# Scianna Blood Group System

## Number of antigens 7

| | |
|---|---|
| Low prevalence | Sc2, Rd |
| High prevalence | Sc1, Sc3, STAR, SCER, SCAN |

## Terminology

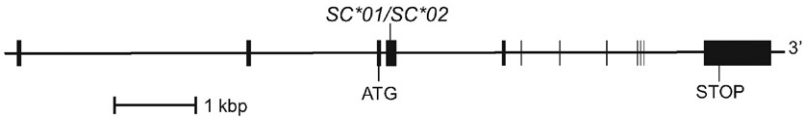
| | |
|---|---|
| ISBT symbol (number) | SC (013) |
| History | Established in 1974; named after the family of the first maker of anti-Sc1. |

## Expression

| | |
|---|---|
| Other blood cells | Weakly expressed on leukocytes[1] |
| Tissues | Fetal liver, thymus, lymph nodes, spleen, and bone marrow in adults[1] |

## Gene

| | |
|---|---|
| Chromosome | 1p34.2 |
| Name | *SC (ERMAP)* |
| Organization | 12 exons spanning 27.89 kbp of gDNA |
| Product | Sc glycoprotein [Erythroid membrane associated protein (ERMAP)] |




## Database accession numbers

| | |
|---|---|
| GenBank | NG_008749 (gene); NM_001017922 (mRNA) |
| Entrez Gene ID | 114625 |



The Blood Group Antigen (3/e). DOI: http://dx.doi.org/10.1016/B978-0-12-415849-8.00015-6

## Molecular bases of Sc phenotypes[2]

The reference allele *SC*01* (Accession number NM_001017922) encodes Sc1 (SC1), SC3, SC5, SC6, SC7. Nucleotide differences, and amino acids affected, are given.

| Allele encodes | Allele name | Exon^ | Nucleotide | Restriction enzyme | Amino acid | Ethnicity (prevalence) |
|---|---|---|---|---|---|---|
| Sc1– Sc2+ or SC:–1,2 | *SC*02* | 4^ | 169G>A | *Sma*I – | Gly57Arg | Mennonites, Others (Several) |
| Rd+ or SC:4 | *SC*01.04* | 4^ | 178C>G | | Pro60Ala | Danes, Jews, Canadians, Blacks (Several) Others (Rare) |
| STAR– or SC:–5 | *SC*01.–05* | 4^ | 139G>A | | Glu47Lys | English, Irish (Rare) |
| SCER– or SC:–6 | *SC*01.–06* | 4^ | 242G>A | | Arg81Gln | German (Rare) |
| SCAN– or SC:–7 | *SC*01.–07* | 4^ | 103G>A | | Gly35Ser | German English-Native American heritage (Rare) |

Note: A change of *SC*54C>T* in exon 3 (previously exon 2; silent; Leu18) and *SC*76C>T* in exon 3 (previously exon 2) are polymorphic, and more common in Caucasians than Blacks[3]. *SC*76C>T* encodes His26Tyr in the leader sequence of Sc glycoprotein, and thus is not in the RBC membrane.
^In 2011, the gene encoding ERMAP was shown to have 12 exons and not 11 as previously published. As the additional exon is upstream of the initiation codon, the exon that harbors nucleotide changes that affect the expression of a blood group is +1 from that given in the original publications, while the nucleotide and amino acid numbers remain the same.

## Molecular bases of silencing of *SC*[2]

Homozygosity or compound heterozygosity leads to the $Sc_{null}$ (SC:–1–2–3) phenotype. The nucleotide difference from *SC*01* reference allele (Accession number NM_001017922), and the amino acid affected, are given.

| Allele name | Exon | Nucleotide | Restriction enzyme | Amino acid | Ethnicity (prevalence) |
|---|---|---|---|---|---|
| *SC*01N.01* | 4^ | 307_308delGA | | 113fs Stop | Saudi Arabian (Rare) |
| *SC*01N.02* | 12^ | 994C>T@ | *Tsp*45I+ | Arg332Stop | Marshallese (Rare) |

^See comment under previous table.
@This allele also may have *SC*1514C>T* in the 3′-UTR portion of exon 12 (previously published as exon 11).

