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Transfusion-related alloimmunization to red cell antigens among pediatric recipients

Maiko Abe, Hitoshi Ohto, Keiji Minakawa, Kinuyo Kawabata, Satoshi Ono, Nozomi Takano, Hiroe Suzuki, Mao Watanabe, Akiko Sugawara, Masami Kikuchi, Saori Miura, Chikako Takeuchi-Baba, Hiroyasu Yasuda, Kenneth E. Nollet, Yoshiko Tamai, Junichi Kitazawa, Kazuhiko Ikeda

ABSTRACT

Aims: Alloimmune response to red cell transfusion has not been widely investigated in pediatric patients. We retrospectively compared the frequency and specificity of red cell antibody formation among pediatric recipients grouped by age, versus an adult control cohort. Methods: A total of 331 pediatric red cell transfusion recipients were studied in four age groups: 0 to 4.9 months (Group A), 5.0 to 11.9 months (Group B), 1.0 to 5.9 years (Group C), and 6.0 to 14.9 years (Group D). Similarly transfused adult males, 20.0 to 59.9 years old, as a control cohort group. Alloimmunization was defined as post-transfusion detection of red cell alloantibodies not detected prior to transfusion. Results: After red cell transfusion, no one in Group A (0 of 106) developed alloantibodies, whereas 8.0% (2 of 25) in Group B, 1.1% (1 of 95) in Group C, and 2.9% (3 of 105) in Group D, versus 2.1% (8 of 380) of adult male controls who developed alloantibodies. However, these differences did not achieve statistical significance. Conclusion: This investigation of alloimmunization in pediatric recipients found no cases in patients younger than five months old, however, the incidence rates of older age groups were statistically indistinguishable from a control cohort of male adults. Until larger studies suggest otherwise, current antibody screening and cross-matching policies should be continued.

Keywords: Alloantibody, Neonates, Pediatric patients, Red cell transfusion

Maiko Abe[1], Hitoshi Ohto[1], Keiji Minakawa[1], Kinuyo Kawabata[1], Satoshi Ono[1], Nozomi Takano[1], Hiroe Suzuki[1], Mao Watanabe[1], Akiko Sugawara[1], Masami Kikuchi[1], Saori Miura[1], Chikako Takeuchi-Baba[1], Hiroyasu Yasuda[1], Kenneth E. Nollet[1], Yoshiko Tamai[2], Junichi Kitazawa[1,3], Kazuhiko Ikeda[1]

Affiliations: [1]Department of Blood Transfusion and Transplantation Immunology, Fukushima Medical University Hospital, Fukushima, Japan; [2]Division of Blood Transfusion Medicine, Hirosaki University Hospital, Hirosaki, Japan; [3]Department of Clinical Laboratory, Aomori Prefectural Central Hospital, Aomori, Japan.

Corresponding Author: Hitoshi Ohto, MD, PhD, Department of Blood Transfusion and Transplantation Immunology and Department of Advanced Cancer Immunology, Fukushima Medical University, Fukushima City, Fukushima-960-1295, Japan; Email: hit-ohto@fmu.ac.jp

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INTRODUCTION

Red blood cell (RBC) alloantibodies, attributable to allogeneic transfusion and pregnancy, are found in 1.43%

of screened patients in Japan (1.32% of males and 1.52% of females) [1]. In contrast, neonates and infants up to four months old rarely produce RBC-associated antibodies, neither IgM anti-A and anti-B, nor clinically significant IgG antibodies [2–6]. Based on these observations and extensive clinical experience, AABB standards [7] and the British Committee for Standards in Hematology Guideline [8] allow ABO-compatible RBC transfusion without repeated antibody screening/cross-matching if initial antibody screening is negative. Reports of patients under one year old to developing alloantibodies after allogeneic RBC transfusion are few [9–15]. This retrospective cohort study investigated the frequency and the specificity of RBC alloimmunization among various age groups.

MATERIALS AND METHODS

Pediatric and adult study cohorts

Consecutive pediatric patients transfused at Fukushima Medical University Hospital between January 2003 and December 2015 were enrolled into a retrospective cohort study. Patients included all children younger than 15 years old who received at least one bag of allogeneic packed RBCs for transfusion. RBC transfusions for pediatric patients, including neonates, were matched for ABO and RhD. Neonates received compatible RBCs (usually type O) if they had maternal anti-A and/or anti-B. If a pediatric patient received two or three aliquots from a single RBC bag, we counted one donor exposure. Recipients who were only transfused fresh frozen plasma and/or autologous blood were excluded.

