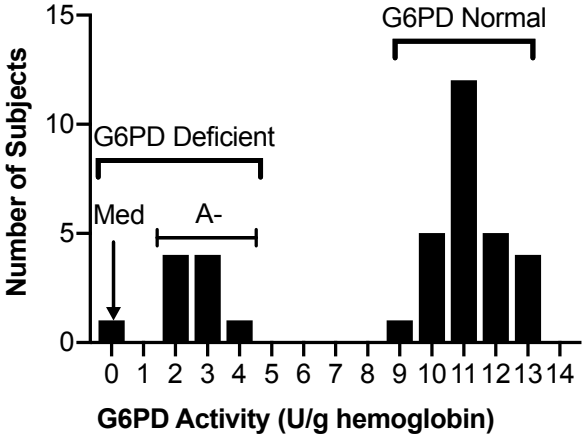
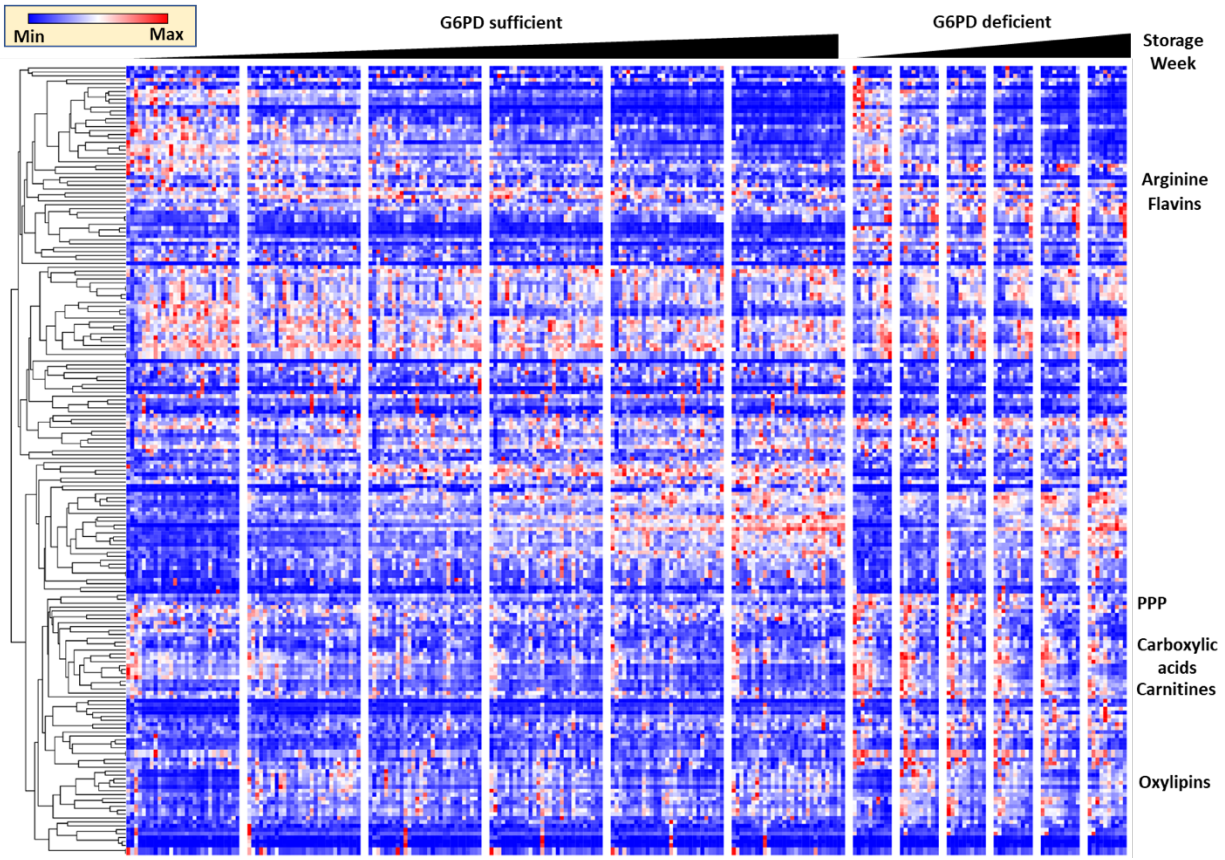
Supplementary Figure 1. G6PD enzyme activity in fresh RBCs of study participants. A histogram of 27 G6PD-normal and 10 G6PD-deficient subjects is shown. One G6PD-deficient subject had the Mediterranean variant and 9 had the A- variant, as labeled.



