Livestock Genomics: The Odyssey

Jim Womack, Texas A&M University

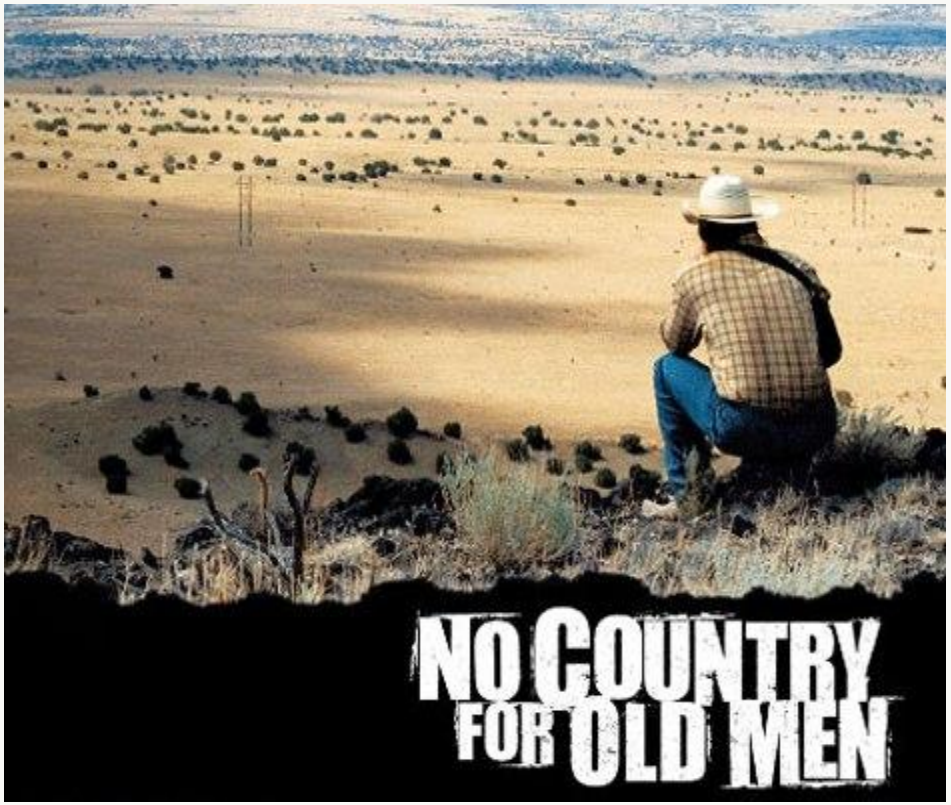
NRSP-8 Animal Genome Workshop

Plant and Animal Genome XX, Jan 15, 2012

Thanks, Geoff and Workshop Committee

- BRD?
- Rift Valley Fever?

HISTORY!!!



New Text for Jeff Foxworthy Act

You might should consider retirement if:

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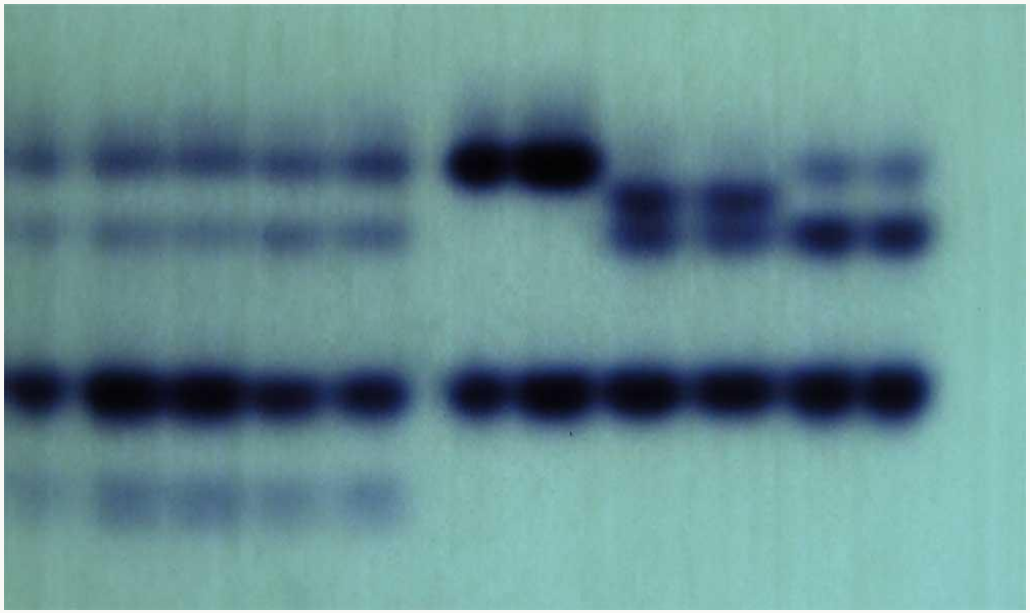
- You have ever cooked a starch gel

