Iron metabolism phenotype: the example of *SLC11A1* genotype in Italian Friesian calves

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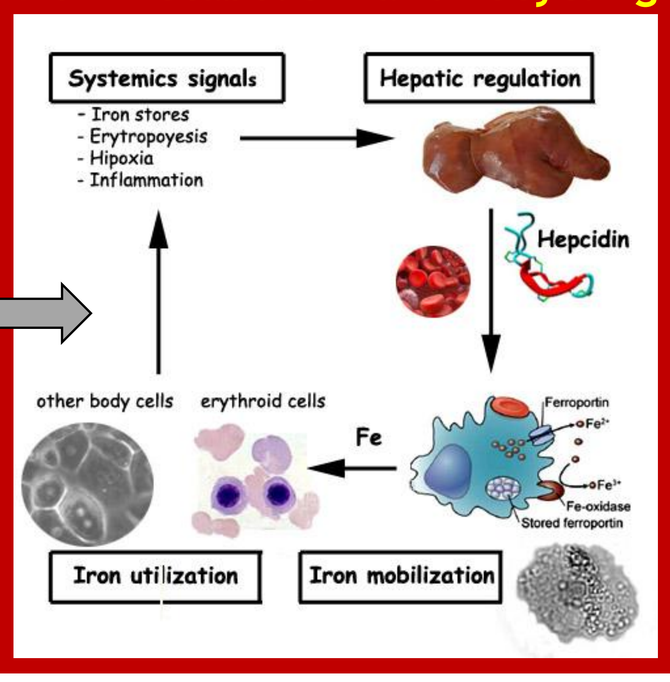
Introduction

- iron (Fe) metabolism plays an important role in critical moments of the life (for example, neonatal phase)
- Fe metabolism is regulated by the action of different genes
- senescent erythrocytes are phagocytised by macrophages for Fe recycling
- *Slc11A1* (formerly NRAMP1) is mainly expressed in macrophages, improving their ability to subtract Fe in competition with pathogens (Ruiz-Larrañaga et al., 2010)

The objective of this study was to evaluate the effect of a *SLC11A1* genotype for a coding SNP at the exon 11 (C>G) on Fe metabolism in young cattle

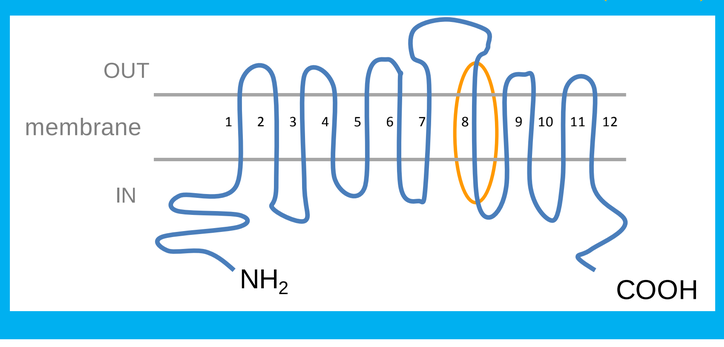
Iron metabolism and recycling



Bovine *Slc11A1* SNPs monitored

promoter → c.93C>T (*Martinez et al. 2008*)
promoter → c.752G>A (*Zanotti et al. 2002*)
exon 11 → c.1067C>G (*Martinez et al. 2008*)

Trans-membrane domain 8 (TM8)



Materials and Methods

42 newborn Italian Friesian calves were genotyped sequencing the exon 11 amplifying a region of 578 bp; distribution: CC n=31; CG n=10; GG n=1

Blood samples: 1, 2, 3, 4, 6, and 8 wk of age
haematological profile → K_3EDTA tubes

plasma Fe; total iron-binding capacity (TIBC);
unsaturated iron-binding capacity (UIBC);
TIBC % of saturation (TIBC-sat) → Li-heparin tubes

Statistical analysis

Mixed model: genotype (CC vs CG, excluding GG), wk of age, and their interaction as main factors, with the animal repeated in time

