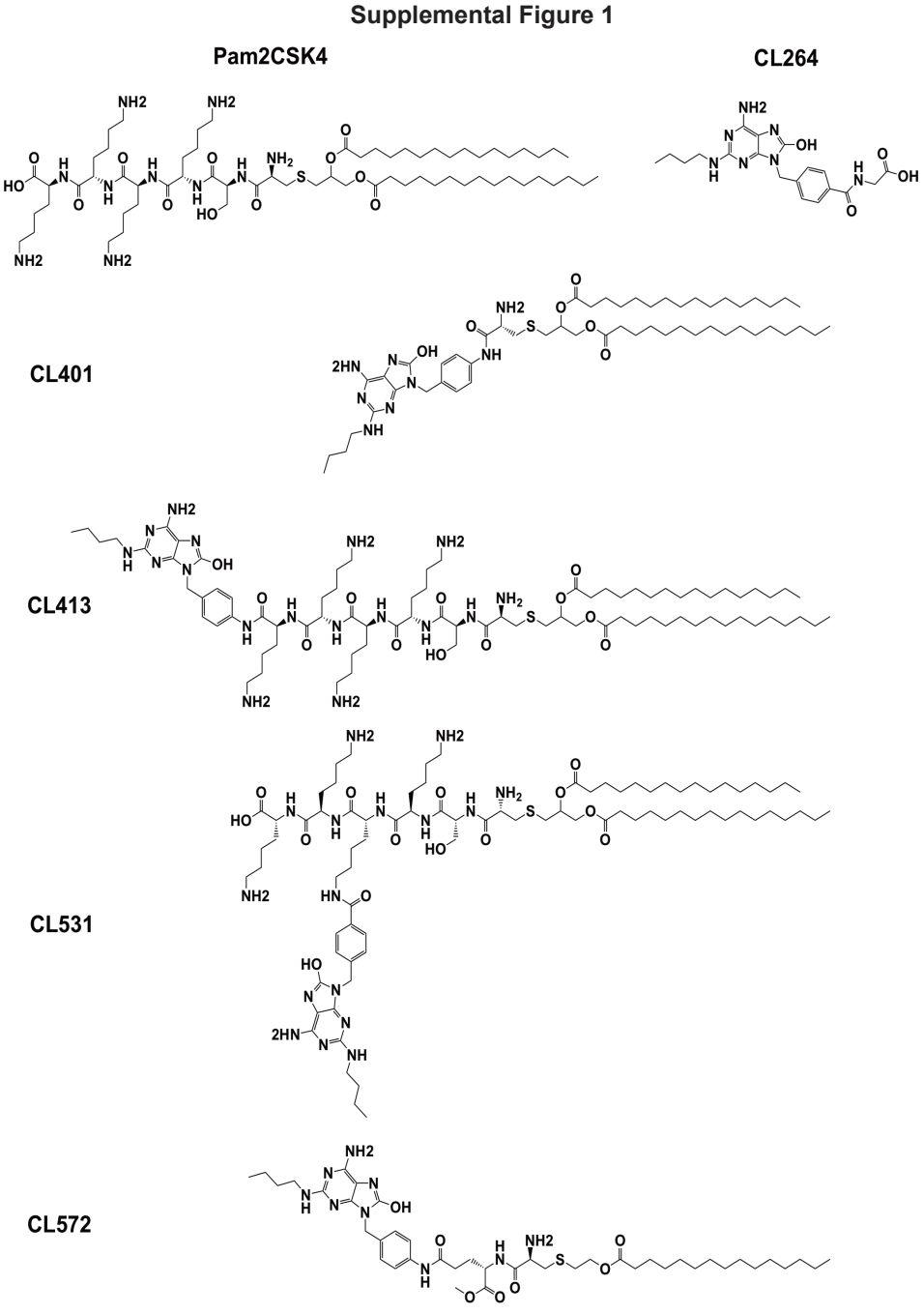
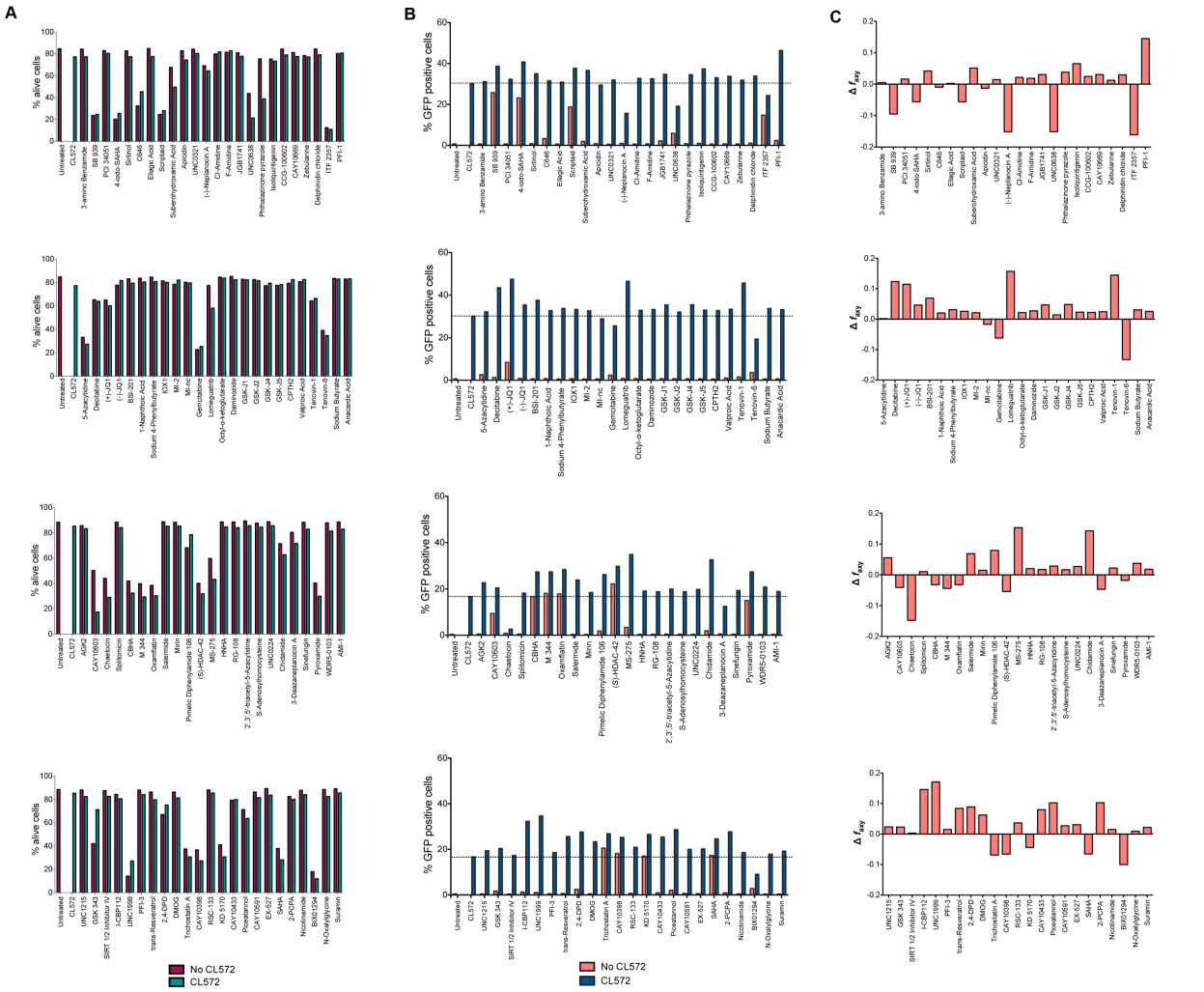


