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Status of Genome and QTL Mapping in Pigs - Data of Hohenheim F₂ Families -

Dedicated to Prof. Dr. Dr. h.c. Gottfried Leuthold on the occasion of his 65th birthday

Summary

Three informative F₂ families (by use of European Wild boar (W), Pietrain (P) and Meishan (M)), each with more than 300 animals, were genotyped for evenly spaced marker loci and recorded for more than 100 quantitative traits. Linkage and QTL mapping data for 8 chromosomes are presented (74, 76 and 75 mapped loci in families WxP, MxP and WxM, resp). Linkage maps gave evidence of heterogeneity in recombination between sexes and families. The male to female recombination ratio were 1.19 (WxP), 1.35 (MxP) and 1.27 (WxM). Several QTLs were mapped for performance traits of growth, carcass and meat quality. These QTLs are located on different chromosomes and influenced by families. Larger effects were found on chromosome 6 and 7, and e.g. up to 60 % of the phenotypic F₂ variance for meat quality traits was associated with chromosome 6. Candidate genes are proposed for some of the QTL intervals. The subsequent QTL mapping use a combined strategy of genome-wide marker mapping with a positional candidate gene approach in order to identify genes which are significant for breeding.

Key words: pig, linkage mapping, QTL mapping, performance traits

Zusammenfassung

Titel der Arbeit: Stand der Genom- und QTL-Kartierung beim Schwein –Daten aus den Hohenheimer F₂-Familien

In drei informativen F₂ Familien (erstellt unter Verwendung der Rassen Europäisches Wildschwein (W), Pietrain (P) und Meishan (M)), die jeweils mehr als 300 Tiere umfassen, wurden gleichmäßig über das Genom verteilte Markerloci genotypisiert und pro Tier mehr als 100 quantitative Merkmale berücksichtigt. Es werden Kopplungs- und QTL-Kartierungsdaten für 8 Chromosomen dargestellt (74, 76 und 75 kartierte Loci bei den Familien WxP, MxP bzw. WxM). Aus den Kopplungskarten läßt sich erkennen, daß Geschlechts- und Familieneffekte auf die Rekombinationshäufigkeiten wirken. Das Verhältnis männlicher zu weiblicher Rekombinationen lag bei 1.19 (WxP), 1.35 (MxP) und 1.27 (WxM). Für die Leistungsmerkmale des Wachstums, des Schlachtkörpers und der Fleischqualität wurden mehrere QTLs kartiert. Diese liegen auf verschiedenen Chromosomen und werden durch die Familien beeinflusst. Größere Effekte wurden auf den Chromosomen 6 und 7 gefunden, z.B. war bis zu 60 % der phänotypischen F₂-Varianz für die Fleischqualitätsmerkmale mit dem Chromosom 6 assoziiert. Für einige der QTL-Intervalle werden Kandidatengene vorgeschlagen. Die nachfolgende QTL-Kartierungsstrategie kombiniert den Einsatz von im gesamten Genom kartierten Markern mit der Auswahl positionaler Kandidatengene, um auf diese Weise züchterisch wichtige Gene identifizieren zu können.

Schlüsselwörter: Schwein, Kopplungskartierung, QTL-Kartierung, Leistungsmerkmale

Introduction

Main tasks of genome research in farm animals are orientated to identify genes affecting economically relevant traits. Values of those traits are often influenced by many, in detail unknown factors and thus quantitatively distributed in populations (quantitative traits). For those traits, LEUTHOLD (1972) and his co-workers used parameters of metabolism which are closely related to the regulation and expression of the genes involved. Another approach for genetic analysis of quantitative traits is the diagnosis of effects arising from chromosome regions. Within families the transfer of chromosome intervals can be traced by polymorphic loci and subsequently used for the analysis of gene effects on quantitative traits (Quantitative Trait Loci, QTL; GELDERMANN, 1975). Among farm animal species this approach was first used in pigs by ANDERSSON et al. (1994). Its success is partly due to some advantages of this species for genetic analysis, e.g. the short generation interval, multiparity, low number of morphologically different chromosomes (GUSTAVSSON, 1988), simple and standardized housing of test animals, numerous and well characterized criteria of production traits and similarity to human physiology. Mapping of the porcine genome has been stimulated and supported by multinational programmes (e.g. PiGMaP – ARCHIBALD et al. (1991) which enabled construction of a middle density linkage map and cytogenetic map needed for QTL mapping). At present these maps encompass 1774 loci, of which 507 are designated genes (Livestock Animal Genome Database - Roslin Institute, Edinburgh; stage 08/1998; <http://www.ri.bbsrc.ac.uk>). The majority of mapped loci are microsatellites, i.e. short repetitive DNA motifs (e.g. LITT and LUTY, 1989; TAUTZ, 1989) which occur interspersed in non repetitive DNA and cover the whole genome with about 60.000 to 100.000 loci.

At Hohenheim, three informative porcine F₂ families have been generated for QTL analysis on growth, carcass and meat quality traits. Objectives of this programme are a detailed recording of quantitative traits, providing of data and samples for joint research, efficient genotyping of DNA loci, genome-wide QTL mapping for a large number of traits as well as comparison of families for intrachromosomal recombination and QTL effects. In this report we give a short review on results so far obtained.

Material and Methods

Genetically diverse resources of pigs (European Wild Boar, Meishan and Pietrain) were used for the generation of three F₂ families (Tab. 1). All pigs were kept in one experimental station under standardized housing and feeding. At ten weeks of age, the piglets were taken into single pens for growth and fattening tests. The pigs were slaughtered at a defined age (210 days). Samples have been collected for measuring additional phenotypic criteria and isolation of genomic DNA.

The F₂ families were optimized for QTL analysis. Based on some marker loci, individuals were selected in the founder generation according to the expected degree of heterozygosity in the F₁ offspring. Then, F₁ animals with the highest information

Table 1
Structure and size of the Hohenheim F₂ families (Aufbau und Umfang der Hohenheimer F₂-Familien)

Generation	W x P	M x P	W x M
Founder	1 boar W x 9 sows P	1 boar M x 8 sows P	1 boar W x 4 sows M
F ₁	2 boars x 28 sows	3 boars x 19 sows	1 boar x 21 sows
F ₂	315	316	335

W: European Wild Boar; P: Pietrain; M: Meishan

values for mapping were mated for the production of the F₂ generation. Only one to three males and a few females were used in the founder and F₁ generation in order to reduce the number of segregating haplotypes in the F₂. More than 300 F₂ animals have been generated per family. Comparison groups were kept for animals from the founder and F₁ generation. All individuals were housed in one station in order to have uniform environmental effects.