Figure 1 - RBC

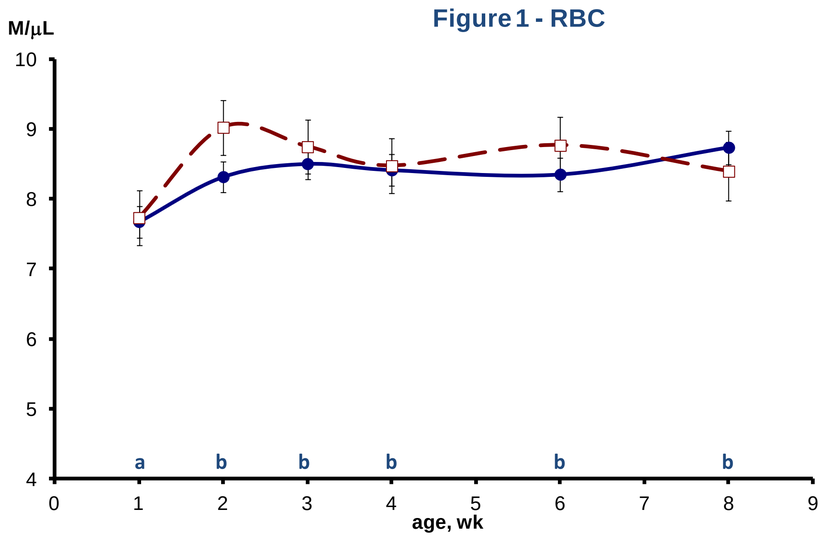
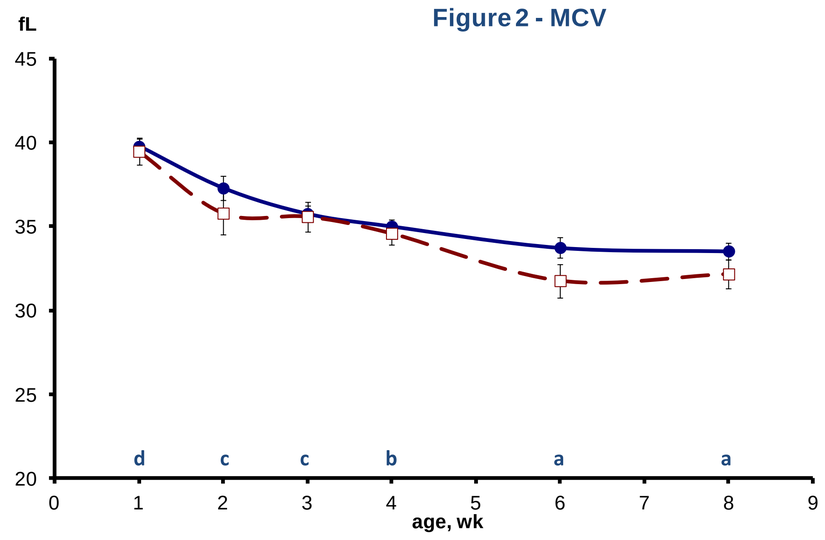


Figure 2 - MCV



Results and Discussion

Age affected all the considered haematological variables (erythrocytes count, haemoglobin, haematocrit, mean erythrocyte volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, red cells distribution wideness), and plasma Fe, TIBC, UIBC, and TIBC-sat
⇒normal post-natal haematopoiesis

Genotype and its interaction with age did not affect haematological traits (Fig. 1 and 2) and TIBC (Fig. 3)

CG genotype had higher (P<0.05) plasma Fe, and TIBC-sat (Fig. 4 and 5)

C allele → MAP susceptibility (Ruiz-Larrañaga et al., 2010)

Position 356 allele C → proline (CCA codon) G → alanine (GCA codon)

GCG (alanine) ancestral codon in mammals ⇒ GCA (alanine) in ruminants

High prevalence C in Holstein-Friesians and other *Bos taurus* → artificial selection, close linkage with nearby allele favourable to yield traits (Ruiz-Larrañaga et al., 2010)

Open questions

Different genotypes ⇒ different Fe recycling ability?
Evaluable differences only when Fe availability is limiting?

