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Gentec-IGF2

A major gene for specific selection in sire and dam lines

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Animal breeding: 4 generations in selection

- exterior
- Measures (e.g. growth, BFT)
- Quantitative Genetics (BLUP)
- Molecular Genetics (DNA markers)

Marker assisted selection and breeding

Contracts with breeding companies and labs

Canadian Centre for Swine Improvement Inc.

BREEDING COMPANIES

COMMERCIAL LABS

…

R&D / Technical support

sublicensing technology

Gentec

Gentec : staff and collaborations

In house

- Prof. Dr. Nadine Buys, Molecular geneticist

External

- 5 Professors (Michel, Leif, Ann, José-Louis, Stefaan)
- 4 Post docs (Wouter, Dominique, Romi, Luis,)
- 5 pHD students (Natacha, Bart, Jo, Karijn, Anneleen)
- 5 lab technicians (Nico, David, Noella, Jo, Tom, Eric)

A major gene
for increased muscle mass and
decreased back fat in pigs resulting
in more uniform pigs

BETTERGEN MUSCLE+ Gentec-IGF2

Gentec-IGF2

effect on:	no effect on:
• % ham ↗	• Daily gain
• % loin ↗	• Birth weight
• % lean meat ↗	• % abdomin. fat
• % back fat ↘	• pH meat

IGF2-intron3-G3072A mutation

- A mutation in the regulatory region of the IGF2 gene has been identified to be the cause underlying the QTL effect on muscle growth and fat deposition (Van Laere et al. Nature, 2003).
- This single nucleotide substitution (G-A), located at position 3072 in the intron 3 of IGF2 gene
  - increases gene expression of IGF2 in muscle threefold
  - stimulates muscle growth at the expense of back fat
  - results in leaner swine carcass and lower back fat.

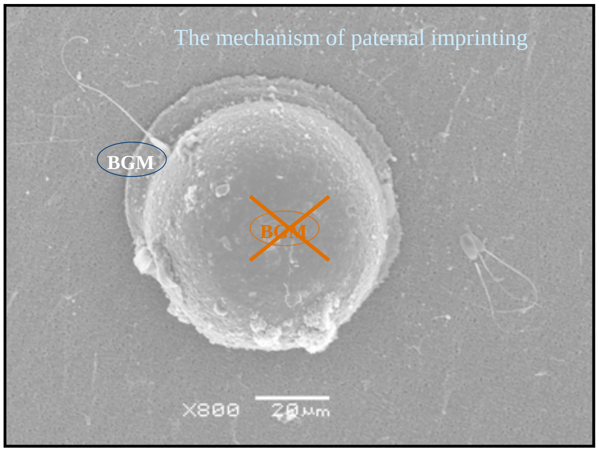
Gentec-IGF2

The gene is inherited in a specific way

PATERNAL IMPRINTING

= only the allele inherited from the father is expressed

The mechanism of paternal imprinting



Use of selection for IGF2 in sire lines

- The large effect of the QTL on lean meat and back fat without influence on growth or meat quality, makes this an attractive QTL to use in the breeding program.
- Terminal sires are selected to be homozygous for the lean allele *(IGF2+/IGF2+)* in order to pass the full effect to their offspring.
- Field results have been reported by several authors (Scheller *et al*., 2002, Buys, 2003; Liu *et al*., 2006).

Gentec-IGF2

Heterozygous boar
IGF2+ / igf2-

Homozygous boar
IGF2+ / IGF2+

descendents :

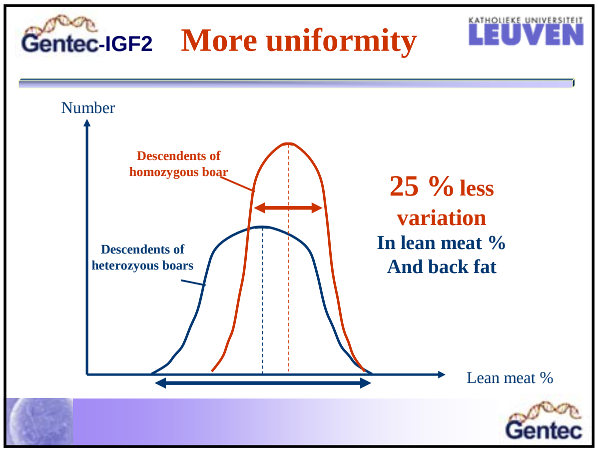
50 % +: more lean meat %
50 % - : less lean meat %