Table 2 gives a review of the traits included. The performance traits belong to stress reaction, fattening, carcass, and meat quality. Moreover, additional traits are included which are highly heritable, and some of them correspond to performance traits.

Table 2
Quantitative traits measured for the F₂ animals (Erfasste quantitative Merkmale an den F₂-Tieren)

Parameter	Number of definitions	Class of traits
Stress reaction	2	Performance traits ^{*)}
Fattening	6	
Carcass	25	
Meat quality	10	
Weight of organs	2	Additional traits ^{**)}
Hair colour	8	
Skin & hair structure	5	
Adipose cell size	6	
Enzyme activities	10	
Muscle tissue	25	
Bone conformation	25	

^{*)} Definitions and trait values are given in detail by MÜLLER et al. (1998).

^{**)} Not all are considered in the QTL mapping presented.

Up to now, 8 chromosomes are mapped in all three pedigrees. Table 3 lists the numbers of markers considered for linkage and QTL mapping in the work presented. 74, 76 and 75 loci were genotyped in the families WxP, MxP and WxM (KNORR, 1996; YUE, 1998; BEECKMANN, 1998). The Type II loci are microsatellites, the Type I loci include biochemical polymorphisms, blood groups, allotypes and DNA variants for potential candidate genes (e.g. CRC, GH). For example, the growth hormone (GH) gene variants were analyzed according to the RFLP method of LARSEN and NIELSEN (1993) by using the restriction enzymes ApaI and HinPI (KNORR, 1996) for which restriction sites are in the promoter and signal peptide coding regions.

Table 3
Summary of linkage maps (Zusammenfassung der Kopplungskarten)

Chromosome	Pedigree	Number of Loci			Total map length (Kosambi cM)		
		Type I	Type II	Total	Average	Male	Female
SSC1	WxP	1	9	10	229	235	230
	MxP	1	9	10	206	223	195
	WxM	0	8	8	147	167	141
SSC3	WxP	1	7	8	158	125	201
	MxP	1	7	8	150	115	192
	WxM	1	7	8	147	108	207
SSC4	WxP	0	5	5	127	127	124
	MxP	1	9	10	135	111	136
	WxM	1	9	10	140	132	161
SSC6	WxP	7	7	14	202	197	210
	MxP	5	7	12	226	136	250
	WxM	3	7	10	171	159	186
SSC7	WxP	6	7	13	192	155	222
	MxP	6	7	13	201	165	246
	WxM	5	8	13	233	190	287
SSC8	WxP	1	6	7	155	138	178
	MxP	1	6	7	150	119	184
	WxM	1	6	7	145	132	161
SSC12	WxP	2	7	9	111	81	161
	MxP	3	5	8	117	86	150
	WxM	2	8	10	159	128	196
SSC13	WxP	2	6	8	143	160	119
	MxP	1	7	8	152	154	153
	WxM	1	8	9	203	206	211
Total	WxP	20	54	74	1317	1218	1445
	MxP	19	57	76	1337	1109	1506
	WxM	14	61	75	1345	1222	1550

Marker loci were chosen to be evenly distributed over all chromosomes. Especially microsatellite loci were selected so that they were variable between founder sources (informative in at least two families), cover the chromosomes with distances less than 20 cM, maximally different in their allelic fragment lengths (2 bp), and suitable for multiplex PCR (similar PCR conditions, different length of PCR products). The large scale genotyping of microsatellites was performed in an automated approach (Fig. 1). Genotype data were verified with help of a computer programme by comparing the observed data with known alleles and with pedigree information (for details see YUE, 1998 and BEECKMANN, 1998).

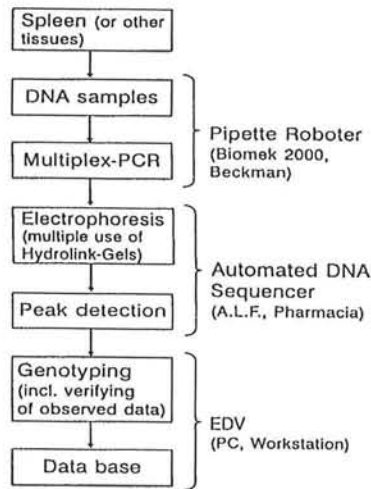


Fig. 1: Scheme of automated microsatellite analysis (Schema der automatisierten Analyse von Mikrosatelliten)

Linkage analyses were performed using the software CRIMAP (GREEN et al., 1990) according to the guidelines in KEATS et al. (1991). Sex-averaged as well as sex-specific maps were constructed. Data were analyzed using the analytical methods and approach developed by HALEY et al. (1994). The analysis for each chromosome included background genetic effects on other linkage groups as suggested by ZENG (1994) and JANSSEN (1993). Background genetic effects were included as covariates using a stepwise selection procedure. Chromosome-specific empirical threshold values of the F test statistic were estimated via permutation tests (CHURCHILL and DOERGE, 1994). Genome-wide thresholds were calculated from the data by applying a Bonferroni correction for the number of chromosomes not included in the current analysis. The 10%, 5% and 1% genome-wide thresholds were estimated as 7.3, 8.1, 10.0 in WxP; 7.3, 8.0, 9.8 in MxP and 7.6, 8.4 and 9.9 in WxM respectively. Associations between GH gene variants (combined alleles of two RFLPs) and trait values were analysed using the statistical package LSMLMW of HARVEY (1987).

Results

Linkage Maps. The linkage data of the chromosomes so far mapped are shown in Table 3. Between 74 and 76 markers were typed on the 8 chromosomes with an average marker distance of about 18 cM. The total genetic length covered per family was between 1317 cM and 1345 cM. On average higher recombination frequencies were observed in females than in males. The male to female recombination ratio was 1.19 (WxP), 1.35 (MxP) and 1.27 (WxM). For chromosome 1 male recombination was higher in all three families. Large differences in the length for some linkage groups were mainly due to markers located at the end of chromosomes that were not informative in all families (e.g. chromosome 6).

