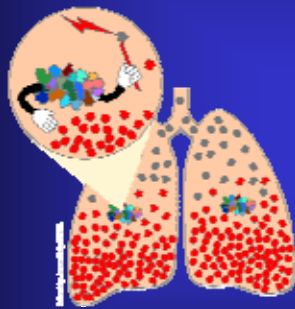


# Bull Selection Strategies Using Genomic Estimated Breeding Values

**Larry Schaeffer**  
**CGIL, University of Guelph**

**ICAR-Interbull Meeting**  
**Niagara Falls, NY**  
**June 18, 2008**

## **Understanding Cancer and Related Topics** **Understanding SNPs and Cancer**



*Developed by:*  
*Susan Greenhut, M.S.*  
*Donna Kerrigan, M.S.*  
*Jeanne Kelly*  
*Brian Hollen*

Explains tiny variations in the human genome called Single Nucleotide Polymorphisms (SNPs) that can influence a person's health. Shows how SNPs occur in both coding and noncoding regions and can cause silent, harmless, harmful, or latent effects. Shows how SNPs can be markers for cancer. Suggests that SNPs may also be involved in the different levels of individual cancer risk observed. Suggests that, in the future, SNPs databases may be used to improve cancer diagnosis and treatment planning.

*These PowerPoint slides are not locked files. You can mix and match slides from different tutorials as you prepare your own lectures. In the Notes section, you will find explanations of the graphics.*