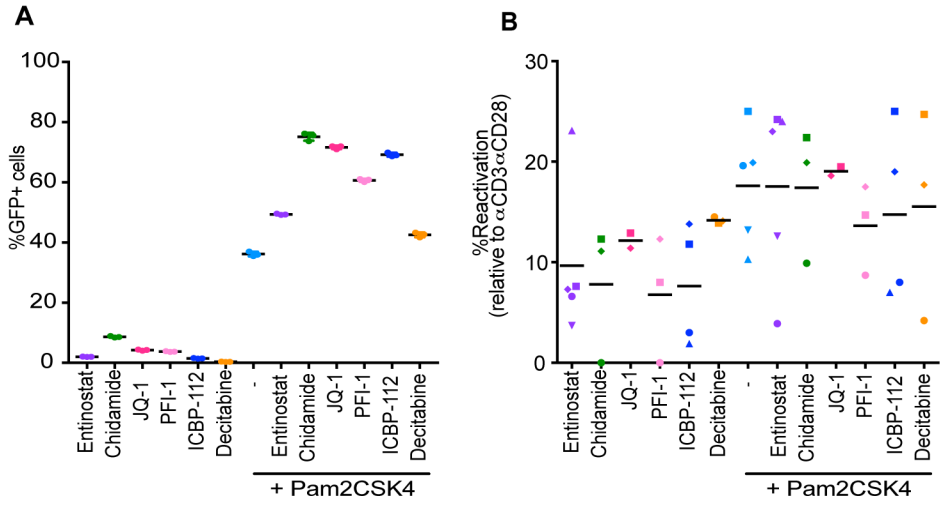
Supplemental Figure 1. Chemical structure of TLR ligands. Chemical structure of Pam2CSK4 (TLR2 agonist), CL264 (TLR7 agonist), and 3 dual TLR2/7 agonists CL413, CL531 and CL572.

