Importance of Genetic Monitoring in Breeding Colonies

Taconic

Smart Solutions To Improve Human Health

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Outlay



- Importance of Genetic Monitoring
- What does Genetic Monitoring mean
- Tailoring Genetic Monitoring to your colony needs
- Examples

Why do Genetic Monitoring

- **Assure Genetic Quality of mice being bred**
  - Preserve the Genetic Background
  - Preserve the mutation(s) of the mouse strain
  - Breed so that the right controls for the experiment are used
- **Assure that strain characteristics, are maintained**
- **Guarantees data reproducibility through space and time**

Steps in Genetic Monitoring

- **What is the make-up of the incoming strain**
  - Inbred/Outbred/Genetically modified/Spontaneous mutant
- **Nomenclature**
  - Need information about genetic background
  - Need information about generation numbers
  - Need information about how the mutations were made and where
  - Breeding history of the model before receipt
- **What are the goals of the project**
  - Backcrossing
  - Breeding Format considering breeding challenges
  - Cohort delivery for project/phenotyping
  - Genotyping Protocols
- **How to minimize genetic drift**
  - Cryopreservation

Genetic Background

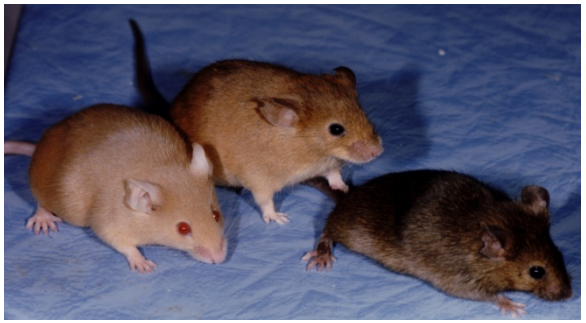


- **Genetic Background is the genetic context where genes are expressed**

- **Inbred or Outbred genetic background**
  - Inbred strains-homozygous at all alleles
  - Outbred strains-heterozygous alleles

- **Mutations or phenotypes are expressed differently depending upon the genetic background they are in**

Inbred Mouse



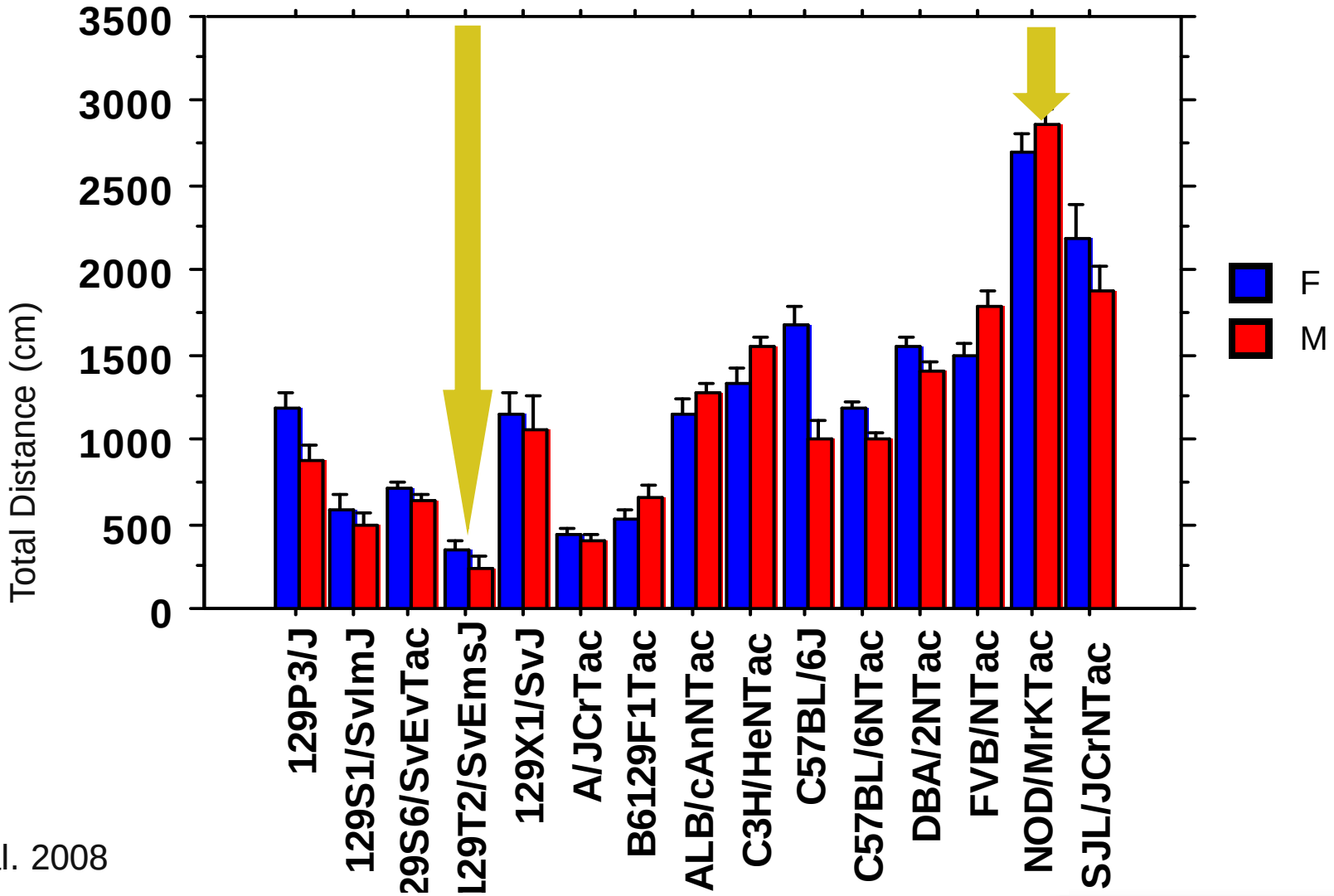
- **Value of inbred mice ~1950**
- **Brother x sister mating for 20 generations**
- **At any one locus/gene—homozygosity: H/H or h/h (not H/h)**
- **No (minimized) segregation over whole genome, so next generation is equivalent to previous one**
- **Each strain approximates multiple copies of a single individual, but are not clones. Thus, each strain has certain characteristics**
  - C57BL/6, FVB, 129S6, etc

Outbred Mouse

- **Maximize genetic diversity**
  - Desirable sizes, weights, fecundity, etc.
  - Sometimes reveal phenotypes not observed on inbred backgrounds
  - Often allows maintenance of mutations that have severe effects on inbred strains

- **Maximal heterozygosity at each locus**
  - Allele segregeation
  - Small colony of outbreds, replace frequently
  - Rederivations, genetic bottlenecks
  - Genetic monitoring checking allele frequencies *

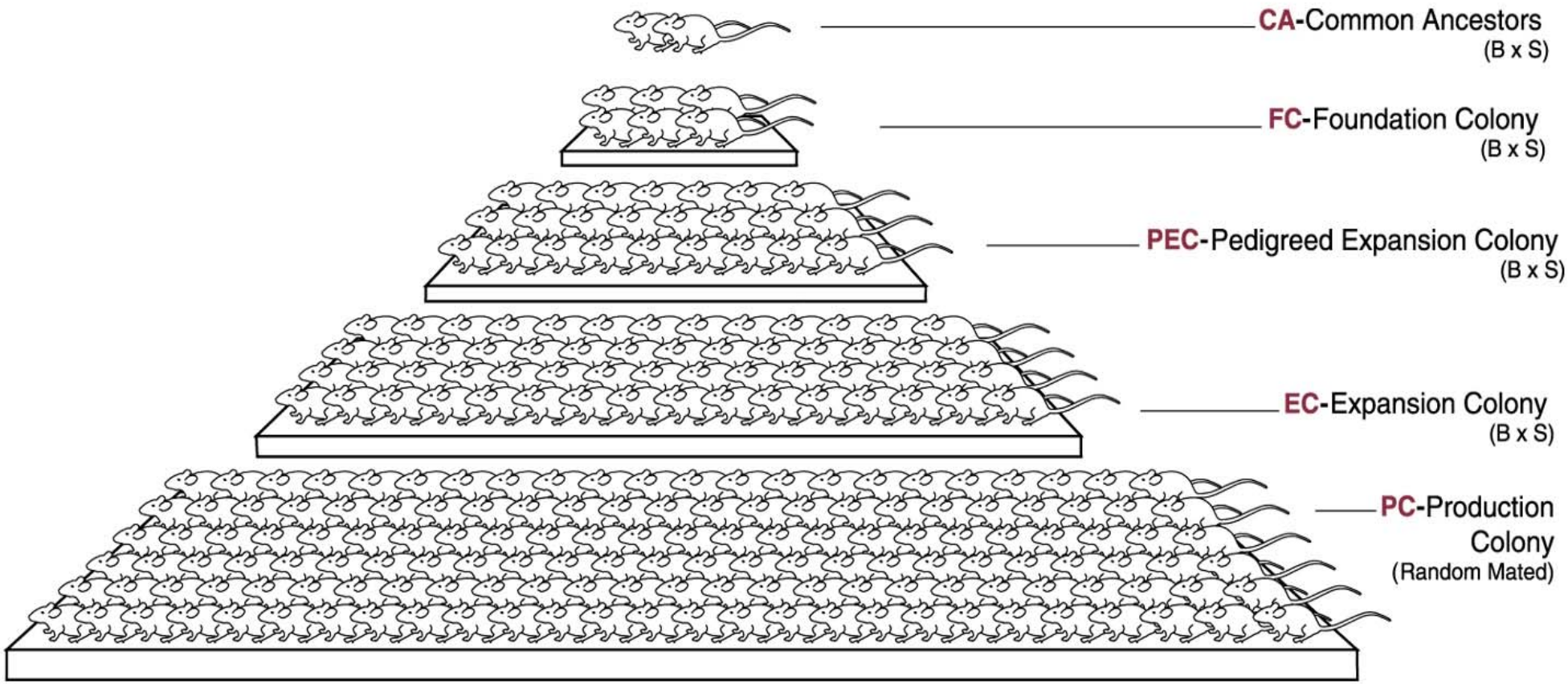
Open Field Activity (first exposure)



