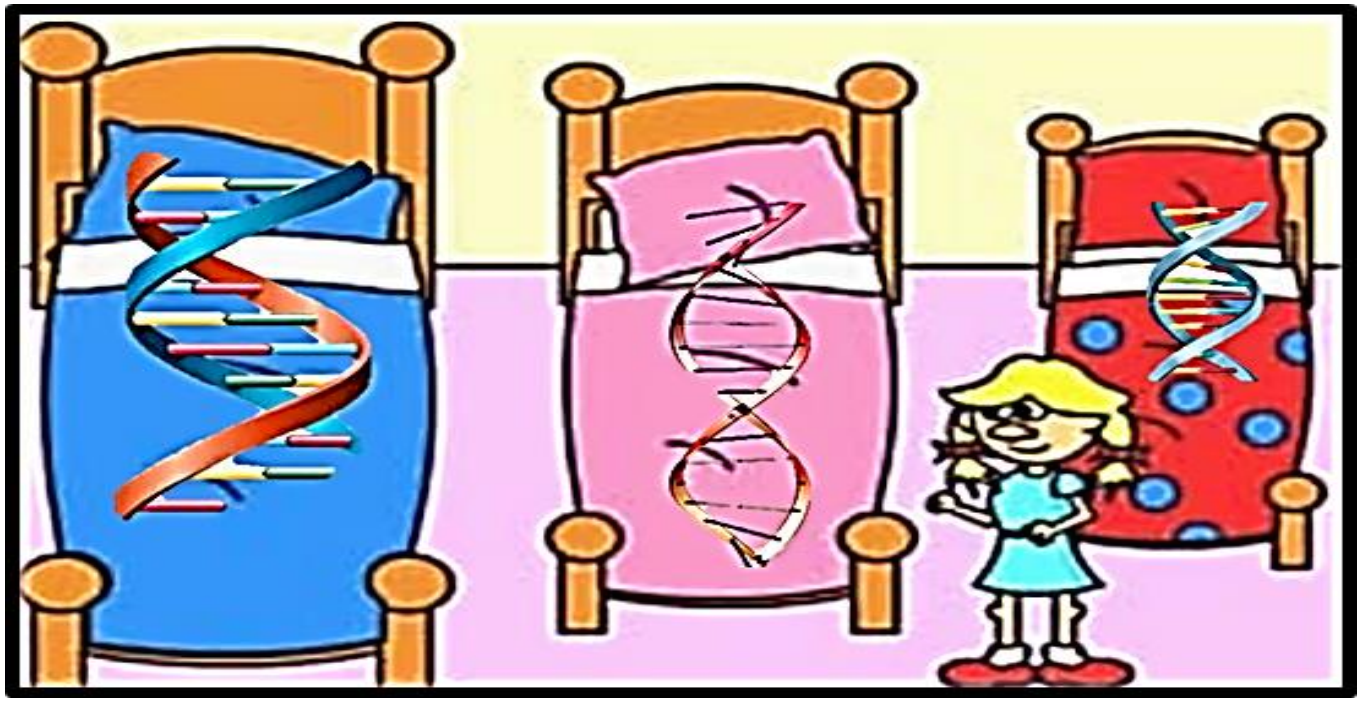
Community Blood Center

Goldie Locks and the Three Bone Marrows



Julie Kirkegaard MT(ASCP)SBB
Aaron Gottschalk, Ph.D.

New York Blood Center

IBR INNOVATIVE BLOOD RESOURCES

Rhode Island Blood Center

NATIONAL CENTER FOR BLOOD GROUP GENOMICS

Blood Bank of Delmarva

Community Blood Center

Expanding our organization to meet clinical, cellular and transfusion product and service needs for patients.

Now providing almost one million blood products, over 450,000 laboratory and multi-assay infectious disease tests, and over 12,500 specialty clinical procedures annually to hospitals nationwide.

NATIONAL CORD BLOOD PROGRAM

NATIONAL CENTER FOR BLOOD GROUP GENOMICS

COMPREHENSIVE CELL SOLUTIONS™

New York Blood Center

IBR INNOVATIVE BLOOD RESOURCES

Rhode Island Blood Center

Blood Bank of Delmarva

OBJECTIVES

- List the antibodies that cannot be ruled out using dithiothreitol treated cells or trypsin treated cells.
- Discuss your institution's policy for transfusion of patients receiving anti-CD38 treatment.
- List technical complications encountered when genotyping patients that have received bone marrow transplants.
- Describe technical strategies to genetically determine a patient's predicted phenotype for recipients of bone marrow transplants.
- Discuss best treatment "policy" for patients needing transfusion post bone marrow/stem cell transplant.