Patients with primary immunodeficiency, any autoimmune disease, those taking immunosuppressive drugs and/or intravenous immunoglobulin (IVIG), and recipients of hematopoietic stem cells and/or solid organ transplants were not excluded from the study. Eligible pediatric patients were grouped by age: 0 to 4.9 months (group A, neonates and younger infants who are rarely alloimmunized), 5.0 to 11.9 months (group B, infants 5 months or older), 1.0 to 5.9 years (group C, preschool children), and 6.0 to 14.9 years old (group D, school children). Adult male patients aged 20 to 59.9 years who received allogeneic RBC during the same study period were used as a control cohort. Those receiving only autologous blood were not included.

All allogeneic blood products are came from Japanese Red Cross Fukushima Blood Center. Japanese Red Cross "units" are based on 200 ml of whole blood, although in modern times 400 ml collections are more common. Whether 200 ml or 400 ml, whole blood is collected in acid-citrate-dextrose solution, made into (packed) RBCs, and stored up to 21 days in Mannitol-Adenine-Phosphate additive solution. Per national Japanese policy, allogeneic cellular blood products are irradiated and all allogeneic blood products, including fresh frozen plasma, are leukoreduced during blood center processing [16].

This study secured approval (#2791) from the Ethics committee of Fukushima Medical University, which is guided by local policy, national law, and the World Medical Association Declaration of Helsinki.

Data collection

Data were collected from an institutional transfusion data base (BLAD, Fujitsu, Tokyo, Japan) and patient medical records.

Transfusion testing

RBC alloantibody screening was carried out on patient samples, or, for neonates, maternal samples, using standard physiological saline and polyethylene glycol-indirect antiglobulin test (PEG-IAT) methods [17, 18, 19]. In the physiological saline method, one drop of red blood cell reagent was mixed with two drops (about 100 μL) of patient plasma, and then interpreted after immediate spin (3400 rpm, 15 seconds). PEG-IAT followed by adding 2 drops of an in-house PEG solution to the test tube after physiological saline interpretation, incubating at 37 °C for 15 minutes, and washing by centrifugation four times (Hitachi MC 450, Tokyo, Japan). Then, after adding two drops of anti-human rabbit IgG serum (Ortho Clinical Diagnostics, NJ, USA), it was centrifuged and interpreted. When a test tube showed no reaction, one drop of in-house anti-D-sensitized RBC reagent was added to validate the result.

Surgiscreen and Ortho Diego A (Di^a) reagent red cells were used for screening, and Resolve Panel A and Panel B were used for identification of alloantibody specificity (all Ortho Diagnostic Diagnostics).

Outcomes and statistical analysis

The primary outcome of this study was the frequency of alloimmunization among pediatric recipients after RBC transfusion. A secondary outcome was the specificity of newly developed alloantibodies after transfusion.

Statistical analysis was performed using SPSS Statistics version 24 (IBM Analytics, IBM Japan, Tokyo, Japan) and StatMate IV for Windows version 4.01 (ATMS, Tokyo, Japan). The Mann-Whitney U test was used to compare the number of transfused bags between two groups, the Kruskal-Wallis test was used among multiple groups, and antibody positive rates were assessed by the Chi-squared test with $p < 0.05$ regarded as statistically significant.

RESULTS

Patients

As shown in Figure 1, a total of 771 children (428 male, 343 females) met the inclusion criteria, whereas 438 patients were excluded: 242 for no pre-transfusion

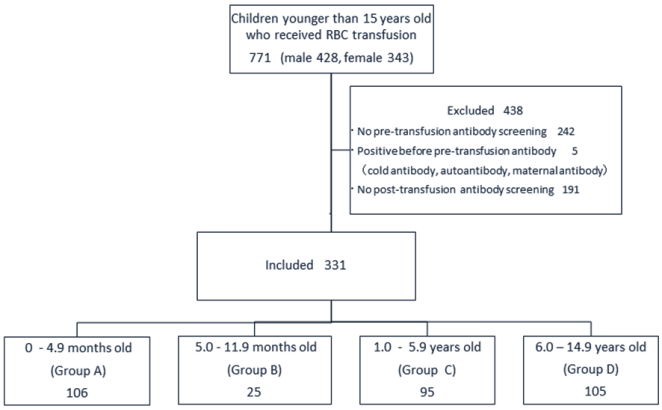

Figure 1: Flowchart of the study.

antibody screening, 5 for positive antibody screening prior to transfusion, and 191 for no post-transfusion antibody screening. Ultimately, 331 were eligible for the study: 106 in group A, 25 in group B, 95 in group C and 105 in group D.