100 % +: more lean meat %

Homozygous :

+ + boars : always BETTERgen muscle⁺

♂	♀					
++	++	++	++	++	++	100% meer
++	+-	++	+-	++	+-	100% meer
++	--	+-	+-	+-	+-	100% meer
+-	++	++	++	-+	-+	50% minder
+-	+-	++	+-	-+	--	50% minder
+-	--	+-	+-	--	--	50% minder
--	++	-+	-+	-+	-+	100% minder
--	+-	-+	--	-+	--	100% minder
--	++	-+	-+	-+	-+	100% minder



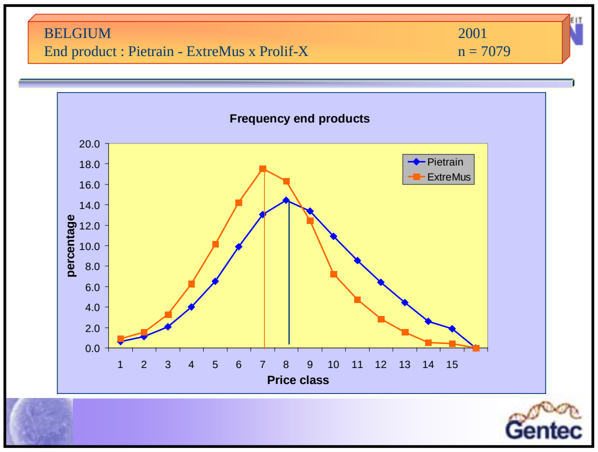
Gentec-IGF2

More uniformity

25 % less variation

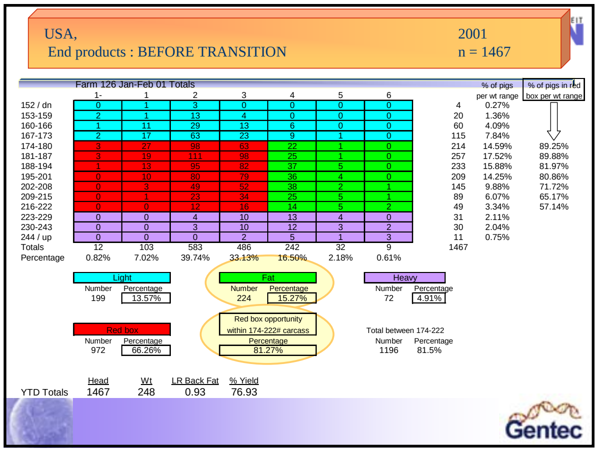
In lean meat %

And back fat



BELGIUM 2001

End product : Pietrain - ExtreMus x Prolif-X n = 7079



USA, 2001

End products : BEFORE TRANSITION n = 1467

Farm 126 Jan-Feb 01 Totals

	1-	1	2	3	4	5	6		% of pigs per wt range	% of pigs in red box per wt range
152 / dn	0	1	3	0	0	0	0	4	0.27%	
153-159	2	1	13	4	0	0	0	20	1.36%	
160-166	1	11	29	13	6	0	0	60	4.09%	
167-173	2	17	63	23	9	1	0	115	7.84%	
174-180	3	27	98	63	22	1	0	214	14.59%	89.25%
181-187	3	19	111	98	25	1	0	257	17.52%	89.88%
188-194	1	13	95	82	37	5	0	233	15.88%	81.97%
195-201	0	10	80	79	36	4	0	209	14.25%	80.86%
202-208	0	3	49	52	38	2	1	145	9.88%	71.72%
209-215	0	1	23	34	25	5	1	89	6.07%	65.17%
216-222	0	0	12	16	14	5	2	49	3.34%	57.14%
223-229	0	0	4	10	13	4	0	31	2.11%	
230-243	0	0	3	10	12	3	2	30	2.04%	
244 / up	0	0	0	2	5	1	3	11	0.75%	
Totals	12	103	583	486	242	32	9	1467		
Percentage	0.82%	7.02%	39.74%	33.13%	16.50%	2.18%	0.61%			

