THETA
Statistical Genetics Group
Institute of Animal Genetics

Inheritance analysis of copy number variation polymorphisms in swine genome

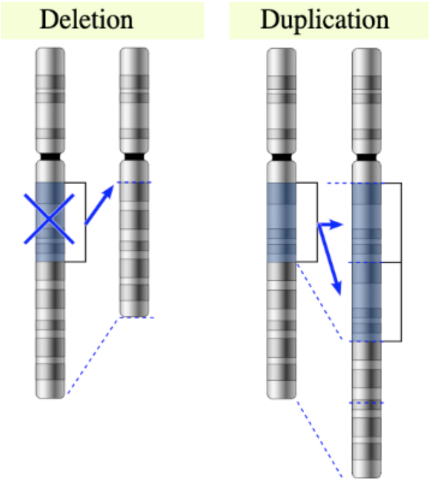
Magdalena Fraszczak, Magdal Mielczarek, Martyna Kaźmierczak, Błażej Nowak, Joanna Szyda

Biostatistics Group, Wrocław University of Environmental and Life Sciences

Objectives

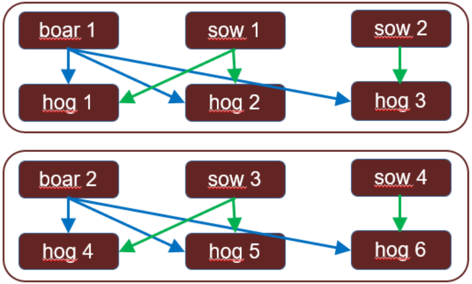
- to analyse of CNV inheritance in full and half siblings
- to determine the prevalence of CNVs formed *de novo* in the genomes of the offspring
- to describe the distribution of CNVs

Copy number variations



Material

- Whole genome sequence with Ilumina HiSeq2000
- 12 swines (6 trios) Polish Large White breed:


boar 1
sow 1
sow 2
hog 1
hog 2
hog 3
boar 2
sow 3
sow 4
hog 4
hog 5
hog 6

Methods

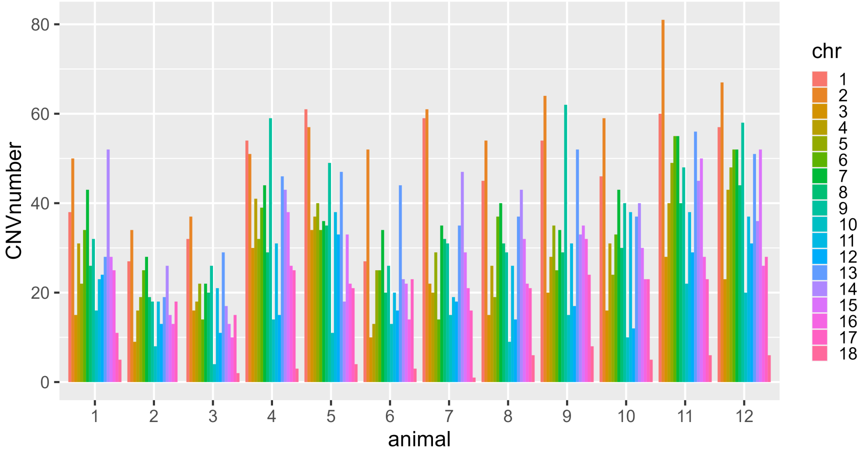
Bioinformatics pipeline

- Alignment to Sscrofa11.1 (BWA-MEM)
- Post alignment filtering (Picard & Samtools)
- CNV detection (CNVnator, Pindel)
- Functional annotation (VeP)