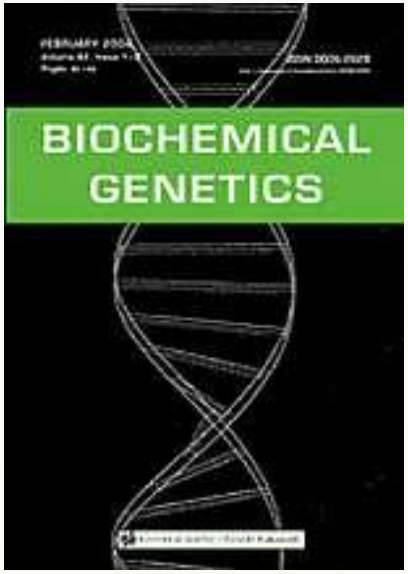
You might should consider retirement if:

- You have ever cooked a starch gel
- You have ever used the words “allozyme” or “isozyme” in a scientific publication



You might should consider retirement if:

- You have ever cooked a starch gel
- You have ever used the word “allozyme” or “isozyme” in a scientific publication
- You have ever published in Biochemical Genetics



‘Genomics’ Emerged from ‘Gene Mapping”

Pontecorvo, Ruddle, and Crick

Why map genes?

Frank Ruddle, 1984. “Because gene mapping is good for you”

Animal Gene Mapping in 1980s

Only Linkage Map was Mouse (and Chicken to lesser extent)

linkage groups

Human Map was a Parasexual Map, generated by somatic cell genetics

synteny groups (Renwick, 1971)

Linkage map of cattle in 1981

Larsen B. Royal Danish Agricultural Society, Copenhagen

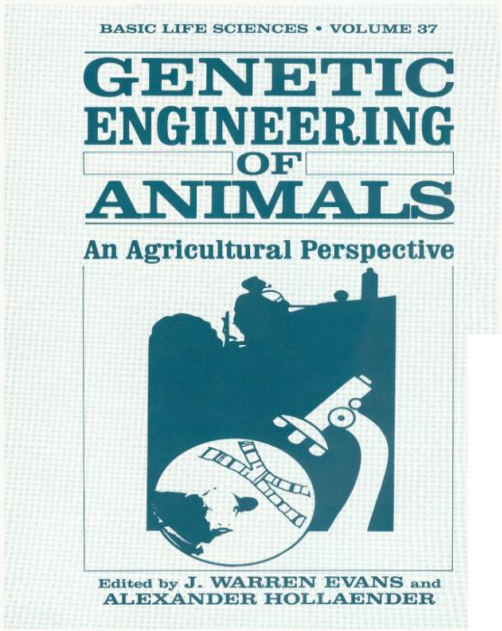
Table 1. *Loci with Established Linkage Relations.*

Linked loci	Recombination %
A and Hb	1.7±1.0
J and Lg	4.1±2.9
Alpha-, beta- and kappa-casein	<1
Tf and Cp	20.5±3.2

- Larsen B. 1966. Test for linkage of the genes controlling haemoglobin, transferrin and blood types in cattle. Royal Vet. Agric. Univ., Copenhagen, Yrb. 41-48.

