A novel single nucleotide polymorphism (SNP) of ARHGEF12 involved in the susceptibility to chemotherapy-induced anemia in acute lymphoblastic leukemia (ALL) patients

SCMC-ALL-2005 cohort including 452 patients

- 31 No RBC transfusion cohort (NRT)
- 31 Multiple RBC transfusions cohort (MRTs)

Genome-wide association study (GWAS) analyses

- 281 genes
  - 12 genes highly expressed in pre-erythroid committed
  - 23 genes highly expressed in erythroid committed

**ARHGEF12** encodes a RhoA guanine nucleotide exchange factor which is essential for embryonic erythropoiesis

**GATA1** binding motif (933bp)

- A SNP significantly associated with patients who need RBC transfusion (P=3.469E-03, odds ratio 5.864)
- rs10892563 homozygosity is associated with a ~61% reduction in **ARHGEF12** expression (P=0.0088)

rs10892563 impairs **GATA1** mediated trans-regulation of **ARHGEF12**

Reduced erythropoiesis at the pro-erythroblast phase

Xie et al., Haematologica, 2020