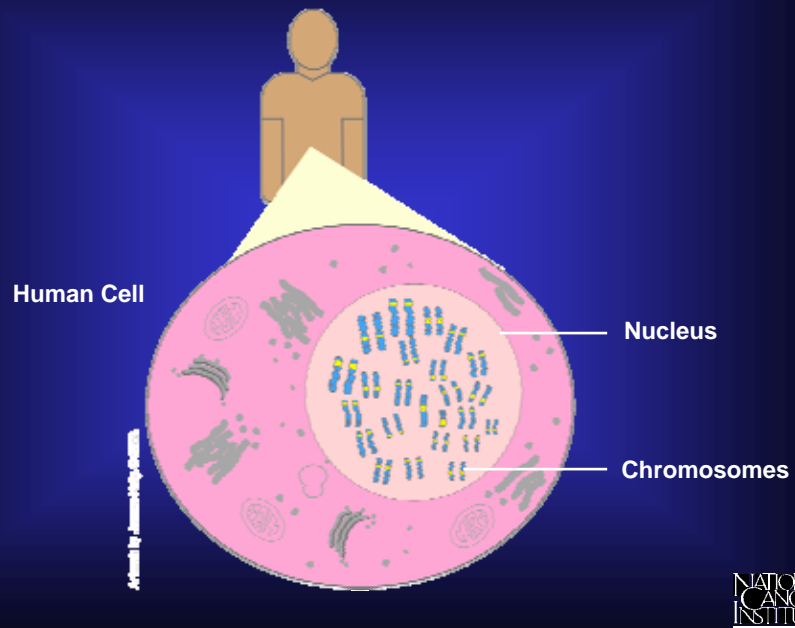
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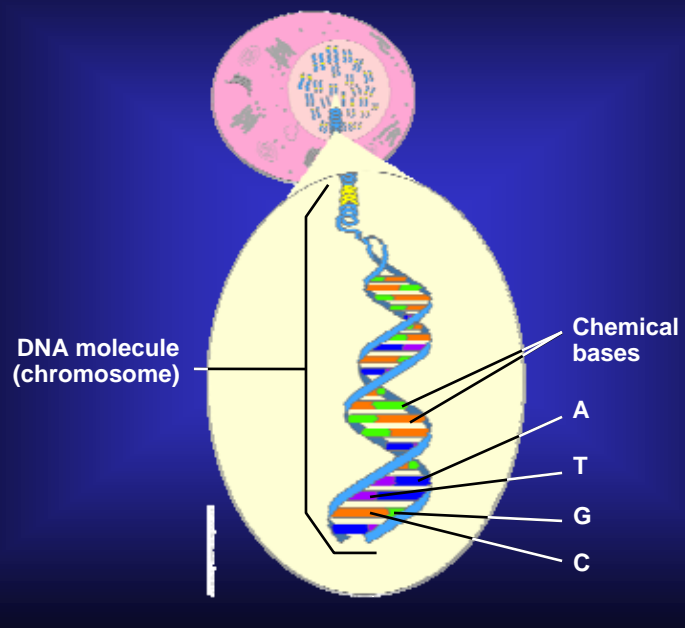
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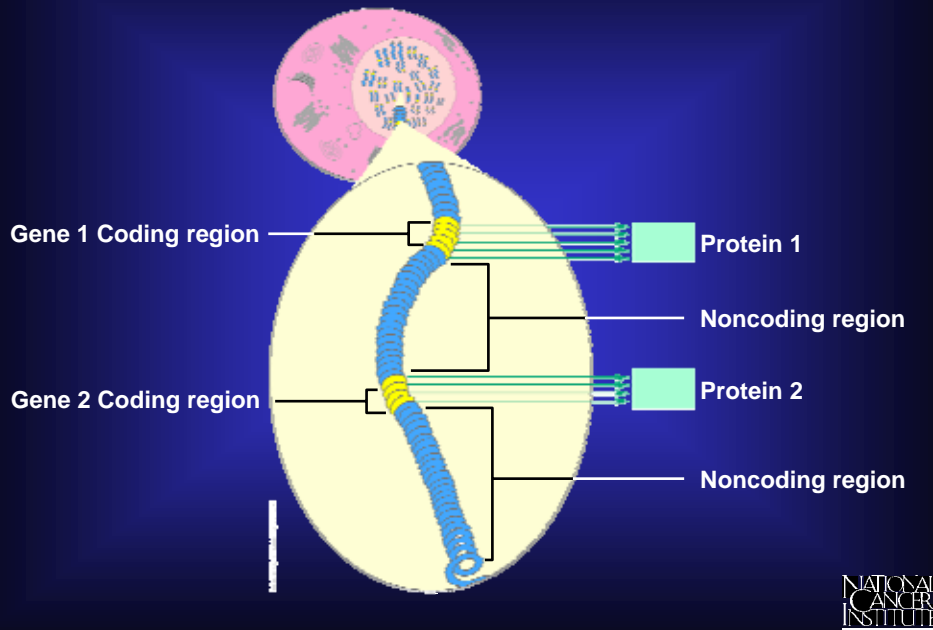
## What Is the Human Genome?