Statistical analysis

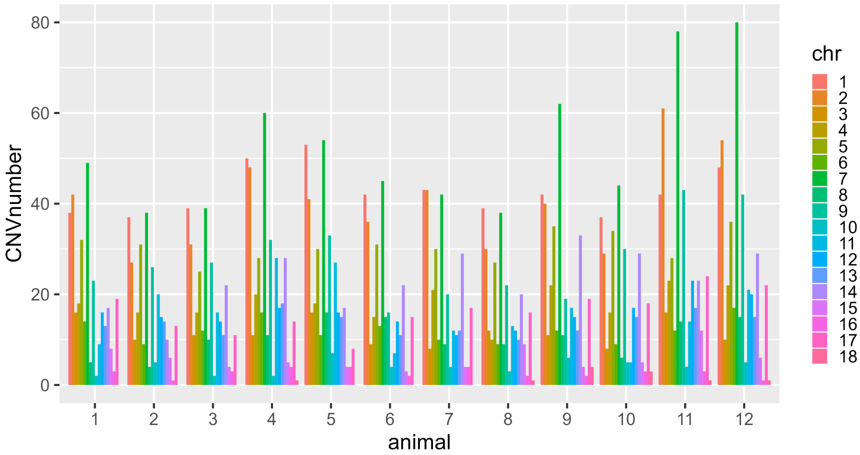
- Descriptive statistics
- Kołmogorov-Lilliefors test
- Wilcoxon signed rank test
- Permutation test
- U- Mann - Withney test
- Multidimensional scalling
- Test for fraction
- Correspondence analysis

Results



- 325 - 753 - del/ind
- max: 34 - 81 chr 2
- min: 0-8 chr 18

Results



- 282 - 444 - dup/ind
- max: 38-80 chr 7
- min: 0-3 chr 18

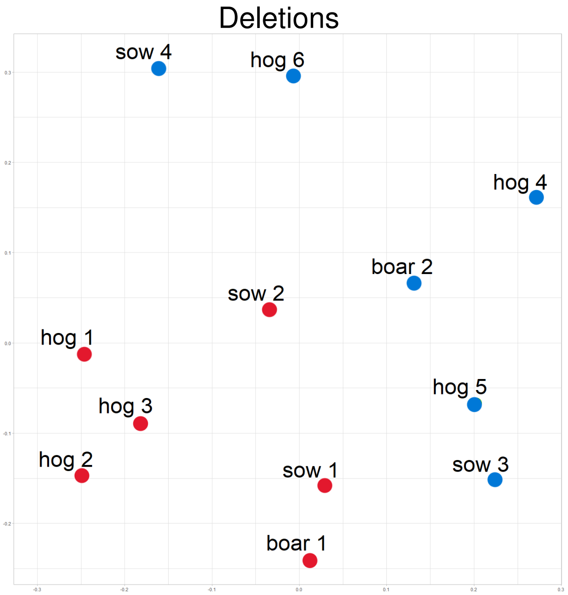
Results

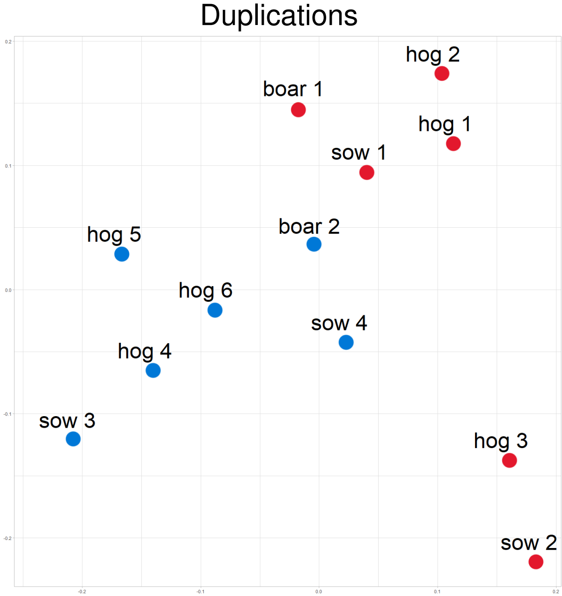
The length of CNVs

- deletions: 600 - 195000 bp (average 6662 ± 13001.5)
- duplications: 1200 - 561400 bp (average 10036 ± 33438.1)

