Bioinformatics

Introduction

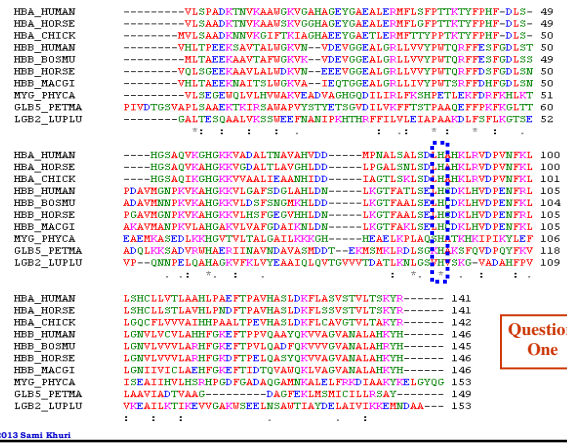
Sami Khuri
Department of Computer Science
San José State University
San José, California, USA
Sami.Khuri@sjsu.edu
www.cs.sjsu.edu/faculty/khuri

Outline

- Ten Questions
- Top 25 Questions for the next 25 years [Science]
- Genetics in Medicine – Sixth and Seventh Editions

Workshop: Introduction to Bioinformatics

- Biology Review & Introduction to Bioinformatics
- Pairwise and Multiple Sequence Alignments
- Phylogenetic Tree Construction
- RNA Secondary Structure
- Gene Prediction
- Human Genome Variation

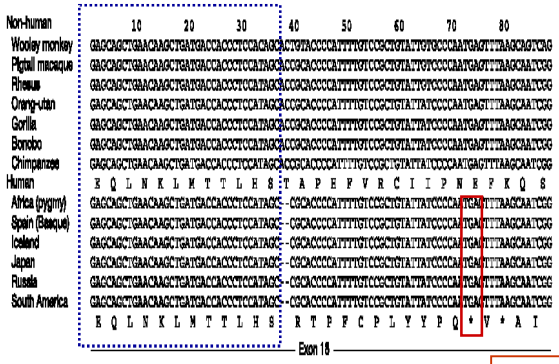


Question One

Quagga: Zebra or Horse?

Died in Amsterdam zoo in 1883.

Question Two



MYH16: Myosin Heavy Gene
Accession Number: BK001410 at NCBI (exon 19)

Question Three

Table 1 Types and Frequencies of β-Thalassemia Mutations and β-Globin variants in Lebanon

Mutation	Phenotype	Number of Chromosomes	Number of homozygotes/heterozygotes	Frequency (%)
IVS-I-110 (G>A)	β^+	178	65/48	34.2
IVS-I-1 (G>A)	β^0	78	29/20	15.0
IVS-I-6 (T>C)	β^+	75	28/19	14.4
cd 29 (C>T)	β^+	50	22/6	9.6
IVS-II-1 (G>A)	β^0	45	17/11	8.6
cd 5 (−CT)	β^0	26	9/8	5.0
cd 30 (G>C)	β^0	14	6/2	2.7
cd 8 (−AA)	β^0	13	5/3	2.5
cd 44 (−C)	β^0	8	3/2	1.5
IVS-II-745 (C>G)	β^+	6	3/0	1.1
β^s	β^s	5	0/5	1.0
−87 (C>G)	β^+	4	1/2	0.8
IVS-I-5 (G>C)	β^+	4	2/0	0.8
−88 (C>T)	β^+	3	1/1	0.6
290 bp deletion	β^0	3	1/1	0.6
25 bp deletion	β^0	2	1/0	0.4
$\delta\beta$-thalassemia (Sicilian type)	$\delta\beta^0$	2	1/0	0.4
cd 8/9 (+G)	β^0	1	0/1	0.2
cd 36/37 (−T)	β^0	1	0/1	0.2
cd 39 (C>T)	β^0	1	0/1	0.2
Unknown		1	0/1	0.2
Total		520	194/132	100

Six mutations are responsible for 86.8% of all beta thalassemias in Lebanon

"**Genetic heterogeneity of beta thalassemia in Lebanon reflects historic and recent population migration**" by N. J. Makhoul, et al.
"Annals of Human Genetics" in 2005 (issue 69, pages 55 to 66).

