each individual is unique -- we are loaded with differences that make us unique**

- **Differences are coded for in our DNA:**

- **Many changes in DNA do not cause disease and are usually located in space between genes, although some are within genes**

- **A few changes in DNA cause disease These are usually located within the genes or very close to them**

- **Genes do not exist or act in a vacuum: they, and their products, interact with other genes and their products -- they “network”**

- **Some genes have more than 1 function**

- **Some genes work only in some tissues, some in all tissues or organs**

- **Some genes only work at specific times during our development and lifetime, while some work all the time**

Just like genes, people do not live in a vacuum but they interact with their environment and are affected by it

- How do various foods affect them?
- How do infectious agents affect them?
- How do weather and pollutants affect them?
- How does activity affect them?
- How do medications affect them?

When there is disease,

Is it environmentally caused?
Like an infectious disease,
or something you ate,
or an allergy ?

Or is it intrinsic to the individual?

Is it genetic?

Our health is a manifestation of

how well our genes are working

and

how well we get along with our environment

“NATURE and NURTURE”

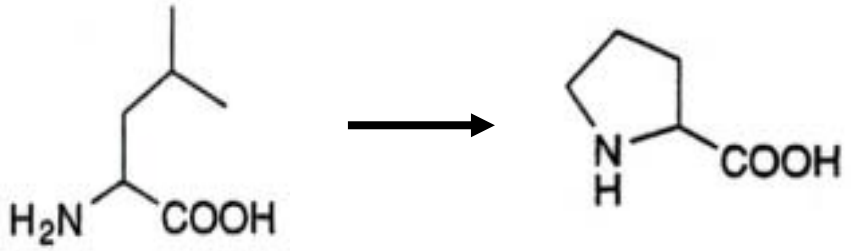
All amino acid substitution mutations found occur at invariant & conserved positions in tafazzin protein

Exon 2	50 *a	51 *t	52	53	54 *a	55 *t	56	57 *a,fs	58	59	60
HU	CTG leu	TAC tyr	GAG glu	CTC leu	ATC ile	GAG glu	AAG lys	CGA arg	GGC gly	CCG pro	GCC ala
CH/GO	CTG leu	TAC tyr	GAG glu	CTC leu	ATC ile	GAG glu	AAC asn	CGA arg	GGC gly	CCG pro	GCC ala
OR / GI	CTG leu	TAC tyr	GAG glu	CTC leu	ATC ile	GAG glu	AAC asn	CGA arg	GGC gly	CCG pro	GCC ala
RH/PAT	CTG leu	TAC tyr	GAG glu	CTC leu	ATC ile	GAG glu	AAC asn	CGA arg	GGC gly	CCG pro	GCC ala
SQM	CTG leu	TAT tyr	GAG glu	CTC leu	ATT ile	GAG glu	AAC asn	CGA arg	GGC gly	CCG pro	GCC ala
MO	CTG leu	TAT tyr	GAG glu	CTC leu	ATT ile	GAG glu	AAC asn	CGA arg	GGC gly	CCT pro	GCC ala
RA	CTG leu	TAC tyr	GAG glu	CTC leu	ATC ile	GAG glu	AAC asn	CGA arg	GGT gly	CCT pro	GCG ala
BOS	CTG leu	TAC tyr	GAG glu	CTC leu	ATC ile	GAG glu	AAC asn	CGA arg	GGC gly	CCA pro	GCC ala
SUS	CTG leu	TAC tyr	GAC asp	CTC leu	ATC ile	GAA glu	AAC asn	CGA arg	GGC gly	CCA pro	GCC ala
Canis	CTG leu	TAT tyr	GAG glu	CTC leu	ATC ile	GAG glu	AAC asn	CGA arg	GGC gly	CCA pro	GCC ala
possum	CTG leu	TAT tyr	GAA glu	CTG leu	ATC ile	GAG glu	AAT asn	CGG arg	GAT asp	CCT pro	GGC gly
Gallus	CTG leu	CAC his	GAG glu	TTG leu	GTG val	GAG glu	CGG arg	CGG arg	GGG gly	CCG pro	CGC arg
XEN	CTG leu	TAT tyr	GAG glu	CTC leu	ATT ile	GAG glu	AAC asn	CGA arg	GGC gly	CCT pro	GCC ala
medaka	TTG leu	TTG leu	AAC asn	CTG leu	ATT ile	GAT asp	CAC his	AGG arg	CCC pro	CCC pro	AAC asn
hapl chil	TTG leu	TTG leu	AAC asn	CTG leu	ATT ile	GAT asp	CAC his	AGG arg	CCC pro	CCC pro	AAC asn
trout	CTA leu	TTTphe	GAC asp	CTG leu	ATA ile	GAC asp	CAA gln	CGT arg	CCA pro	CCT pro	GAC asp
Danio	TTG leu	TTG leu	AAC asn	CTG leu	GTT val	GAT asp	GAG glu	CGT arg	CCT pro	CAG gln	GAC asp