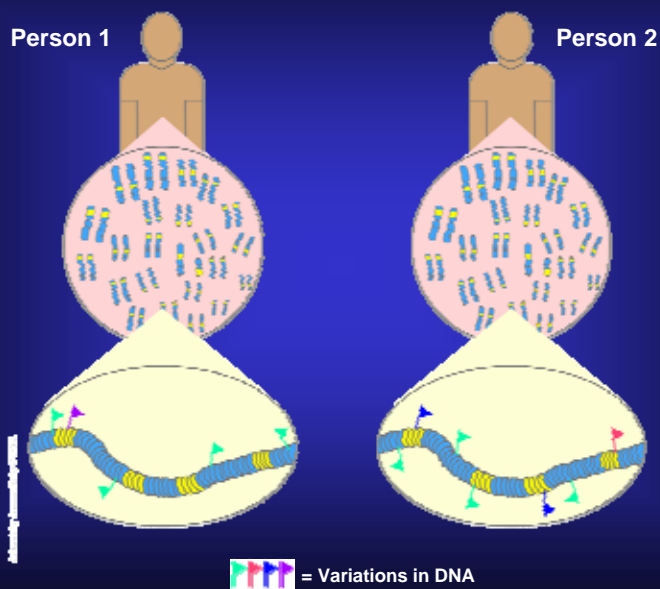
## DNA and Chromosome Structure



## The Genome Contains Genes



## Variation in the Human Genome



# What Is Variation in the Genome?

Common Sequence



Variations



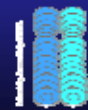
Polymorphism



Deletions



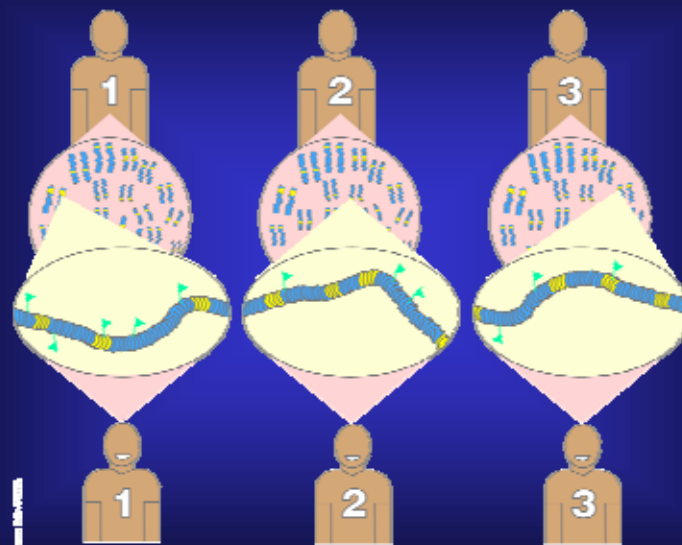
Insertions



Chromosome

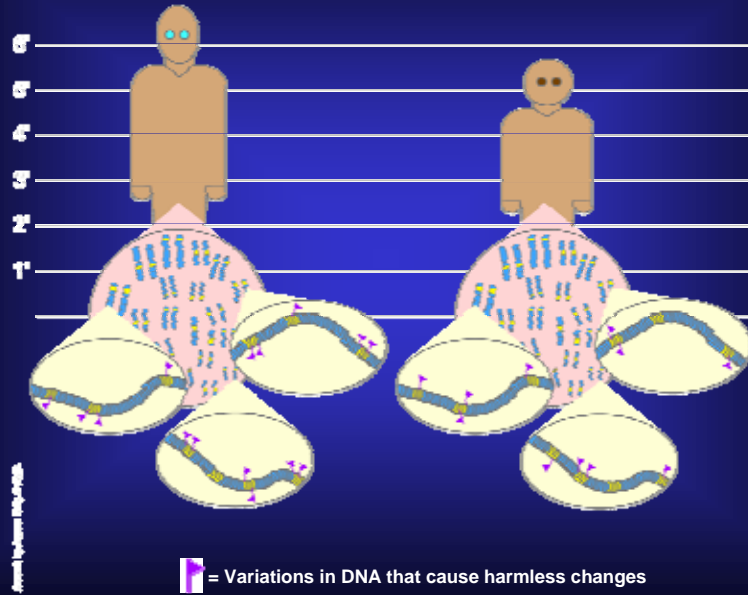
Translocations

# Variations Causing No Changes

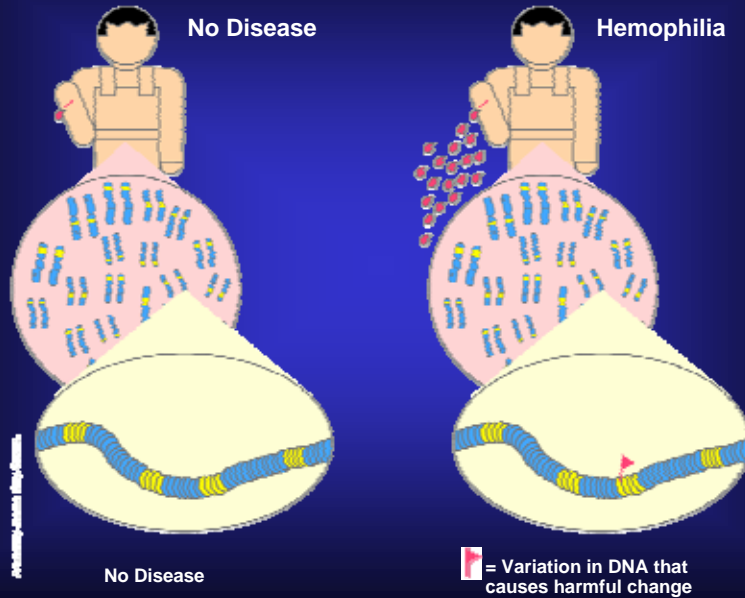


= Variations in DNA that cause no changes

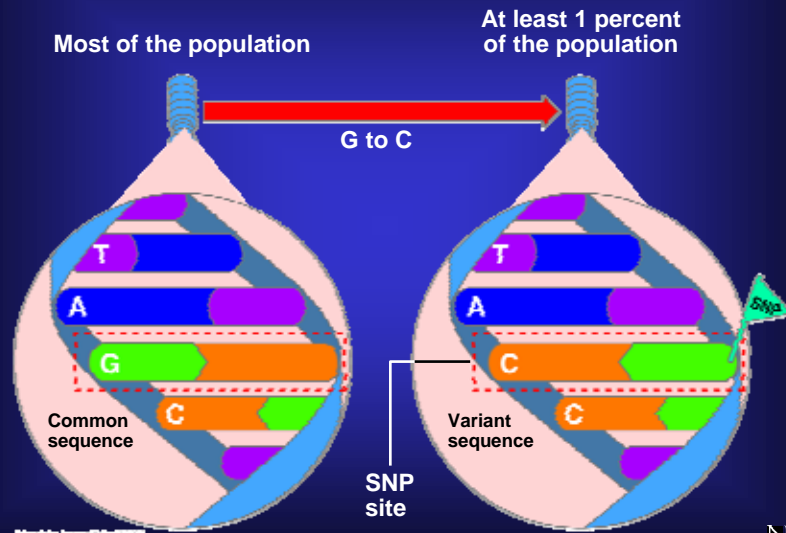
## Variations Causing Harmless Changes



## Variations Causing Harmful Changes



# SNPs Are the Most Common Type of Variation



## Design and Application of the BovineSNP50.



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301-504-6501

**Curt Van Tassell**

USDA  
Agricultural Research Service

## History

- Goals
  1. Implement whole genome selection
  2. QTL detection
- Challenge
  - Needed at least 30,000 good markers
- Problem
  - Product did not exist

## Cattle SNP Collaboration iBMAC

- Develop 60,000 Bead Illumina iSelect® assay
  - USDA-ARS Beltsville Agricultural Research Center: Bovine Functional Genomics Laboratory and Animal Improvement Programs Laboratory
  - University of Missouri
  - University of Alberta
  - USDA-ARS US Meat Animal Research Center
- Starting 60,800 beads – expected 53,000 SNPs to result
- Plan to genotype ~30,000 animals for multiple projects