Taconic -G. Bothe et al. 2008

Inbred Colony Management at Taconic

The Pyramid System



Areas of Genetic Risk





- **Initiation of a New Colony**
  - Importation and checking of genetic quality
  - Contamination during rederivation or cryopreservation
- **Movement animals from one location to another**
- **Co-housing more than one strain of animals with the same coat color**
- **Hybrid colonies sharing a coat color of breeders**
- **Mice of different Genotypes**
  - Genetic contamination is not detected unless it is tested for it

Genetic Monitoring Program

- **Phenotypic Characteristics**
  - Coat Color
  - Phenotype of strain, i.e. obese, nude
- **Husbandry procedures to minimize risk**
  - Colored cage cards by line
  - Minimize the number of lines with similar coat colors in one location
  - Minimize the number of animals moves of similar coat color at the same time
- **Cryopreservation**
  - Sperm/embryo
- **Genetic Testing**
  - Biochemical/DNA based

Genetic Testing

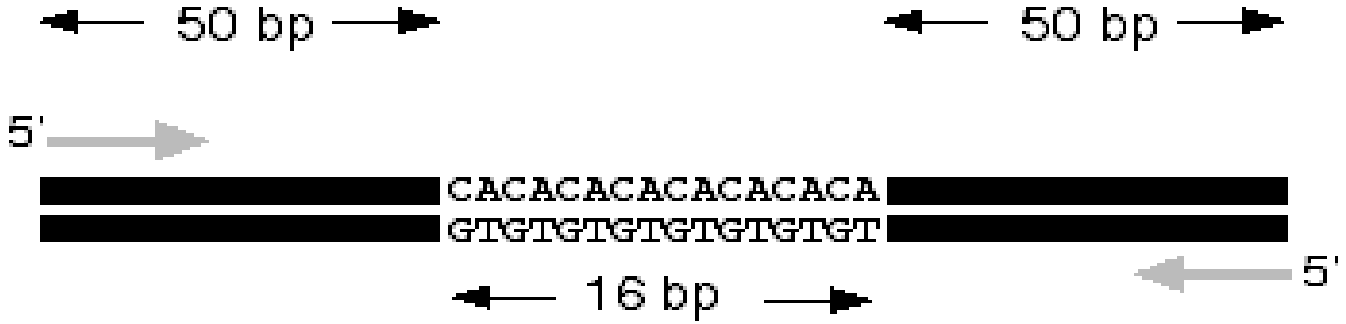
- **Genetic Background Testing**
  - Biochemical testing- tests for proteins /genetic polymorphisms
  - DNA Microsatellites
  - Single Nucleotide Polymorphisms or SNPs

- **Genotyping**
  - Southern Blot
  - Polymerase Chain Reaction or PCR
  - Quantitative PCR
  - Phenotyping, i.e. Flow Cytometry

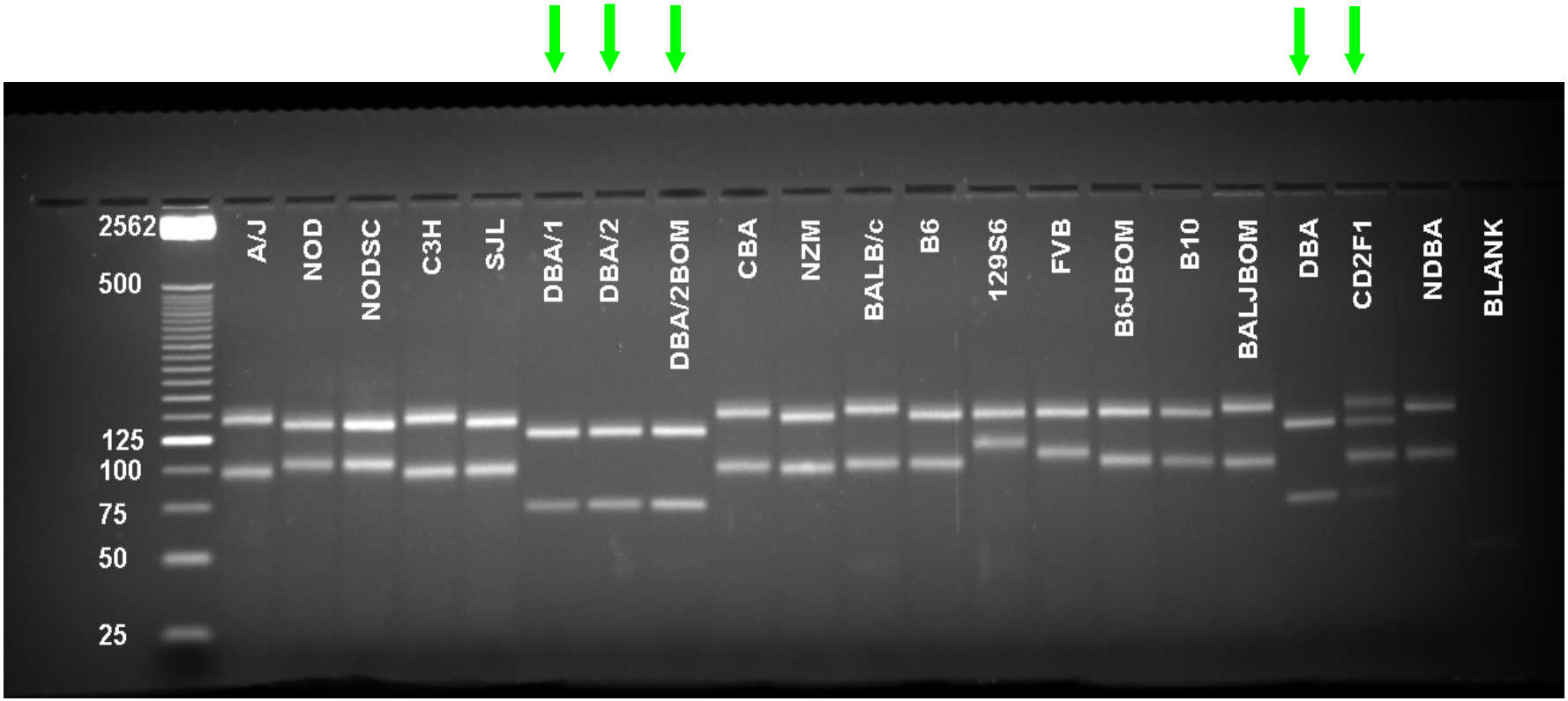
Genetic Background Testing



- **DNA microsatellites**
  - Short segments of DNA that have a repeated sequence
  - The length of the sequence repeat varies from species to species and from strain to strain
  - It is somewhat unstable, higher mutation rate
  - Artifact/Technical problems
  - It is difficult to perform in a high-throughput manner