FIRST ENCOUNTER

- **Saw patient 1st time in Feb 2013**
- **8 years old**
- **Group O Rh Positive**
- **DAT negative**
- **Diagnosis was B-cell acute lymphocytic leukemia**
- **Pre bone marrow transplant**
- **Sent for A titers**
  - Titer with A_1 cells: IgM/IgG 2, IgG < 2
  - Titer with A_2 cells: IgM/IgG < 2, IgG < 2
- **His own bone marrow wasn't quite right… Too soft?**

SECOND ENCOUNTER

- **Saw patient 2nd time in July 2015**
- **10 years old**
- **Group A Rh Positive**
- **DAT negative**
- **Received group A bone marrow transplant July 2013**
- **Sent for B titers**
  - IgM/IgG titer with B cells: 4
  - IgG Titer with B cells: 2

THIRD ENCOUNTER

- **October 2017**
- **Diagnosis ALL relapsed x 2**
- **1st bone marrow transplant in 2013**
  - Donor was his sister
  - Went from group O to group A
- **2nd bone marrow transplant in 2015**
  - Sister's bone marrow wasn't quite right… Too hard??
  - 2nd donor was his father
  - Maybe this bone marrow will be just right!

THIRD ENCOUNTER

- **Patient on multiple medications including Daratumumab**
- **Daratumumab is monoclonal anti-CD38**
  - FDA approved in 2015 to treat relapsed/refractory multiple myeloma
  - Multiple ongoing clinical trials using anti-CD38 to treat plasma cell dyscrasias & malignancies (hematologic & solid)
  - Causes interference in antibody detection tests since CD38 is present on red blood cells

TESTING RESULTS

- **DAT**

Polyspecific	IgG specific	Complement
(+)	(+)	**(0)✓**

- **Acid Eluate**
  - All cells were nonreactive

PLASMA RESULTS

		Rh					MNSs				Lewis		Kell		P	Duffy		Kidd		Lutheran		Results
		D	C	E	c	e	M	N	S	s	Le a	Le b	K	k	P1	Fy a	Fy b	Jk a	Jk b	Lu a	Lu b	PEG IAT
1	R1R1w	+	+	0	0	+	+	+	0	+	0	+	+	+	+	+	0	+	0	0	+	1+
2	R1R1	+	+	0	0	+	+	0	0	+	0	+	0	+	+	+	+	0	+	+	+	1+
3	R2R2	+	0	+	+	0	+	0	0	+	+	0	0	+	+	0	+	+	0	0	+	1+
4	rr	0	0	0	+	+	0	+	+	+	0	+	+	+	+	0	+	+	0	0	+	1+
5	rr	0	0	0	+	+	+	0	+	0	0	0	0	+	0	+	+	+	+	0	+	1+
6	rr	0	0	0	+	+	0	+	0	+	0	+	0	+	+	+	0	0	+	0	+	1+
7	R2R2	+	0	+	+	0	0	+	+	0	+	0	0	+	0	0	+	0	+	0	+	1+
8	R1R1	+	+	0	0	+	+	0	+	0	0	+	0	+	0	0	+	+	0	0	+	1+
9	Auto																					1+w

New York Blood Center · Community Blood Center · IBR Innovative Blood Resources · Rhode Island Blood Center · Blood Bank of Delmarva

PLASMA RESULTS

DTT TREATED CELLS

		Rh					MNSs				Lewis		Kell		P	Duffy		Kidd		Lutheran		Results
		D	C	E	c	e	M	N	S	s	Le a	Le b	K	k	P1	Fy a	Fy b	Jk a	Jk b	Lu a	Lu b	PEG IAT
1	R1R1w	+	+	0	0	+	+	+	0	+	0	+	+	+	0	+	0	+	0	0	+	0✓
2	R1R1	+	+	0	0	+	+	0	+	0	0	+	0	+	+	+	+	0	+	+	+	0✓
3	R2R2	+	0	+	+	0	+	0	0	+	+	0	0	+	+	0	+	+	0	0	+	0✓
4	rr	0	0	0	+	+	+	0	+	0	0	0	0	+	0	+	+	+	+	0	+	0✓
5	rr	0	0	0	+	+	0	+	0	+	0	+	+	+	+	+	0	0	+	0	+	0✓
6	R2R2	+	0	+	+	0	0	+	+	0	+	0	0	+	0	0	+	0	+	0	+	0✓