Table 4a

Summary of significant QTL effects for production traits (WxP) (Zusammenfassung der signifikanten QTL-Effekte für Leistungsmerkmale)

Chromosome / Trait	F ratio	Map position ¹⁾	Additive effect ²⁾	Dominance effect ²⁾	Per cent of F ₂ variance ³⁾
SSC1					
Average daily gain (g)	10.7	124	-33.1 ± 7.61	18.1 ± 10.2	7.2
Average back fat depth (mm)	12.5	124	-1.78 ± 0.36	0.55 ± 0.49	8.2
Head weight (kg)	15.2	119	-0.20 ± 0.04	0.11 ± 0.05	10.1
Half carcass weight (kg)	15.2	122	-2.29 ± 0.45	1.52 ± 0.62	10.1
SSC4					
Bacon weight (kg)	10.3	99	-0.89 ± 0.20	0.46 ± 0.51	6.8
Bacon meat weight (kg)	13.7	92	-0.77 ± 0.15	0.42 ± 0.40	9.1
Shoulder meat weight (kg)	14.4	102	-0.40 ± 0.08	0.23 ± 0.19	14.4
Head weight (kg)	16.1	86	-32 ± 0.06	0.10 ± 0.15	16.1
SSC6					
Chops meat weight (kg)	14.0	75	-0.42 ± -0.08	-0.01 ± 0.12	9.3
Lean cuts (%)	18.6	94	-1.45 ± 0.26	-1.18 ± 0.45	12.0
CK ₂₀ -value (U/ml)	98.4	75	-0.37 ± 0.03	-0.09 ± 0.04	43.0
Conductivity 24h <i>M. long. dorsi</i> (mS/cm)	196.2	76	-3.01 ± 0.15	0.82 ± 0.22	60.1

Only up to 4 traits with F ratios ≥ 10 are given per chromosome. Additional traits with F ratios ≥ 10 are given below.

SSC1: Back fat depth at 13th/14th vertebra, back fat depth at back, back fat weight, bacon external fat weight, shoulder meat weight, chops meat weight, bacon meat weight, bacon meat weight / half carcass weight, live weight at slaughter, carcass weight.

SSC4: Chops meat weight, weight of liver.

SSC6: pH 45 min *M. long. dorsi*, pH 45 min *M. semimembranosus*, conductivity 45 min *M. long. dorsi*, conductivity 45 min *M.*

semimembranosus, conductivity 24 h *M. semimembranosus*, stiffness of *M. semimembranosus*, meat colour, fat cuts, bacon meat weight / half carcass weight, bacon meat weight, shoulder meat weight, bacon weight.

¹⁾ The most likely positions are given in centimorgans from the proximal end of the chromosome.

²⁾ Estimates are given as mean ± SE.

³⁾ The reduction of the residual variance in the F₂ generation by including a QTL at the most likely position.

Table 4b

Summary of significant QTL effects for production traits (MxP) (Zusammenfassung der signifikanten QTL-Effekte für Leistungsmerkmale)

Chromosome / Trait	F ratio	Map position ¹⁾	Additive effect ²⁾	Dominance effect ²⁾	Per cent of F ₂ variance ³⁾
SSC1					
Fat cuts (%)	10.6	166	1.12 ± 0.27	0.57 ± 0.44	6.8
Meat : Fat ratio	11.2	166	0.08 ± 0.02	0.03 ± 0.03	7.1
SSC4					
Chops meat weight (kg)	10.4	55	-0.38 ± 0.09	-0.19 ± 0.12	6.5
Head weight (kg)	13.5	94	0.29 ± 0.06	-0.13 ± 0.08	8.6
Carcass length (cm)	14.2	67	-2.04 ± 0.38	-0.20 ± 0.56	9.0
SSC6					
Bacon meat weight (kg)	13.8	95	0.49 ± 0.09	-0.05 ± 0.13	8.8
Lean cuts (%)	31.1	96	-2.07 ± 0.28	-0.82 ± 0.35	18.6
CK ₂₀ -value (U/ml)	45.7	96	-0.26 ± 0.03	-0.11 ± 0.04	25.5
Conductivity 24h <i>M. long. dorsi</i> (mS/cm)	69.1	97	-2.34 ± 0.20	0.20 ± 0.25	33.5

Table 4b (continued)

Chromosome / Trait	F ratio	Map position ¹⁾	Additive effect ²⁾	Dominance effect ²⁾	Per cent of F ₂ variance ³⁾
SSC7					
Meat area (cm ²)	13.3	90	-1.92 ± 0.40	-0.92 ± 0.59	8.5
Carcass length (cm)	23.4	71	2.75 ± 0.40	0.10 ± 0.57	14.3
Back fat depth at back (mm)	23.9	78	-3.05 ± 0.44	-0.04 ± 0.65	14.9
Head weight (kg)	50.7	76	0.56 ± 0.06	0.13 ± 0.08	27.2

Only up to 4 traits with F ratios ≥ 10 are given per chromosome. Additional traits with F ratios ≥ 10 are given below.

SSC6: pH 45 min *M. long. dorsi*, pH 45 min *M. semimembranosus*, conductivity 45 min *M. long. dorsi*, conductivity 45 min *M. semimembranosus*, conductivity 24 h *M. semimembranosus*, meat colour, stiffness of *M. semimembranosus*, back fat depth at 13th/14th vertebra, average back fat depth, shoulder external fat weight, fat cuts, bacon meat weight / lean cuts weight, dressing percentage, bacon weight / half carcass weight, , meat:fat ratio, bacon meat weight / half carcass weight.

SSC7: Average back fat depth, abdominal fat weight, back fat depth at hip, back fat depth at 13th/14th vertebra.

¹⁾ The most likely positions are given in centimorgans from the proximal end of the chromosome.

²⁾ Estimates are given as mean ± SE.

³⁾ The reduction of the residual variance in the F₂ generation by including a QTL at the most likely position.

Table 4c

Summary of significant QTL effects for production traits (WxM) (Zusammenfassung der signifikanten QTL-Effekte für Leistungsmerkmale)

Chromosome / Trait	F ratio	Map position ¹⁾	Additive effect ²⁾	Dominance effect ²⁾	Per cent of F ₂ variance ³⁾
SSC1					
Back fat weight (kg)	10.0	121	-0.20 ± 0.06	0.27 ± 0.09	5.9
Lean cuts (%)	11.1	129	1.38 ± 0.29	-0.18 ± 0.48	6.6
Bacon meat weight / half carcass weight (%)	11.4	125	0.59 ± 0.13	-0.38 ± 0.21	6.7
Bacon weight / half carcass weight (%)	12.2	135	0.41 ± 0.08	-0.04 ± 0.13	12.2
SSC4					
Shoulder meat weight (kg)	11.1	82	-0.16 ± 0.03	0.03 ± 0.04	6.5
SSC7					
Back fat depth at back (mm)	12.0	85	2.26 ± 0.47	-0.49 ± 0.73	7.1
Shoulder meat weight (kg)	18.6	79	-0.16 ± 0.03	0.09 ± 0.04	10.8
Carcass length (cm)	32.4	85	-2.86 ± 0.36	0.95 ± 0.55	17.8
Head weight (kg)	33.8	78	-0.35 ± 0.04	0.05 ± 0.06	18.5
SSC13					
Conductivity 24 h <i>M. long. dorsi</i> (mS/cm)	10.1	73	0.30 ± 0.07	-0.21 ± 0.1	5.8

Only up to 4 traits with F ratios ≥ 10 are given per chromosome. Additional traits with F ratios ≥ 10 are given below.

