CORRECTION

Correction to: A pharmacogenomic study on the pharmacokinetics of tacrolimus in healthy subjects using the DMET™ Plus platform

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The authors identified errors in the published article. Corrections are in **bold**. These corrections do not affect the results, discussion, or conclusions. The authors regret the errors and sincerely apologize to the Journal and readers of the Journal for any inconvenience.

1. There were errors in Tables 1 and 2. Corrections to the tables have been made, as well as their corresponding entries in the INTRODUCTION section. The "Reference allele" and "Mutant allele" columns in Tables 1 and 2 previously contained the information based on the PharmGKB database and PubMed database. But the authors found that the allele information from different databases can cause discrepancies. Therefore, a correction has been made based on the dbSNP database which is the largest public repository for genetic variation to clarify any confusion or misunderstanding. The corrected INTRODUCTION section, Table 1 and 2 appear below.

INTRODUCTION

Although rs776746 **T** > **C** (also known as *CYP3A5*3*), which is a nonfunctioning allele of the *CYP3A5* gene, is associated with decreased tacrolimus metabolism[4], the role of other genes, including the *ABCB1*, *CYP2C19*, *POR*, *UGT1A8*, *NOD2*, and *PPARA*, in the pharmacokinetics of tacrolimus was either inconsistent or insignificant[3].

Table 1. Generic variants associated with tacrolimus AUC_{last} based on the FDR-adjusted multiple testing analysis. The four most significant associations are shown here.

SNP	Gene	Reference allele‡	Mutant allele‡	*P*-value	FDR adjusted *P*-value
rs776746	*CYP3A5*	T	C	0.00001	0.00466
rs2257401	*CYP3A7*	G	C	0.00001	0.00466
rs2242480	*CYP3A4*	**C**	**T**	0.00029	0.06444
rs3814055	*NR1I2*	C	T	0.00073	0.12125

‡ Reference and mutant alleles designated in this study were based on the dbSNP database in National Center for Biotechnology Information (NCBI).
AUC_{last}: area under the concentration curve from time zero to the last quantifiable time point; SNP: single nucleotide polymorphism; FDR: false discovery rate.

Table 2. Genetic variants having a coefficient greater than zero in the LASSO models for tacrolimus AUC_{last} and C_{max}.

	SNP	Gene	Reference allele‡	Mutant allele‡	Coefficient
AUC_{last}	rs4986949	*GSTP1*	**G**	**T***	0.28485
	rs776746	*CYP3A5*	**T**	**C**	0.18146
	rs3814055	*NR1I2*	C	T	0.10679
	rs2257401	*CYP3A7*	G	C	0.05650
	rs16947	*CYP2D6*	**G**	**A***	0.05085
	rs7496	*GSTA4*	C	T	0.03105
	rs1736565	*FMO6P*	C	T	0.02985
	rs2020861	*FMO2*	A	G*	0.02571
	rs6068816	*CYP24A1*	**C**	**T**	0.01274
	rs3803390	*SLC28A1*	C	T*	0.00302
	rs1783811	*SLC22A11*	A	G*	0.00050
	rs1080983	*CYP2D6*	**C**	**T**	0.00008
C_{max}	rs776746	*CYP3A5*	T	C	0.10999
	rs3814055	*NR1I2*	**C**	**T**	0.00039

‡ Reference and mutant alleles designated in this study were based on the dbSNP database in National Center for Biotechnology Information (NCBI).
* Multiple alleles exist.
AUC_{last}, area under the concentration curve from time zero to the last quantifiable time point; C_{max}, maximum **whole-blood** concentration; SNP: single nucleotide polymorphism.

2. There was an error in the SUBJECTS and METHODS section, subsection "Determination of plasma concentrations of tacrolimus", subsection "Pharmacokinetic analysis", where "plasma concentration" should be "whole blood concentration". A correction has been made, as well as their corresponding entries in Figure 1 and the caption on Table 3.

SUBJECTS AND METHODS

Determination of tacrolimus concentrations in whole blood

Whole-blood concentrations of tacrolimus were determined using a previously published LC/MS/MS method[18] with some modifications. The **blood** sample preparation involved a liquid/liquid extraction with methyl tert-butyl ether.

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Pharmacokinetic analysis

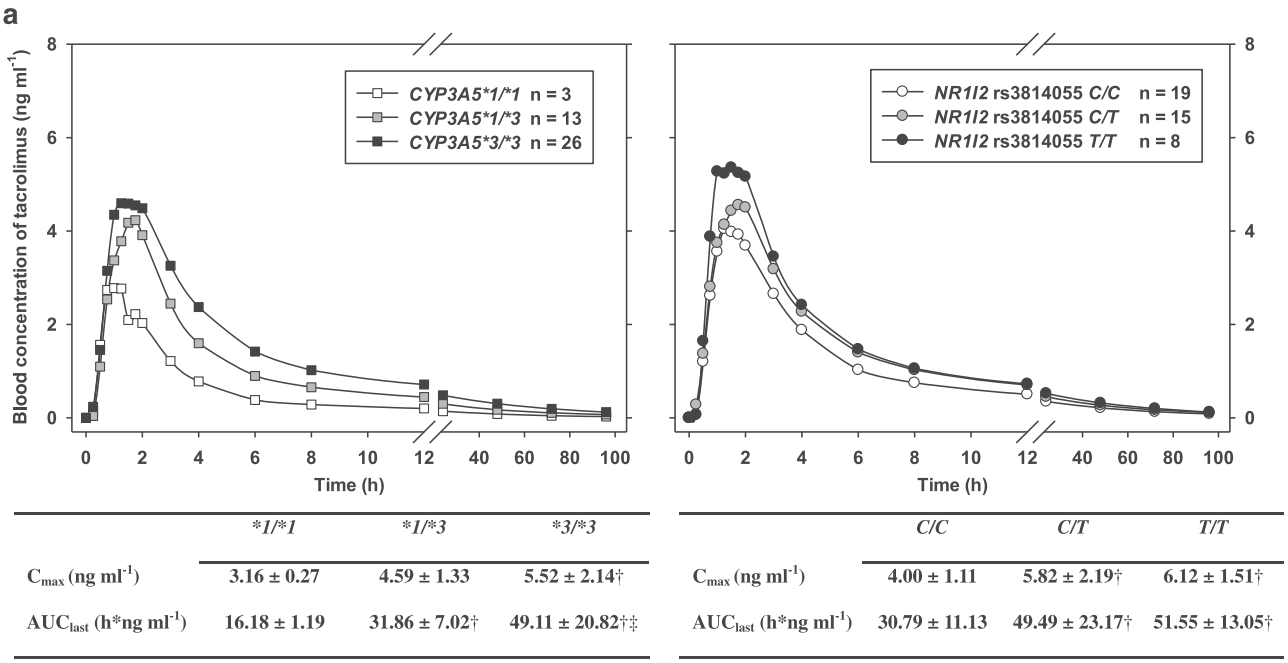
Tacrolimus concentrations from the reference formulation were used for the pharmacokinetic analysis in the present study. The maximum **whole-blood** concentration (C_{max}) of tacrolimus was determined directly from the observed **whole-blood** concentration data.