Genetic Markers - Microsatellites



Genetic Background Testing



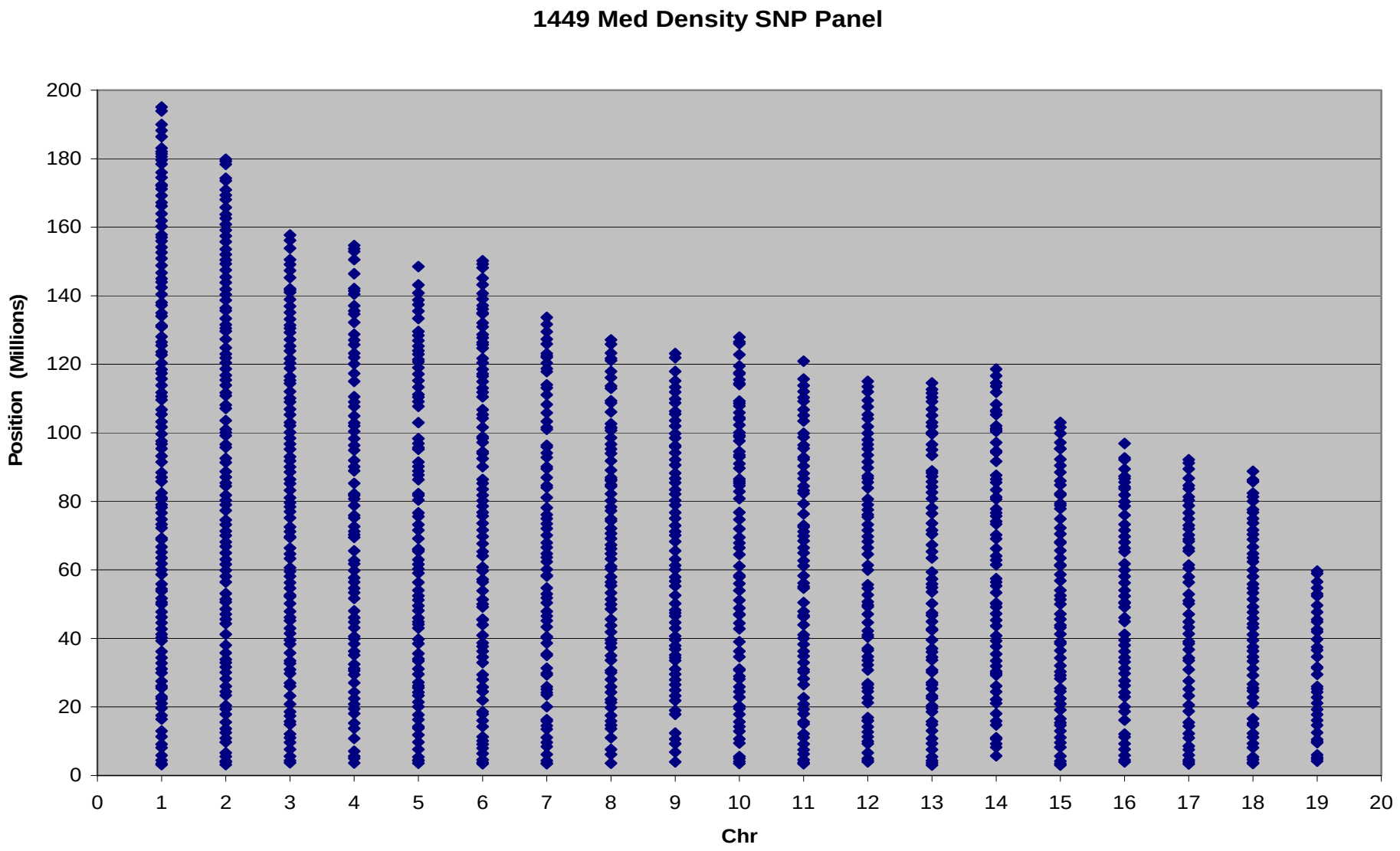
- **Single Nucleotide Polymorphisms or SNPs**
  - DNA sequence variations that occur when a single nucleotide (A,T,C,or G) in the genome sequence is altered
  - More stable than microsatellites
  - Scalable for high-throughput, tested in the order of thousands

    AAGGCTAA to
    ACGGCTAA

  - SNPs allow us to detect strain differences

Genomic Profiling Illumina 1449 SNP Panel





MDL (1449) SNP Panel Differences

Table 2: Strain Differences in 1449 Marker Panel

	129P3/J	129S4/SvJae	129S6/SvEvTac	A/JCrTac	BALB/cAnNTac	BALB/cJBomTac	BTBR T<+>	C3H/HeNTac	C57BL/10SgSnAiTac	C57BL/6J	C57BL/6NTac	C57BL6/JBomTac	CBA/JBomTac	DBA/1JBomTac	DBA/2NTac	FVB/NTac	NOD/Tac	SJL/JCrNTac
129P3/J		19	39	716	666	683	451	685	844	869	857	866	699	696	725	619	638	592
129S4/SvJae	19		22	713	662	678	443	667	847	872	860	869	683	687	716	621	638	599
129S6/SvEvTac	39	22		704	652	669	447	659	854	879	867	876	675	678	707	620	630	595
A/JCrTac	716	713	704		326	337	650	413	904	953	941	950	477	638	650	519	546	567
BALB/cAnNTac	666	662	652	326		0	644	452	795	832	820	829	486	612	629	579	561	562
BALB/cJBomTac	683	678	669	337	0		664	464	828	864	852	861	497	628	647	600	578	584
BTBR T<+>	451	443	447	650	644	664		668	690	715	703	712	673	666	688	598	617	639
C3H	685	667	659	413	452	464	668		880	923	911	920	202	482	476	593	610	606
C57BL/10SgSnAiTac	844	847	854	904	795	828	690	880		68	56	65	856	838	856	797	793	766
C57BL/6J	869	872	879	953	832	864	715	923	68		12	3	901	877	892	822	820	795
C57BL/6NTAC	857	860	867	941	820	852	703	911	56	12		9	889	865	880	810	808	783
C57BL6/JBomTac	866	869	876	950	829	861	712	920	65	3	9		898	874	889	819	817	792
CBA/JBomTac	699	683	675	477	486	497	673	202	856	901	889	898		439	454	597	618	632
DBA/1JBOMTAC	696	687	678	638	612	628	666	482	838	877	865	874	439		99	641	634	629
DBA/2NTac	725	716	707	650	629	647	688	476	856	892	880	889	454	99		646	616	630
FVB	619	621	620	519	579	600	598	593	797	822	810	819	597	641	646		491	382
NOD/Tac	638	638	630	546	561	578	617	610	793	820	808	817	618	634	616	491		521
SJL	592	599	595	567	562	584	639	606	766	795	783	792	632	629	630	382	521	

Genetic Monitoring-Genetically Modified Mice

- **Nomenclature**
  - –Genetic Background
  - –Allele Nomenclature

C57BL/6-*Bmp15*^{tm1Zuk}

B6.129- *Bmp15*^{tm1Zuk}

Strain Nomenclature

Guidelines for Nomenclature of Mouse and Rat Strains
Revised: September 2010

International Committee on Standardized Genetic Nomenclature for Mice
Chairperson: Dr. Janan T. Eppig
(e-mail: jte@informatics.jax.org)

Rat Genome and Nomenclature Committee
Chairperson: Dr. Goran Levan
(e-mail: Goran.Levan@gen.gu.se)

•In 2001, the International Committee on Standardized Nomenclature for Mice and the Rat Genome and Nomenclature Committee agreed to establish a joint set of rules for strain nomenclature, applicable to strains of both species. These rewritten guidelines reflect this collaboration, in addition to documenting new and revised rules for the naming of strains. This document is updated annually by the international nomenclature committees for mouse and rat.

Allele Nomenclature



Guidelines for Nomenclature of Genes, Genetic Markers, Alleles, and Mutations in Mouse and Rat

Revised: September 2010

International Committee on Standardized Genetic Nomenclature for Mice

Chairperson: Dr. Janan T. Eppig

(e-mail: jte@informatics.jax.org)