Question Four

TABLE 2. FREQUENCY DISTRIBUTION OF THE MOST COMMON β-THALASSEMIA MUTATIONS IN MOROCCO AND IN ARAB AND MEDITERRANEAN COUNTRIES

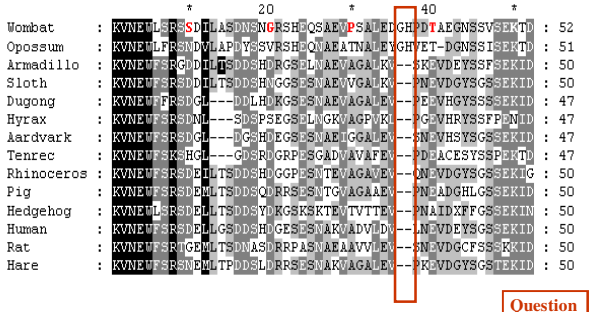
Mutations	Morocco (160)[a]	Algeria (239)	Tunisia (233)	Portugal (561)	Spain (324)	Italy (325)	Egypt (337)	Lebanon (520)	Turkey (795)
Codon 39 (C→T)	26.58	27.6	40	36.8	36	40	1.5	0.5	3.8
FSC-8 (-AA)	13.91	–	0.9	–	0.4	0.1	1.8	2.5	5.4
IVS-II-745 (C→G)	7.6	0.9	2.5	–	–	5	5.6	1.2	5
−29 (A→G)	6.33	3.8	–	–	–	–	–	–	–
FSC-6 (-A)	5.7	17	6.65	1	1	1.9	0.9	–	0.4
IVS-I-110 (G→A)	5.7	24.7	20.5	10	13	19.9	32.9	34.2	39.2
IVS-I-2 (T→C)	5.06	3.3	0.76	–	–	–	–	–	–
IVS-I-1 (G→A)	5.06	11.7	1	28	35	10.2	11.3	15	5
Total	76	89	72.3	75.8	85.4	77	54	53.4	58.8
References[b]		1	2,3	4	5,6	7	8	9	10

[a]Values in parenthesis indicate the total number of chromosomes studied.
[b]1, Bennani *et al.* (1994); 2, Fattoum *et al.* (1991); 3, Haj Khelil *et al.* (2004); 4, Faustino *et al.* (1999); 5, Amselem *et al.* (1988); 6, Ribeiro *et al.* (1997); 7, Rosatelli *et al.* (1992b); 8, Waye *et al.* (1999); 9, Makhoul *et al.* (2005); 10, Tadmouri *et al.* (1998).

"**Molecular basis of beta thalassemia in Morocco: possible origins of the molecular heterogeneity**" by I. Agouti et al. In "Genetic Testing" Volume 12, Number 4, 2008.

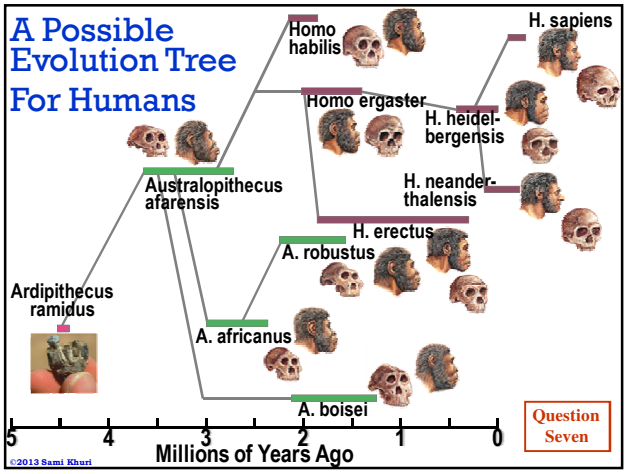
Question Five

Aligning BRCA1 Sequences



Question Six

A Possible Evolution Tree For Humans



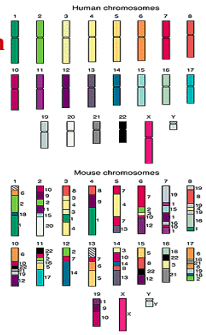
Question Seven

The Mighty Mouse

Mouse versus Human

Approximately the same number of chromosomes and local gene order in mammals.

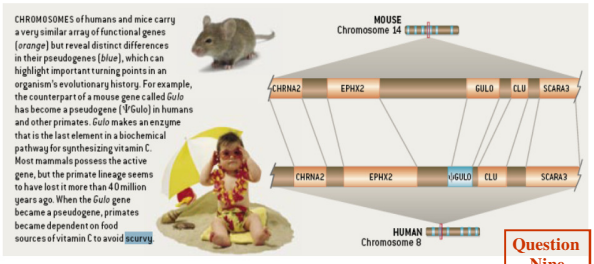
Insights into mouse genetics are likely to **illuminate** human genetics as well.



Question Eight

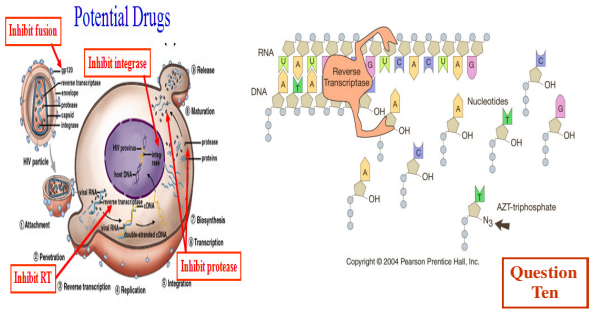
Pseudogenes

"The Real Life of Pseudogenes" by By Mark Gerstein and Deyou Zheng Scientific American, August 2006.