SSC7: Bacon meat weight, chops meat weight.

¹⁾ The most likely positions are given in centimorgans from the proximal end of the chromosome.

²⁾ Estimates are given as mean ± SE.

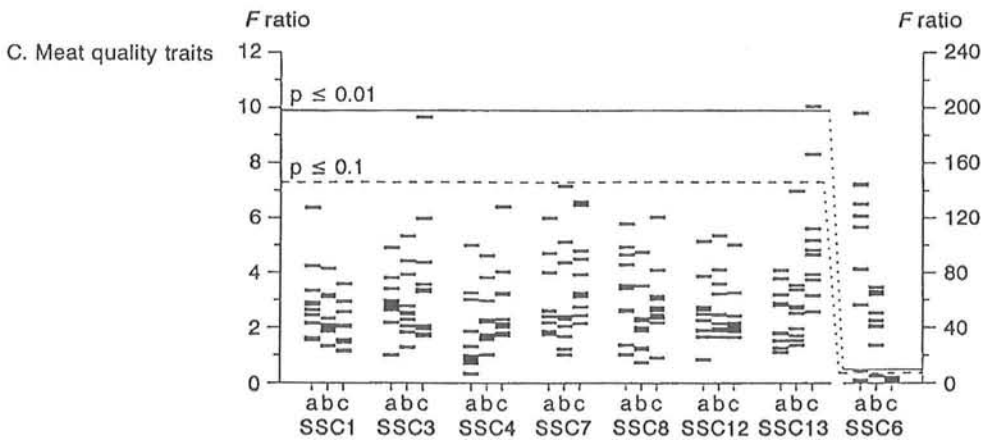
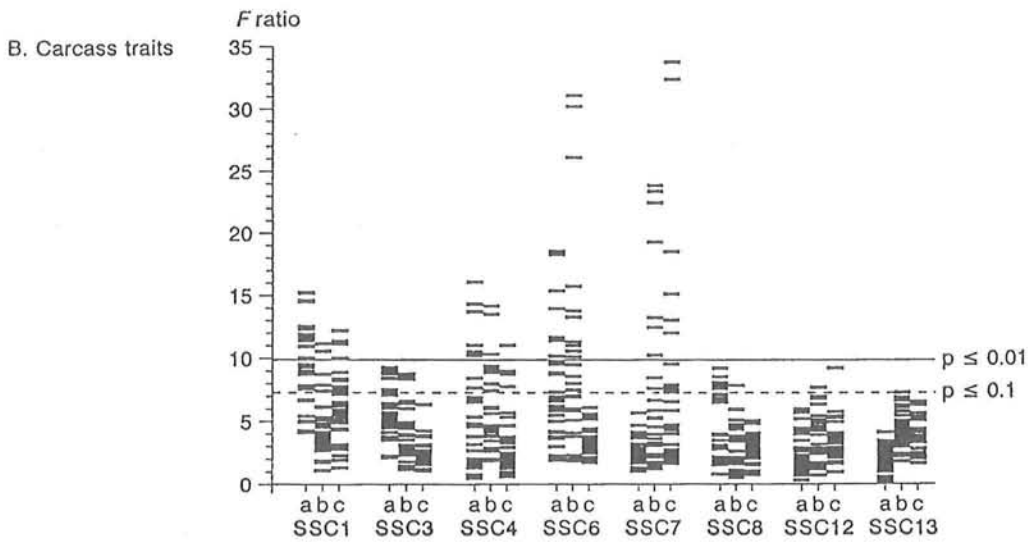
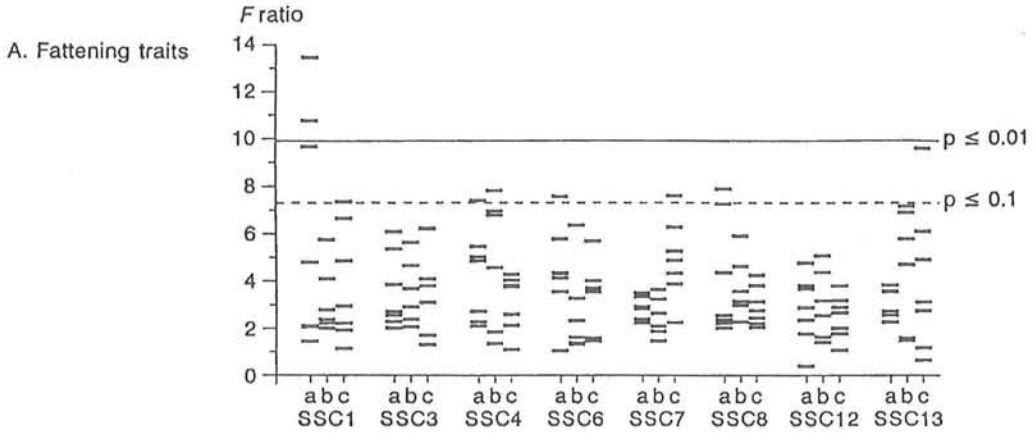
³⁾ The reduction of the residual variance in the F₂ generation by including a QTL at the most likely position.

Fig. 2 (see page 74)

Fig. 2: F ratio maxima for QTLs. Individual marks on the plot represent the F values for investigated traits (F-Wert-Maxima der QTLs. F-Werte für die untersuchten Merkmale sind durch Striche gekennzeichnet)

A: Mastleistungsmerkmale; B: Schlachtkörpermerkmale; C: Fleischbeschaffenheitsmerkmale

a: WxP; b: MxP; c: WxM; A: Fattening traits B: Carcass traits C: Meat quality traits



Map positions and effects of QTLs. The estimates for the most likely position and effects of QTLs detected at a highly significant level of linkage ($P < 0.01$; F ratio > 10.0) are given in Table 4. The F values for all investigated traits of different trait complexes are shown in Figure 2. First it can be seen, that QTLs differ in the size of their effects on traits of the same trait complex between pedigrees. Moreover, for the same traits QTLs were not mapped in all families. For example, major QTLs for fattening traits were only identified in WxP. For carcass traits highly significant QTLs were mapped in all three families on chromosomes 1 and 4, on chromosome 6 in WxP and MxP and on chromosome 7 in MxP and WxM. Smaller effects were found on chromosomes 3 (WxP; MxP), 8 (WxP; MxP) and 12 (MxP; WxM). QTLs for meat quality traits were located on chromosome 6 in WxP and MxP and on chromosomes 3 and 13 in WxM. In the families WxP and MxP, QTLs for carcass composition and meat quality were located in the region of the CRC gene, which had segregating alleles at position +1843 bp in these families. In WxM the CRC locus had a fixed allele (C) at position +1843 bp, but the microsatellite-ETH5001 within the CRC gene was informative. As given in Table 4, the gene action of the QTLs was largely additive. Surprisingly, for back fat traits, the alleles of the QTLs on chromosome 7 inherited from Meishan had allelic effects opposite of what would be expected based on the phenotype of this breed and were associated with a lower fatness of the carcass. The