Supplemental Figure 2



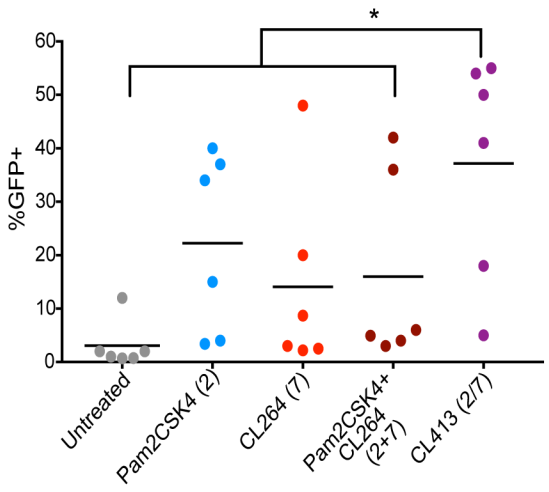
Supplemental Figure 2. Screening of epigenetic modulators in JLAT-TLR2. 94 epigenetic modulators were tested for their ability to reactivate latent HIV in JLAT-TLR2 at 10 μM either alone or in combination with 1 μM of CL572. Cell viability (**A**) and viral reactivation (**B**) were assessed by flow cytometry. (**C**) Synergism between the epigenetic modulator and CL572 was calculated using the Bliss independence model.

Supplemental Figure 3



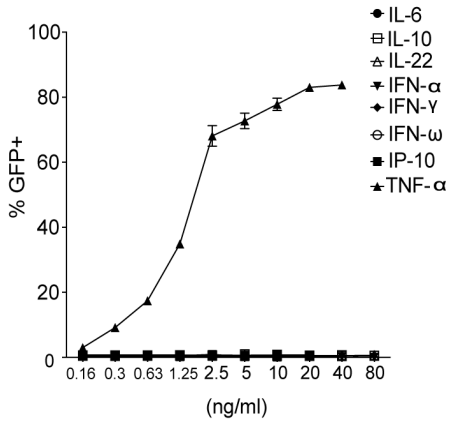
Supplemental Figure 3. HIV reactivation by combination of epigenetic modulators with Pam2CSK4. (**A**) Viral reactivation mediated by 6 epigenetic modulators at 10 μM either alone or in the presence of 1 μM of the TLR2 agonist Pam2CSK4 in JLAT-TLR2. Data is representative of 3 independent experiments using triplicates and horizontal line represent mean. (**B**) Viral reactivation relative to αCD2/αCD28 mediated by 6 epigenetic modulators at 10 μM either alone or in the presence of 1 μM of the TLR2 agonist Pam2CSK4 in the T_{CM} model of latency. Each symbol corresponds to a different donor and horizontal line represent mean.