## SNP Available for Assay Design

### With MAF (18%)

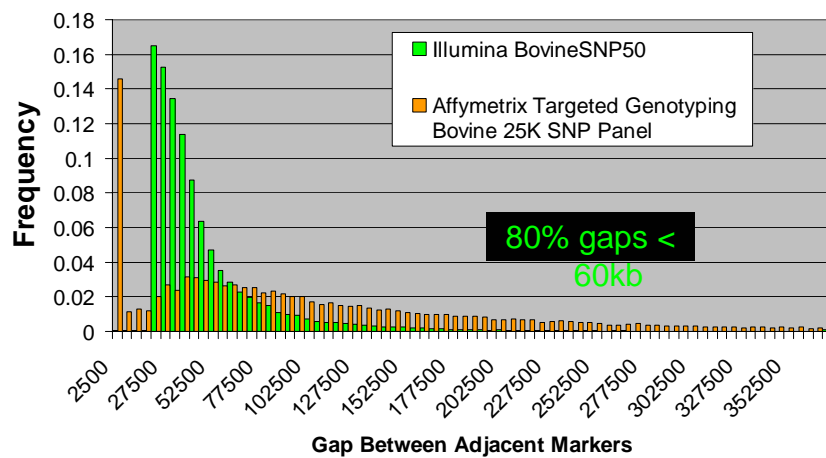
▪ Next Generation Sequencing	62,042
▪ Bovine HapMap Consortium	33,836
▪ DPI, US-MARC,UA	10,574

### InSilico SNPs (72%)

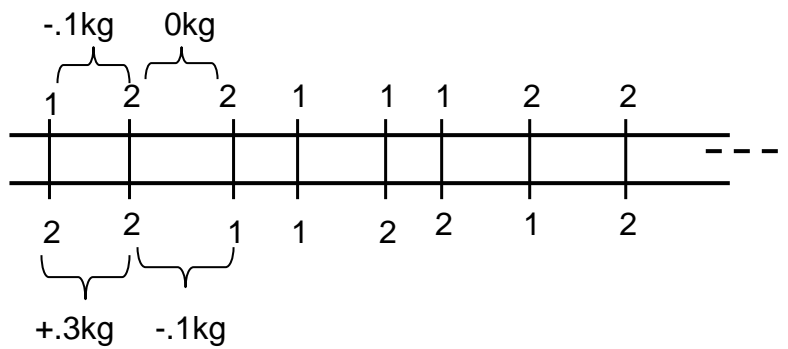
▪ Assembly SNP (Filtered)	278,429
▪ Baylor Interbreed	123,049
▪ BAC and BAC-end Derived	89,832
▪ INRA	764

**Total: 598,648**    **85% Infinium II (1 Bead)**  
**15% Infinium I (2 Beads)**

## Gap Distribution







50,000+ interval estimates

Haplotypes or Genotypes

Hotspots, blocks of markers

GEBV = (Sum of estimates | Genotypes )

## GEBV

1. Estimate 50,000+ genotypes or haplotypes and sum together estimates given genotypes
2. Use genotypes to get more precise A matrix
3. Use polygenic model and add in significant explanatory markers (100-200 markers)
4. Apply data-mining, machine learning to select 3,000 to 5,000 SNP markers

## Advantages of GEBV??

- Better accuracy than Parent Average EBV
- Can be obtained at birth of animal

## Disadvantages??

- SNP interval estimates deteriorate over time
- Effects need to be re-estimated
- Estimates differ between populations
- SNP panels will change over time

## Implications on Bull Selection

Assume that GEBV works

- Accurate, stable
- Available at birth

## Progeny Testing Scheme (PT)

1 Million cows

400 young bulls per year (100 daus)

50 proven bulls per year

Top 20 used as sires of sons

Dams from top 5% of population (0.50)