- No underlying alloantibodies detected
- Cannot rule out Kell, Dombrock, Lutheran, Cartwright, LW and Indian system antibodies

New York Blood Center · Community Blood Center · IBR Innovative Blood Resources · Rhode Island Blood Center · Blood Bank of Delmarva

PLASMA RESULTS

TRYPSIN TREATED CELLS

		Rh					MNSs				Lewis		Kell		P	Duffy		Kidd		Lutheran		Results
		D	C	E	c	e	M	N	S	s	Le a	Le b	K	k	P1	Fy a	Fy b	Jk a	Jk b	Lu a	Lu b	PEG IAT
1	R1R1w	+	+	0	0	+	+	+	0	+	0	+	+	+	+	+	0	+	0	0	+	0✓
2	R2R2	+	0	+	+	0	+	0	0	+	+	0	0	+	+	0	+	+	0	0	+	0✓
3	rr	0	0	0	+	+	0	+	+	+	0	+	+	+	+	0	+	+	0	0	+	0✓
4	rr	0	0	0	+	+	+	0	+	0	0	0	0	+	0	+	+	+	+	0	+	0✓

- No underlying alloantibodies detected
- Cannot rule out presence of Dombrock, Lutheran, Cartwright, LW and Indian system antibodies

New York Blood Center · Community Blood Center · IBR Innovative Blood Resources · Rhode Island Blood Center · Blood Bank of Delmarva

AABB RECOMMENDATIONS

- **Association Bulletin # 16-02**
- **Prior to patient taking anti-CD38:**
  - Perform baseline type and antibody screen
  - A baseline phenotype or genotype is recommended
- **After patient begins taking anti-CD38:**
  - Antibody detection & identification using DTT-treated cells can be used to eliminate interference
    - DTT destroys Kell antigens, K-negative units should be provided unless patient is K-positive
    - Antibodies to other DTT-sensitive blood group antigens will not be detectable

WHY DETERMINE PHENOTYPE/GENOTYPE??

- Know what the patient's extended phenotype is
- Know what potential alloantibodies the patient can produce
- Know what antibodies you have to exclude during antibody identification, if needed.
- If phenotype matched units are desired, know what antigen negative units to order.

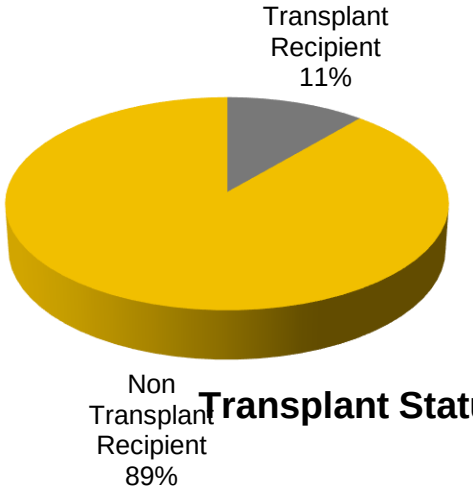
PHENOTYPE VS. GENOTYPE

- **Phenotype typically includes common blood group antigens**
  - C, E, c, e; K; Fy^a, Fy^b; Jk^a, Jk^b; S, s
  - Have to be untransfused in prior 3 months
  - Need to have negative DAT for IAT reagents
- **How do you phenotype a recently transfused patient with history of 2 bone marrow transplants????**
  - Can't reliably do phenotyping on whole blood sample
- **Genotype can be done after transfusion and after anti-CD38 treatment has started**
  - No interference by positive DAT or prior transfusion
  - Provides more information
    - Common antigens and others (total of 38 antigens)

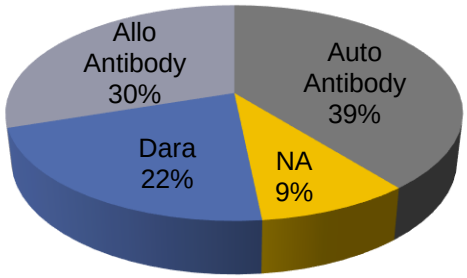
GENOTYPING GOLDIE LOCKS

- **Whose genotype will we be getting?**
  - Whole blood sample – bone marrow donor type
    - Depends on engraftment of bone marrow
    - Our patient has had 2 bone marrow transplants from family members (sister and father)
  - Buccal swab from patient's cheek- original patient type
- **Recommended submitting:**
  - Whole blood sample and buccal swabs from patient
  - Whole blood sample from bone marrow donors
    - Sister-1st donor and father -2nd donor