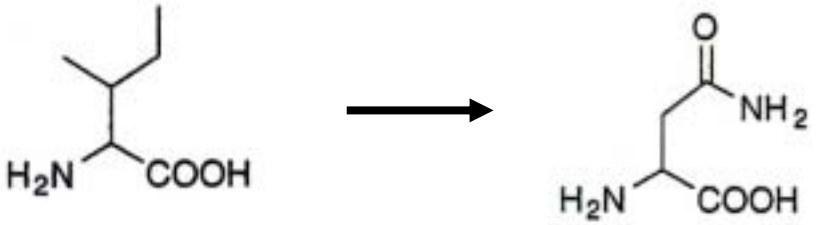
a = amino acid subst, t = STOP codon, fs = frame shift

50: leucine → proline 54: isoleucine → asparagine 57: arginine → leucine

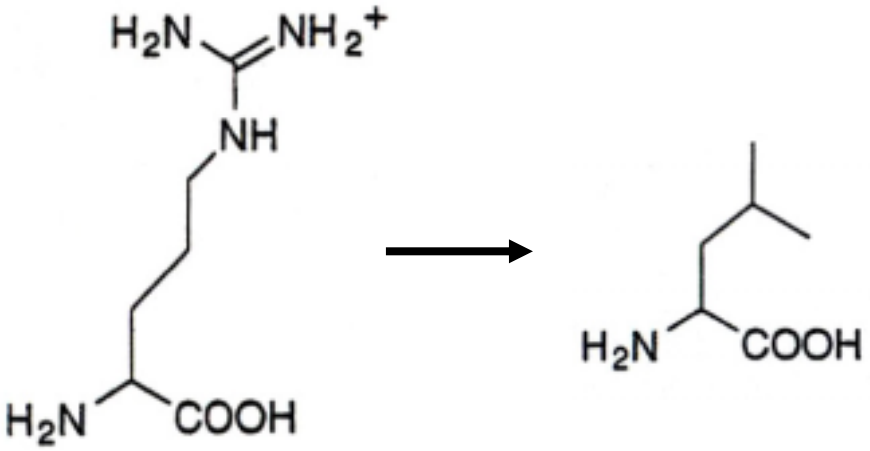
50: leucine → **proline**



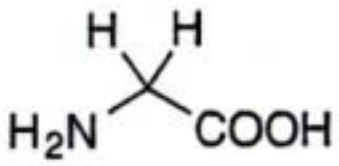
54: isoleucine → **asparagine**



57: arginine → **leucine**

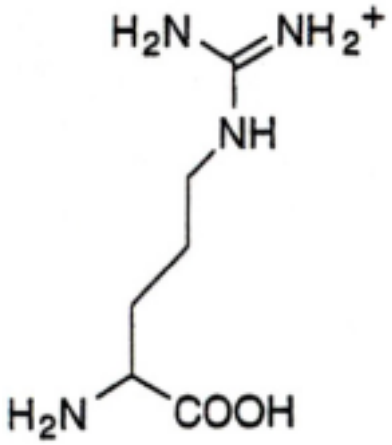


Exon 8

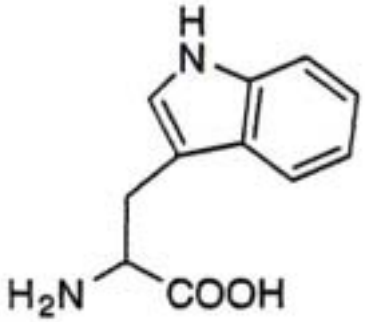


Glycine 197

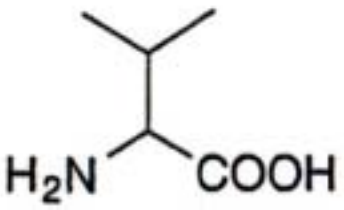
“hotspot”
GGG



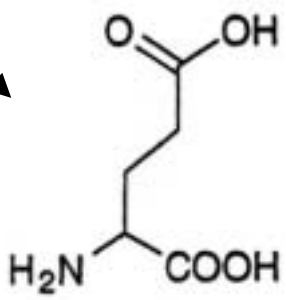
Arginine
AGG



Tryptophan
TGG



Valine
GTG



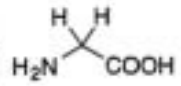
Glutamic
GAG

Amino Acid Structures

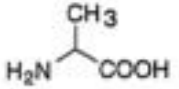
Notice the many different shapes and sizes

Each amino acid is accompanied by its three- and one-letter code, residue molecular weight (actual molecular weight minus water) and side-chain pK_a where appropriate.