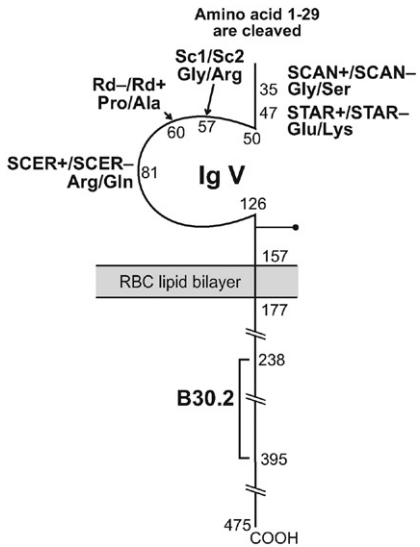
## Amino acid sequence[1,4]

```
MEMASSAGSW  LSGCLIPLVF  LRLSVHVSGH  AGDAGKFHVA  LLGGTAELLC   50
PLSLWPGTVP  KEVRWLRSPF  PQRSQAVHIF  RDGKDQDEDL  MPEYKGRTVL  100
VRDAQEGSVT  LQILDVRLED  QGSYRCLIQV  GNLSKEDTVI  LQVAAPSVGS  150
LSPSAVALAV  ILPVLVLLIM  VCLCLIWKQR  RAKEKLLYEH  VTEVDNLLSD  200
HAKEKGKLHK  AVKKLRSELK  LKRAAANSGW  RRARLHFVAV  TLDPDTAHPK  250
LILSEDQRCV  RLGDRRQPVP  DNPQRFDFVV  SILGSEYFTT  GCHYWEVYVG  300
DKTKWILGVC  SESVSRKGKV  TASPANGHWL  LRQSRGNEYE  ALTSPQTSFR  350
LKEPPRCVGI  FLDYEAGVIS  FYNVTNKSHI  FTFTHNFSGP  LRPFFEPCLH  400
DGGKNTAPLV  ICSELHKSEE  SIVPRPEGKG  HANGDVSLKV  NSSLLPPKAP  450
ELKDIILSLP  PDLGPALQEL  KAPSF                            475
```

*SC* encodes a signal peptide of 29 amino acids.

## Carrier molecule[1,2,5]

Single pass type 1 membrane glycoprotein, a member of the immunoglobulin superfamily (IgSF) with one IgV domain.



| | |
|---|---|
| $M_r$ (SDS-PAGE) | 60,000–68,000 |
| CHO: N-glycan | 4 sites |
| Cysteine residues | 11 |
| Copies per RBC | Not determined |

## Function

Human ERMAP is an erythroid transmembrane adhesion/receptor protein.

## Disease association

Not known

## Phenotypes (% occurrence)

| Phenotype | Caucasians | Blacks |
|---|---|---|
| SC:1,–2 | 99 | 100 |
| SC:1,2 | 1 | 0 |
| SC:–1,2 | Very rare | 0 |
| SC:1,–2, Rd+ | Very rare | Very rare |
| SC:1,2, Rd+ | Very rare | 0 |
| Null: SC:–1,–2,–3 | | |



## Comments

The extracellular IgV domain of ERMAP is homologous with the butyrophilin family of milk proteins, autoantigens, and avian blood group antigens[1].
The intracellular B30.2 domain is highly homologous with a similar domain in a diverse group of proteins, including butyrophilin, pyrin, and MID1[1].

## References

[1] Su, Y.Y., et al., 2001. Human ERMAP: an erythroid adhesion/receptor transmembrane protein. Blood Cells Mol Dis 27, 938–949.
[2] Brunker, P.A.R., Flegel, W.A., 2011. Scianna: the lucky 13th blood group system. Immunohematology 27, 41–57.
[3] Fuchisawa, A., et al., 2009. The polymorphism nt 76 in exon 2 of *SC* is more frequent in Whites than in Blacks. Immunohematology 25, 18–19.
[4] Xu, H., et al., 2001. Cloning and characterization of human erythroid membrane-associated protein, human ERMAP. Genomics 76, 2–4.
[5] Wagner, F.F., et al., 2003. The Scianna antigens including Rd are expressed by ERMAP. Blood 101, 752–757.