Red cell alloimmunization incidence

Among 331 eligible pediatric recipients, 6 (1.8%, 95% CI: 0.4–3.2%) developed new alloantibodies. Although none of 106 in group A formed alloantibody, 2 of 25 in Group B, 1 of 95 in Group C, 3 of 105 Group D, and 8 of 380 in controls developed new RBC alloantibodies after transfusion. Thus, alloimmunization incidence was 0% [95% CI: 0.0–0.34%] in Group A, 8.0% [95% CI: 0.1–26.0%] in Group B, 1.1% [95% CI: 0.0–5.7%] in Group C, 2.9% [95% CI: 0.3–10.5%] in Group D, 2.1% [95% CI: 0.7–3.5%] among controls (Table 1).

Transfusion characteristics

Among patients under one year old (Groups A and B), transfusion necessitated by congenital disease accounted for 50% or more of cases. On the other hand, from the age of one year and above, blood transfusion was performed more frequently for hematological diseases. The median number of transfused bags was three in Groups A and B, 8 in Group C, and 13 in Group D. Among adult controls, the median was 8 bags. When comparing the number of transfused bags in each group, significant differences (p

Table 1: Number of transfusion recipients and RBC alloimmunization after transfusion

	(Group A) 0.0–4.9 months old	(Group B) 5.0–11.9 months old	(Group C) 1.0–5.9 years old	(Group D) 6.0–14.9 years old	(Control) adult male: 18.0–59.9 years old	p-value
No. of transfused patients	432	61	138	140	1184	
No. of infants screened for antibody (%)	106 (24.5)	25 (41.0)	95 (68.8)	105 (75.0)	380 (32.1)	
No. of antibody positive (%)	0 (0)	2 (8.0)	1 (1.1)	3 (2.9)	8 (2.1)	NS
[95% CI] Diseases (%)	[0.0–3.4%]	[1.0–26.0%]	[0.0–5.7%]	[0.3–10.5%]	[0.7–3.5%]	
Anemia (low-birth-weight)	14 (13.2)	0	0	0	0	
Surgery (congenital disease)	71 (67.0)	14 (56.0)	13 (13.7)	1 (1.0)	Bleeding/anemia 62(26.8)	
Hematologic disease	4 (3.8)	1 (4.0)	46 (48.4)	65 (61.9)	Tumors 49 (21.2)	
Trauma	4 (3.8)	1 (4.0)	1 (1.1)	3 (2.9)	Cardiovascular surg. 39 (16.9)	
Others	13(12.3)	9 (36.0)	35 (36.8)	36 (34.3)	Orthopedic surg. 13 (5.6) Disseminated intravascular coagulation 11 (4.8) Others 57 (24.7)	
Number of transfused bags among eligible recipients Median (range)	3 (1–27)	3 (1–26)	8 (1–66)	13 (1–326)	8 (1–257)	
P-values	vs Group B: p=0.56 vs Group C: p<0.001 vs Group D: p<0.001 vs Control: p<0.001	vs Group C: p<0.001 vs Group D: P<0.001 vs Control: P<0.001	vs Group D: P=0.01 vs Control: P=0.58	vs Control: P<0.01		

<0.001) were found in Group A versus Groups C, D and adult controls, and in Group B versus Groups C, D and adult controls. There were also significant differences (p =0.01) in Group C versus Group D, and Group D versus adult controls. The median number of transfused bags by diagnosis were: 2 for low-birth-weight, three each for congenital disease surgery and trauma, 13 for hematological disease, and seven for other diseases. Most RBC components were used for hematological diseases, and significant differences were observed compared with all other conditions.