Rat Genome and Nomenclature Committee

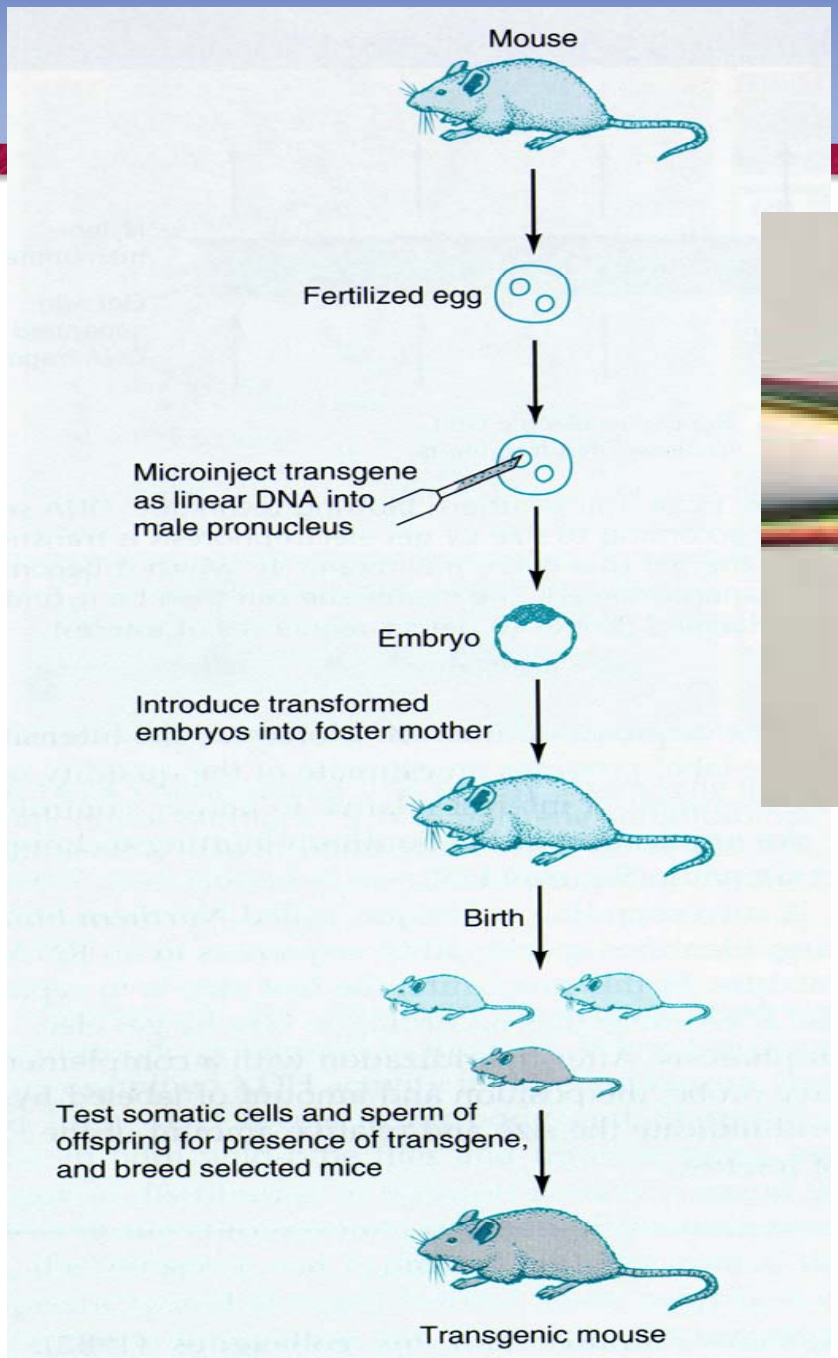
Chairperson: Dr. Goran Levan

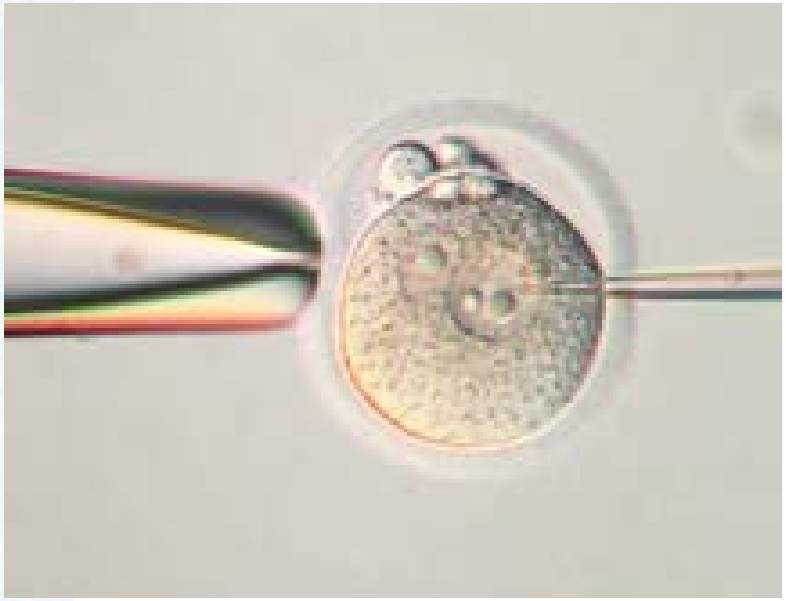
(e-mail: Goran.Levan@gen.gu.se)

•Rules for mouse genetic nomenclature were first published by Dunn, Gruneberg, and Snell (1940) and subsequently revised by the International Committee for Standardized Genetic Nomenclature in Mice (1963, 1973, 1981, 1989, 1996). The most recent publication of mouse nomenclature guidelines can be found in Eppig (2006). Users should be advised, however, that this web version represents the current nomenclature policies of the International Committee for Standardized Genetic Nomenclature for Mice and takes precedent over previously published versions.

•Rules for rat genetic nomenclature were first published by the Committee on Rat Nomenclature in 1992 and then by Levan *et al.* in 1995.

Pronuclear Injections= Transgenic Mice







Genetic Modified Models

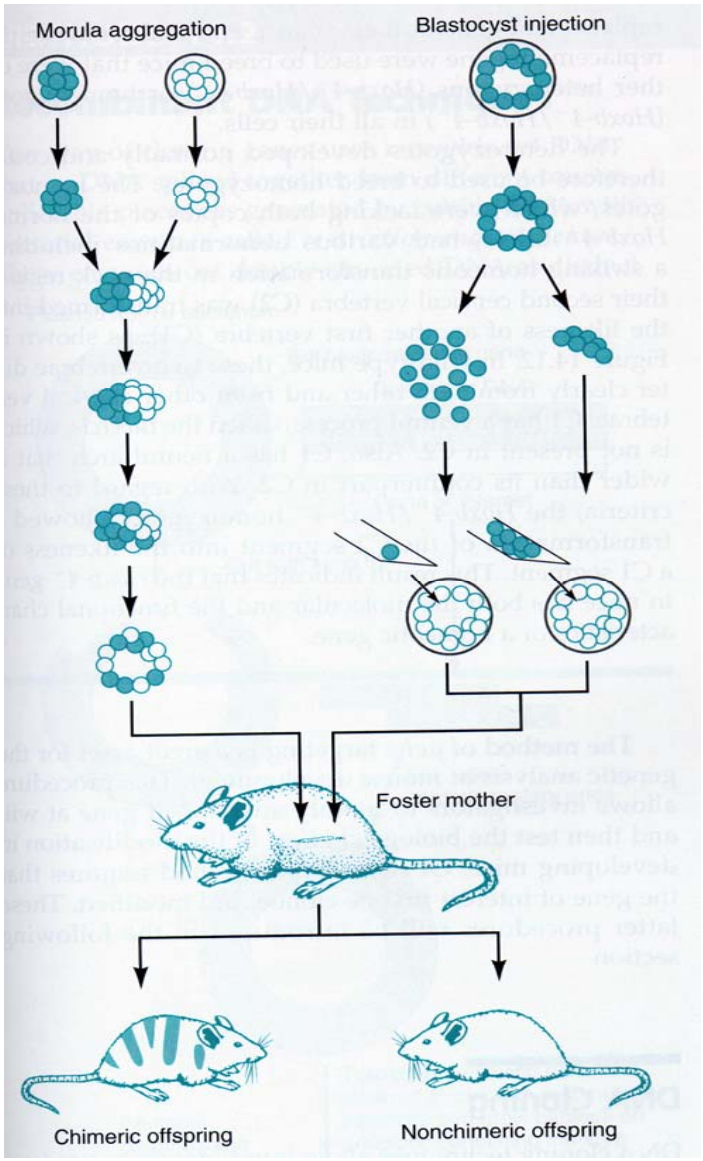


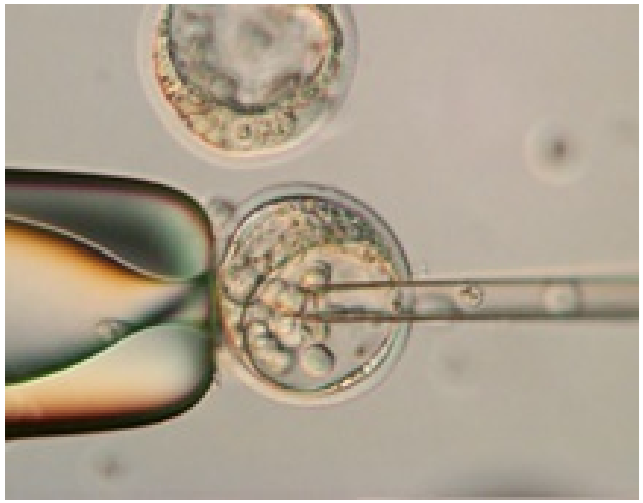
- **Pronuclear Injections**
  - Integrates anywhere in the genome
  - Several copies are usually integrated in a head to tail manner
  - Depending upon the site of integration there could be genetic instability of the transgene
  - Difficult to map the site of integration
  - Rules of Nomenclature

    Formal nomenclature is: Tg(Prom-YYY)#Zzz

Knock-Out or Knock-In Mice







Genetic Modified Models



- **Targeted Mutagenesis**
  - DNA insertion is by homologous recombination, so there is sequence similarity between the injected DNA and the targeted DNA
  - There is only one copy in the site of integration
  - In the chimaera there are two strains in one mouse (two genomes)
  - Rules of Nomenclature

    Formal nomenclature is: YYY$^{tm\#Zzz}$

What 's in a Name?

STOCK *Bmp15^{tm1Zuk} Tg(Pgk1-EGFP)1Arte*

STOCK= genetic background

Bmp15= Bone morphogenetic protein 15

tm1 = targeted mutant 1

Tg =Transgenic

(Pgk1-EGFP)

- **Promoter = Phosphoglycerate kinase 1**
- **Gene = enhanced green fluorescent protein**

1 = laboratory assigned number (founder number)

Zuk & Arte= Laboratory registration codes

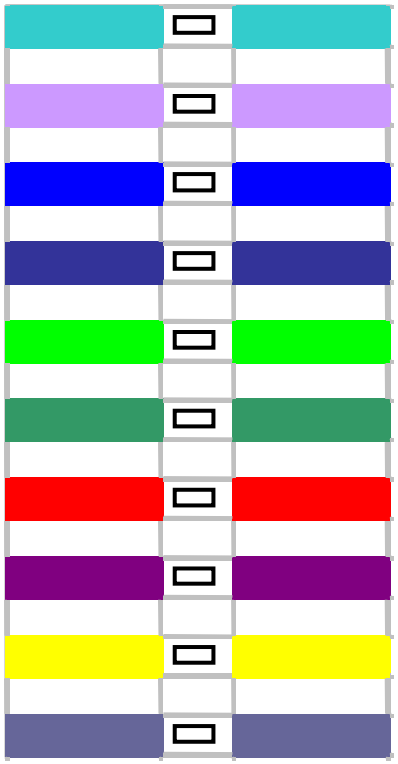
Congenic Strain

Definition: An (inbred) strain that is produced by repeated backcrosses to an inbred (background; partner) strain, with selection for a particular marker / gene / locus from a donor strain

Result: An inbred strain that differs from the standard “partner” inbred strain background by a small number of genes, mostly (but not entirely) surrounding the selected gene locus