- Hines H.C. et al. 1969. Linkage among cattle blood groups and milk polymorphisms. Genetics 62: 401-412.

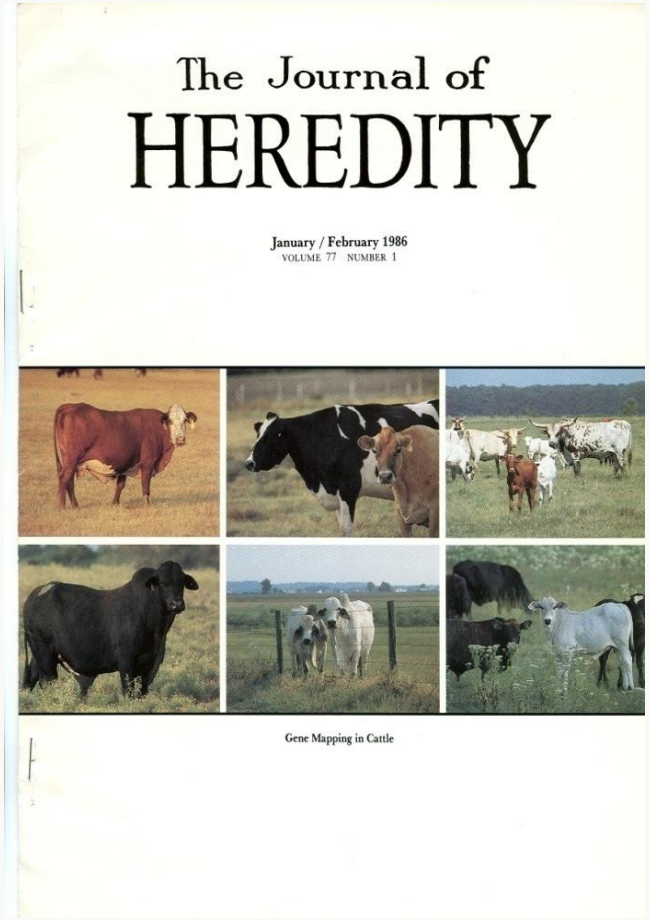
Genetic Engineering of Animals, UC Davis, 1985



Tab. 2. Status of the gene maps of some domestic species.

Species	Number of linkage or synteny groups	Number of chromosomal assignments
Cow (Bos taurus)	25	34
Sheep (Ovis aries)	12	22
Goat (Capra hircus)	0	0
Pig (Sus scrofa)	10	17
Chicken (Gallus gallus)	10	29