Table 5

Association between GH haplotypes and performance traits (Beziehungen zwischen GH-Haplotypen und Leistungsmerkmalen)

Trait	Significance ¹⁾	Per cent of F ₂ variance (%)	LSQ mean ± S.E	
			max	min
MxP				
Back fat weight (kg)	**	12.6	2.94 ± 0.15	1.74 ± 0.18
Back fat depth at hip (mm)	**	13.1	27.34 ± 1.28	15.70 ± 1.56
Average back fat depth (mm)	*	11.7	31.41 ± 1.09	21.76 ± 1.33
Back fat depth at 13/14 vertebra (mm)	***	15.2	26.71 ± 1.08	16.46 ± 1.31
Fat area (cm ²)	*	12.2	24.75 ± 0.99	16.20 ± 1.19
Meat : Fat ratio	***	17.7	0.91 ± 0.04	0.58 ± 0.04
Fat cuts (%)	**	14.5	21.14 ± 0.57	15.33 ± 0.70
WxM				
Bacon weight / half carcass weight (%)	***	12.5	27.11 ± 0.15	25.45 ± 0.26
Back fat depth at hip (mm)	*	6.7	32.76 ± 1.16	25.97 ± 1.00
Back fat depth at 13/14 vertebra (mm)	*	6.7	37.60 ± 2.00	28.03 ± 1.18
Fat area (cm ²)	*	6.5	28.65 ± 1.52	21.39 ± 0.90
Meat : Fat ratio	***	9.6	1.60 ± 0.08	1.08 ± 0.05

¹⁾ genom-wide significance * $P < 0.05$, ** $P < 0.01$ und *** $p < 0.001$. ²⁾ The reduction of the residual variance in the F₂ generation by including GH haplotypes in the model.

direction of the QTL effects on other chromosomes was in the expected direction. The locations of QTLs significant at least at the 10% genome-wide thresholds are shown in Figure 3, where the three pedigrees were visually merged on the map of one family. In general, QTLs were localized at few positions. The positions of QTL showed some similarities between families, as demonstrated e.g. for chromosomes 1, 4, 6, 7 and 8.

A. Fattening traits

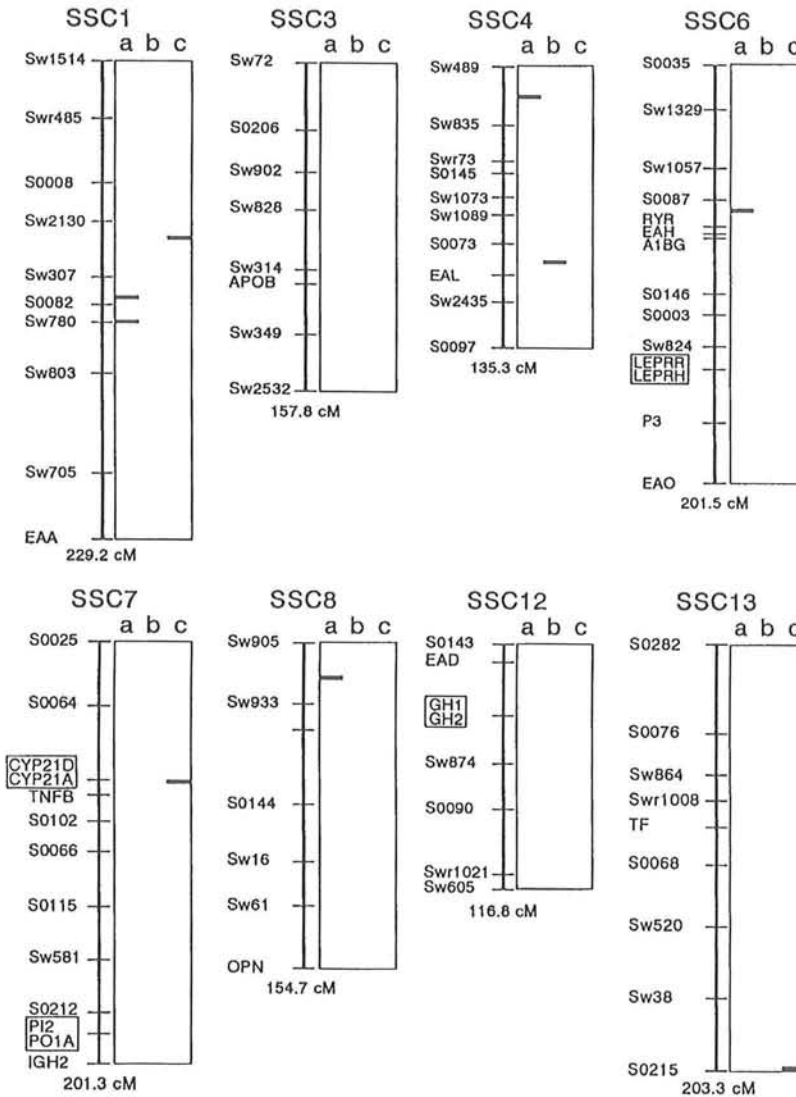


Fig. 3A: Positionen signifikanter QTL-Effekte (Positionen signifikanter QTL-Effekte)

A: Mastleistungsmerkmale

A: Fattening traits a: WxP; b: MxP; c: WxM

Associations between GH genotypes and performance traits. In the F₂ families, RFLPs of the GH gene were considered in an association analysis. Associations between GH gene variants and performance traits were detected in pedigrees MxP and WxP. The results given in Table 5 show that the GH locus explained 12% to 18% of the phenotypic variance in MxP and between 7% to 13% in WxM. In both pedigrees