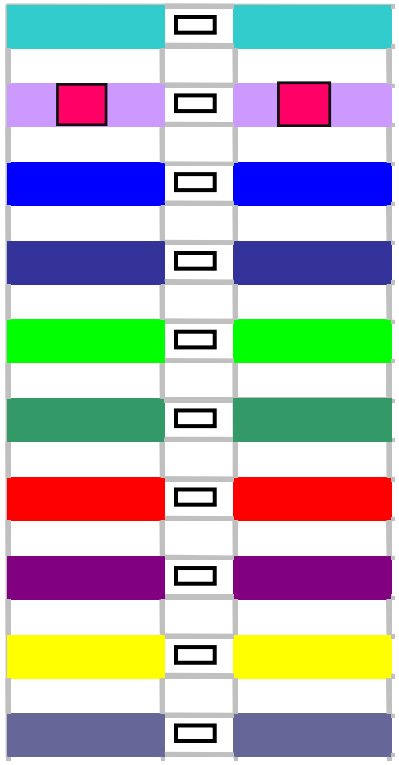
How to obtain a Congenic Strain

B6



Ptprc^{b}

Line 4007



Ptprc^{a}

a small segment of the chromosome derived from the SJL inbred strain by generations of backcrossing to B6

"Almost" a B6 mouse with a slightly different marker protein on its white cells, useful for transplantation studies

X and Y Chromosomes in a backcross

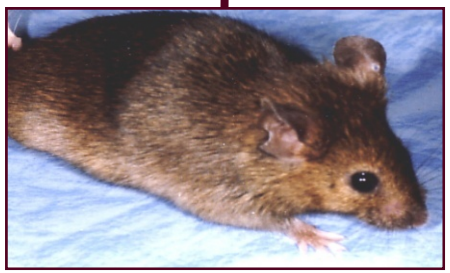


B6 Female
Ptprc^{b}

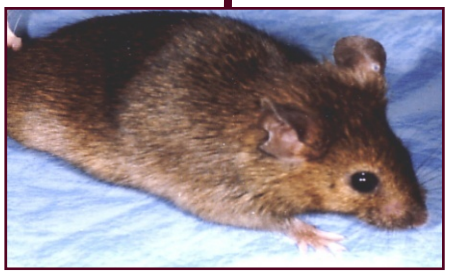
XX

XY

SJL Albino
Ptprc^{a}



Agouti
Female



Agouti Male

XX

F1

XY

X Y Chomosomes in a Backcross



B6 Female

XX

XY from N4

Black Male

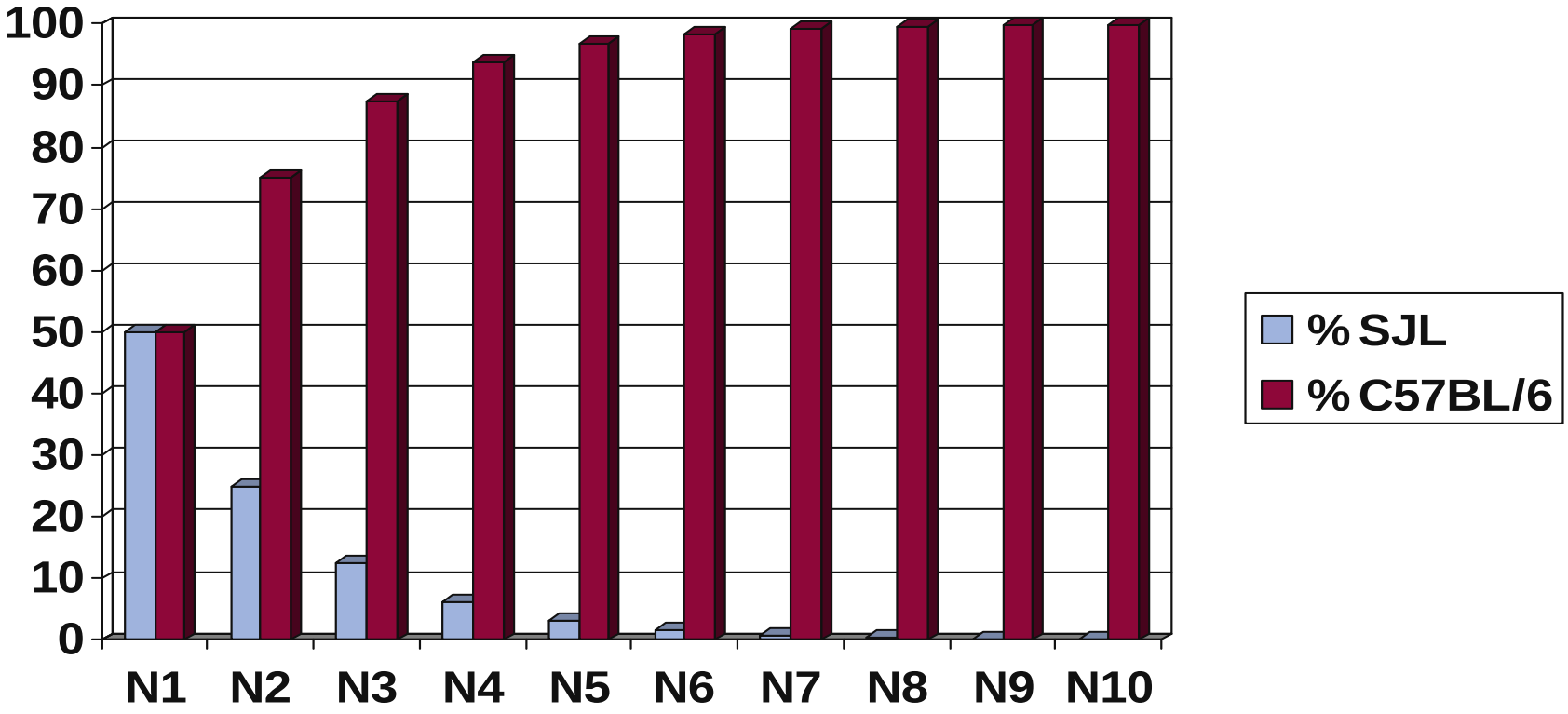
N5

Offspring will be XX and XY

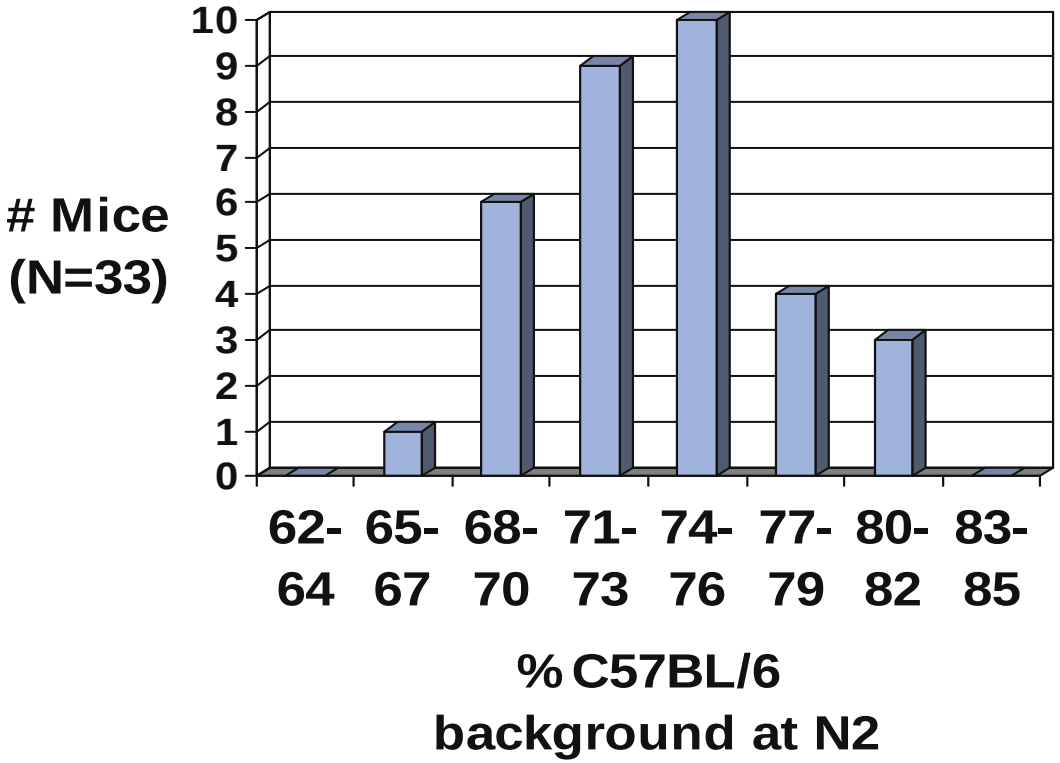
You can continue to choose all males to backcross on the next generations