Supplementary Figure 2. G6PD-deficient RBCs undergo similar metabolic changes as G6PD-normal RBCs with some specific differences. G6PD-deficient RBCs are also characterized by specific changes in arginine and flavin metabolism, the PPP, carboxylates, carnitines, and oxylipins. A vectorial (scalable) version of this figure, including metabolite names, is provided in **Supplementary Figures 3** and **4** for RBCs and supernatants, respectively.



Supplementary Figure 3. G6PD-deficient RBCs undergo similar metabolic changes as G6PD-normal RBCs with some specific differences (RBCs). A vectorial (scalable) version of **Supplementary Figure 2** for RBCs.

Annotation

3 8.5 14

Annotation-1

- week1+
- week1-
- week2+
- week2-
- week3+
- week3-
- week4+
- week4-
- week5+
- week5-
- week6+
- week6-

relative

row min row max

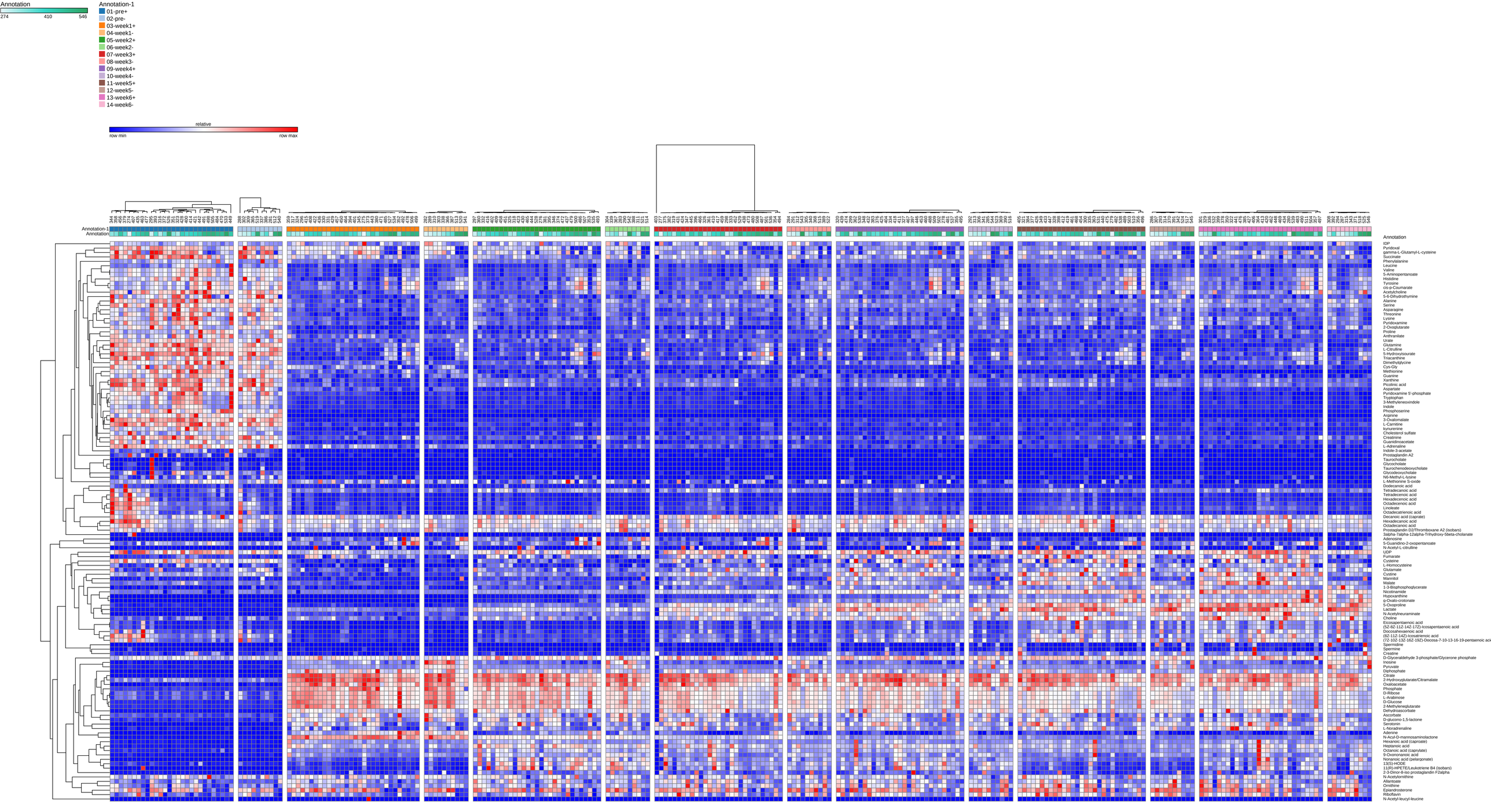
Annotation-1

Annotation

Annotation

IDP
4-Acetamidobutanoate
Ethanolamine phosphate
Asparagine
UDP-N-acetyl-D-glucosamine
GTP
ADP
UDP-glucose
ATP
D-Fructose 1-6-bisphosphate
1-3-Bisphosphoglycerate
2/3-Phospho-D-glycerate
Phosphoenolpyruvate
Methionine
L-Methionine S-oxide
sn-glycero-3-Phosphoethanolamine
CMP-N-acetylneuraminate
Glutathione disulfide
Leucocyanidin
Adenine
Glutamine
5-Hydroxyisourate
3-Oxalomalate
Glycerol 3-phosphate
D-Ribitol 5-phosphate
Glutamate
Phosphoserine
acyl-C6-DC
D-Glyceraldehyde 3-phosphate/Glycerone phosphate
GMP
Octadecanoyl-L-carnitine
Epiandrosterone
S-Adenosyl-L-homocysteine
S-Adenosyl-L-methionine
acyl-C5-OH
Nicotinamide
Alanine
Putrescine
Creatine
Methylenediurea
Ascorbate
Inosine
Pyruvate
6-Pyruvoyltetrahydropterin
Pyridoxal
Biliverdin
propionyl-carnitine
octenoyl-l-carnitine
Spermine
Bilirubin
N-Acetyl-leucyl-leucine
Proline
Serine
Threonine
Tryptophan
Leucine
Valine
5-Aminopentanoate
Tyrosine
cis-p-Coumarate
Urate
3',5'-Cyclic AMP
Glutathione
Cys-Gly
2S-5S-Methionine sulfoximine
Histidine
Lysine
Ornithine
4-Pyridoxate
3-Methylenexindole
Serotonin
Riboflavin
5-Guanidino-2-oxopentanoate
5-Hydroxyindoleacetate
N-Acetylmethionine
Arginine
Aspartate
Dimethylglycine
Anthranilate
N-formyl kynurenine
Peptide tryptophan
N-Acetylornithine
N5-Methyl-L-glutamine