	Number	Percentage
Light	199	13.57%
Fat	224	15.27%
Heavy	72	4.91%
Red box	972	66.26%

Red box opportunity within 174-222# carcass

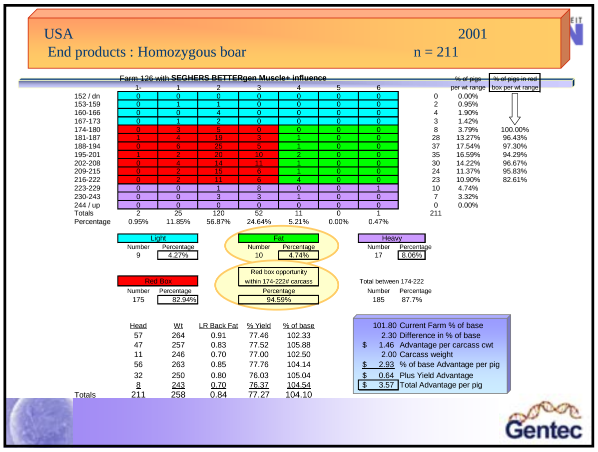
Percentage

81.27%

Total between 174-222

Number	Percentage
1196	81.5%

	Head	Wt	LR Back Fat	% Yield
YTD Totals	1467	248	0.93	76.93



USA 2001

End products : Homozygous boar n = 211

Farm 126 with **SEGHERS BETTERgen Muscle+ influence**

	1-	1	2	3	4	5	6		% of pigs per wt range	% of pigs in red box per wt range
152 / dn	0	0	0	0	0	0	0	0	0.00%	
153-159	0	1	1	0	0	0	0	2	0.95%	
160-166	0	0	4	0	0	0	0	4	1.90%	
167-173	0	1	2	0	0	0	0	3	1.42%	
174-180	0	3	5	0	0	0	0	8	3.79%	100.00%
181-187	1	4	19	3	1	0	0	28	13.27%	96.43%
188-194	0	6	25	5	1	0	0	37	17.54%	97.30%
195-201	1	2	20	10	2	0	0	35	16.59%	94.29%
202-208	0	4	14	11	1	0	0	30	14.22%	96.67%
209-215	0	2	15	6	1	0	0	24	11.37%	95.83%
216-222	0	2	11	6	4	0	0	23	10.90%	82.61%
223-229	0	0	1	8	0	0	1	10	4.74%	
230-243	0	0	3	3	1	0	0	7	3.32%	
244 / up	0	0	0	0	0	0	0	0	0.00%	
Totals	2	25	120	52	11	0	1	211		
Percentage	0.95%	11.85%	56.87%	24.64%	5.21%	0.00%	0.47%			

	Number	Percentage
Light	9	4.27%
Fat	10	4.74%
Heavy	17	8.06%
Red Box	175	82.94%

Red box opportunity within 174-222# carcass

Percentage

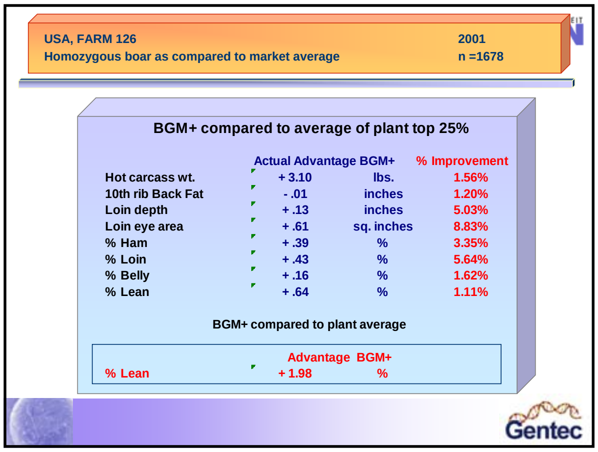
94.59%

Total between 174-222

Number	Percentage
185	87.7%

	Head	Wt	LR Back Fat	% Yield	% of base
	57	264	0.91	77.46	102.33
	47	257	0.83	77.52	105.88
	11	246	0.70	77.00	102.50
	56	263	0.85	77.76	104.14
	32	250	0.80	76.03	105.04
	8	243	0.70	76.37	104.54
Totals	211	258	0.84	77.27	104.10