1986



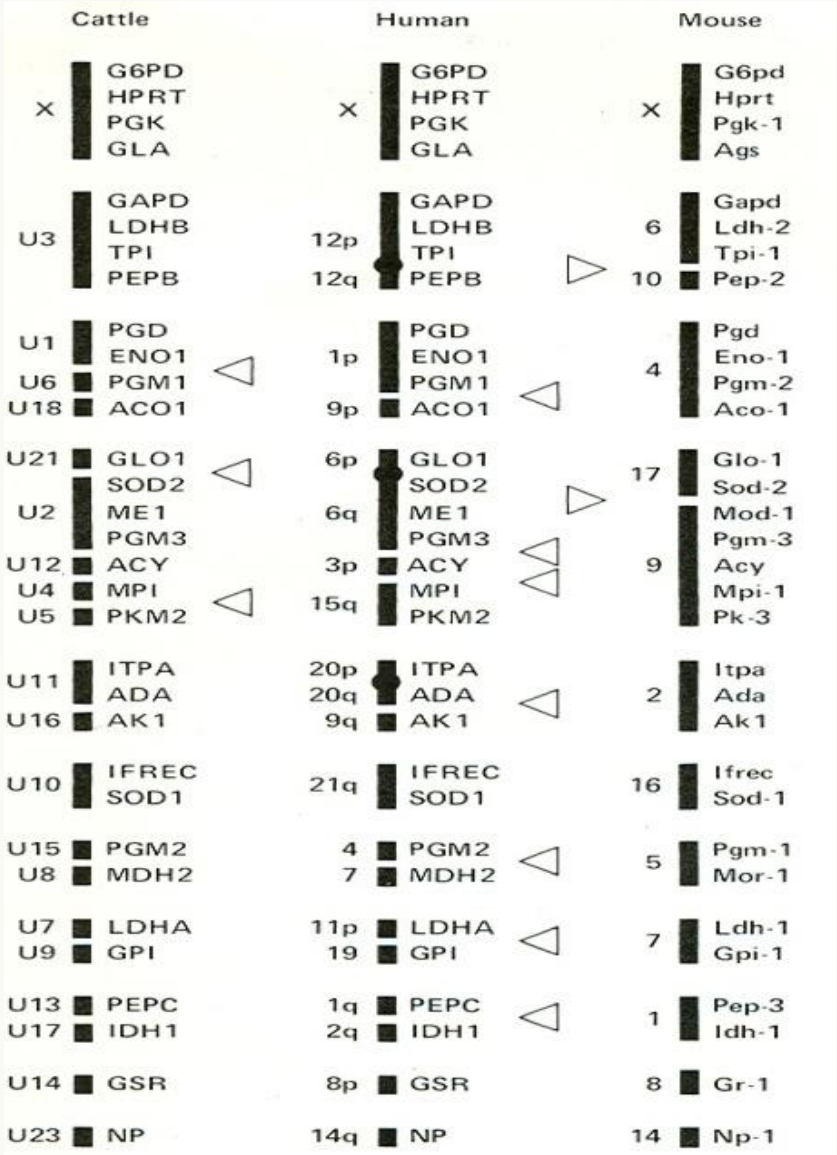
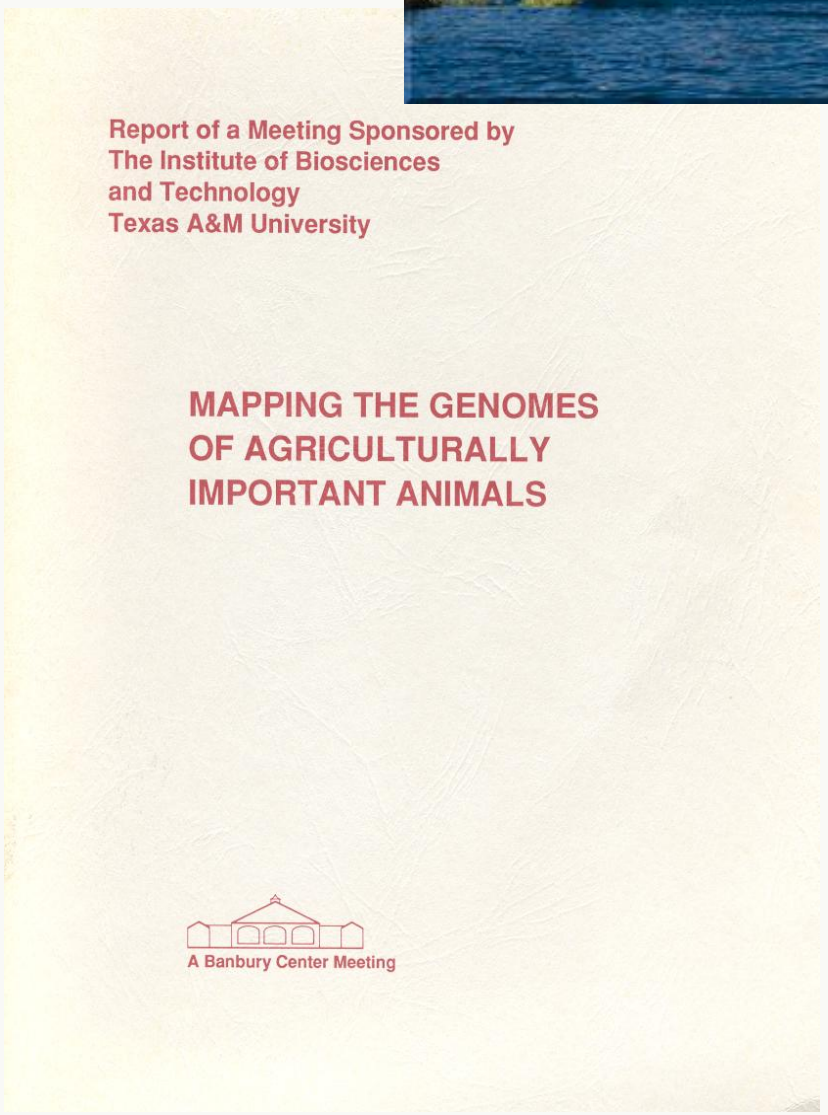