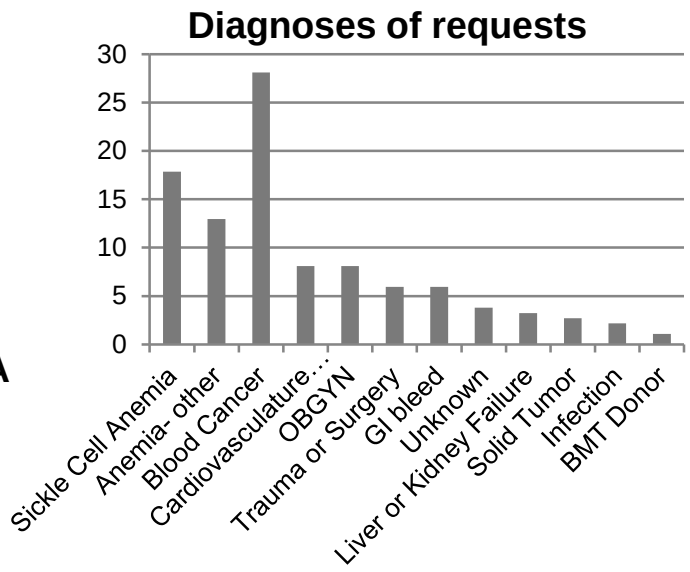
TRANSPLANT AND COMPLEX CASES IN 2017



Transplant Status



Technical Reasons for HEA



- 11% patients at NCBGG have had BMT
- 22% of patients are on Daratumumab
- ~30% are diagnosed with hematologic malignancy

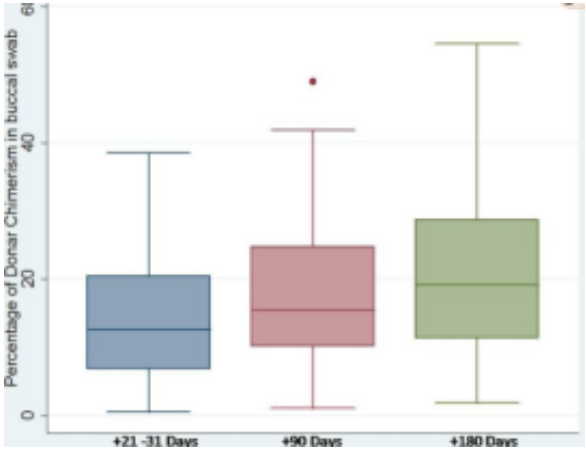
New York Blood Center | Community Blood Center | IBR INNOVATIVE BLOOD RESOURCES | Rhode Island Blood Center | Blood Bank of Delmarva

GENOTYPING PATIENTS WITH ALLOGENEIC TRANSPLANTS

Int J Legal Med. 2013 Jan;127(1):49-54. doi: 10.1007/s00414-012-0687-5. Epub 2012 Mar 9.

Chimerism in DNA of buccal swabs from recipients after allogeneic hematopoietic stem cell transplantations: implications for forensic DNA testing.

Berger B[1], Parson R, Clausen J, Berger C, Nachbaur D, Parson W.



- Transplants present unique obstacles to Genotyping
- Blood samples are always chimeric with donor WBCs
- Buccal Swabs better (only 10-20% relative donor chimerism)
- Strongly recommend pre-transplant samples be provided

New York Blood Center · Community Blood Center · IBR INNOVATIVE BLOOD RESOURCES · Rhode Island Blood Center · Blood Bank of Delmarva