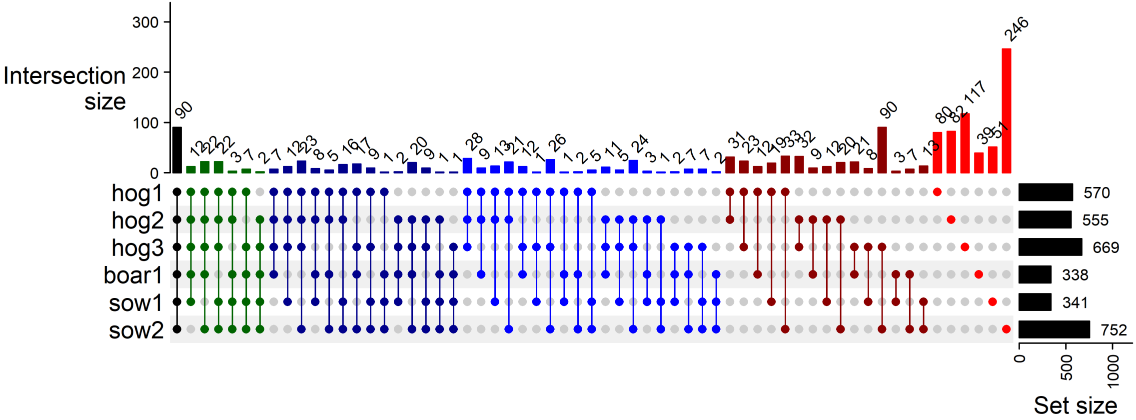
The percentage of genome covered

- deletions: 0.11% - 0.21%
- duplications: 0.26%-0.35%

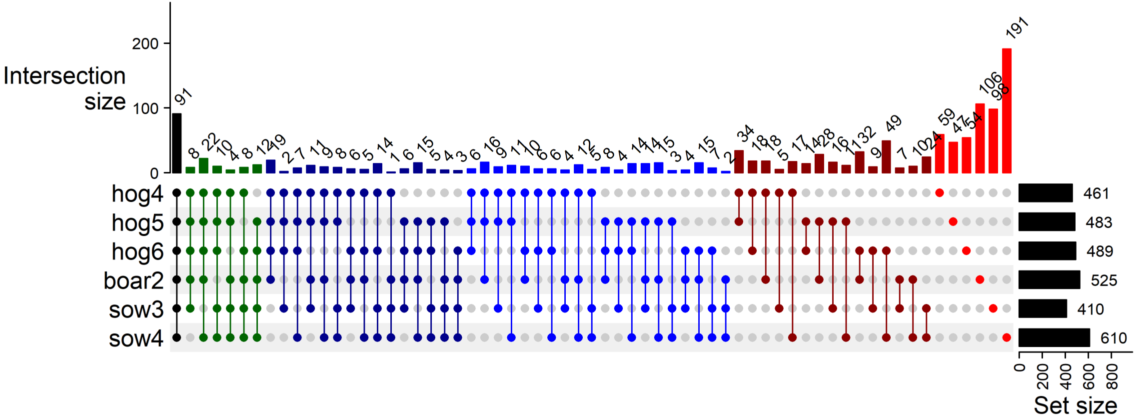

Deletions


Duplications

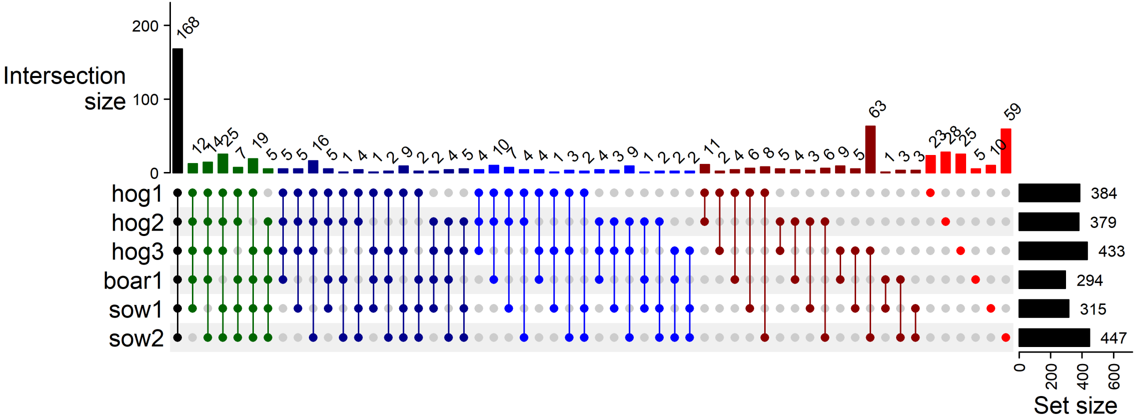
Results - common deletions



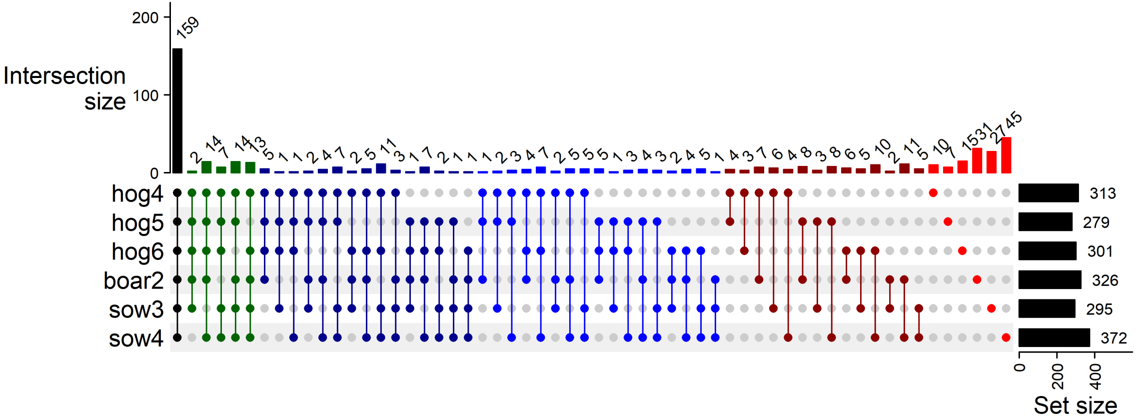
Results - common deletions