FIGURE 3 Comparative maps of homologous gene loci mapped in cattle, human beings, and mice. Arrows indicate discordancies between the cattle and mouse maps with the reference human map.

1990: The Big Bang

- Banbury Conference on Mapping Genomes of Agriculturally Important Animals, Cold Spring Harbor. Feb. 25-28
- Allerton Conference on Mapping Domestic Animal Genomes: Needs and Opportunities, Urbana, April 9-10
- ISAG Gene Mapping Workshop in East Lansing, attended by 250 people, individual species workshops established, August 25-31
- Many other meetings world wide over next 5 years
- NRSP-8 formed in 1993



Banbury Conference 1990

Cold Spring Harbor Laboratory

Participants

- Charles J. Arntzen
- Stephen Ashley
- D. Allan Bromley
- Neville P. Clarke
- Neal L. First
- Michel S. Georges
- Florence P. Haseltine
- Jay Hetzel
- David H. Housman
- Neal Jorgensen
- Brian W. Kirkpatrick
- Harry Lewin
- Joan Lunney
- Victor McKusick
- Harry Mussman
- David L. Nelson
- Andrew H. Paterson
- Leslie Roberts
- Lawrence B. Schook
- Linda A. Schuler
- Ruth M. Shuman
- Loren C. Skow
- Morris Soller
- Alan Teale
- James D. Watson
- Raymond L. White
- J. Michael Wilson
- James E. Womack

The Banbury Conference Maps- 1990

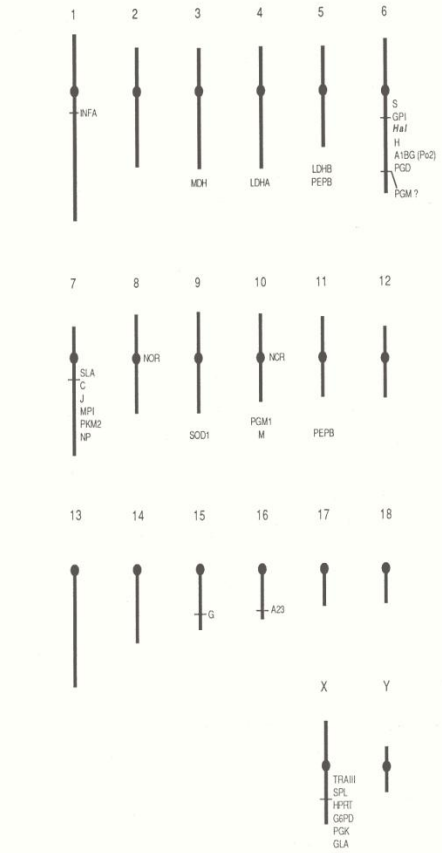


Figure 1 Current gene map of the pig.