	101.80	Current Farm % of base
	2.30	Difference in % of base
$	1.46	Advantage per carcass cwt
	2.00	Carcass weight
$	2.93	% of base Advantage per pig
$	0.64	Plus Yield Advantage
$	3.57	Total Advantage per pig



USA, FARM 126 **2001**

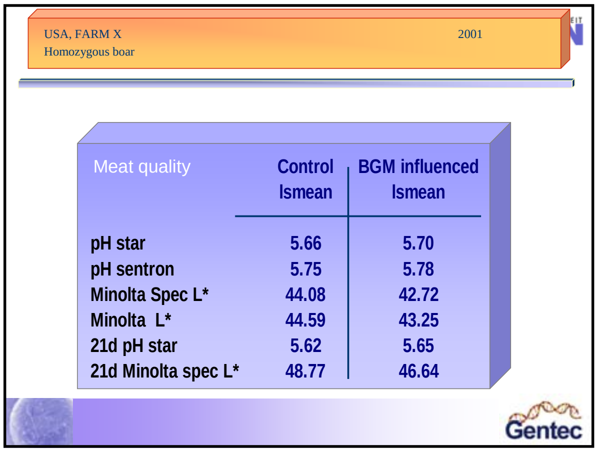
Homozygous boar as compared to market average **n =1678**

BGM+ compared to average of plant top 25%

	Actual Advantage BGM+		% Improvement
Hot carcass wt.	+ 3.10	lbs.	1.56%
10th rib Back Fat	- .01	inches	1.20%
Loin depth	+ .13	inches	5.03%
Loin eye area	+ .61	sq. inches	8.83%
% Ham	+ .39	%	3.35%
% Loin	+ .43	%	5.64%
% Belly	+ .16	%	1.62%
% Lean	+ .64	%	1.11%

BGM+ compared to plant average

	Advantage BGM+	
% Lean	+ 1.98	%



USA, FARM X 2001

Homozygous boar

Meat quality	Control lsmean	BGM influenced lsmean
pH star	5.66	5.70
pH sentron	5.75	5.78
Minolta Spec L*	44.08	42.72
Minolta L*	44.59	43.25
21d pH star	5.62	5.65
21d Minolta spec L*	48.77	46.64

Terminal sires : homozygous IGF2+/IGF2+

Heterozygous boar (+/-)

Homozygous boar (+/+)

Slaughter pigs

50 % +: higher lean meat yield
50 % - : lower lean meat yield

100 % +: higher lean meat content

IGF2 in dam lines?

- Prolificacy and sow longevity was said to be reducing as a result of the genetic selection for increased leanness and lowering fat deposition (Mathur and Liu, 2003).
- Body fat deposition is necessary to sustain sow reproduction performance, for example to support adequate milk production and to limit body weight loss.
- The selection for leaner carcasses, demanded by the packing industry and consumers, may conflict with the prolificacy and longevity of the sow and lead to increased replacement costs of sows in pig production

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IGF2 in dam lines?

- IGF2+/IGF2+ terminal sires give the full effect to the slaughter pigs
- Genotype of the mother does not influence the muscle mass of the slaughter pig

⇒ Can we make the GP boar homozygous (igf2-/igf2-)?

- All parent sows will receive the igf2- allele from their father
- Parent sows will have more back fat = more body reserve = better prolificacy???
- The fat allele of the sows will not influence the carcass quality of the pigs

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Set up

- **Animals:**
  - 565 purebred sows of 3 closed dam lines based on Landrace and Large White
  - blood bank of 1999 until 2005
- **Measurements :**
  - total born, live born, stillborn, weaned piglets per litter and parity per sow
  - Backfat thickness, loin eye depth and lean meat % using PigLog105 at 110 kg
- **Genotyping :** of sows and their respective parents with an allelic discrimination assay (Taqman)
- **Statistical analysis :** SAS

PROC FREQ for gene frequencies
PROC GLM for effects of paternal or maternal allele taking parity and sire into account

On a dataset from sows sired by heterozygous boars : effect of paternal allele and effect of maternal allele
On a dataset from sows from heterozygous dams: effect of maternal allele.