Small

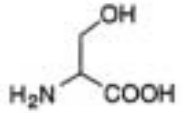


Glycine (Gly, G)
MW: 57.05

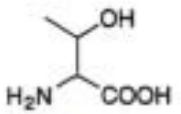


Alanine (Ala, A)
MW: 71.09

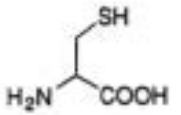
Nucleophilic



Serine (Ser, S)
MW: 87.08, pK_a – 16

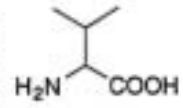


Threonine (Thr, T)
MW: 101.11, pK_a – 16

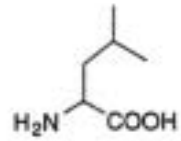


Cysteine (Cys, C)
MW: 103.15, pK_a = 8.35

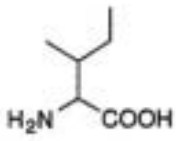
Hydrophobic



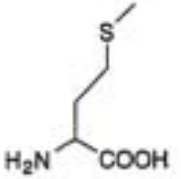
Valine (Val, V)
MW: 99.14



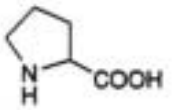
Leucine (Leu, L)
MW: 113.16



Isoleucine (Ile, I)
MW: 113.16

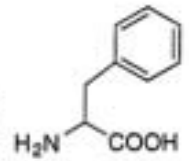


Methionine (Met, M)
MW: 131.19

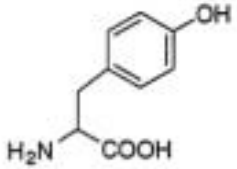


Proline (Pro, P)
MW: 97.12

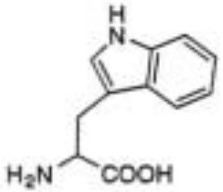
Aromatic



Phenylalanine (Phe, F)
MW: 147.18

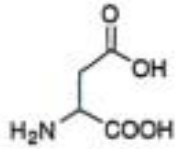


Tyrosine (Tyr, Y)
MW: 163.18