B. Carcass traits

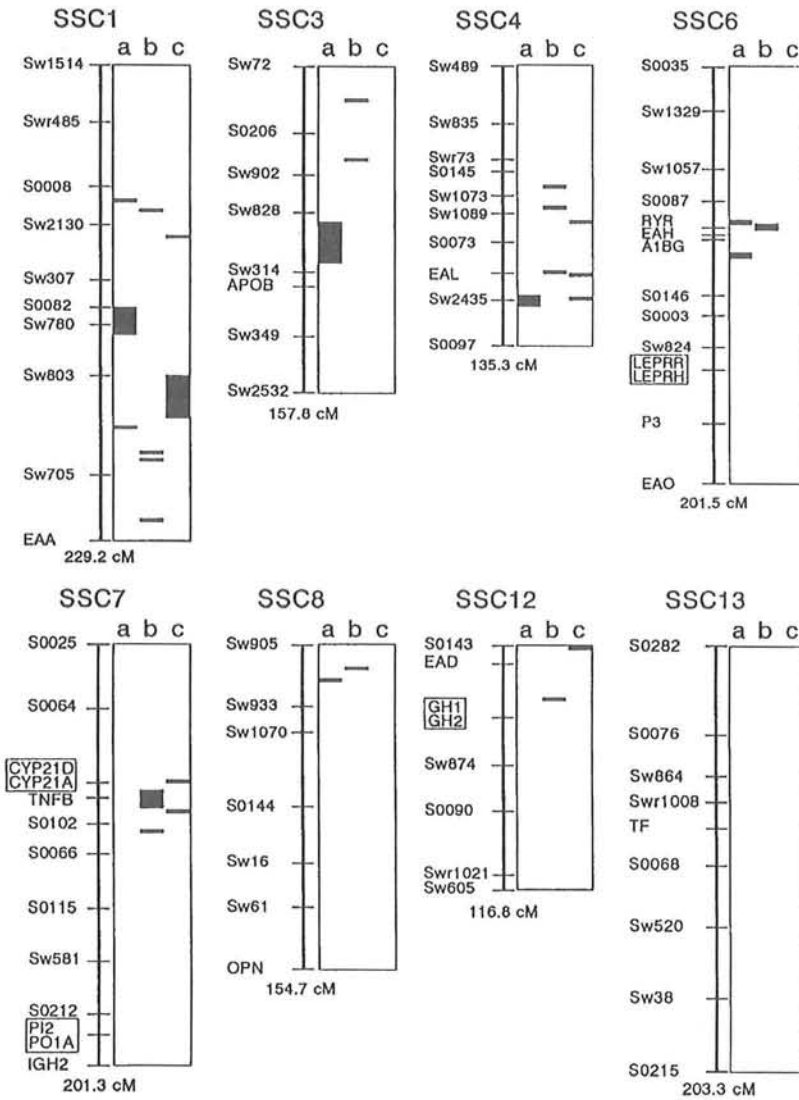


Fig. 3B: Positions of significant QTL effects ((Positionen signifikanter QTL-Effekte)
 B: Schlachtkörpermerkmale
 B: Carcass traits a: WxP; b: MxP; c: WxM

traits mainly related to fatness were significantly associated. No association was found between the breed origin of GH genotypes and values of quantitative traits. The statistical model including the breed origin of haplotypes is similar to the model used for QTL mapping, where the two founder breeds are assumed to be fixed for alternative alleles at the QTL. The QTL mapping reveal smaller effects in the chromo-

C. Meat quality traits

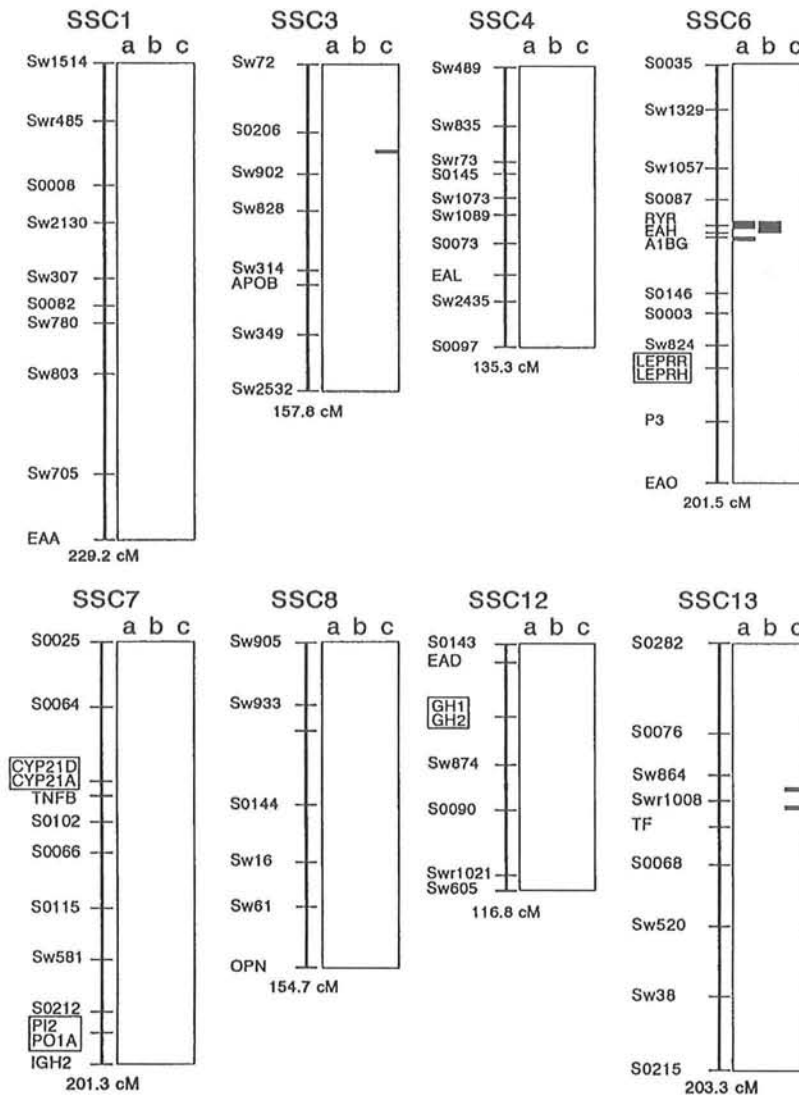


Fig. 3C: Positionen von signifikanten QTL-Effekten (Positionen signifikanter QTL-Effekte)

C: Fleischbeschaffenheitsmerkmale

C: Meat quality traits a: WxP; b: MxP; c: WxM

somal region of the GH gene (see Table 4 and Fig. 3). Therefore, we presume the associations found are caused by variants within the GH gene and not by a linked QTL with fixed alternative alleles in the founder breeds.