Figure 3 - TIBC

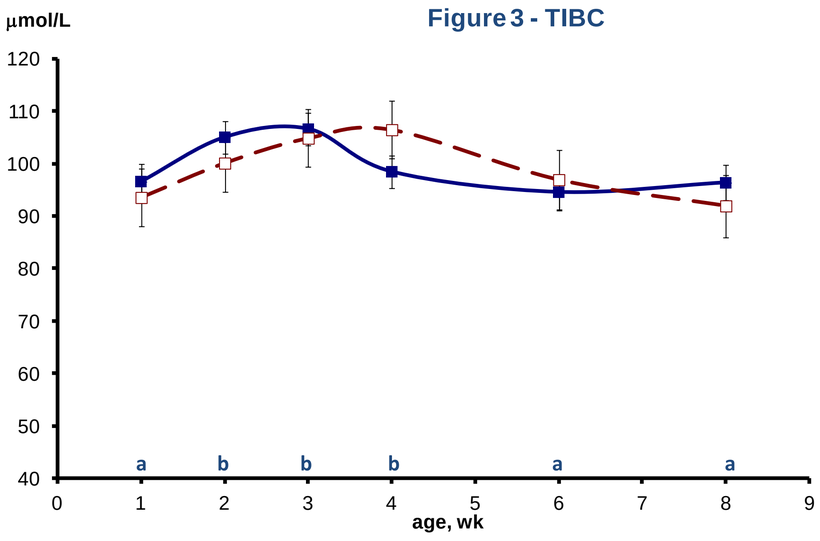


Figure 4 - Fe

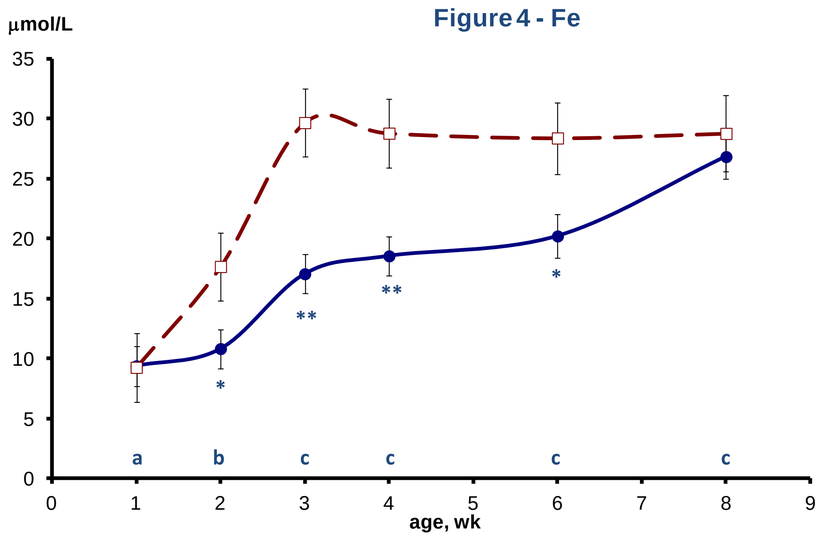
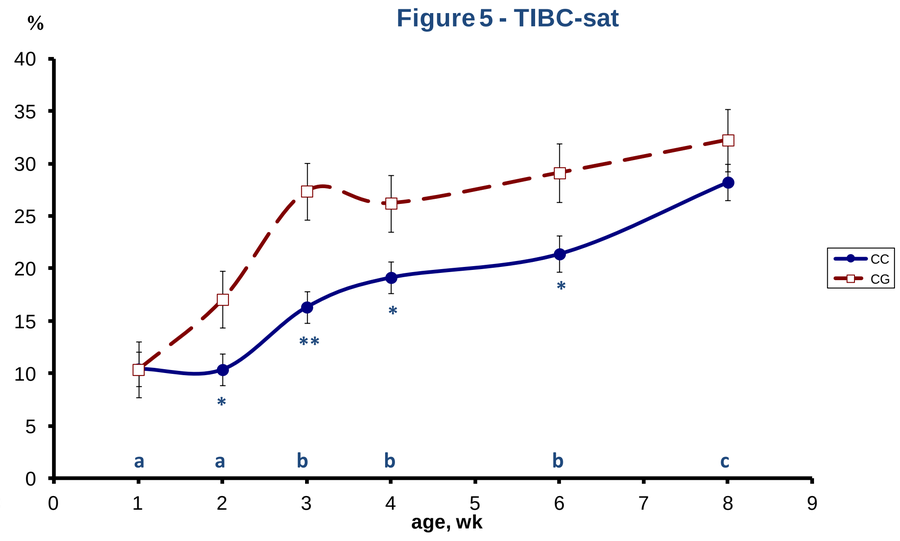


Figure 5 - TIBC-sat



Conclusion

In light of the role of macrophage in the clearance of senescent erythrocytes, we suppose that the studied SNP at exon 11, which affects the protein structure in the TM8, could determine a different capacity in Fe recycling (and a different susceptibility to pathogens?)