Young bulls \$10,000 purchase,  
\$6,000/yr

Single trait, heritability=0.30

## PT Time Frame

Year 0 – young bull is born

Year 1 – test matings are made for young bulls

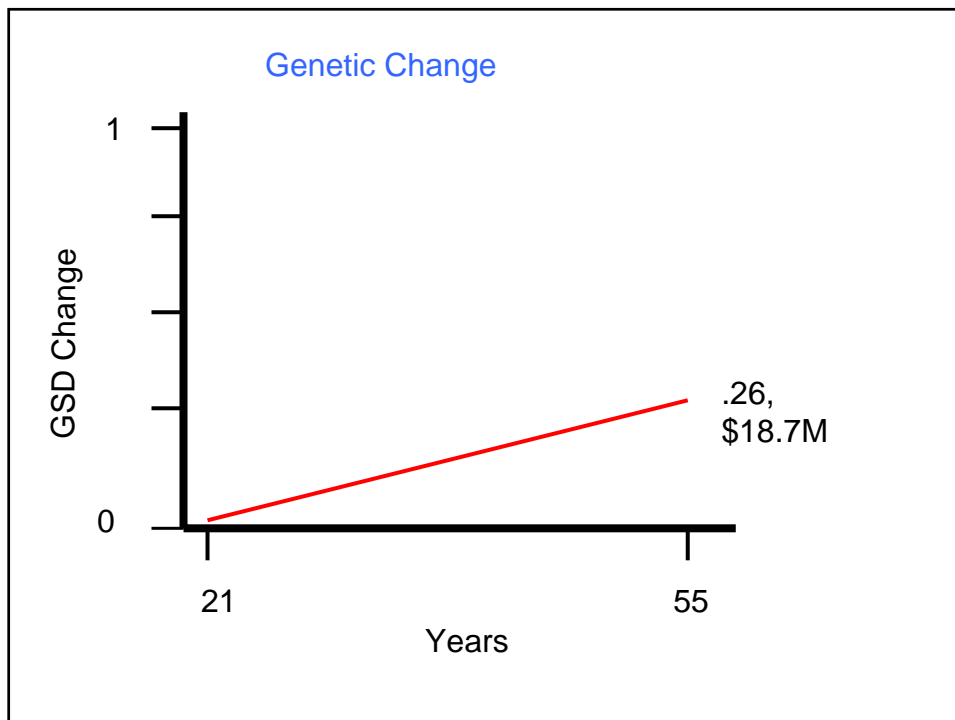
Year 2 – daughters are born

Year 3 – daughters are bred

Year 4 – daughters calve, first lactations begin

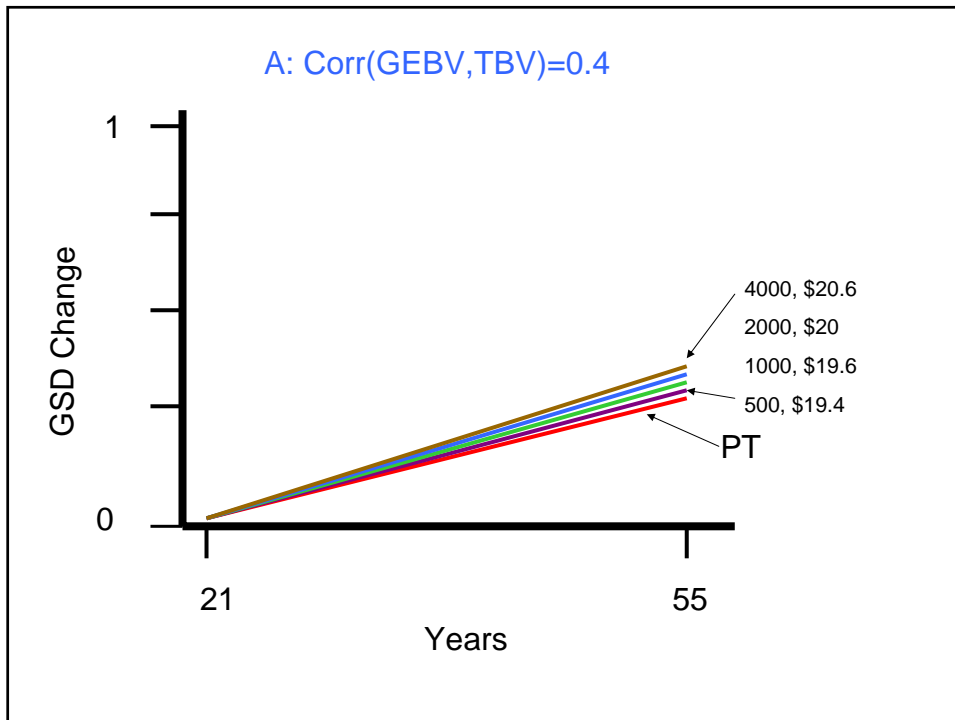
Year 5 – young bulls receive first proofs, culled or returned to service, second crop of daughters started

6 years from birth to proof.



