

Supplementary Table S5: Descriptions of phenotypes measured as part of the MAP pan-GWAS analysis

This file contains detailed descriptions of traits measured at cow level and sample level.

General characteristics of sample

1. **Source:** potentially linked to introductions of new MAP strains into a farm.
 - 0 = cow was homebred,
 - 1 = cow was purchased,
 - NA = missing data and sample type “environmental”.
2. **Environment:** sample type.
 - 0 = Isolate was sampled from a cow, incl. fecal or tissue samples,
 - 1 = Isolate was sampled from the environment.

Reduced milk production

MAP is described to have an effect on the milk productivity of cows. As disease progresses, milk yield may tend to decrease.

3. **LactIndex:** lactation index - how constant was the cow's milk yield over lifetime compared to her herd. This index was calculated in three steps:
 - 1) Milk yield of the cow's first standard lactation (milk yield over the first 305 days after she had her first calf) was compared to the average first standard lactation of her herd. If the cow's milk yield was among the lowest quartile of cows, she was assigned an index of 1; in the second quartile an index of 2, etc. up to an index of 4. (“*Lact1 - index*”).
 - 2) Milk yield of the cow's second to last standard lactation (milk yield over the first 305 days after she had her second to last calf, averaged over all lactation periods) was compared to the second to last standard lactations of her herd. If the cow's milk yield was among the lowest quartile of cows, she was assigned an index of 1; in the second quartile an index of 2, etc. up to an index of 4 (“*Lact2+ - index*”).
 - 3) Calculation: “*Lact2+ - index*” minus “*Lact1 - index*”. Negative values indicate a decrease in milk production over lifetime, and positive values indicate that the cow improved her milk production over lifetime compared to her herd. Cows that stayed with their *Lact1 - index* and *Lact2+ - index* in the same quartile, stayed constant in their milk production.
 - 0 = Milk yield of cow stayed constant or improved over lifetime compared to her herd,
 - 1 = milk yield of cow decreased over lifetime compared to her herd,
 - NA = for sample type “environmental”; cows with only one lactation, cows with missing data.

Immune response

Direct measure of humoral immune response (antibodies against MAP) of cow.

4. **SeroStatus:** serological status in serum samples (test system: ELISA).

- 0 = Cow had only negative serological test results,
 - 1 = Cow had at least one positive serological test result,
 - NA = for sample type “environmental”.
5. **ODcat:** maximum optical density (OD) level measured during the cow’s life, expressed in categories. The laboratory result for serum samples tested with the ELISA system is given in OD values.
- 0 = OD values of 0 – 1 → ~ 0 – 90th percentile of OD values,
 - 1 = OD values >1 → ~ highest 10 % OD values,
 - NA = for sample type “environmental”.

Tissue or feces infection

6. **STpos:** sample types that were MAP positive. Hypothesis: some strains of MAP may harbor loci that facilitate tissue infection.
- 0 = cow was only pos in feces (with tissue tested neg)
 - 1 = cow was pos in tissue (with or without additional positive feces or serum samples)
 - NA = environmental samples; cows that did not fulfil the inclusion criteria: at least 1 pos or 2 neg samples in each sample type (serum, feces, tissue).

Onset of shedding

Age or phase of life when cow started shedding MAP.

7. **AnteFC:** phase of life when feces was tested MAP positive - *ante mortem* (during lifetime) or *post mortem* (after culling/at slaughter).
- 0 = Only fecal samples taken from the cow’s carcass after culling/slaughter (*post mortem*) were positive (= missing proof of MAP shedding on farm):
 - 1 = Cow had at least one positive fecal culture during lifetime (= proof of MAP shedding on farm).
 - NA = for sample type “environmental”.
8. **FFS<3:** first fecal shedding at younger age (up to 3 years) or at older age (>3 years).
- 0 = Cow had first positive fecal sample at age of 3 years or older
 - 1 = Cow had first positive fecal sample <3yrs
 - NA = for sample type “environmental”.

Shedding level

Measure of infectiousness of cow due to fecal MAP shedding and MAP burden in intestinal tissues. The MAP strain was isolated from a cow that at some stage in her life shed a certain number of bacteria or had a certain bacterial load in its tissues.

9. **FecalShedGroup:** maximum number of colony forming units (cfu)/tube cultured from fecal samples of a cow (sampled *ante mortem* or *post mortem* at slaughter).
- 0 = Cow had only fecal samples with 0 - 50 cfu/tube = negative to moderate fecal shedder.
 - 1 = Cow had at least one fecal sample with >50 cfu/tube = high fecal to super shedder.

Disease progress

Infection pattern.

10. **Prog:** Schukken et al. (2015) observed two distinct infection patterns: “progressors” show an increase in their fecal shedding level over time, whereas “non-progressors” show no increase in their fecal shedding level and have negative fecal samples in between / after positive fecal samples.

Inclusion criteria: Only animals with a.) at least 4 fecal MAP culture results and b.) at least 1 fecal MAP culture taken after a positive MAP culture are included in this analysis.

- 0 = Fecal culture negative cow or non-progressor: Cow with no positive fecal sample or cow with no increase in fecal shedding levels (measured in cfu/tube) over time,
- 1 = Progressor: Cow showed an increase in fecal shedding levels (measured in cfu/tube) over time, and had no negative sample (0 cfu/tube) after previous positive samples.
- NA = Cows with 0 – 3 fecal samples; cows that were only in their last fecal sample positive (no valid assumption on further progress possible); sample type “environmental”.

References

Schukken, Y.H., Whitlock, R.H., Wolfgang, D., Grohn, Y., Beaver, A., VanKessel, J., Zurakowski, M., Mitchell, R., 2015. Longitudinal data collection of Mycobacterium avium subspecies paratuberculosis infections in dairy herds: the value of precise field data. Veterinary research 46, 65p.