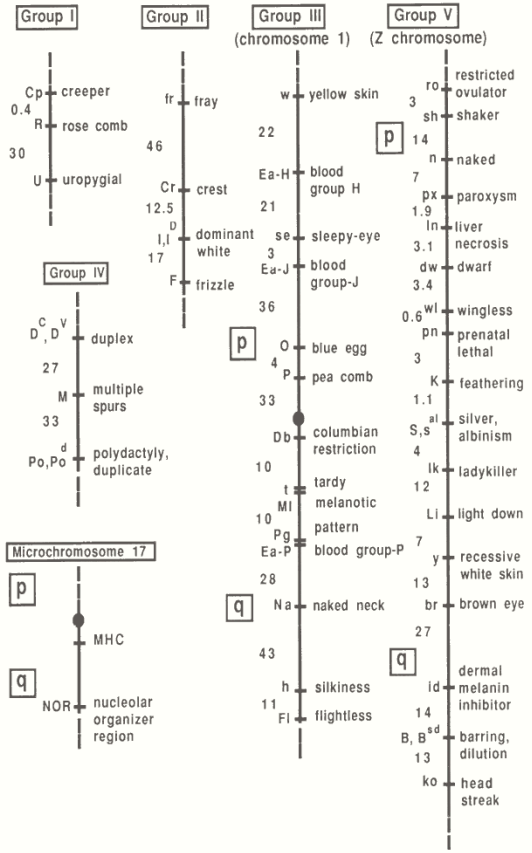


Figure 1 Linkage map of the domestic chicken.

Table 1 The Synteny Map

(a) *Syntenic groups*

Syntenic group	Chromosomal location	Gene locus
U1		PGD, ENO1, AT3 ABLL, REN
U2		SOD2, ME1, PGM3
U3	5	GAPD, LDHB, TPI1, PEPB, IFNG, A2M, INT1, HOX3, LALBA, KRAS2, GLI, PAH, NKNB, KRTB, GDH, LYS, PFKM, IGF1
U4	21	MPI, CYP11A, FES, IGH, D21S16
U5	10	PKM2, NP, HEXA, FOS, KRT8L1, B2M
U6		PGM1, AMY1
U7		LDHA, TYR
U8		MDH2, ASL, PRM, GUSB, HBA1
U9	18	GPI, DIA4
U10		SOD1, IFREC, PRGS, PAIS, CRYA1, SST, APP, ETS2, S100B, COL6A1, COL6A2, CBS, GAP43, PFKL, CD18, TF, CP, SI
U11		ITPA, ADA, VIM, IL2R, SRC, HCK
U12		ACY1, RHO, GPX1
U13		HOX1, MET, COL1A2, ESD, IL6
U14		GSR, PLAT
U15	6	PGM2, PEPS, CASAS1, CASAS2, CASB, CASK, ADH2, IGJ, IF
U16		ABL, ASS, AK1, GRP78, LGB, J, IGHML1
U17	8	IDH1, FN1, CRYG, VIL1
U18		ACO1, IFNA1, IFNA2, IFNB, GSN, GGTB2, ALDOB, ALDH1, C5, ITIL, NEFM, NEFL, CLTLA2
U19	15	CAT, A, PTH, HBB, CRYA2, FSHB
U20	23	GLO1, CYP21, BOLAA, BOLAB, BOLAD, PRL, TCP1, M, HSPA1, MUT
U21	19	GH, HOX2, KRTA, POLR2
U22		AMH, SPARC, CLTLB
U23		ALDH2, IL2, IGL, FGB, FGG
U24	14	TG, MOS, CA2, MYC, CYP11B
U25		CLTLA1
U26		GOT1, CYP17A, ADRA2R
U27		
U28		MBP, YES1
U29		PLAU, RBP3
X	X	G6PD, HPRT, PGK1, GLA, F9, DMD
Y	Y	DYZB, DYZ1