Normal Backcrossing-Congenics

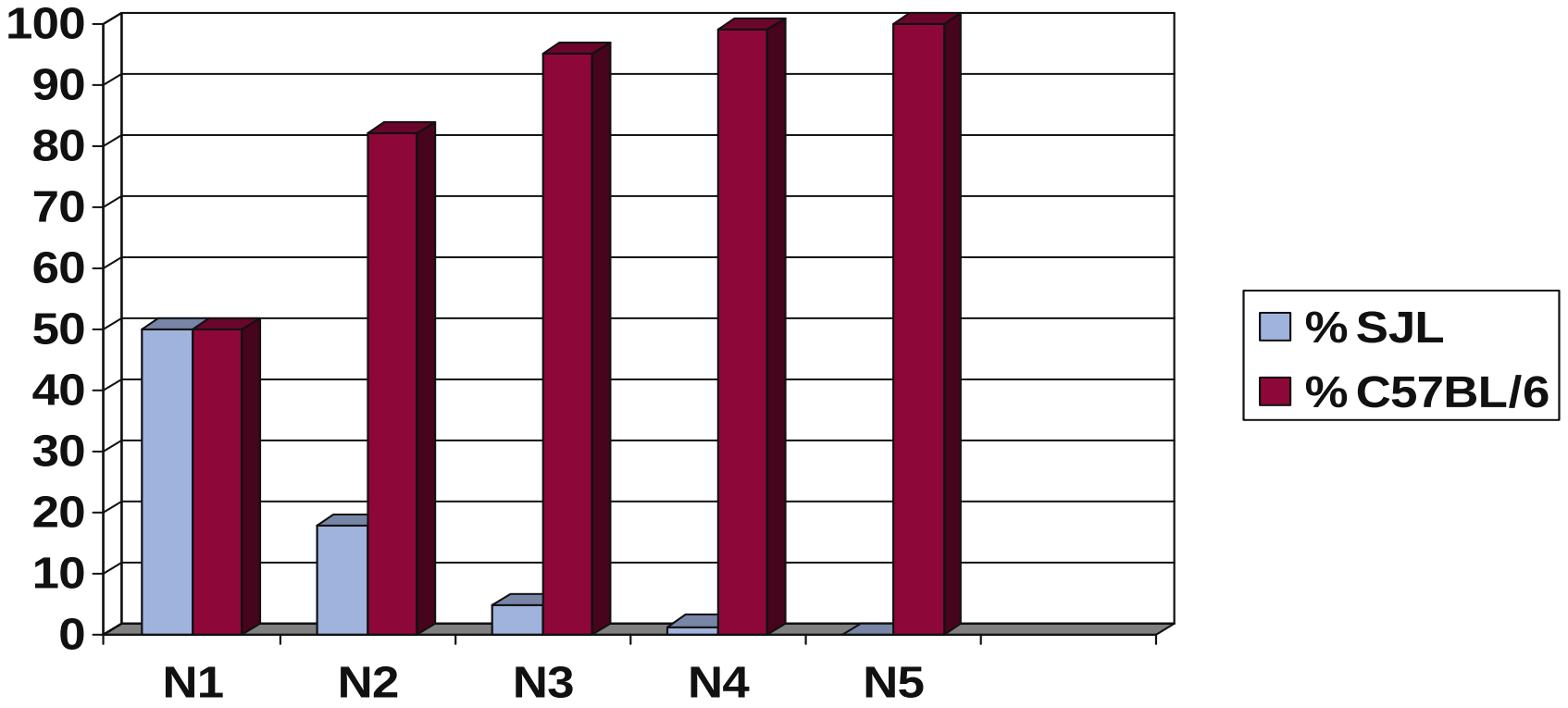




Distribution of Normal Backcrossing



Speed Congenics



Taconic SNP Panel Testing Report: Data



				Genotyping Result						Congenic Result			
Index	Chr	Position	SNPs that differentiate between C57BL/6N ar	60_129S6_Ref_Ref_0836 (377).GType	B6N(377).GType2	14A_UNK_BKG_0916.GType	18A_UNK_0916.GType	20A_UNK__0916.GType	21A_UNK___0916.GType	14A_UNK_BKG_0916.GType2	18A_UNK_0916.GType3	20A_UNK__0916.GType4	21A_UNK___0916.GType5
8	17	37478448		AA	AA	AA	AA	AA	AA	1	1	1	1
316	17	41235453		AA	BB	BB	BB	BB	BB	1	1	1	1
376	17	44325625		BB	AA	AA	AA	AA	AA	1	1	1	1
170	17	46772416		BB	BB	BB	BB	BB	BB	1	1	1	1
52	17	61947366		AA	AA	AA	AA	AA	AA	1	1	1	1
63	17	64224877		BB	BB	BB	BB	BB	BB	1	1	1	1
201	17	67483047		BB	AA	AA	AA	AA	AA	1	1	1	1
171	17	73981248		AA	BB	BB	BB	BB	BB	1	1	1	1
218	17	77914489		AA	BB	BB	BB	BB	BB	1	1	1	1
64	17	85857606		AA	BB	BB	BB	BB	BB	1	1	1	1
9	17	86913143		BB	BB	BB	BB	BB	BB	1	1	1	1
45	18	10431432		BB	AA	AA	AA	AA	AA	1	1	1	1
280	18	12221563		BB	BB	BB	BB	BB	BB	1	1	1	1
358	18	16784949		BB	AA	AB	AB	AB	AB	0.5	0.5	0.5	0.5
172	18	19671420	X	BB	BB	BB	BB	BB	BB	1	1	1	1
233	18	30952210		AA	BB	AB	AB	AB	AB	0.5	0.5	0.5	0.5
285	18	33572164		BB	BB	BB	BB	BB	BB	1	1	1	1
253	18	33968545		BB	BB	BB	BB	BB	BB	1	1	1	1
217	18	58570705		AA	BB	BB	BB	BB	BB	1	1	1	1
317	18	63022572		BB	BB	BB	BB	BB	BB	1	1	1	1
351	18	65694361		BB	AA	AA	AA	AA	AA	1	1	1	1

Taconic

Congenic Genetically Modified Strain

B6.FVB– *Bmp15^{tm1Zuk} Tg(Pgk1-EGFP)1Arte*

B6.FVB= genetic background

Bmp15= Bone morphogenetic protein 15, this is X-linked

tm1 = targeted mutant 1

Tg =Transgenic

(Pgk1-EGFP)

- **Promoter = Phosphoglycerate kinase 1**
- **Gene = enhanced green fluorescent protein**

1 = laboratory assigned number (founder number)

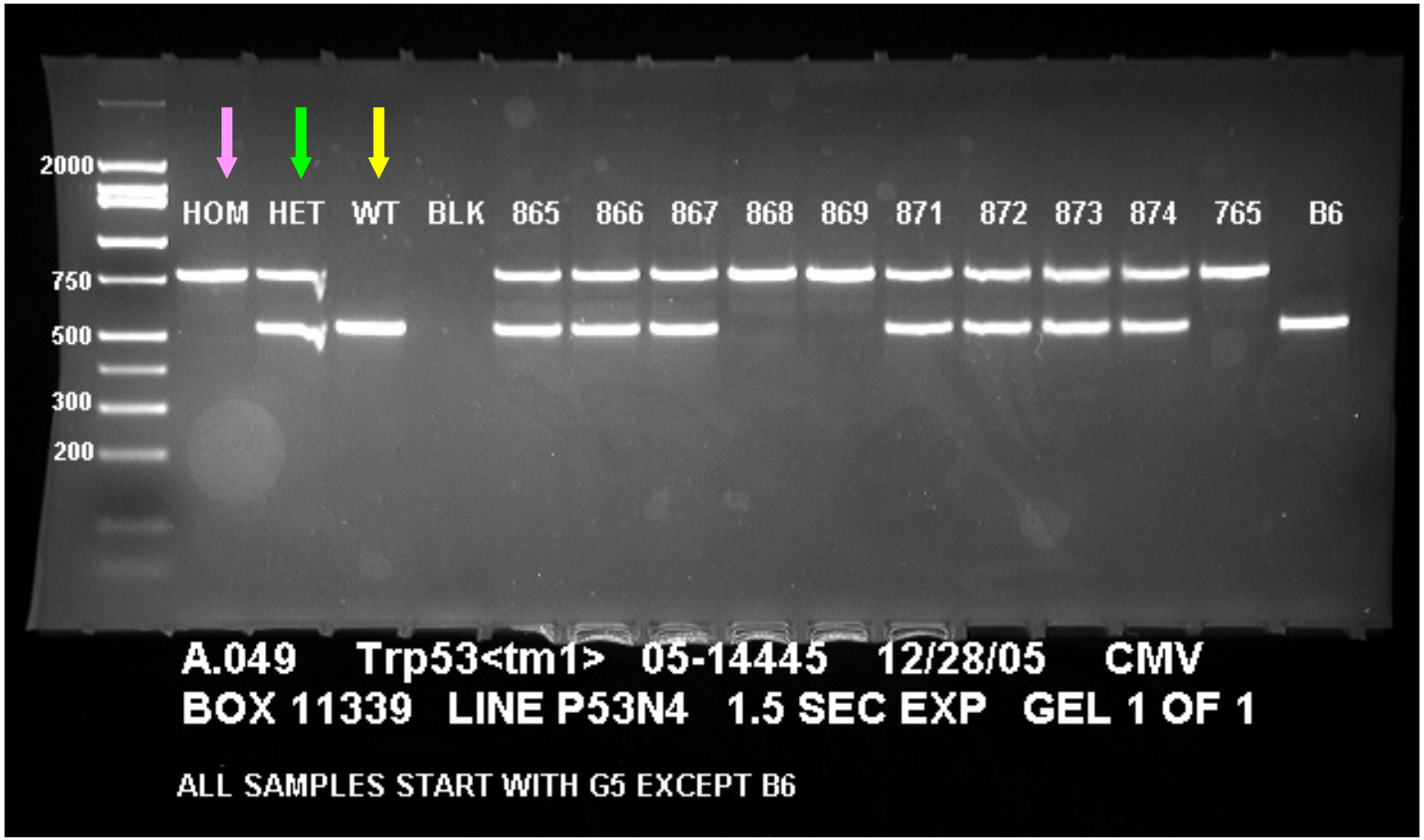
Zuk & Arte= Laboratory registration codes

Genotyping

- **Southern Blot**
  - Laborious and time consuming
  - Need information of genetic construct
  - Allows assessment of mutation in the whole context of the genome
- **PCR**
  - Easy to execute and scalable
  - High through-put
  - Need only minor sequence information
- **Quantitative PCR**
  - Same advantages of PCR
  - Able to assess copy number

Genotyping by PCR

Example: Mating Format Het x Het



Fragment 1 (upper) is associated with mutant allele; Fragment 2 (lower) is wild-type

Steps in Genetic Monitoring

- **What is the make-up of the incoming strain**
  - Inbred/Outbred/Genetically modified/Spontaneous mutant
- **Nomenclature**
  - Need information about genetic background
  - Need information about generation numbers
  - Need information about how the mutations were made and where
  - Breeding history of the model before receipt
- **What are the goals of the project**
  - Backcrossing
  - Genotyping Protocols
  - Breeding Format considering breeding challenges
  - Cohort delivery for phenotyping
- **How to minimize genetic drift**
  - Cryopreservation

Project Goals



B6.FVB– *Bmp15^{tm1Zuk}* *Tg(Pgk1-EGFP)1Nrl*

x

C57BL/6– *Tg(GFAP-Cre)25Mes*

B6.FVB–*Bmp15^{tm1Zuk}* *Tg(Pgk1-EGFP)1Nrl* *Tg(GFAP-Cre)25Mes*

Beware of Genetic Contamination!!!!!