Details of antibody-producing cases

Table 2 shows clinical details of patients who formed alloantibody. Among six pediatric patients, five were females and only one was a male. In two patients younger than one year old, anti-Jk^a was detected after latent periods of 49 and 51 days after the first transfusion. The number of latent days until antibody production following the first transfusion ranged from 8 to 51, median of 28.5 days.

The number of transfused bags was 1 to 12, median 3.5.

Two cases of antibody production in age Group B are detailed as follows.

A seven-month-old Japanese girl, type O, RhD (-), Ccee, Jk (a-b+), received cross-matched RBCs since five months of life, totaling 7 aliquots of ~140 mL, derived from 4 bags. Anti-E and anti-Jk^a were detected simultaneously at seven months of age, on the 49th-day after the first transfusion. IVIG was not administered within 5 weeks prior to anti-Jk^a detection. Hemolysis following RBC transfusion was not observed. Thereafter, the patient was transferred to another hospital, and soon passed away without further RBC transfusion [Case 1].

An eight-month-old Japanese boy, type B, RhD (+), Jk (a-b+), received cross-matched RBCs since six months of life, totaling 4 aliquots of ~140 mL, derived from two bags. Anti-Jk^a was identified after the last transfusion with no hemolysis. IVIG was not administered prior to antibody detection. Thereafter, he did not need further RBC transfusion. Phenotyping revealed that the first bag was Jk (a-b+), whereas the second bag was Jk (a+b-), and thereafter deemed to be causative. It took 24 days to detect the antibody after the first exposure to the causative antigen [Case 2].

DISCUSSION

In this study, we found that the overall alloimmunization frequency in pediatric recipients was 1.8% [95% CI: 0.4–3.2%], which was remarkably similar to adult male controls (2.1%, [95% CI: 0.7–3.5%]. As anticipated, the incidence (0%) in Group A (those younger than 5-month-old) was very low compared to older pediatric groups; nevertheless, the differences did not achieve statistically significance. This result is in line with previous reports that no neonates or infants aged four months or less produce RBC-reactive alloantibodies after RBC transfusion [3, 4, 6].

Recently, an interesting German study of 1641 neonates and children up to three years of age reported that only two (0.12%) developed antibodies at ages of 181 and 611 days, which cannot exclude the possibility of “naturally occurring” anti-E and anti-M. The authors

Table 2: Clinical background of pediatric recipients who developed antibody

Case #	Age	Sex	ABO	RhD	Specificity	No. of transfused bags	Disease	Outcome	Days from the first transfusion to antibody detection
1	7-month-old	F	O	−	anti-E+anti-Jk^a	4	Congenital disease, acute encephalopathy, acute hepatitis	Death	49
2	8-month-old	M	B	+	anti-Jk^a	2	Idiopathic dilated cardiomyopathy	Discharge	51
3	2-year-old	F	A	+	anti-M	1	Congenital biliary atresia	Discharge	8
4	9-year-old	F	O	+	anti-E	12	Hemolytic uremic syndrome（HUS	Discharge	19
5	11-year-old	F	A	+	anti-E (+anti-HLA)	3	Aplastic anemia	Discharge	31
6	14-year-old	F	A	+	anti-Jk^a	5	Aplastic anemia	Death	26
						Median 3.5		Median 28.5	

concluded that repeat antibody screening and cross-matching during the first months of life can be safely omitted [20]. Our results include two infants aged seven and eight months who formed clinically significant anti-Jk^a, in contrast to the above work and a previous study in which none of 78 infants up to 11 months old developed antibody [2].

To explain apparent differences in alloantibody production among pediatric recipients between 5.0 and 11.9 months of age, we offer some conjectures. First, genetic background should be considered. We previously observed that none of 52 low-birth-weight Japanese infants who received RBCs - 25 leukoreduced and 27 not, developed anti-HLA at 3 months and 5 to 11 years of age [21]. In contrast, Strauss et al. found that 13% (4/30) of American preterm infants who were multiply transfused with non-leukoreduced RBCs produced white cell antibodies [6]. Moreover, when anti-human leukocyte antigens (HLA) alloimmunization of parous women is compared, a markedly incidence among parous female donors in the USA (31%) is reported [22], compared to 0.6% of Japanese parous blood donors, or 9.4% of Japanese women currently pregnant when tested by classical lymphocyte toxicity test [23]. As the detection sensitivities of the techniques are markedly different, and Japanese are genetically more homogenous [24], we cannot draw any conclusions.