Figure 1. Mean concentration-time profiles of tacrolimus (**a**) by different *CYP3A5* and *NR1I2* genotypes ($n = 42$) and (**b**) by two different combined *CYP3A5* and *NR1I2* genotypes ($n = 9$) where the genotypes represented the highest (*CYP3A5 *3/*3* and *NR1I2* T/T) and the lowest (*CYP3A5 *1/*1* and *NR1I2* C/C) exposure to tacrolimus. The error bars represent the standard deviations.

Table 3. P-values from a general linear model of the pharmacokinetic parameters for tacrolimus, where the *CYP3A5* (rs776746) and *NR1I2* (rs3814055) genotypes and their interaction term were the independent variables.

	P-value			Adjusted $r^{2\,a}$
	CYP3A5	*NR1I2*	Interaction	
AUC_{last}	<0.01	<0.05	0.16	0.54
C_{max}	0.20	<0.05	0.34	0.24

AUC_{last}, area under the concentration curve from time zero to the last quantifiable timepoint; C_{max}, maximum **whole-blood** concentration.
[a] Proportion of variability that can be explained by the model consisting of the *CYP3A5* and *NR1I2* genotypes.



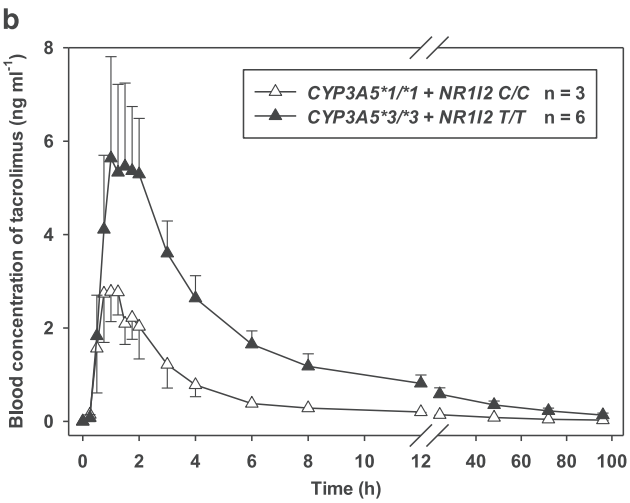
	**1/*1*	**1/*3*	**3/*3*
C_{max} (ng ml^{-1})	3.16 ± 0.27	4.59 ± 1.33	5.52 ± 2.14†
AUC_{last} (h*ng ml^{-1})	16.18 ± 1.19	31.86 ± 7.02†	49.11 ± 20.82†‡

	C/C	*C/T*	*T/T*
C_{max} (ng ml^{-1})	4.00 ± 1.11	5.82 ± 2.19†	6.12 ± 1.51†
AUC_{last} (h*ng ml^{-1})	30.79 ± 11.13	49.43 ± 23.17†	51.55 ± 13.05†

†, $P < 0.05$, compared with the wild-type (*CYP3A5*1/*1* or *rs3814055 C/C*) groups.

‡, $P < 0.05$, compared with the *CYP3A5*1/*3* group.

P values were calculated by Mann-Whitney U test.



3. There was an error in the RESULTS section, subsection "Genetic effects of *CYP3A5* and *NR1I2* on tacrolimus pharmacokinetics", where "*CYP2A5*3/*3*" should be "*CYP3A5*3/*3*".

RESULTS

Genetic effects of *CYP3A5* and *NR1I2* on tacrolimus pharmacokinetics

The greater the number of nonfunctioning **3* alleles in the *CYP3A5* gene, the greater the mean exposure to tacrolimus (Figure 1a). Consequently, the geometric mean AUC_{last} and C_{max} of tacrolimus was 2.78 (95% CI: 1.66–4.66) and 1.64 (95% CI: 1.04–2.60) times greater, respectively, in the ***CYP3A5*3/*3*** homozygote than in the **1/*1* wild-type ($P < 0.05$; Figure 1a).

4. There was a typo in the DISCUSSION section. The corrected sentence appears below.

DISCUSSION

Recently, a clinical trial in 32 kidney transplant patients showed that subjects with the rs3814055 **C/C** genotype had 1.2 and 1.5 times greater clearance of tacrolimus than the rs3814055 T carriers**, C/T and T/T genotypes, respectively,**[27] which supports the findings in our study.