Mating Format for Project Goals

B6.FVB– *Bmp15^{tm1Zuk}* *Tg(Pgk1-EGFP)1Nrl*

X

XX *Bmp15$^{-/-}$; EGFP$^{0/-}$*

C57BL/6– *Tg(GFAP-Cre)25Mes*

XY Cre$^{+/-}$

B6.FVB–*Bmp15^{tm1Zuk}* *Tg(Pgk1-EGFP)1Nrl* *Tg(GFAP-Cre)25Mes*

XY *Bmp15$^{-/0}$; EGFP$^{+/-}$* Cre$^{+/-}$

Mating Format for Project Goals

B6.FVB– *Bmp15^{tm1Zuk}* *Tg(Pgk1-EGFP)1Nrl*

X

XX *Bmp15$^{-/+}$; EGFP$^{0/-}$*

C57BL/6– *Tg(GFAP-Cre)25Mes*

XY Cre$^{+/-}$

B6.FVB–*Bmp15^{tm1Zuk}* *Tg(Pgk1-EGFP)1Nrl* *Tg(GFAP-Cre)25Mes*

XY *Bmp15$^{-/0}$; EGFP$^{+/0}$;* Cre$^{+/0}$

XY *Bmp15$^{+/0}$; EGFP$^{+/0}$;* Cre$^{+/0}$

Genetic Background for Project Goals

B6.FVB– *Bmp15^{tm1Zuk}* *Tg(Pgk1-EGFP)1Nrl*

X

XX *Bmp15$^{-/+}$; EGFP$^{0/-}$*

C57BL/6– *Tg(GFAP-Cre)25Mes*

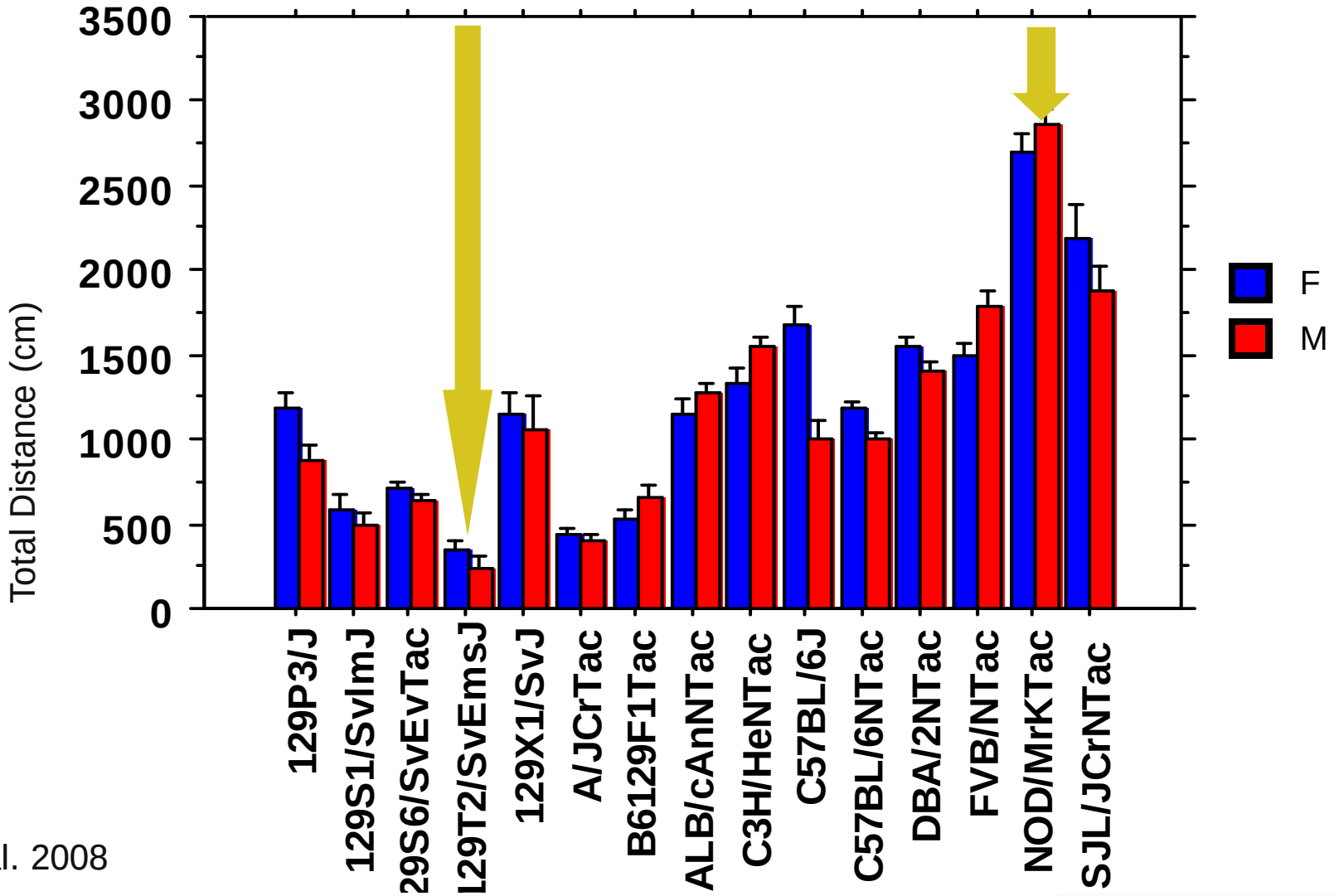
XY Cre$^{+/-}$

B6.FVB–*Bmp15^{tm1Zuk}* *Tg(Pgk1-EGFP)1Nrl* *Tg(GFAP-Cre)25Mes*

XY *Bmp15$^{-/0}$; EGFP$^{+/0}$;* Cre$^{+/0}$

XY *Bmp15$^{+/0}$; EGFP$^{+/0}$;* Cre$^{+/0}$

Open Field Activity (first exposure)



Taconic -G. Bothe et al. 2008

Nnt and Snca mutations



- **Nnt- N**icotinamide **n**ucleotide **t**ransferase, associated with impair glucose homeostasis and reduced insulin secretion. Reported as ~17 Kbp deletion

- **Snca- S**y**n**u**c**lein **a**lpha, associated with resistance to the effects of MPTP (1-methyl-4 phenyl -1,2,3,6-tetrahydropyridine, used as prototypical toxin) on dopamine levels. Reported as 365 Kbp deletion

Differences between C57BL/6 sub-strains



- **Different Flavors of C57BL/6: C57BL/6J, C57BL/6NTac, C57BL/6JBom, C57BL/6NHsd**

C57BL/6 Sub-strain	Nnt Mutation	Snca Mutation
C57BL/6J	Yes	No
C57BL/6JOlaHsd	Yes	Yes
C57BL/6JBom	No	No
C57BL/6NTac	No	No

Importance of Genetic Background

- **What's a researcher to do?**
  - Know the genetic background of your mice
  - Check the background of your mice
  - Do not mix backgrounds for experiments, if you do try to normalize the genetic background to a reference strain

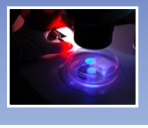
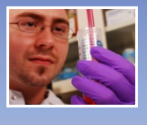
- **How do we help?**
  - Background Characterization
  - Speed Congenics