Discussion

For comparison and confirmation, evaluation of QTL effects and positions require data from several families. By comparing the data of our three F₂ families with other results (ANDERSSON et al., 1994; ANDERSSON-EKLUND et al., 1998; ROTHSCILD et al., 1995), data show strong influences of families on QTL profiles. However, some chromosomal regions, especially those with larger effects, carry similar QTLs in several families. In correspondence with other reports (ANDERSSON-EKLUND et al., 1998; KNOTT et al., 1998), we found QTLs affecting a distinct quantitative trait to be located on several chromosomes. The GH gene locus gives evidence that genotypes for potential candidate genes should be analysed by both, QTL mapping as well as association analysis.

The programme for a genome-wide QTL mapping is still under progress. In the frame of a cooperative programme*), marker loci are presently genotyped for all porcine chromosomes. Moreover, further additional phenotypic criteria are prepared to be included in the QTL analysis. After finishing the genome-wide QTL mapping it will follow a candidate gene approach which will make use of mapped QTLs for a pre-selection of potential candidate genes. Only those genes which are located in chromosomal intervals with major QTL effects are regarded. Potential candidate genes are screened from comparative mapping results, as well as according to their functions and tissue specific expression (EST from cDNA libraries). As far as possible, the potential candidate genes are genotyped by use of DNA variants in functional sites.

Finally, QTLs are mapped by including the markers already typed combined with the newly regarded potential candidate genes. For such a strategy the co-operative programme can use a number of pre-conditions: many phenotypic criteria of fattening, carcass and meat quality traits, large number of loci already mapped in pig, information on a number of potential candidate genes for growth, carcass composition, muscle structure etc., homology in location of genes between mammalian species, knowledge of QTLs already identified in several F₂ families, application of additional DNA techniques for screening and genotyping of potential candidate genes (e.g. muscle and fat tissue specific cDNA).

QTL analysis and association studies in families are able to resolve effects of chromosomal intervals not much less than +5 cM. Once QTLs have been assigned to an interval between two markers, the next target will be to isolate and identify the

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nature of the QTLs themselves. Such an analysis of candidate gene variants need combinations of further techniques and their application *in vitro*, *in vivo* as well as in different populations. The challenge in animal genetics analysis will be the analysis of effects arising from single gene sites on trait values. For this target and in combination with other approaches, the QTL mapping is of high significance.

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References

- ANDERSSON, L.; HALEY, C.S.; ELLEGREN, H.; KNOTT, S.A.; JOHANSSON, M. ANDERSSON, K.; ANDERSSON-EKLUND, L.; EDFORS-LILJA, I.; FREDHOLM, M.; HANSSON, I.; HAKANSSON, J.; LUNDSTRÖM, K.:
Genetic mapping of quantitative trait loci for growth and fatness in pigs. *Science*, Washington 263 (1994), 1771-1774
- ANDERSSON-EKLUND, L.; MARKLUND, L.; LUNDSTRÖM, K.; HALEY, C.S.; ANDERSSON, K.; HANSSON, I.; MOLLER, M.; ANDERSSON, L.:
Mapping quantitative trait loci for carcass and meat quality traits in a Wild boar x Large White intercross. *J. Anim. Sci.*, Edinburgh 76 (1998), 694-700
- ARCHIBALD, A.; HALEY, C.S.; ANDERSSON, L.; GUSTAVSSON, I.; BOSMA, A.A.; DAVIES, W.; FREDHOLM, M.; GELDERMANN, H.; GELLIN, J.; GROENEN, M.; OLLIVIER, L.; TUCKER, E.M.; Van DE WEGHE, A.:
PiGMAP: A European initiative to map the porcine genome. *Anim. Genet.* 23 (1991), Suppl. 1, 82
- BEECKMANN, P.:
Kartierung von Geneffekten auf quantitative Merkmale beim Schwein mit Hilfe von Markerloci. Univ. Hohenheim, Diss., 1998
- CHURCHILL, G.A.; DOERGE, R.W.:
Empirical threshold values for quantitative trait mapping. *Genetics* 138 (1994), 963-971
- GELDERMANN, H.:
Investigations on inheritance of quantitative characters in animals by gene markers. I. *Methods Theor. Appl. Genet.* 46 (1975), 319-330
- GREEN, P.; FALLS, K.; CROOKS, S. :
Documentation for CRIMAP Version 2.4. Washington Univ. School of Medicine, St. Louis (1990), Polykopie
- GUSTAVSSON, I.:
Standard karyotype of the domestic pig. *Hereditas* 109 (1988), 151-157
- HALEY, C.S.; KNOTT, S.A.; ELSEN, J.M.:
Mapping quantitative trait loci in crosses between outbred lines using least squares. *Genetics* 136 (1994), 1195-1207
- HARVEY, W.R.:
User's guide for LSMLMW. Mixed model least squares and maximum likelihood computer program. Ohio State Univ. (1987), Polykopie

JANSEN, R.C.:

Controlling the type I and type II errors in mapping quantitative trait loci. *Genetics* 138 (1993), 871-881
 KEATS, B.J.B.; SHERMAN, S.L.; MORTON, N.E.; ROBSON, E.B.; BUETOW, K.H.; CARTWRIGHT, P.E.;
 CHAKRAVARTI, A.; FRANKE, U.; GREEN, P.P.; OTT, J:

Guidelines for human linkage maps; an international system for human linkage maps (ISLM 1990),
Genomics 9 (1991), 557-560

KNORR, C.:

QTL-Effekte im Chromosom 6 und von Wachstumshormon-Genvarianten auf Merkmale der Mastleistung, des Schlachtkörperwertes und der Streßresistenz in F2-Familien beim Schwein. Univ. Hohenheim, Diss., 1996

KNORR, C.; MOSER, G.; MÜLLER, E.; GELDERMANN, H.:

Associations of GH gene variants with performance traits in F2 generations of European Wild boar, Pietrain and Meishan pigs. *Anim. Genet.* 28 (1997), 124-128

KNOTT, S.A.; MARKLUND, L.; HALEY, C.S.; ANDERSSON, K.; DAVIES, W.; ELLEGREN, H.; FREDHOLM, M.; HANSSON, I.; HOYHEIM, B.; LUNDSTRÖM, K.; MOLLER, M.; ANDERSSON, L.:

Multiple marker mapping of quantitative trait loci in a cross between outbred Wild boar and Large White pigs. *Genetics* 149 (1998), 1069-1080

LARSEN, N.J.; NIELSEN, V.H.:

ApaI and CfoI polymorphisms in the porcine growth hormone gene. *Anim. Genet.* 24 (1993), 71

LEUTHOLD, G.:

Aspekte der Nutzenanwendung von Erkenntnissen der biochemisch-physiologischen Genetik in der Tierzucht. Arch. Tierz., Berlin 15 (1972), 143-161