(Unassigned linkage groups)
LG VI ALB, GC
LGV II S, PI2

Marker Development

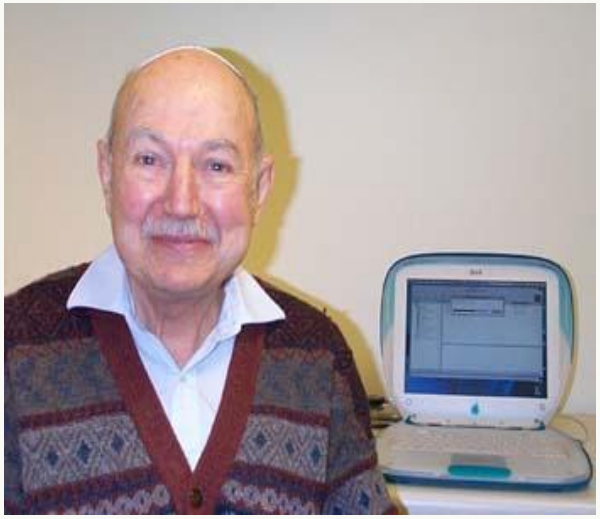
- Morphological variants, diseases
- Histo-compatibility, blood groups
- Biochemical (allozymes)
- DNA: RFLPs
- DNA: Microsatellites
- DNA: SNPs
- DNA: Sequence

Marker/Trait Associations:
Evolution of the Concept

- Neimann-Sorensen A. and Robertson A. 1961. The association between blood groups and several production characters in three Danish cattle breed. Acta. Agr. Scand. 11: 163-196.

- Geldermann H. 1975. Investigations on inheritance of quantitative characters in animals by gene markers. 1. Methods Theor. Appl. Genet. 46: 319.

- Smith C. and Simpson S.P. 1986. The use of genetic polymorphisms in livestock improvement. J. Anim. Breed. Genet. 103: 205-217.



- Soller M. 1978. The use of loci associated with quantitative traits in dairy cattle improvement. Anim. Prod. 27: 133.

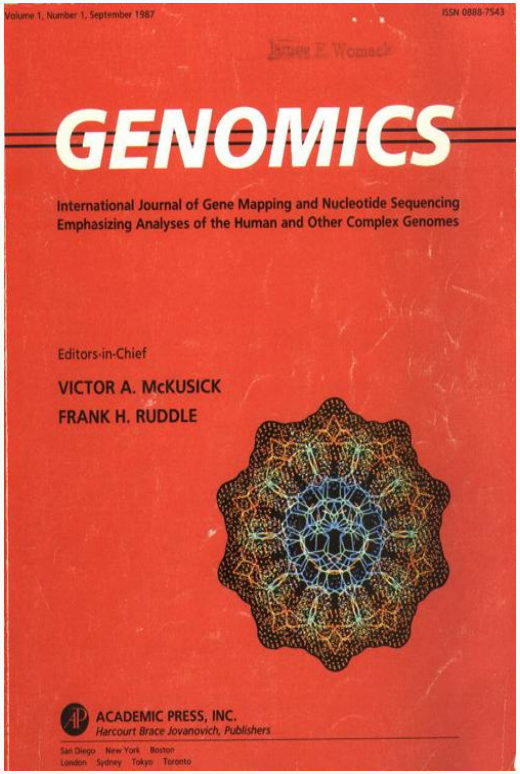
- Beckman J.S. and Soller M. 1987. Molecular markers in genetic improvement of farm animals. Biotechnology 5: 573-576.

- Beckman J.S. and Soller M. 1988. Detection of linkage between marker loci and loci affecting quantitative traits in crosses between segregating populations. Theor. Appl. Genet. 76: 228-236.

From Genetics to Genomics

Genome, a word coined in 1920 by Hans Winkler (U. of Hamburg botanist) from a hybrid of **gen***e* and *chromos***ome**: to describe 'all the genes on a haploid set of chromosomes.'

Genomics, no known use of the word prior to 1986. Coined by Dr. Thomas H. Roderick as a suggestion for title of a new journal to meet the needs of the human genome project.



Journal of the National Cancer Institute, Vol. 90, No. 2, January 21, 1998

News

Beer, Bethesda, and Biology: How "Genomics" Came Into Being

Over the last decade, molecular genetics has spun off a lexicon of new words that scientists, including cancer researchers, now use to describe their work. One word that has become standard fare at many cancer meetings is "genomics," meaning the study and comparison of genomes across species.