Question Nine

Azidothymidine (AZT) Blocks Reverse Transcriptase in HIV

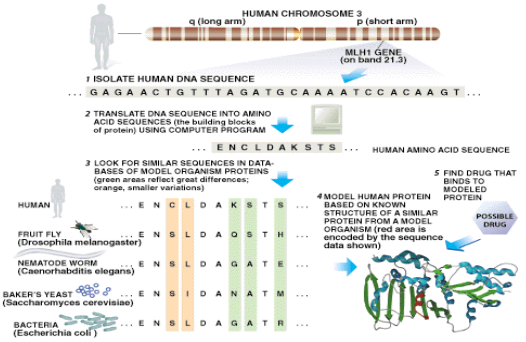


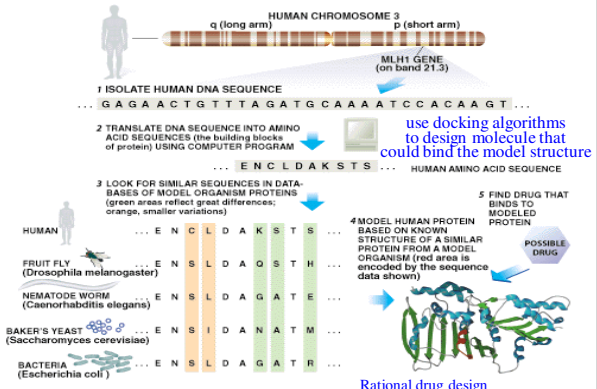
Question Ten

Why Study Bioinformatics (I)

- Bioinformatics is intrinsically interesting.
- Bioinformatics offers the prospect of finding better drug targets earlier in the drug development process.
  - By looking for genes in model organisms that are similar to a given human gene, researchers can learn about protein the human gene encodes and search for drugs to block it.

How can Bioinformatics Help?





use docking algorithms to design molecule that could bind the model structure

Rational drug design
Structure-based drug design

Scientific American July 2000

Why Study Bioinformatics (II)

- Molecular biology is the new frontier of 21st century science.
  - DNA, RNA, genes, stem cells, etc.. are everywhere in the news.
- Science Magazine celebrated its 125th anniversary by issuing twenty five big questions facing science over the next quarter-century.

www.sciencemag.org/sciext/125th

Science: Top 25 Questions (I)

* What Is the Universe Made Of?
* What is the Biological Basis of Consciousness?
- **Why Do Humans Have So Few Genes?**
- **To What Extent Are Genetic Variation and Personal Health Linked?**

* Can the Laws of Physics Be Unified?
* How Much Can Human Life Span Be Extended?

- **What Controls Organ Regeneration?**
- **How Can a Skin Cell Become a Nerve Cell?**
- **How Does a Single Somatic Cell Become a Whole Plant?**

* How Does Earth's Interior Work?
* Are We Alone in the Universe?
* How and Where Did Life on Earth Arise?

Science: Top 25 Questions (II)

- **What Determines Species Diversity?**
- **What Genetic Changes Made Us Uniquely Human?**

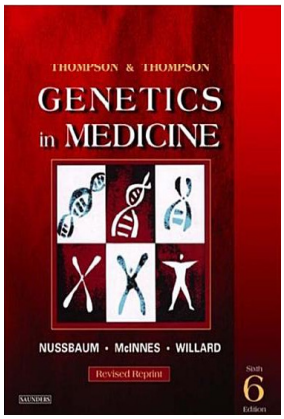
* How Are Memories Stored and Retrieved?

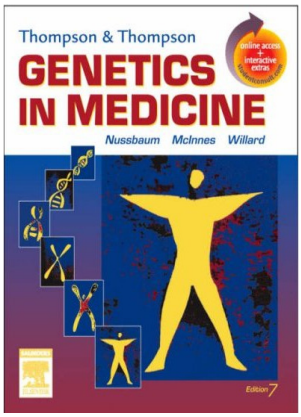
- **How Did Cooperative Behavior Evolve?**
- **How Will Big Pictures Emerge from a Sea of Biological Data?**

* How Far Can We Push Chemical Self-Assembly?
* What Are the Limits of Conventional Computing?

- **Can We Selectively Shut Off Immune Responses?**
- Do Deeper Principles Underlie Quantum Uncertainty and Nonlocality?
- **Is an Effective HIV Vaccine Feasible?**

* How Hot Will the Greenhouse World Be?
* What Can Replace Cheap Oil -- and When?





Preface of the Seventh Edition

Much has changed, however, since the last edition of this book. Completion of the HGP provides us with a catalogue of all human genes, their sequence, and an extensive, and still growing, database of human variation. Genomic information has stimulated the creation of powerful new tools that are changing human genetics research and medical genetics practice. We therefore have expanded the scope of the book to incorporate the concepts of "**Personalized Medicine**" into ***Genetics in Medicine*** by providing more examples of how genomics is being used to identify the contributions made by genetic variation to disease susceptibility and treatment outcomes.