Gene frequencies in dam lines

Line	IGF2+/IGF2+	IGF2+/igf2-	Igf2-/igf2-
A	0.04 (4)	0.28 (25)	0.68 (61)
B	0.30 (42)	0.37 (52)	0.33 (46)
C	0.80 (259)	0.19 (62)	0.01 (4)

Effect of paternal allele inherited from heterozygous sires on prolificacy

Trait	Paternal IGF2+	Paternal igf2-	P value
Number of records	240	276	
Born alive / litter	10.37 ± 0.18	10.90 ± 0.16	0.0075
Total born / litter	11.04 ± 0.19	11.48 ± 0.17	0.0371
Stillborn / litter	0.63 ± 0.07	0.59 ± 0.06	NS
Weaned / litter	9.11 ± 0.21	9.92 ± 0.16	0.0134
Parity	2.95 ± 0.12	3.54 ± 0.12	0.0035

Maternal allele: no effect

Effect of paternal allele inherited from heterozygous sires on carcass quality at 110 kg live weight

Trait	Paternal IGF2+	Paternal igf2-	Significance
Number of records	70	64	
Back fat 1 (mm)	14.90 ± 0.27	15.08 ± 0.27	NS
Back fat 2 (mm)	13.20 ± 0.29	14.14 ± 0.30	NS
Loin depth (mm)	56.28 ± 0.45	55.72 ± 0.41	NS
% lean meat	57.31 ± 0.26	56.69 ± 0.28	NS

Second analysis : Animal Model

Dataset:

Only daughters from heterozygous sires:

- 516 records
- 1129 animals in pedigree (sows /+ ancestors) selected from 6649 records

Model:

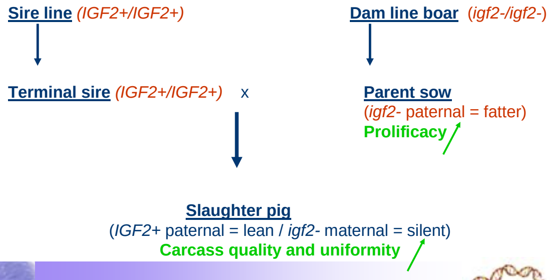
- Born alive, total born and weaned
- Fixed effects : parity, year of birth, line and paternal allele
- Contrast between the two levels of paternal allele “2”-”1” was estimated (mixed model equations solved using PEST)

Animal Model: results

Number of records, estiamtion of residual and additive genetic variance (VE and VA), estimate of the contrast for Paternal allele and probability value for the estimated contrast

	N	VE	VA	EST. CONTRAST (SE)	P-VALUE
Total born	498	7.172	0.742	0.509 (0.32)	0.115
Live born	516	5.799	0.799	0.712 (0.31)	0.022
weaned	485	5.587	0.658	0.535 (0.29)	0.069

MAS for GENTEC-IGF2



Sire line *(IGF2+/IGF2+)*

Dam line boar *(igf2-/igf2-)*

Terminal sire *(IGF2+/IGF2+)* x

Parent sow
(*igf2-* paternal = fatter)
Prolificacy ↗

Slaughter pig
(*IGF2+* paternal = lean / *igf2-* maternal = silent)
Carcass quality and uniformity ↗

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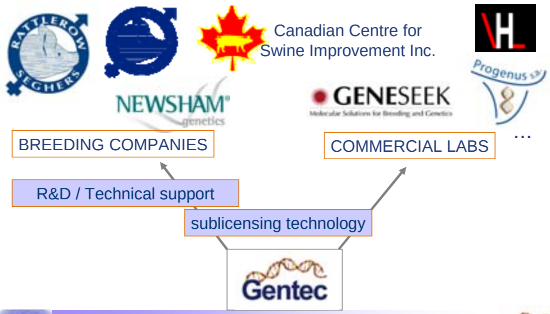
patent

- Inventors and owners
  - Prof. Michel Georges, Université de Liège (België)
  - Prof. Leif Andersson, Swedish University of Agricultural Sciences
  - Prof. Nadine Buys, GENTEC
- Claims
  - IGF2 mutation in pigs
  - All parentally imprinted QTL in all domestic animals

Contracts with breeding companies and labs



Canadian Centre for Swine Improvement Inc.

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COMMERCIAL LABS

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