N6-Methyl-L-lysine
L-Citrulline
Indole
Indole-3-acetaldehyde
acyl-C4-OH
3alpha-7alpha-12alpha-Trihydroxy-5beta-cholanate
5-6-Dihydrothymine
Creatinine
Acetylcholine
Guanidinoacetate
O-dodecanoyl-carnitine
tetradecenoyl-Carnitine
O-tetradecanoyl-L-carnitine
Hexadecenoyl-carnitine
acyl-C18:2
Choline
acyl-C4-DC
D-Ribose 5-diphosphate
Adenosine
AMP
Mannitol
S-Glutathionyl-L-cysteine
Guanine
D-Rhamnose
Cysteine
L-Homocysteine
2-Oxoglutaramate
3',5'-Cyclic IMP
Lactate
N-Acetylneuraminate
2-Hydroxyglutarate/Citramalate
L-Noradrenaline
Glycine
UDP
Hypoxanthine
5-Oxoproline
Docosahexaenoic acid
Eicosatetraenoic acid
(8Z-11Z-14Z)-Icosatrienoic acid
(7Z-10Z-13Z-16Z-19Z)-Docosa-7-10-13-16-19-pentaenoic acid
N-Acyl-D-mannosaminolactone
Allantoate
Pyridoxamine
Octadecenoic acid
Linoleate
Octadecatrienoic acid
Eicosapentaenoic acid
(5Z-8Z-11Z-14Z-17Z)-Icosapentaenoic acid
acyl-C18:2-OH
13(S)-HODE
Prostaglandin A2
Leukotriene A4
Fumarate
Malate
trans-4-Hydroxy-L-proline
Uracil
Xanthine
D-Glucose 6-phosphate
D-Glucono-1-5-lactone 6-phosphate
D-Erythrose 4-phosphate
Oxaloacetate
Citrate
Dehydroascorbate
alpha-D-Ribose 1-phosphate
Sedoheptulose 1-phosphate
gamma-Glutamyl-Se-methylselenocysteine
D-Ribose
Phosphate
Diphosphate
Decanoic acid (caprate)
D-Glucose
1-4-beta-D-Xylan
2-Methylenoglutarate
3D-(3-5/4)-Trihydroxycyclohexane-1-2-dione
6-Phospho-D-gluconate
D-gluconо-1,5-lactone
9-Oxononanoic acid
2-Deoxy-alpha-D-glucoside
Taurine
2-Oxoglutarate
O-octadecenoyl-L-carnitine
6-Hydroxykynurenic acid
L-Tryptophanamide
Spermidine
N1-Acetylspermine
L-Adrenaline
L-Carnitine
Carnosine
Succinate
L-octanoylcarnitine
O-Decenoyl-L-carnitine
O-Decanoyl-L-carnitine
acetyl-carnitine
Tiracanthine
butanoyl-l-carnitine
acyl-C5
acyl-C5:1
gamma-L-Glutamylputrescine
11(R)-HPETE/Leukotriene B4 (isobars)
Heptanoic acid
Octanoic acid (caprylate)
Nonanoic acid (pelargonate)
Tetradecanoic acid
Hexanoic acid (caproate)
Tetradecenoic acid
Hexadecenoic acid
Octadecanoic acid
Hexadecanoic acid
Prostaglandin D2/Thromboxane A2 (isobars)
Dodecanoic acid
IMP
N-Carbamyl-L-glutamate
L-Palmitoylcarnitine
Hydroxycholesterol
Glycocholate
Taurocholate
Taurochenodeoxycholate
Glycodeoxycholate
Glycochenodeoxycholate