## A: Use GEBV to select young bulls

Young bulls selected using GEBV  
Still go through usual PT scheme  
 $\text{Corr}(\text{GEBV}, \text{TBV}) = 0.4 \text{ to } 0.8$   
500 to 4000 young bulls genotyped at birth  
Purchase price is still \$10,000 per bull  
\$300 to genotype an animal



**Scheme A:**

$\text{Corr}(\text{GEBV}, \text{TBV})$

Increasing from 0.4 to 0.8, no change in GSD per year – about 0.34.

Number of Young Bulls Genotyped

More is better, balance against costs

Number Chosen for PT (400 – 200 – 100)

No drop in GSD, costs decrease to \$6.1 M for 100 bulls

## B: Use Young Bulls as Sire of Sons

Genotype 500-4000 young bulls at birth, GEBV

Select 50, best 20 as Sires of Sons for next generation

---

Cost of purchasing a bull = \$20,000

Special contracts may be needed

## Scheme B: Time Frame

Year 0 – young bull is born AND GENOTYPED, GEBV

Year 1 – Use as though a proven sire, sire of sons

Year 2 –

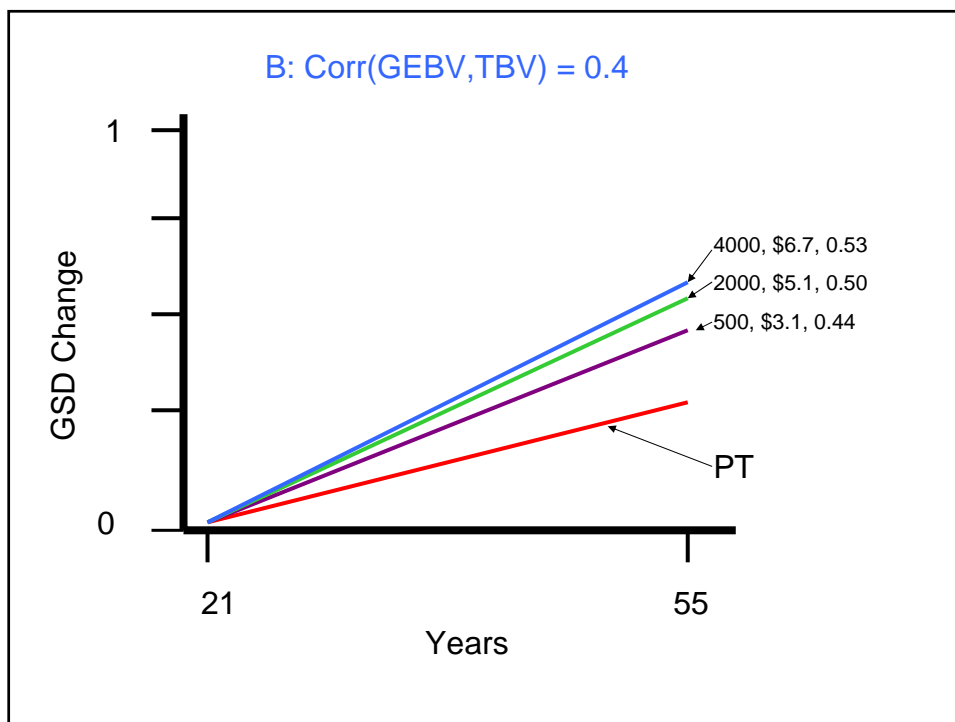
Year 3 –

Year 4 –

Year 5 – young bulls receive usual first proof

0 years from birth to proof, no need to wait 6 years

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**Scheme B:**

$\text{Corr}(\text{GEBV}, \text{TBV})$

Increasing from 0.4 to 0.8, increase GSD 0.50 to 0.55  
for 2000 genotyped young bulls