MDL (1449) SNP Panel Differences

Table 2: Strain Differences in 1449 Marker Panel

	129P3/J	129S4/SvJae	129S6/SvEvTac	A/JCrTac	BALB/cAnNTac	BALB/cJBomTac	BTBR T<+>	C3H/HeNTac	C57BL/10SgSnAiTac	C57BL/6J	C57BL/6NTac	C57BL6/JBomTac	CBA/JBomTac	DBA/1JBomTac	DBA/2NTac	FVB/NTac	NOD/Tac	SJL/JCrNTac
129P3/J		19	39	716	666	683	451	685	844	869	857	866	699	696	725	619	638	592
129S4/SvJae	19		22	713	662	678	443	667	847	872	860	869	683	687	716	621	638	599
129S6/SvEvTac	39	22		704	652	669	447	659	854	879	867	876	675	678	707	620	630	595
A/JCrTac	716	713	704		326	337	650	413	904	953	941	950	477	638	650	519	546	567
BALB/cAnNTac	666	662	652	326		0	644	452	795	832	820	829	486	612	629	579	561	562
BALB/cJBomTac	683	678	669	337	0		664	464	828	864	852	861	497	628	647	600	578	584
BTBR T<+>	451	443	447	650	644	664		668	690	715	703	712	673	666	688	598	617	639
C3H	685	667	659	413	452	464	668		880	923	911	920	202	482	476	593	610	606
C57BL/10SgSnAiTac	844	847	854	904	795	828	690	880		68	56	65	856	838	856	797	793	766
C57BL/6J	869	872	879	953	832	864	715	923	68		12	3	901	877	892	822	820	795
C57BL/6NTAC	857	860	867	941	820	852	703	911	56	12		9	889	865	880	810	808	783
C57BL6/JBomTac	866	869	876	950	829	861	712	920	65	3	9		898	874	889	819	817	792
CBA/JBomTac	699	683	675	477	486	497	673	202	856	901	889	898		439	454	597	618	632
DBA/1JBOMTAC	696	687	678	638	612	628	666	482	838	877	865	874	439		99	641	634	629
DBA/2NTac	725	716	707	650	629	647	688	476	856	892	880	889	454	99		646	616	630
FVB	619	621	620	519	579	600	598	593	797	822	810	819	597	641	646		491	382
NOD/Tac	638	638	630	546	561	578	617	610	793	820	808	817	618	634	616	491		521
SJL	592	599	595	567	562	584	639	606	766	795	783	792	632	629	630	382	521	

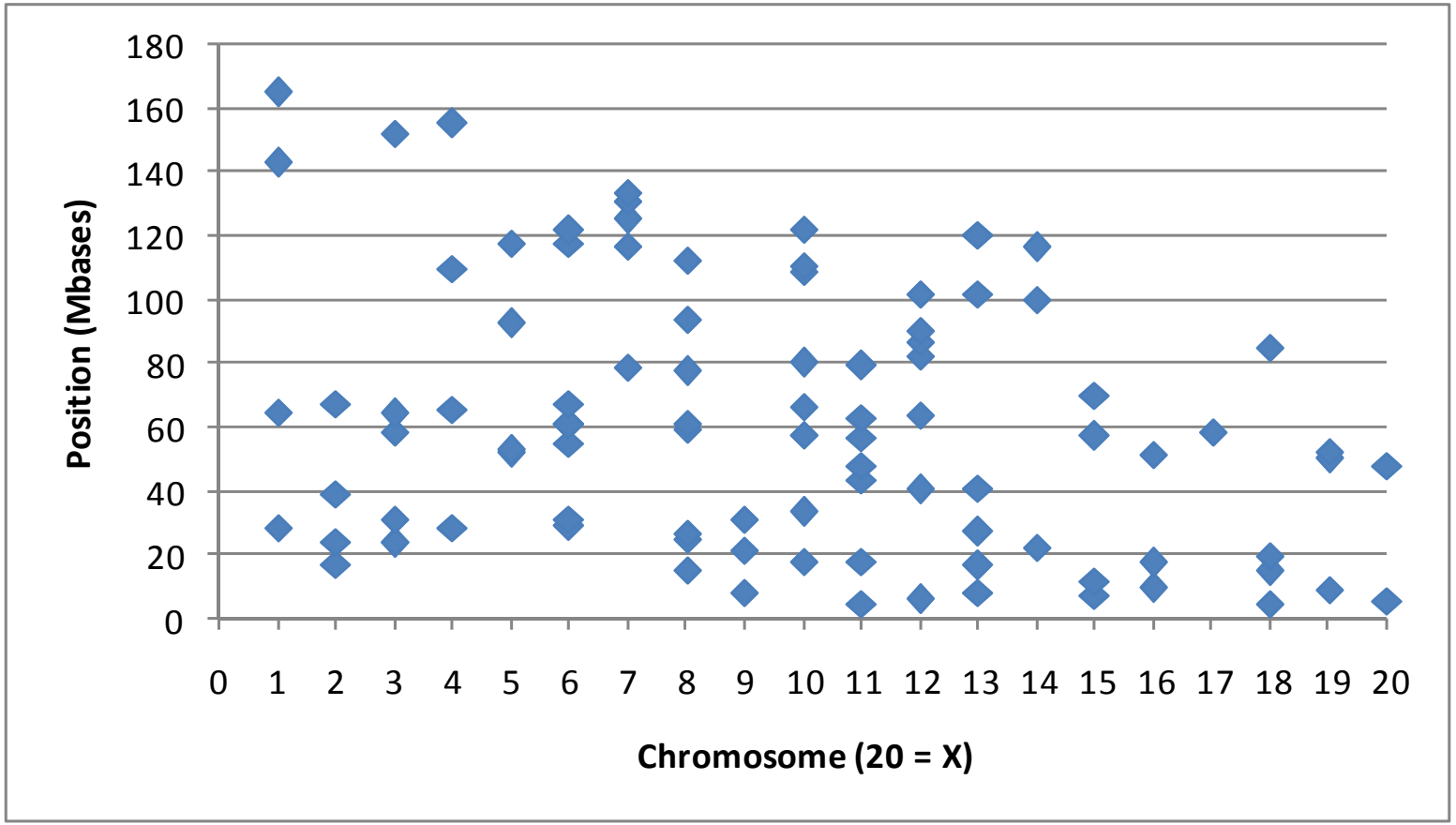
LDL (377) SNP Panel Differences


	129S2/SvHsd	129S4/SvJae	129S6/SvEvTac	A/Jtac	BALB/cAnNTac	BALB/cJBomTac	BTBR/J	C3H/HeNTac	C57BL/10SgSnAiTac	C57BL/6J	C57BL/6JBomTac	C57BL/6NTac	CBA/JBomTac	DBA/1JBomTac
129S2/SvHsd		1	6	160	166	166	108	160	225	241	235	230	153	152
129S4/SvJae	1		5	161	167	167	109	161	224	240	234	229	154	153
129S6/SvEvTac	6	5		160	162	162	114	158	227	243	237	232	153	152
A/Jtac	160	161	160		76	76	166	116	251	271	265	260	129	159
BALB/cAnNTac	166	167	162	76		0	166	106	225	245	239	234	129	165
BALB/cJBomTac	166	167	162	76	0		166	106	225	245	239	234	129	165
BTBR/J	108	109	114	166	166	166		164	177	193	187	182	155	159
C3H/HeNTac	160	161	158	116	106	106	164		239	259	253	248	55	131
C57BL/10SgSnAiTac	225	224	227	251	225	225	177	239		28	22	17	226	222
C57BL/6J	241	240	243	271	245	245	193	259	28		6	11	248	242
C57BL/6JBomTac	235	234	237	265	239	239	187	253	22	6		5	242	236
C57BL/6NTac	230	229	232	260	234	234	182	248	17	11	5		237	231
CBA/JBomTac	153	154	153	129	129	129	155	55	226	248	242	237		118
DBA/1JBomTac	152	153	152	159	165	165	159	131	222	242	236	231	118	
DBA/2NTac	167	168	167	152	162	162	162	124	231	251	245	240	121	23

Distribution of Markers for C57BL/6 Panel





C57BL/6 SNP Panel Differences



Mouse Strain	vs. 129SVE	vs. B10	vs. B6	vs. B6JBom	vs. C57BL/6NCrl	vs. C57BL/6NHsd	vs. C57BL/6J -lyst<bg>	vs. C57BL/6J	vs. C57BL/6ByJ	vs. C57BL/6NJ
129SVE (129S6/SvEvTac)		0	1	46	1	1	86	89	0	3
B10 (C57BL/10SgSnAiTac)	0		1	46	1	1	86	89	0	3
B6 (C57BL/6NTac)	1	1		47	0	0	87	90	1	2
B6JBom (C57BL6/JBomTac)	46	46	47		47	47	40	44	46	49
C57BL/6NCrl	1	1	0	47		0	87	90	1	2
C57BL/6NHsd	1	1	0	47	0		87	90	1	2
C57BL/6J-lyst<bg>	86	86	87	40	87	87		10	86	89
C57BL/6J	89	89	90	44	90	90	10		89	92
C57BL/6ByJ	0	0	1	46	1	1	86	89		3
C57BL/6NJ	3	3	2	49	2	2	89	92	3	

Cryopreservation

- **Back-up in case of genetic contamination**
- **Back up in case of genetic instability**
- **Back-up in case of undesirable genotypes in conditional models**
- **Back-up in case of natural disasters**
- **Back-up to minimize genetic drift**
- **Archiving genetic model**

Steps in Genetic Monitoring

- **What is the make-up of the incoming strain**
  - Inbred/Outbred/Genetically modified/Spontaneous mutant
- **Nomenclature**
  - Need information about genetic background
  - Need information about generation numbers
  - Need information about how the mutations were made and where
  - Breeding history of the model before receipt
  - Genotyping Protocols
- **What are the goals of the project**
  - Backcrossing
  - Breeding Format considering breeding challenges
  - Cohort delivery for phenotyping
- **How to minimize genetic drift**
  - Cryopreservation

Conclusion

- **Awareness of all checkpoints and considerations for Genetic Quality**
- **There are two parts in Genetic Monitoring to keep the integrity of the model**
  - Genetic Background
  - Genotype
- **Other important factors that may affect Genetic Quality**
  - Mating Formats for desired cohort
  - Intrinsic Problems of models