Supplemental Figure 4



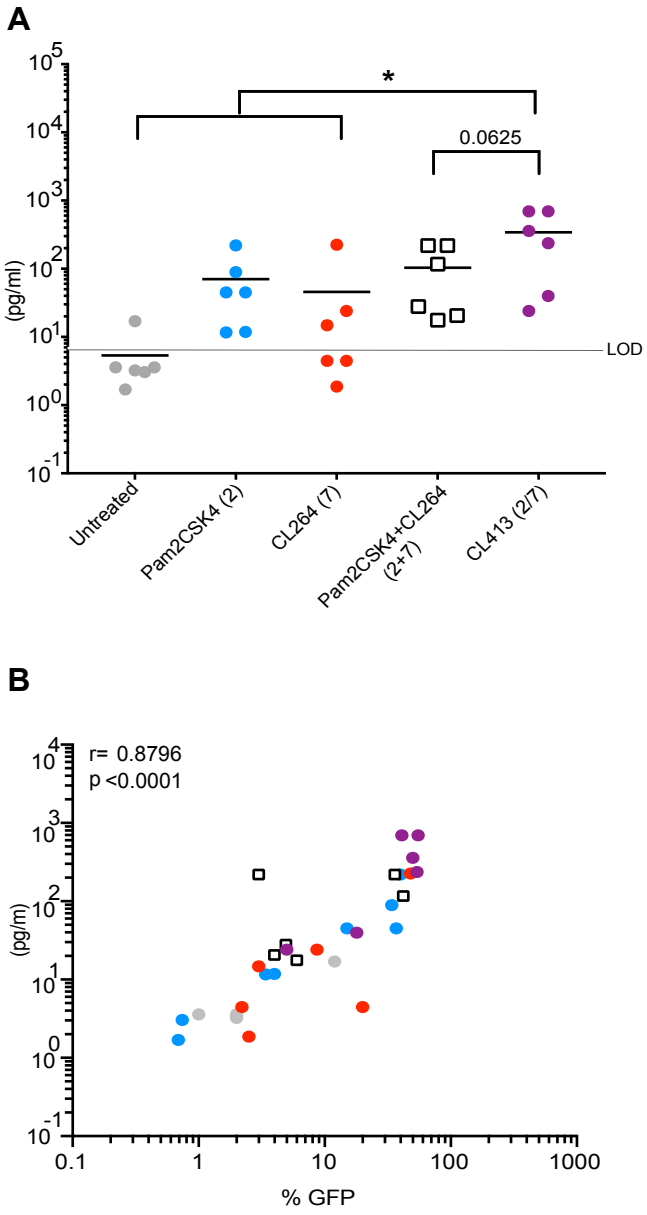
Supplemental Figure 4. Comparison between dual TLR2/7 agonists and simultaneous administration of a TLR2 and a TLR7 agonist. PBMCs were either left untreated or treated with either Pam2CSK4, CL264, a combination of both, or the dual TLR2/7 agonist CL413. Supernatants were tested in their ability to induce viral reactivation in JLAT10.6 (n=6). Horizontal lines indicate media of values. *P < 0.05, by two-tailed Wilcoxon matched-pairs signed-ranks. Each dot corresponds to one donor.

Supplemental Figure 5



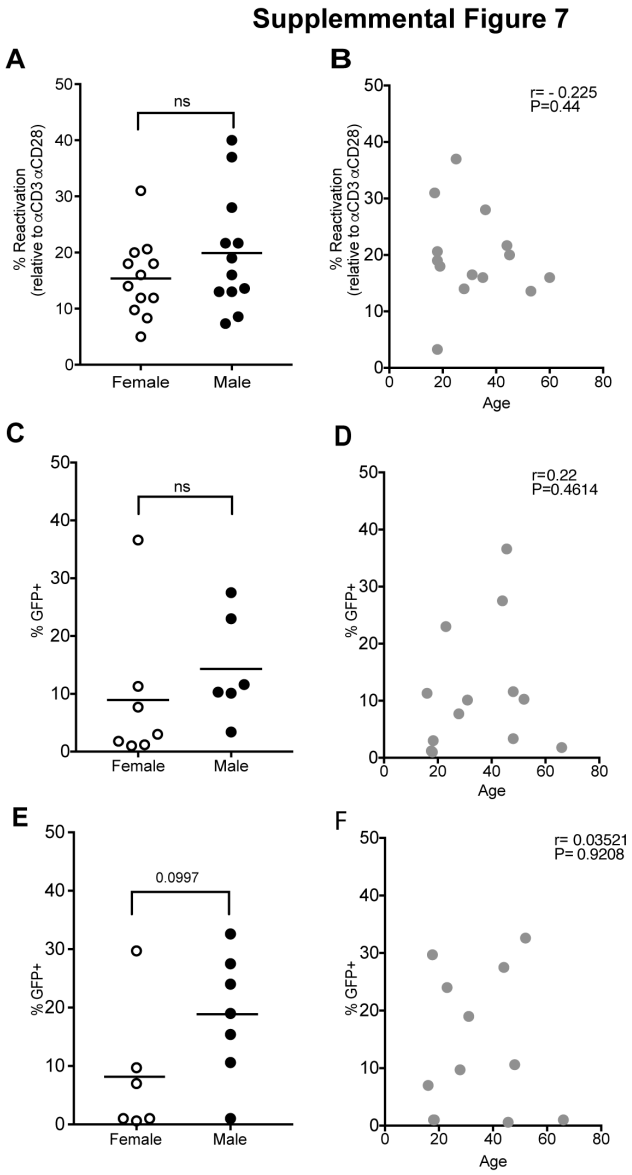
Supplemental Figure 5. Reactivation of latent HIV in the cell line JLAT10.6 by several cytokines. Dose-response of several recombinant cytokines in J-LAT-10.6. Data is representative of 3 independent experiments using triplicates. Values represent mean ± SD.