# Sc1 Antigen

## Terminology

| | |
|---|---|
| ISBT symbol (number) | SC1 (013001 or 13.1) |
| Obsolete name | Sm |
| History | Identified in 1962; name changed from Sm to Sc1 in 1974 when the Scianna system was established. Named for the first maker of anti-Sc1. |

## Occurrence

| | |
|---|---|
| All populations | >99% |

## Antithetical antigen

Sc2 (**SC2**)

## Expression

| | |
|---|---|
| Cord RBCs | Expressed |

## Molecular basis associated with Sc1 antigen[1]

| | |
|---|---|
| Amino acid | Gly57 |
| Nucleotide | G at bp 169 in exon 4 (previously published as exon 3) |

## Effect of enzymes and chemicals on Sc1 antigen on intact RBCs[2]

| | |
|---|---|
| Ficin/Papain | Resistant |
| Trypsin | Resistant |
| α-Chymotrypsin | Resistant |
| DTT 200 mM/50 mM | Resistant/resistant (thus resistant to WARM™ and ZZAP) |

## *In vitro* characteristics of alloanti-Sc1

| | |
|---|---|
| Immunoglobulin class | IgG |
| Optimal technique | IAT |

## Clinical significance of alloanti-Sc1

| | |
|---|---|
| Transfusion reaction | Not reported |
| HDFN | Positive DAT but no clinical HDFN |

## Autoanti-Sc1

Yes[3]. Some examples are reactive in tests using serum but not plasma[4].

### Comments

Siblings of patients with anti-Sc1 should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

### References

[1] Wagner, F.F., et al., 2003. The Scianna antigens including Rd are expressed by ERMAP. Blood 101, 752–757.
[2] Velliquette, R.W., et al., 2011. The effect of proteases or DTT on Scianna antigens, revisited [abstract]. Transfusion 51 (Suppl.), 146A.
[3] Owen, I., et al., 1992. Autoimmune hemolytic anemia associated with anti-Sc1. Transfusion 32, 173–176.
[4] Tregellas, W.M., et al., 1979. An example of autoanti-Sci demonstrable in serum but not in plasma [abstract]. Transfusion 19, 650.

## Sc2 Antigen

### Terminology

| | |
|---|---|
| ISBT symbol (number) | SC2 (013002 or 13.2) |
| Obsolete names | Bu$^a$; Bullee |
| History | Identified in 1962 and named Bu$^a$; renamed Sc2 in 1974 when it was shown to be antithetical to Sm (now Sc1). |

### Occurrence

1% in people of European ancestry; more common in Mennonites.

### Antithetical antigen

Sc1 (**SC1**)

### Expression

| | |
|---|---|
| Cord RBCs | Expressed |

### Molecular basis associated with Sc2 antigen[1]

| | |
|---|---|
| Amino acid | Arg57 |
| Nucleotide | A at bp 169 in exon 4 (previously published as exon 3) |

### Effect of enzymes and chemicals on Sc2 antigen on intact RBCs[2]

| | |
|---|---|
| Ficin/Papain | Resistant |
| Trypsin | Variable |
| α-Chymotrypsin | Variable |
| DTT 200 mM/50 mM | Variable/resistant (thus variable with WARM™ and ZZAP) |

### *In vitro* characteristics of alloanti-Sc2

| | |
|---|---|
| Immunoglobulin class | IgG |
| Optimal technique | IAT |

### Clinical significance of alloanti-Sc2

| | |
|---|---|
| Transfusion reaction | No |
| HDFN | Positive DAT but no clinical HDFN to mild[3] |

### Comments

Sc2 antigen has variable expression among different people.

