Note: Example of human error resulting in discordant phenotype and genotype: *A technologist is performing an extended phenotype for a patient who will receive a monoclonal therapy that interferes with blood bank testing. The patient has not received a transfusion and the DAT is negative. After performing quality control for the antisera, the tubes are labeled. While adding the antisera, the phone rings and testing is put on hold to answer questions regarding another patient. Once off the phone, the technologist continues adding the antisera to the remaining tubes and ensures each tube has antisera in it. However, in error, the anti-s was dropped into the anti-S tube. The patient is incorrectly typed as S+s+, when S−s+ is correct. DNA testing of the patient's sample would be S−s+ and discordant with the S+s+ serologic typing. Extensive serologic or molecular investigation would not be needed. Rather, repeat serologic testing that would show the patient's red cell type as S−s+ would be enough for resolution. Distractions can cause errors in any area, including DNA testing.*

Discordant Examples and Resolutions

This section highlights the limitations for serologic and/or DNA-based testing that lead to discordant results between the two, followed by one or more examples, or scenarios. The serology results are broadly summarized, and the extensive work performed for cases involving antibody identification will not be described. These examples are "true" discordances and presume preanalytical or similar factors mentioned above were ruled out. For many of the examples, the resolution of serologic/DNA discordant results requires testing beyond commercially available blood group genotyping platforms. As these examples illustrate, gene sequencing or amplification assays that target larger (or different) regions of the gene(s) are often required for resolution.

Table 6-1 highlights different examples of discordance between serology and predictions by DNA.

Table 6-1. Examples of Discordances between Serology and DNA Testing*

Discordance			Impact		
Serology	**DNA**	**Cause**	**When Present in the Patient**	**When Present in a Donor**	**Example(s)**
Negative	Positive	Weak antigen expression not detected by serology	No. I risk for alloimmunization to the corresponding antigen, **except if** the antigen is partial	Transfusion to antigen-negative individual may stimulate antibody to the antigen; if patient has the antibody, possible compromised survival of transfused red cells	Weak Fy^b (Fy^X) encoded by *FY*02W.01*[1-4] Weak D encoded by *RHD*weak D type 2*[6] Weak K encoded by *KEL*01.02*[6] Weak e encoded by *RHCE*ceMO*[7] Weak c due to *RHCE*ceJAL*[8]
		Weak antigen expression not detected due to change(s) in another gene	No risk for alloimmunization	May stimulate antibody to corresponding antigen Loss of rare donor	In(Lu) phenotype associated with *KLF1*BGM06*[9]

Positive	Negative	Unexpected antigen expression	Patient may not be recognized as antigen negative; risk for alloimmunization to the conventional antigen	May stimulate antibody to the epitope	False C-positive associated with *RHD*DIVa*[10] D epitope encoded by *RHCE*ceCF*[11,12] E-like epitope on a Ce protein encoded by *RHCE*Ce674G*[13]
Negative	Positive	Silenced or null allele not interrogated by the genotyping assay	Risk of alloimmunization to corresponding antigen Assumption of antigen positive could lead to autoantibody interpretation when actually an alloantibody	No clinical impact Loss of antigen-negative unit	Jk_{null} or Jk(b–) encoded by silenced *JK*B* (*JK*02N.01*)[14] E– due to silenced *RHCE*cE* (*RHCE*cE907C*) (D– – when homozygous)[15]
Positive	Negative	Allele dropout	Not a risk for alloimmunization Potential risk for alloimmunization to the corresponding antigen **if** the antigen is partial	Transfusion to antigen-negative patient could stimulate antibody production	Allele not detected due to intron change(s) Dropout of S on PreciseType HEA due to *GYPB*Mit* (*GYPB*24*)[16]

*Some antigens may type negative or positive depending on the reagent (or genotyping kit/assay) used for typing. Note: The examples are not comprehensive.