LITT, M.; LUTY, J.A.:

A hypervariable microsatellite revealed by in vitro amplification of a dinucleotide repeat within the cardiac muscle actin gene. *Am. J. Hum. Genet.* 44 (1989), 397-401

MÜLLER, E.; MOSER, G.; KNORR, C.; GELDERMANN, H.:

Performance traits in Wild boar, Meishan and Pietrain pigs and their F1 and F2 generations of diverse crosses. In preparation (1998)

ROTHSCHILD, M.F.; LIU, H.C.; TUGGLE, C.K.; YU, T.P.; WANG, L.:

Analysis of pig chromosome 7 genetic markers for growth and carcass performance traits. *J. Anim. Breed. Genet.* 112 (1995), 341-348

TAUTZ, D.:

Hypervariability of simple sequences as a general source for polymorphic DNA markers. *Nucl. Acids Res.* 17 (1989), 6463-6471

YUE, G.:

Gen- und QTL-Kartierung beim Schwein für die Chromosomen 6, 7, 12 und 13 in informativen F2-Familien. Univ. Hohenheim, Diss., 1998

ZENG, Z.B.:

Precision mapping of quantitative trait loci. *Genetics* 136 (1994), 1457-1468

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Buchbesprechungen

Homöopathie und biologische Medizin für Haus- und Nutztiere

ALOIS TIEFENTHALER

2. verbesserte und erweiterte Auflage, 279 Seiten, Karl F. Haug, Hüthig Fachverlage GmbH, Heidelberg, 1997, ISBN 3-7760-1643-4, 89,- DM, 650,- ÖS, 80,50 Sfr

Naturheilkundlich-biologische Heilmethoden finden auch in der Tiermedizin zunehmend mehr Beachtung. Im Gegensatz zur Humanmedizin, bei der seit längerem umfangreiche Standardliteratur verfügbar ist, gibt es für die Tierbehandlung nur wenig Literatur, die eine gute homöopathische Therapie ermöglicht. Es ist das Verdienst des Autors mit diesem Titel über Möglichkeiten und Formen des Einsatzes homöopathischer und biologischer Heilverfahren zu informieren.

Im ersten Abschnitt des Buches werden vor allem für den mit diesen Methoden wenig erfahrenen Nutzer, sowohl als Tierhalter als auch als Tiermediziner, allgemeine Informationen vermittelt. Beginnend mit der Beschreibung der homöopathischen Prinzipien, der Arzneimittel und deren Prüfung werden u.a. auch Anwendungsgebiete, Grenzen und Vorteile beschrieben. Die Hauptabschnitte des Buches beinhalten die homöopathische Behandlung von Erkrankungen bei Rind, Schwein, Pferd, Hund und Katze. Die Besprechung der Erkrankungen sind nach dem Kopf - Fuß - Prinzip den einzelnen Körperorganen zugeordnet. Bei den meisten Erkrankungen werden die Ursachen, Symptome, Prophylaxe, Therapie, die wichtigsten homöopathischen Heilmittel und deren Verabreichungsempfehlungen, wo notwendig, auch ergänzt mit Methoden der Schulmedizin, dargestellt. Der letzte Teil des Buches beinhaltet eine kurzgefaßte Charakteristik der wichtigsten homöopathischen Heilmittel mit der Beschreibung der jeweiligen Organbeziehung, Symptomen, klinischer Anwendung und Potenzen. Das umfangreiche Sachregister enthält die besprochenen Erkrankungen und genannten Krankheits-symptome und ermöglicht die bereits durch die Gliederung gegebene gute Handhabung des Buches.

Es informiert sowohl den Tierhalter über Möglichkeiten alternativer Prophylaxe und Therapie bei Tiererkrankungen als auch dem praktischen Tierarzt und kann diesem helfen die Symptome und homöopathischen Mittel zu finden, die zur Auswahl des heilenden Arzneimittels wichtig sind. Es stellt auf diesem Gebiet ein unverzichtbares, gut nutzbares, empfehlenswertes Hilfsmittel dar, welches beiden Nutzergruppen als Nachschlagewerk und Basisinformation zur Homöopathie nützliche Dienste leisten kann.

ERNST RITTER, Dummerstorf

Pferdekrankheiten in Frage und Antwort

SUE J. DYSON

293 Seiten, 309 Abbildungen, Ferdinand Enke Verlag, Stuttgart, 1998, ISBN 3 432 30181 2, 88,- DM, 642,- ÖS, 80,- Sfr

Das in Übersetzung von Bellinghausen vorliegende Buch beschreibt in Frage und Antwort über 300 Fallbeispiele aus der veterinärmedizinischen Pferdepraxis. Im ersten Teil des mit präzisen Farbfotos ausgestatteten Buches werden Fragen zu auftretenden Auffälligkeiten am Tier, Histologie-, Labor-, Ultraschall-, Arthroskopie- oder anderen Befunden gestellt. Sie beziehen sich u.a. auf Lahmheiten, Gelenkerkrankungen, Koliken, Durchfall oder Gewichtsabnahme, Verletzungen, fiebrige oder erregerbedingte Krankheiten, Fruchtbarkeitsstörungen, Atemwegserkrankungen, Husten und weitere. Die Fallbeschreibungen, ergänzt durch die die Anamnese unterstützenden wichtigen Farbbildungen, illustrieren die typischen Befunde jedes vorgestellten Falles sehr gut und erfragen die jeweilige Verdachtsdiagnose, Diagnosemaßnahmen und Therapiemöglichkeiten. Die einzelnen Fälle widerspiegeln die in der täglichen Praxis auftretenden unterschiedlichsten, häufigsten Fallsituationen. Sie führen dem Leser wesentliche Merkmale tierärztlicher diagnostischer Tätigkeit vor Augen. Der zweite Buchteil enthält den sehr ausführlichen Antwortteil, wobei für jedes Fallbeispiel auf die mögliche Diagnose, Ätiologie sowie Therapieempfehlungen eingegangen wird. Besonderen Wert erfährt dieses Buch auch durch das konsequente Ansprechen der jeweiligen Differentialdiagnosen wodurch das diagnostische Denken geschult wird. Ein empfehlenswertes Buch, welches nicht Lehrbuch oder Nachschlagewerk sein will, sondern als Farbatlas den Studierenden oder praktischen Tierärzten wissenvermittelnde, praxisrelevante Übung ermöglicht. Der besondere Wert des Buches liegt in dem logischen ineinandergreifen von Frage und Antwort sowie von Bild und Information. Es bereichert das Spektrum guter veterinärmedizinischer Fachliteratur.

ERNST RITTER, Dummerstorf