Second, we have used standard tube IAT for antibody screening, whereas the German study used anti-human globulin (AHG)-gel column in 12 of 20 years in their study. The latter is less sensitive in detecting weak but clinically significant antibodies compared to standard tube IAT [19] and solid-phase IAT, especially anti-Jk^a [25, 26] Third, effects of donor exposure numbers between the two studies can be excluded, as the median number of donors are 4 in the German study versus 3 among our Group B cohort of patients between 5.0 to 11.9 months of age. Fourth, emergent antibodies might go undetected as a matter of timing. Using mathematical best-fit line equations, Stack and Tormey estimated that only 31.6% of alloantibodies have been detected, owing to antibody testing that is done too early, too late, or not at all [27].

As the alloantibody response in Group C (ages 1.0 to 5.9 years) and Group D (ages 6.0 to 14.9 years) did not differ from adult male recipients, it remains justified to perform pre-transfusion antibody screening and cross-matching in these ages as are done for adults.

In conclusion, pre-transfusion antibody screening is essential for all infants 5.0 months or older, along with post-transfusion follow up. Moreover, it is reasonable to use maternal blood samples for pre-transfusion testing of infants under 5 months of age. Although this single-center study evaluated every eligible case over 13-year interval, and no patients under 5 months of age developed red cell alloantibodies, statistical power was insufficient to justify curtailing current testing strategies. We anticipate a prospective, multicenter design with large number of recipients will inform future practices.

REFERENCES

1. Takeshita A, Watanabe H, Fijihara H, et al. Collaborative study of irregular erythrocyte antibodies in Japan: Results from the Japanese study group of allo-immunity and antigen diversity in Asian populations. Transfus Apher Sci 2010 Aug;43(1):3–8.
2. Pass MA, Johnson JD, Schulman IA, et al. Evaluation of a walking-donor blood transfusion program in an intensive care nursery. J Pediatr 1976 Oct;89(4):646–51.
3. Floss AM, Strauss RG, Goeken N, Knox L. Multiple transfusion fail to provoke antibodies against blood cell antigens in human infants. Transfusion 1986 Sep-Oct;26(5):419–22.
4. Ludvigsen CW Jr, Swanson JL, Thompson TR, McCullough J. The failure of neonates to form red blood cell alloantibodies in response to multiple transfusions. Am J Clin Pathol 1987 Feb;87(2):250–1.
5. Strauss RG, Cordle DG, Quijana J, Goeken NE. Comparing alloimmunization in preterm infants after transfusion of fresh unmodified versus stored leukocyte-reduced red blood cells. J Pediatr Hematol Oncol 1999 May-Jun;21(3):224–30.
6. Strauss RG, Johnson K, Cress G, Cordle DG. Alloimmunization in preterm infants after repeated transfusions of WBC-reduced RBCs from the same donor. Transfusion 2000 Dec;40(12):1463–8.
7. Standards for blood banks and transfusion services. 30ed. Bethesda, MD: AABB; 2016. [Available at: https://marketplace.aabb.org/ebusiness/Marketplace/Standards-for-Blood-Banks-and-Transfusion-Services-30th-edition---Portal/ProductDetail/12991997]
8. New HV, Berryman J, Bolton-Maggs PH, et al. Guidelines on transfusion for fetuses, neonates and older children. Br J Haematol 2016 Dec;175(5):784–828.
9. Smith MR, Storey CG. Allo-anti-E in an 18-day old-infant. Transfusion 1984 Nov–Dec;24(6):540.
10. Palma L, Criss VR, Roseff SD, Luban NL. Presence of the red cell antibody anti-E in 11-week-old infant. Transfusion 1992 Feb;32(2):177–9.
11. Maniatis A, Theodoris H, Aravani K. et al. Neonatal immune response to red cell antigens. Transfusion 1993 Jan;33(1):90–1.
12. Albiero AL, Novaretti MC, Llacer PE, Chamone DA. Early primary immune response against erythrocytes: A case report. Transfus Med 2003 Apr;13(2):93–7.
13. Tyler LN, Harville TO, Blackall DP. Multiple alloantibodies after transfusion in an infant treated with infliximab. N Engl J Med 2007 Nov 15;357(20):2092–3.
14. Hata JL, Johnson MS, Booth GS. Neonatal alloimmunization: A rare case of multiple alloantibody formation in a patient with disseminated histoplasmosis. Transfusion 2013 May;53(5):1140–1.
15. Kumeta M, Sato H, Osanai T, et al. A case of 7-month-old child with leukemia who produced anti-E antibody after allogeneic red blood cell transfusion. [Article in Japanese]. Jpn J Transfus Med 2016:62;367.
16. Asai T, Inaba S, Ohto H, et al. Guidelines for irradiation of blood and blood components to prevent