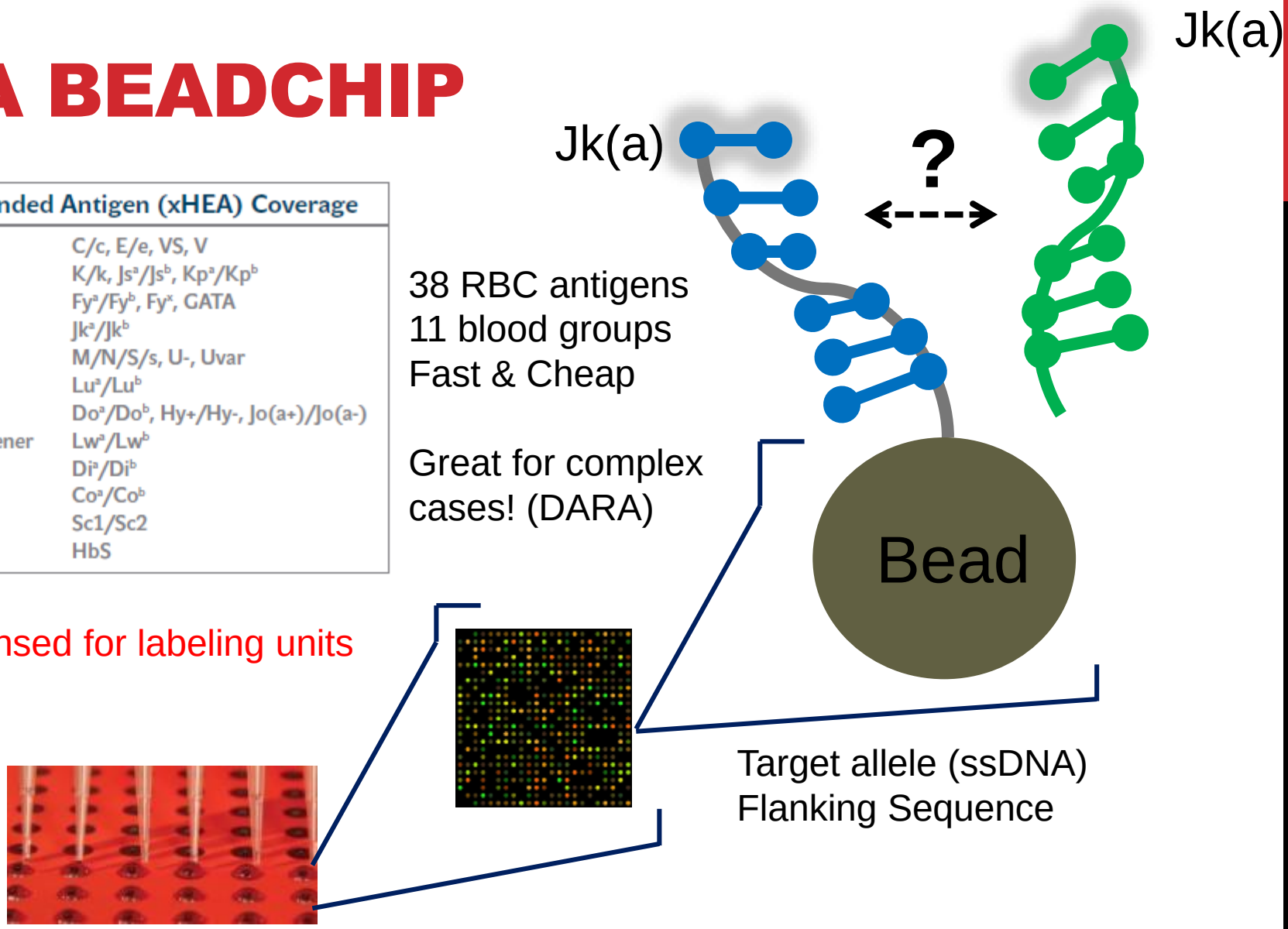
HEA BEADCHIP

Assay Extended Antigen (xHEA) Coverage	
Rh	C/c, E/e, VS, V
Kell	K/k, Js^a/Js^b, Kp^a/Kp^b
Duffy	Fy^a/Fy^b, Fy^x, GATA
Kidd	Jk^a/Jk^b
MNS	M/N/S/s, U-, Uvar
Lutheran	Lu^a/Lu^b
Dombrock	Do^a/Do^b, Hy+/Hy-, Jo(a+)/Jo(a-)
Landsteiner Wiener	Lw^a/Lw^b
Diego	Di^a/Di^b
Colton	Co^a/Co^b
Scianna	Sc1/Sc2
Hemoglobin S	HbS

38 RBC antigens
11 blood groups
Fast & Cheap

Great for complex cases! (DARA)

FDA Licensed for labeling units



New York Blood Center · Community Blood Center · INNOVATIVE BLOOD RESOURCES · Rhode Island Blood Center · Blood Bank of Delmarva