Results - common duplications



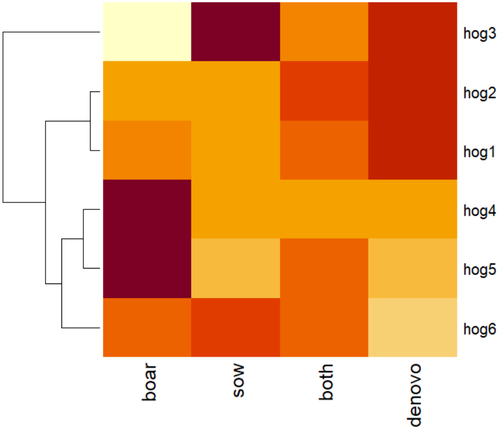
Results - common duplications

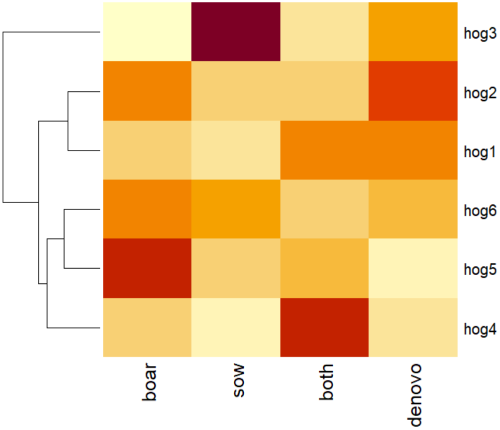


Results

- Most of inherited deletions - chromosome 11
- Most of inherited duplications - chromosome 5
- No differences in numbers of CNV inherited from sow and boar
  - deletions $P = 0.84$
  - duplications $P = 0.41$

