Recitation Section 22
May 2-3, 2005

From Yeast to Humans—Essential Genes on the Evolutionary Continium.

A. CBS protein in yeast and humans

Recall that earlier in the term we considered the human gene CBS and its yeast analog cys4. Recall that these genes each encode the protein cystathionine β-synthase that is responsible for converting homocysteine into cystathionine in the cellular pathway of creating cysteine.

1. What is cysteine? Is it important for organism's survival?

2. What would you expect to be the result of complete absence of the protein product of the yeast *CYS4* gene to be? What about the same question for the human CBS protein?

3. Would you expect cells that contain no functional copy of CBS enzyme to accumulate some kind of a compound? If no, why not? If yes, what kind of a compound would you expect that compound to be?

4. In the experiments we discussed earlier in the term, what was the phenotype of the *cys4* mutants on complete media?

5. As we told you a number of sessions ago, the deficiency in the human analog of *CYS4* gene, CBS, lead to a disease called cysteineurea, resulting in variety of serious conditions, including mental retardation, heart attack, and stroke. What accounts for such a big difference in phenotype between CBS protein deficient yeast and humans?

B. Phylogenetic analysis

Below is a figure from a research paper showing alignment of the amino acid sequences of human, rat, yeast, and *E. coli* CBS proteins.

Figure removed due to copyright reasons.
Please see:
Kruger, W. D., and D. R. Cox. "A yeast system for expression of human cystathionine beta-synthase: structuraland functional conservation of the human and yeast genes." *Proc Natl Acad Sci USA* 91, no. 14 (July 5, 1994): 6614-8.

1. What do the dashes in the sequence represent?

2. Are the DNA sequences encoding amino acids that are conserved across species above necessarily the same? Why or why not?

3. What properties of the particular amino acids allow them to be grouped into the conservative groupings as described in the figure legend above?

4. Look at the genetic code table. Is there a relationship between the codons encoding amino acids in conservative groupings?

5. Is CBS a good candidate for creating a phylogenetic tree on the basis of its sequence? Why or why not?

6. Are human disease alleles of CBS likely to help with phylogenetic tree construction? Why or why not?

7. If constructing a phylogenetic tree on the basis of CBS alignment, would it be more useful to work with the protein or cDNA sequences? cDNA sequences or DNA sequences? Why?

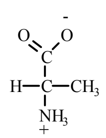
8. Do you expect the human wild type gene to complement yeast *CYS4* deficiency? Why or why not?

9. Is there a way to explore the relationship between human CBS protein and yeast *CYS4* protein?

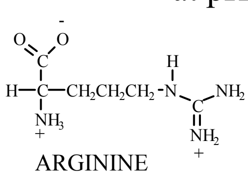
The Genetic Code

	U	C	A	G	
U	UUU **phe (F)** UUC **phe** UUA **leu (L)** UUG **leu**	UCU **ser (S)** UCC **ser** UCA **ser** UCG **ser**	UAU **tyr (Y)** UAC **tyr** **UAA STOP** **UAG STOP**	UGU **cys (C)** UGC **cys** **UGA STOP** UGG **trp (W)**	U C A G
C	CUU **leu (L)** CUC **leu** CUA **leu** CUG **leu**	CCU **pro (P)** CCC **pro** CCA **pro** CCG **pro**	CAU **his (H)** CAC **his** CAA **gln (Q)** CAG **gln**	CGU **arg (R)** CGC **arg** CGA **arg** CGG **arg**	U C A G
A	AUU **ile (I)** AUC **ile** AUA **ile** **AUG met (M)**	ACU **thr (T)** ACC **thr** ACA **thr** ACG **thr**	AAU **asn (N)** AAC **asn** AAA **lys (K)** AAG **lys**	AGU **ser (S)** AGC **ser** AGA **arg (R)** AGG **arg**	U C A G
G	GUU **val (V)** GUC **val** GUA **val** GUG **val**	GCU **ala (A)** GCC **ala** GCA **ala** GCG **ala**	GAU **asp (D)** GAC **asp** GAA **glu (E)** GAG **glu**	GGU **gly (G)** GGC **gly** GGA **gly** GGG **gly**	U C A G

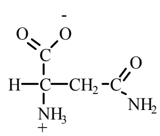
STRUCTURES OF AMINO ACIDS
at pH 7.0



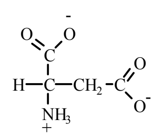
ALANINE
(ala)



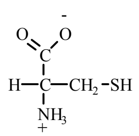
ARGININE
(arg)



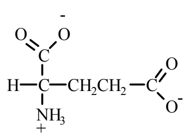
ASPARAGINE
(asN)



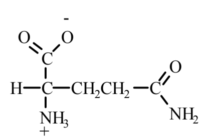
ASPARTIC ACID
(asp)



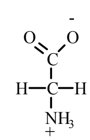
CYSTEINE
(cys)



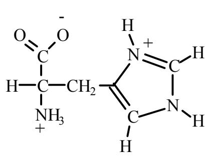
GLUTAMIC ACID
(glu)



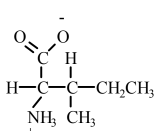
GLUTAMINE
(glN)



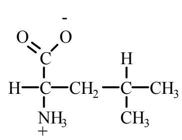
GLYCINE
(gly)



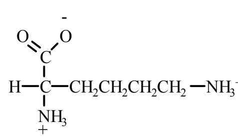
HISTIDINE
(his)



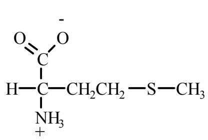
ISOLEUCINE
(ile)



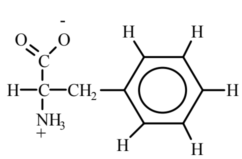
LEUCINE
(leu)



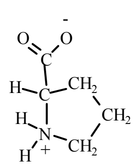
LYSINE
(lys)



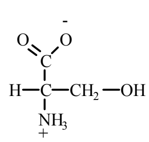
METHIONINE
(met)



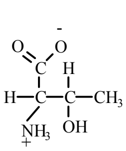
PHENYLALANINE
(phe)



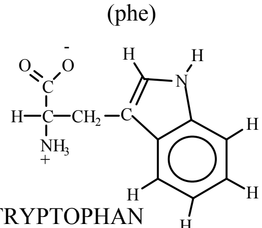
PROLINE
(pro)



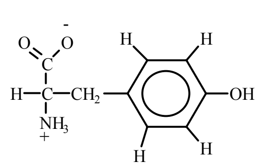
SERINE
(ser)



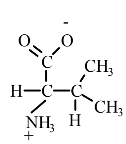
THREONINE
(thr)



TRYPTOPHAN
(trp)



TYROSINE
(tyr)



VALINE
(val)