Blood Group	Antigen	Patient (Blood)	Patient (Buccal)	Donor
Rh	c	+	+	+
	C	+	+	+
	e	+	+	+
	E	0	0	0
	V	0	0	0
	VS	0	0	0
Kell	K	0	0	0
	k	+	+	+
	Kp^a	0	0	0
	Kp^b	+	+	+
	Js^a	0	0	0
	Js^b	+	+	+
Duffy	Fy^a	+	+	+
	Fy^b	0	0	0
Kidd	Jk^a	+	+	+
	Jk^b	+	+	0
MNS	M	+	+	+
	N	+	0	+
	S	0	0	0
	s	+	+	+
	U	+	+	+
Lutheran	Lu^a	0	0	0
	Lu^b	+	+	+
Diego	Di^a	0	0	0
	Di^b	+	+	+
Colton	Co^a	+	+	+
	Co^b	0	0	0
Dombrock	Do^a	0	0	0
	Do^b	+	+	+
	Hy	+	+	+
	Jo^a	+	+	+
Landsteiner-Wiener	LW^a	+	+	+
	LW^b	0	0	0
Scianna	Sc1	+	+	+
	Sc2	0	0	0

HEA RESULTS

N antigen mismatch (Patient Buccal/Blood)

-Likely patient natively lacking N antigen

-N(+) in blood suggests chimerism

Patient Jkb(+) in both blood and buccal

-Patient could natively express Jkb, or

-Patient could have chimerism w/ first donor

Most BMT patients do not match this well
-transfusion recommendations?

New York Blood Center

Community Blood Center

IBR INNOVATIVE BLOOD RESOURCES

Rhode Island Blood Center

Blood Bank of Delmarva

TRANSFUSION DECISIONS

- **Facilities need to decide on protocols for these patients**
- **Some options:**
  - Patients with negative screen using DTT treated cells
    - Electronic or immediate spin crossmatch ABO/Rh compatible K-negative units
    - Antigen matched units
  - Patients with known alloantibodies
    - Antigen negative units for known antibody
    - Phenotypically or genotypically matched units
  - IAT crossmatch using DTT-treated donor cells
  - In emergency, uncrossmatched ABO/Rh compatible units

PHENOTYPICALLY MATCHED

- **For our patient:**
  - What are phenotypically matched units?
  - Matched to whom?
    - Patient original type?
    - Bone marrow donor type?
    - Combination of both – what patient and donor are both negative for
- **Physicians decided to match for combination of both**
  - Sent units that were E-negative, K-negative, Fy(b-), S-negative

SURVEY OF IRLS

- **7 IRLs across the country all do:**
  - Obtain genotype/phenotype before anti-CD38 treatment if possible
  - Give antigen negative units for any existing clinically significant alloantibodies
- **1 IRL gives RH and K matched units**
  - Look back on the few patients encountered – no new antibodies
- **1 IRL just provides K-negative units**
  - Avoids antigen matching and saves those units for patients with actual antibodies
- **2 IRLs have not dealt with transplanted patients on anti-CD38**
  - Most hospitals not asking for phenotype matched units

New York Blood Center | Community Blood Center | IBR INNOVATIVE BLOOD RESOURCES | Rhode Island Blood Center | Blood Bank of Delmarva

SURVEY OF IRLS

- **1 IRL assesses level of chimerism post transplant**
  - If 100% donor type then, match the donor's phenotype
  - If immediate post-transplant and 60-day engraftment window???
  - Some patients have marrow re-emerge up to 1 year post transplant
- **1 IRL would match for patient genotype until engrafted at least 50% or better**
  - Then match for donor genotype
- **1 IRL tries to use modified workup protocol and give phenotype matched units**
  - Some facilities just want DTT-treated cell workup and K- units
  - Transplant patients try to get clear genotype and honor that genotype until patient engrafts
    - Buccal swab does not always get clear genotype
  - After engraftment, medical team would try to provide units antigen negative for what both patient and transplant donor are negative for

OBJECTIVES

- List the antibodies that cannot be ruled out using dithiothreitol treated cells or trypsin treated cells.
- Discuss your institution's policy for transfusion of patients receiving anti-CD38 treatment.
- List technical complications encountered when genotyping patients that have received bone marrow transplants.
- Describe technical strategies to genetically determine a patient's predicted phenotype for recipients of bone marrow transplants.
- Discuss best treatment "policy" for patients needing transfusion post bone marrow/stem cell transplant.

New York Blood Center

IBR INNOVATIVE BLOOD RESOURCES

Rhode Island Blood Center

Blood Bank of Delmarva

NATIONAL CENTER FOR BLOOD GROUP GENOMICS