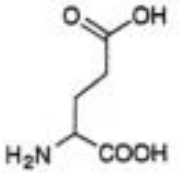


Tryptophan (Trp, W)
MW: 186.21

Acidic

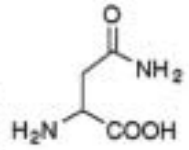


Aspartic Acid (Asp, D)
MW: 115.09, pK_a = 3.9

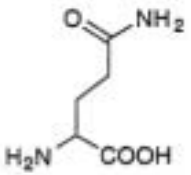


Glutamic Acid (Glu, E)
MW: 129.12, pK_a = 4.07

Amide

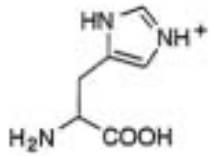


Asparagine (Asn, N)
MW: 114.11

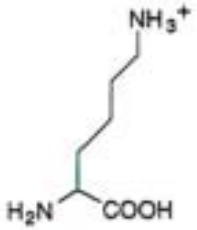


Glutamine (Gln, Q)
MW: 128.14

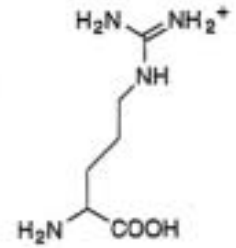
Basic



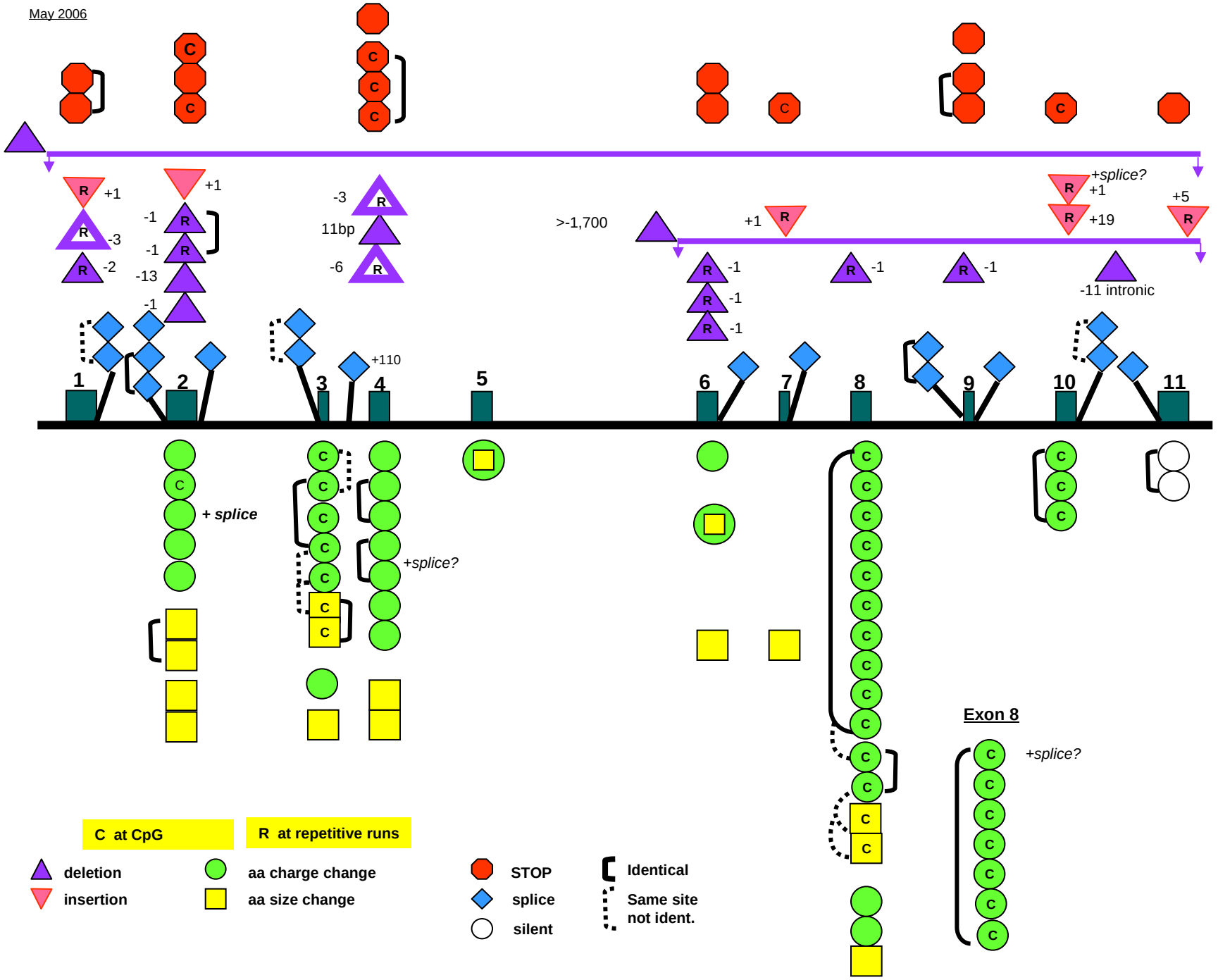
Histidine (His, H)
MW: 137.14, pK_a = 6.04



Lysine (Lys, K)
MW: 128.17, pK_a = 10.79



Arginine (Arg, R)
MW: 156.19, pK_a = 12.48


May 2006
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+1
+splice?
+1
+5
+19
-11 intronic
+110
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11
+ splice
+splice?
Exon 8
+splice?
C at CpG
R at repetitive runs
deletion
insertion
aa charge change
aa size change
STOP
splice
silent
Identical
Same site not ident.