---

Number of Young Bulls Genotyped

More is better, balance against costs - 2000

---

Turnover rate – 36 out of 50 bulls per year

Costs are less than \$10 M per year



## C: Between Schemes A and B

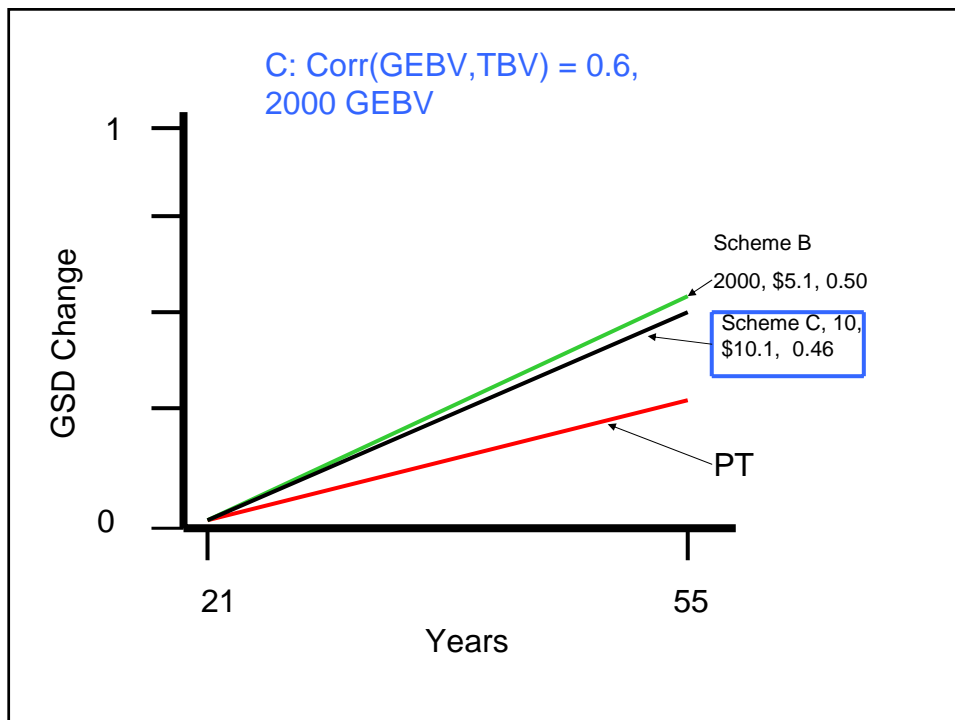
Genotype 2000 young bulls at birth, GEBV

Select best 200 for usual PT

Best 5 or 10 used as Sires of Sons at 1 yr for 1 year

Cost of purchasing a bull = \$10,000

$\text{Corr}(\text{GEBV}, \text{TBV}) = 0.6$



## Results

- Genotype 2000 bulls per year, GEBV
- Reduce number for PT to 100-200
- Use top 10 as Sires of Sons
- Gradually phase out PT and go to Scheme B
- Share SNP results with world

## Genotyping Females

- Genotype at birth, GEBV
- Use top 5000 as dams of bulls
- Use top cows as herd replacements
- No point in genotyping current dams of bulls – already known entities.
- GEBV better than EBV – no pref trt.

## Conclusions

- Use GEBV to select, and use young animals as though they were proven
- Costs may increase for young animals
- Inbreeding should be studied
- Strategies for producers to be involved
- International implications (share or not)

## More

- SNP panels, ever changing
- SNPs to QTLs (patents?)
- G x E
- Breeds