Where did the word genomics come from? It is the brainchild of Thomas H. Roderick, Ph.D., a geneticist at the Jackson Laboratory, Bar Harbor, Maine, who dreamed up the word in 1986 as the name of the then yet-to-be-published journal *Genomics*. In a recent interview, Roderick tells the *News* the story behind the word.

***News*: How did you come up with the word genomics?**

Roderick: In 1986, I attended a good-sized international meeting in Bethesda to discuss the feasibility of mapping the entire human genome. The meeting had adjourned for the day, and Frank Ruddle, Ph.D. [Yale University], and Victor McKusick, M.D. [The Johns Hopkins University], convened a short submeeting involving about 50 people, including myself, to discuss starting a new genome-oriented scientific journal. The journal was to be a place to include sequencing data and as well to include discovery of new genes, gene mapping, and

Dr. Thomas H. Roderick

Bethesda. It was called the McDonald's Raw Bar [which has since been torn down]. There might have been 10 of us that night who went there and sat around drinking beer — actually a lot of beer. It was great fun.

We kept moving on the name. Some of us really wanted to name the journal, Genome. But the *Canadian Journal of Genetics and Cytology* had already announced their intention to change its name to "Genome," with their first issue to appear in 1987, about the time the new journal of McKusick and Ruddle was supposed to appear. Several names were considered using "Genome" as part of the title, but it was agreed they all were too cumbersome.

was in high school, so it must have played a part in the name. In fact, I'm sure it did.

I said the word to Frank Ruddle. Frank recognized it as a name that encompassed what we wanted to do. It wasn't just the objectives of the journal. It was GE-NOM-ICS. It was an activity, a new way of thinking about biology.

We adjourned that evening thinking genomics wasn't a bad name. But I didn't hear any more about it until Victor and Frank decided that was what they wanted to name the journal. Frank told me later that Victor had done some scholarly study of the word to be certain it was etymologically appropriate.

***News*: When you proposed the term genomics, what was the definition that was in your mind?**

Roderick: Well, it certainly encompassed what the journal wanted to cover. It encompassed sequencing, mapping, and new technologies. But we felt it also had the comparative aspect of genomes of various species, their evolution, and how they related to each other. Although we didn't come up with the term "functional genomics," we thought of the genome as a functioning whole beyond just single genes or sequences spread around a chromosome.

***News*: Did you ever think when you left the raw bar in Bethesda that this name would become such a big part of biology?**

Roderick: No. Victor and Frank

Time Line of Human Genome Project

- 1953, Watson and Crick discover the double helix structure of DNA
- 1977, Maxam and Gilbert (Harvard) and Sanger (U.K. MRC) independently develop methods to sequence DNA
- 1985, Santa Cruz conference to discuss feasibility of sequencing the human genome
- 1986, Leroy Hood and Lloyd Smith develop first automated DNA sequencer
- 1988, NIH establishes Office of Human Genome Research with James Watson as its head
- 1990, NIH and DOE announce plans for complete genetic map, a physical map with markers at 100kb, and sequencing of 20 Mb of DNA in model organisms by 2005

Time Line, continued

- 1992, Craig Venter leaves NIH, establishes The Institute for Genome Research (TIGR)
- 1993, Francis Collins is named director of the NCHGR. NIH and DOE announce revised plans which includes complete sequence of human genome by 2005
- 1995, Venter, Fraser and Smith publish first sequence of genome of a free living organism (Haemophilus influenzae), 1.8 Mb.
- 1998, Venter announces a new company, Celera, and declares that it will sequence the human genome within 3 yr for $300 million
- 2000, Celera announces sequencing the Drosophila genome with “shotgun” method (180 Mb)
- 2001, NIH and Celera publish draft sequences of human genome
- 2003, “Finished” sequence… less than 2% error

“The bovine genome will probably never be sequenced…” Jim Womack 1998, Grant proposal to the USDA.

NIH Call for White Papers for Sequencing Additional Model Organisms

January, 2002

International Collaborations

Thanks Y'all

- Students
- Laboratory staff
- Collaborators
- Animal genetics community
- Family