### References

[1] Wagner, F.F., et al., 2003. The Scianna antigens including Rd are expressed by ERMAP. Blood 101, 752–757.
[2] Velliquette, R.W., et al., 2011. The effect of proteases or DTT on Scianna antigens, revisited [abstract]. Transfusion 51 (Suppl), 146A.
[3] DeMarco, M., et al., 1995. Hemolytic disease of the newborn due to the Scianna antibody, anti-Sc2. Transfusion 35, 58–60.

## Sc3 Antigen

### Terminology

| | |
|---|---|
| ISBT symbol (number) | SC3 (013003 or 13.3) |
| History | Named in 1980 when a person with SC:–1,–2 RBCs made an antibody to a high-prevalence antigen. |

### Occurrence

Most SC:–1,–2,–3 people have originated from the Marshall Islands or other Pacific Islands, including Papua New Guinea.

### Expression

| | |
|---|---|
| Cord RBCs | Expressed |

### Molecular basis associated with Sc3 antigen

For molecular bases of the SC:–1,–2,–3 (the null phenotype) see System pages.

### Effect of enzymes and chemicals on Sc3 antigen on intact RBCs[1]

| | |
|---|---|
| Ficin/Papain | Resistant (enhanced) |
| Trypsin | Variable |
| α-Chymotrypsin | Variable |
| DTT 200 mM/50 mM | Resistant/resistant (thus resistant to WARM™ and ZZAP) |

### *In vitro* characteristics of alloanti-Sc3

| | |
|---|---|
| Immunoglobulin class | IgG |
| Optimal technique | IAT |

### Clinical significance of alloanti-Sc3

| | |
|---|---|
| Transfusion reaction | No to mild/delayed |
| HDFN | Mild |

### Autoanti-Sc3

Autoanti-Sc3-like antibody in two patients with suppressed Sc antigens (one patient with lymphoma; one with Hodgkins disease)[2].

### References

[1] Velliquette, R.W., et al., 2011. The effect of proteases or DTT on Scianna antigens, revisited [abstract]. Transfusion 51 (Suppl.), 146A.

[2] Peloquin, P., et al., 1989. Anti-Sc3 as an apparent autoantibody in two patients [abstract]. Transfusion 29 (Suppl.), 49S.



## Sc4 Antigen

### Terminology

| | |
|---|---|
| ISBT symbol (number) | Rd (013004 or 13.4) |
| Obsolete names | Radin; Rd[a]; 700015 |
| History | Named after the first family in which the antibody caused HDFN. Became part of the SC system when the associated polymorphism in human ERMAP was identified. |

### Occurrence

| | |
|---|---|
| All populations | Less than 0.01% |
| Danes | 0.5% |
| Jews, Canadians | 0.1% |
| African Blacks | 0.1% |

### Expression

| | |
|---|---|
| Cord RBCs | Expressed |

### Molecular basis associated with Rd antigen[1]

| | |
|---|---|
| Amino acid | Ala60 |
| Nucleotide | G at bp 178 in exon 4 (previously published as exon 3) |
| Rd-negative | Pro60 and C at bp 178 |

### Effect of enzymes and chemicals on Rd antigen on intact RBCs[2]

| | |
|---|---|
| Ficin/Papain | Resistant |
| Trypsin | Variable, but often sensitive |
| α-Chymotrypsin | Variable, but often sensitive |
| DTT 200 mM/50 mM | Resistant/resistant (thus resistant to WARM™ and ZZAP) |

### *In vitro* characteristics of alloanti-Rd

| | |
|---|---|
| Immunoglobulin class | IgG |
| Optimal technique | IAT |

### Clinical significance of alloanti-Rd

| | |
|---|---|
| Transfusion reaction | No |
| HDFN | Mild to severe |

### References

[1] Wagner, F.F., et al., 2003. The Scianna antigens including Rd are expressed by ERMAP. Blood 101, 752–757.

[2] Velliquette, R.W., et al., 2011. The effect of proteases or DTT on Scianna antigens, revisited [abstract]. Transfusion 51 (Suppl.), 146A.