post-transfusion graft-vs.-host disease in Japan. Transfus Med 2000 Dec;10(4):315–20.
17. Yamaguchi T, Yasuda H, Sato K, Iwabuchi N, Akama T, Ohto H. Evaluation of the polyethylene glycol-indirect antiglobulin test for routine antibody screening: A prospective study. [Article in Japanese]. Jpn J Transfus Med 1999;45(4):462–5.
18. Okutsu M, Ohto H, Yasuda H, et al. Increased detection of clinically significant antibodies and decreased incidence of delayed haemolytic transfusion reaction with the indirect antiglobulin test potentiated by polyethylene glycol compared to albumin: A Japanese study. Blood Transfus 2011 Jul;9(3):311–9.
19. Ono T, Ohto H, Yasuda H, et al. Comparative study of two automated pre-transfusion testing systems (microplate and gel column methods) with standard tube technique. Int J Blood Transfus Immunohematol 2017;7:15–25.
20. Türkmen T, Qiu D, Cooper N, et al. Red blood cell alloimmunization in neonates and children up to 3 years of age. Transfusion 2017 Nov;57(11):2720–6.
21. De Clippel D, Baeten M, Torfs A, et al. Screening for HLA antibodies in plateletpheresis donors with a history of transfusion or pregnancy. Transfusion 2014 Dec;54(12):3036–42.
22. Ishibashi N, Ohto H, Ujiie N, Ariga H, Ishii T, Suzuki H. Low frequency of observed anti-HLA among transfused preterm infants. Transfusion 2003 May;43(5):663–7.
23. Enomoto T, Maruoka H, Hanagaki S, et al. Pregnancy-induced alloimmunization against platelet antigens: HLA and human platelet antigens (HPA). [Article in Japanese]. Jpn J Transfus Med 2000;46(5):467–73.
24. Ohto H, Yasuda H, Noguchi M, Abe R. Risk of transfusion-associated graft-versus-host disease as a result of directed donations from relatives. Transfusion 1992 Sep;32(7):691–3.
25. Knowles SM, Milkins CE, Chapman JF, Scott M. The United Kingdom national external quality assessment scheme (blood transfusion laboratory practice): Trends in proficiency and practice between 1985 and 2000. Transfus Med 2002 Feb;12(1):11–23.
26. Kay B, Poisson JL, Tuma CW, Shulman IA. Anti-Jk^a that are detected by solid-phase red blood cell adherence but missed by gel testing can cause hemolytic transfusion reactions. Transfusion 2016 Dec;56(12):2973–9.
27. Stack G, Tormey CA. Detection rate of blood group alloimmunization based on real-world testing practices and kinetics of antibody induction and evanescence. Transfusion 2016 Nov;56(11):2662–7.

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Author Contributions

Maiko Abe – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Hitoshi Ohto – Substantial contribution to conception and design, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

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Nozomi Takano – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Hiroe Suzuki – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Mao Watanabe – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Akiko Sugawara – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Masami Kikuchi – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Saori Miura – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Mao Watanabe – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Chikako Takeuchi-Baba – Substantial contribution to acquisition of data, Drafting the article, Final approval of the version to be published

Hiroyasu Yasuda – Substantial contribution to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Kenneth E. Nollet – Substantial contribution to interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Yoshiko Tamai – Substantial contribution to conception and design, Drafting the article, Final approval of the version to be published

Junichi Kitazawa – Substantial contribution to conception and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Kazuhiko Ikeda – Substantial contribution to conception and design, Drafting the article, Final approval of the version to be published

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Authors declare no conflict of interest.

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