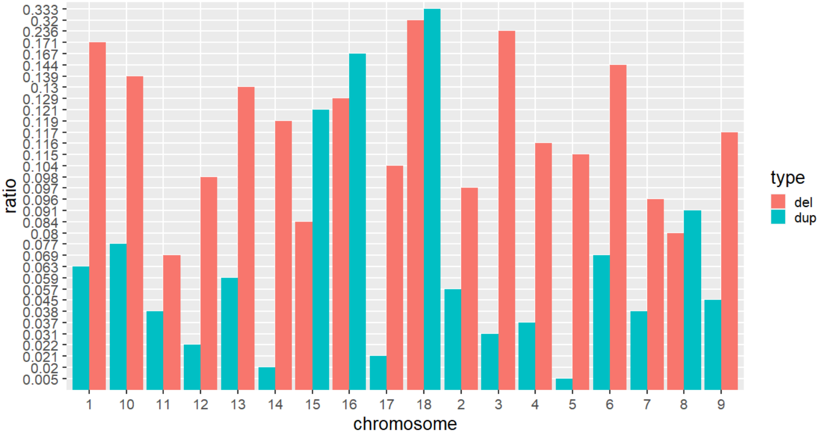
Results


hog3
hog2
hog1
hog4
hog5
hog6
boar
sow
both
denovo


hog3
hog2
hog1
hog6
hog5
hog4
boar
sow
both
denovo

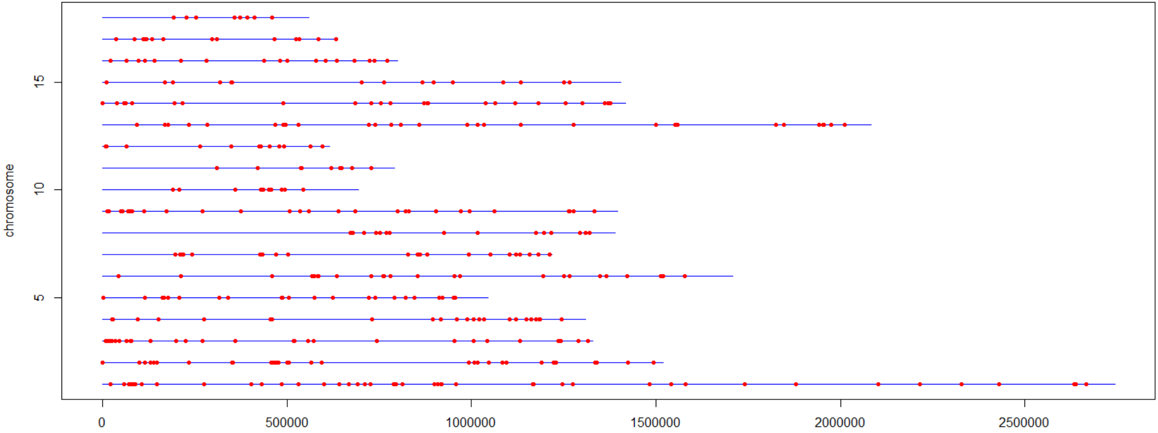
Results - *de novo* CNVs

- deletions
  422 (47 – 117)
- duplications
  96 (7 – 28)
- 72 CNV - chr 1
  55 - del, 17 - dup