Supplementary Figure 4. G6PD-deficient RBCs undergo similar metabolic changes as G6PD-normal RBCs with some specific differences (supernatant). A vectorial (scalable) version of **Supplementary Figure 2** for supernatants.


Annotation
274
410
546
Annotation-1
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02-pre-
03-week1+
04-week1-
05-week2+
06-week2-
07-week3+
08-week3-
09-week4+
10-week4-
11-week5+
12-week5-
13-week6+
14-week6-
relative
row min
row max
Annotation-1
Annotation
Annotation
IDP
Pyridoxal
gamma-L-Glutamyl-L-cysteine
Succinate
Phenylalanine
Leucine
Valine
5-Aminopentanoate
Histidine
Tyrosine
cis-p-Coumarate
Acetylcholine
5-6-Dihydrothymine
Alanine
Serine
Asparagine
Threonine
Lysine
Pyridoxamine
2-Oxoglutarate
Proline
Anthranilate
Urate
Glutamine
L-Citrulline
5-Hydroxyisourate
Triacanthine
Dimethylglycine
Cys-Gly
Methionine
Guanine
Xanthine
Picolinic acid
Aspartate
Pyridoxamine 5'-phosphate
Tryptophan
3-Methylenexoindole
Indole
Phosphoserine
Arginine
3-Oxalomalate
L-Carnitine
kynurenine
Cholesterol sulfate
Creatinine
Guanidinoacetate
L-Adrenaline
Indole-3-acetate
Prostaglandin A2
Taurocholate
Glycocholate
Taurochenodeoxycholate
Glycodeoxycholate
N6-Methyl-L-lysine
L-Methionine S-oxide
Dodecanoic acid
Tetradecanoic acid
Tetradecenoic acid
Hexadecenoic acid
Octadecenoic acid
Linoleate
Octadecatrienoic acid
Decanoic acid (caprate)
Hexadecanoic acid
Octadecanoic acid
Prostaglandin D2/Thromboxane A2 (isobars)
3alpha-7alpha-12alpha-Trihydroxy-5beta-cholanate
Adenosine
5-Guanidino-2-oxopentanoate
N-Acetyl-L-citrulline
UDP
Fumarate
Cysteine
L-Homocysteine
Glutamate
Cystine
Mannitol
Malate
1-3-Bisphosphoglycerate
Nicotinamide
Hypoxanthine
g-Oxalo-crotonate
5-Oxoproline
Lactate
N-Acetylneuraminate
Choline
Eicosapentaenoic acid
(5Z-8Z-11Z-14Z-17Z)-Icosapentaenoic acid
Docosahexaenoic acid
(8Z-11Z-14Z)-Icosatrienoic acid
(7Z-10Z-13Z-16Z-19Z)-Docosa-7-10-13-16-19-pentaenoic acid
Spermidine
Spermine
Creatine
D-Glyceraldehyde 3-phosphate/Glycerone phosphate
Inosine
Pyruvate
Diphosphate
Citrate
2-Hydroxyglutarate/Citramalate
Oxaloacetate
Phosphate
D-Ribose
L-Arabinose
D-Glucose
2-Methyleneglutarate
Dehydroascorbate
Ascorbate
D-glucono-1.5-lactone
Serotonin
L-Noradrenaline
Adenine
N-Acyl-O-mannosaminolactone
Hexanoic acid (caproate)
Heptanoic acid
Octanoic acid (caprylate)
9-Oxononanoic acid
Nonanoic acid (pelargonate)
13(S)-HODE
11(R)-HPETE/Leukotriene B4 (isobars)
2-3-Dinor-8-iso prostaglandin F2alpha
N-Acetylornithine
Allantoate
Ornithine
Epiandrosterone
Riboflavin
N-Acetyl-leucyl-leucine