## STAR Antigen

### Terminology

| | |
|---|---|
| ISBT symbol (number) | SC5 (013005 or 13.5) |
| History | Named in 2005 after the STAR– proband. |

### Occurrence

The only STAR– proband was of English-Irish heritage.

### Molecular basis associated with STAR antigen[1]

| | |
|---|---|
| Amino acid | Glu47 |
| Nucleotide | G at bp 139 in exon 4 (previously published as exon 3) |
| SCAN– | Lys47 and A at bp 139 |

### Effect of enzymes and chemicals on STAR antigen on intact RBCs

| | |
|---|---|
| Ficin/papain | Resistant (Enhanced) |

### *In vitro* characteristics of alloanti-STAR

| | |
|---|---|
| Immunoglobulin class | IgG |
| Optimal technique | IAT |

### Clinical significance of alloanti-STAR

No information because antibody is rare.

### Comments

Siblings of patients with anti-STAR should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

### Reference

[1] Hue-Roye, K., et al., 2005. STAR: a novel high prevalence antigen in the Scianna blood group system. Transfusion 45, 245–247.



## SCER Antigen

### Terminology

| | |
|---|---|
| ISBT symbol (number) | SC6 (013006 or 13.6) |
| History | Named in 2005 after "SC" for Scianna and "ER" from the second and third letters of the SCER– proband's name. |

### Occurrence

The only SCER– proband was of German heritage.

### Molecular basis associated with SCER antigen[1]

| | |
|---|---|
| Amino acid | Arg81 |
| Nucleotide | G at 242 in exon 4 (previously published as exon 3) |
| SCER– | Gln81 and A at bp 242 |

### Effect of enzymes and chemicals on SCER antigen on intact RBCs

| | |
|---|---|
| Ficin/papain | Resistant |
| Trypsin | Resistant |
| DTT 200/50 mM | Resistant/resistant (thus resistant to WARM™ and ZZAP) |

### *In vitro* characteristics of alloanti-SCER

| | |
|---|---|
| Immunoglobulin class | IgG |
| Optimal technique | IAT |

### Clinical significance of alloanti-SCER

| | |
|---|---|
| Transfusion reaction | No information because the antibody is rare, but an *in vivo* $^{51}$Cr-labelled RBC survival study indicated reduced survival of antigen-positive RBCs |
| HDFN | No information because antibody is rare |

### Comments

Siblings of patients with anti-SCER should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

### Reference

[1] Flegel, W.A., et al., 2005. SCER and SCAN: two novel high-prevalence antigens in the Scianna blood group system. Transfusion 45, 1940–1944.

## SCAN Antigen

### Terminology

| | |
|---|---|
| ISBT symbol (number) | SC7 (013007 or 13.7) |
| History | Named in 2005 after "SC" for Scianna and "AN" from the second and third letters of the SCAN– proband's name. |

### Occurrence

The only SCAN– proband was of German, English, and Native American heritage.

### Molecular basis associated with SCAN antigen[1]

| | |
|---|---|
| Amino acid | Gly35 |
| Nucleotide | G at bp 103 in exon 4 (previously published as exon 3) |
| SCAN– | Ser35 and A at bp 103 |

The SCAN– proband also had the *SC*54C>T* silent nucleotide change and *SC*76C>T* (His26Tyr).

## Effect of enzymes and chemicals on SCAN antigen on intact RBCs

| | |
|---|---|
| Ficin/papain | Resistant |
| DTT 200/50 Mm | Resistant/resistant (thus resistant to WARM™ and ZZAP) |

## *In vitro* characteristics of alloanti-SCAN

| | |
|---|---|
| Immunoglobulin class | IgG |
| Optimal technique | IAT |

## Clinical significance of alloanti-SCAN

| | |
|---|---|
| Transfusion reaction | Delayed (only one case reported) |
| HDFN | No information because antibody is rare |

## Comments

Siblings of patients with anti-SCAN should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

## Reference

[1] Flegel, W.A., et al., 2005. SCER and SCAN: two novel high-prevalence antigens in the Scianna blood group system. Transfusion 45, 1940–1944.