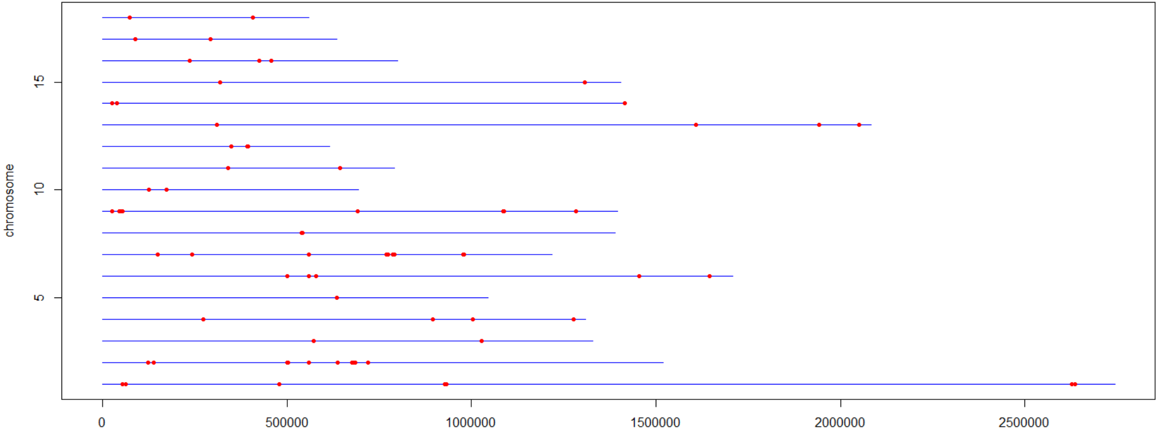


Magdalena Fraszczak magdalena.fraszczak@upwr.edu.pl

Results - density of *de novo* deletions along the genome



Results - density of *de novo* duplications along the genome



Results

- Significantly less CNVs arise *de novo* than inherited (P=0.008 for deletions, 0.006 for duplications)
- Fraction of *de novo* CNVs depends on animal in both deletions (P=0.007) duplications (P=0.004)

	hog 1	hog 2	hog 3	hog 4	hog 5	hog 6
deletion	0.129	0.131	0.150	0.111	0.089	0.094
duplication	0.058	0.072	0.045	0.018	0.021	0.044

Results

- *De novo* deletions are shorter than inherited in all animals.

	hog 1	hog 2	hog 3	hog 4	hog 5	hog 6
P-value	$3.76 \cdot 10^{-5}$	$1.26 \cdot 10^{-6}$	$6.49 \cdot 10^{-7}$	$0.13 \cdot 10^{-1}$	$0.17 \cdot 10^{-3}$	$8.18 \cdot 10^{-7}$

- no differences in length of *de novo* and inherited duplications

Results

	deletions	duplications
variants	422	96
overlapped genes	268	81
intergenic variant	14%	21%
genic coding variants	4.2%	13%
others	81.8%	66%

Results - Enrichment analysis

- Common duplications in all 12 pigs are related to the regulation of basic biological processes (metabolic and olfactory receptor activity, as well as G protein-coupled receptor signaling pathway)
- No significant results found for common deletions
- No significant results found for *de novo* CNVs

Conclusions:

- CNVs formed *de novo* account for 2%-15% of all CNVs
- deletions formed de novo are shorter than inherited
- full siblings are more simmilar each other in structure of CNVs than to other individuals
- *de novo* CNVs are not uniformly distributed
- duplications in genes are considered to be essential sources of evolutionary innovation and duplications with beneficial effects are likely to be kept
- deletions bring severe consequences by interrupting gene products and causing loss of the biological functions; polymorphisms with large negative effects are likely to be removed from the population by natural selection

THANK YOU FOR YOUR ATTENTION!

Biostatistics Group
Department of Genetics
Wrocław University of Environmental
and Life Sciences
http://theta.edu.pl

Any questions?