Trial record **1 of 1** for: NCT04081272

Previous Study | Return to List | Next Study

Effect of G6PD Deficiency on Red Blood Cell Storage

ClinicalTrials.gov Identifier: NCT04081272

Recruitment Status : Completed
First Posted : September 9, 2019
Last Update Posted : September 17, 2019

Sponsor:
Columbia University

Collaborator:
New York Blood Center

Information provided by (Responsible Party):
Columbia University

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

Study Description

Go to

Brief Summary:
The proposed study will determine whether G6PD-deficient RBCs store differently than normal RBCs under standard blood banking conditions. The investigators plan to screen a large number of healthy male volunteers for G6PD deficiency in order to identify 10 G6PD deficient and 30 matched normal individuals using a blood sample obtained from a finger-stick. The identified individuals will then be asked to donate a unit of blood that will be stored for up to 42

days and various tests will be performed on these units during storage. At 6 weeks of storage a portion of the unit will be radioactively labeled and re-infused into the volunteer. Blood samples will be drawn before, during, and after the infusion to measure how well or poorly the red blood cells survive after transfusion.

Condition or disease	Intervention/treatment
G6PD Deficiency	Drug: Sodium Chromate Cr51

Detailed Description:
Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme deficiency, affecting approximately 400 million people world-wide. It manifests as red blood cell (RBC) destruction in response to oxidative stress, which can be precipitated by infection, and by the ingestion of certain medications and foods. The prevalence of G6PD deficiency varies among populations and is most commonly found in individuals from sub-Saharan Africa, the Mediterranean region, and south-east Asia. Although in most studies G6PD-deficient individuals have normal RBC survival at steady-state, this may vary based upon the G6PD variant present, and some individuals may have shortened RBC survival. While it is not routine practice to screen blood donors for G6PD deficiency, G6PD deficient donor RBCs may store more poorly than normal RBCs. In addition, the transfusion of stored G6PD-deficient RBCs may result in decreased RBC survival after transfusion compared to RBCs from normal donors.

Study Design

Go to

Study Type :
Observational

Actual Enrollment :
40 participants

Observational Model:
Cohort

Time Perspective:
Prospective

Official Title:
Effect of Glucose-6-phosphate Dehydrogenase Deficiency on Donor Red Blood Cell Storage

Actual Study Start Date :
November 2012

Actual Primary Completion Date :
August 2017

Actual Study Completion Date :
October 2017

Resource links provided by the National Library of Medicine

Genetics Home Reference related topics: Glucose-6-phosphate dehydrogenase deficiency

MedlinePlus related topics: Blood Transfusion and Donation G6PD Deficiency

Drug Information available for: Sodium chromate Cr 51

Genetic and Rare Diseases Information Center resources: Glucose-6-phosphate Dehydrogenase Deficiency

U.S. FDA Resources

Groups and Cohorts

Go to

Group/Cohort	Intervention/treatment
G6PD-normal Donated blood from G6PD-normal subjects	Drug: Sodium Chromate Cr51 Sodium Chromate Cr 51 will be used to perform a red blood cell recovered study 24 hours post-transfusion. Other Name: Chromitope
G6PD-deficient Donated blood from G6PD-deficient subjects	Drug: Sodium Chromate Cr51 Sodium Chromate Cr 51 will be used to perform a red blood cell recovered study 24 hours post-transfusion. Other Name: Chromitope

Outcome Measures

Go to

Primary Outcome Measures :

1. 24-hour post-transfusion red blood cell recovery [Time Frame: 24 hours]

   Percentage of radio-labeled red blood cells remaining 24 hours after infusion

Secondary Outcome Measures :

1. In vitro hemolysis rate [Time Frame: 42 days]

   Percent hemolysis in the red blood cell unit in vitro

Other Outcome Measures:

1. Number of samples with metabolites detected [Time Frame: Pre-donation to 42 days after donation]

   Metabolomics analysis: metabolites that are representative of major metabolic pathways will be measured in the red blood cells or supernatant during storage. Quantitative measurements will be performed using high performance liquid chromatography and mass spectrometry and the data obtained will be analyzed to detect correlations with the primary outcome measure of 24-hour post-transfusion red blood cell recovery.

Biospecimen Retention: Samples With DNA

Blood will be collected to conduct a complete blood count (CBC), testing for the presence of abnormal hemoglobin types (hemoglobinopathy screen), blood type and antibody screen, and confirmation of G6PD deficiency by measuring enzyme activity. In addition, DNA will be extracted and preserved for genetic testing for G6PD deficiency.

Eligibility Criteria

Go to

Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:

18 Years to 70 Years (Adult, Older Adult)

Sexes Eligible for Study:

Male

Accepts Healthy Volunteers:

Yes

Sampling Method:

Non-Probability Sample

Study Population

Healthy male volunteers will be screened for G6PD deficiency in order to identify 10 G6PD deficient and 30 matched normal individuals using a blood sample obtained from a finger-stick.

Criteria

Inclusion Criteria:

- Male
- Weight greater than 110 pounds
- Hemoglobin greater than 11.5 g/dL
- African (e.g., Afro-American, Afro-Caribbean, Sub-Saharan), Asian, Hispanic, Middle Eastern, or Mediterranean (e.g., Italian, Greek) based on mother's ancestry
- English speaking

Exclusion Criteria:

- Presence of hemoglobin variant
- Ineligible for donation based on the New York Blood Center donor autologous questionnaire
- Systolic blood pressure >180 or <90 mm Hg, diastolic blood pressure >100 or <50 mm Hg
- Heart rate <50 or >100
- Temperature >99.5°F prior to donation
- Temperature >100.4°F or subjective feeling of illness prior to transfusion (this criterion is to avoid concurrent illness affecting post-transfusion measurements)
- Positive results on standard blood donor infectious disease testing

Contacts and Locations

Go to

Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT04081272***

Locations

United States, New York

Columbia University Irving Medical Center
New York, New York, United States, 10032

New York Blood Center
New York, New York, United States, 10065

Sponsors and Collaborators

Columbia University

New York Blood Center

Investigators

Principal Investigator: Richard O Francis, MD, PhD Columbia University Irving Medical Center

More Information

Go to

Responsible Party:
Columbia University

ClinicalTrials.gov Identifier:
NCT04081272 History of Changes

Other Study ID Numbers:
AAAJ6862

First Posted:
September 9, 2019 Key Record Dates

Last Update Posted:
September 17, 2019

Last Verified:
September 2019

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD:
Yes

Plan Description:
We will share all individual study data results upon request once the study is published.

Supporting Materials:

Study Protocol

Statistical Analysis Plan (SAP)

Informed Consent Form (ICF)

Clinical Study Report (CSR)

Analytic Code

Time Frame:

upon request once the study is published

Access Criteria:

email study PI to request data

Studies a U.S. FDA-regulated Drug Product:

Yes

Studies a U.S. FDA-regulated Device Product:

No

Product Manufactured in and Exported from the U.S.:

No

Keywords provided by Columbia University:

transfusion

post-transfusion recovery

Additional relevant MeSH terms:

Glucosephosphate Dehydrogenase Deficiency

Anemia, Hemolytic, Congenital

Anemia, Hemolytic

Anemia

Hematologic Diseases

Genetic Diseases, Inborn

Carbohydrate Metabolism, Inborn Errors

Metabolism, Inborn Errors

Metabolic Diseases