Supplemental Figure 6



Supplemental Figure 6. Comparison between dual TLR2/7 agonists and simultaneous administration of a TLR2 and a TLR7 agonist in their ability to induce TNF-α. (**A**) PBMCs were either left untreated or treated with either Pam2CSK4, CL264, a combination of both, or the dual TLR2/7 agonist CL413. Supernatants were tested in their ability to induce produce TNF-α (n=6). Horizontal lines indicate media of values. *P

< 0.05, by two-tailed Wilcoxon matched-pairs signed-ranks. Each dot corresponds to one donor **(B)** Spearman correlation between the concentration of TNF-α with the ability of the supernatants to reactivate JLAT10.6.



Supplemental Figure 7. Influence of sex in direct and indirect reactivation of HIV by TLR2 or TLR7 agonists. A. Comparison of the levels of reactivation by Pam2CSK4 in the T_{CM} model between female and male donors (n=12 each group). **B.** Correlation between age and the ability of Pam2CSK4 to reactivate HIV. **C.** Comparison of the ability of supernatants from PBMC stimulated with GS-9620 from female and male donors to reactivate latent HIV in the cell line JLAT10.6 (n=7 each group). **D.** Correlation between

age and the ability of supernatants of GS-9620-treated PBMCs to reactivate latent HIV. **E.** Comparison of the ability of supernatants from PBMC stimulated with CL413 from female and male donors to reactivate latent HIV in the cell line JLAT10.6 (n=7 each group). **F.** Correlation between age and the ability of supernatants of CL413-treated PBMCs to reactivate latent HIV. Mann-Whitney U test was used for comparisons between female and male. Correlations were determined using two-tailed non parametric Spearman correlation coefficient.

Supplemental Tables

Supplemental Table 1. NK cell activation

versus	Pam2CSK4	CL264	GS9620	CL413	CL531	CL572	PMA/ION
Media	***	***	***	***	***	***	***
Pam2CSK4		**	ns	ns	ns	*	ns
CL264			***	**	***	***	**
GS-9620				ns	ns	ns	ns
CL413					*	ns	ns
CL531						***	ns
CL572							ns

Supplemental Table 1. Statistical analysis of the ability of the different TLR agonists to induce NK cell activation. *P < 0.05, **P < 0.01, and ***P < 0.001, by two-tailed Wilcoxon matched-pairs signed-ranks.

Supplemental Table 2. CD4T cell activation

versus	Pam2CSK4	CL264	GS9620	CL413	CL531	CL572	PMA/ION
Media	**	**	***	***	***	***	***
Pam2CSK4		ns	ns	ns	ns	ns	***
CL264			**	***	***	**	***
GS-9620				ns	ns	ns	***
CL413					ns	ns	***
CL531						ns	***
CL572							***

Supplemental Table 2. Statistical analysis of the ability of the different TLR agonists to induce CD4T cell activation. **P < 0.05, **P < 0.01, and ***P < 0.001, by two-tailed Wilcoxon matched-pairs signed-ranks.

Supplemental Table 3. CD8T cell activation

versus	Pam2CSK4	CL264	GS9620	CL413	CL531	CL572	PMA/ION
Media	**	*	***	***	**	***	***
Pam2CSK4		**	**	ns	ns	**	***
CL264			***	**	***	***	***
GS-9620				**	***	ns	***
CL413					ns	**	***
CL531						***	***
CL572							***

Supplemental Table 3. Statistical analysis of the ability of the different TLR agonists to induce CD8T cell activation. *P < 0.05, **P < 0.01, and ***P < 0.001, by two-tailed Wilcoxon matched-pairs signed-ranks.

Supplemental Table 4. IL-6

versus	Pam2CSK4	CL264	GS9620	CL413	CL531	CL572	PMA/ION
Media	**	**	**	**	**	**	**
Pam2CSK4		ns	ns	ns	ns	ns	ns
CL264			ns	**	**	**	ns
GS-9620				**	*	**	*
CL413					ns	ns	ns
CL531						ns	ns
CL572							ns

Supplemental Table 4. Statistical analysis of the ability of the different TLR agonists to induce IL-6 secretion. *P < 0.05, **P < 0.01, and ***P < 0.001, by two-tailed Wilcoxon matched-pairs signed-ranks.

Supplemental Table 5. IL-10

versus	Pam2CSK4	CL264	GS9620	CL413	CL531	CL572	PMA/ION
Media	**	ns	**	**	**	**	**
Pam2CSK4		ns	ns	**	ns	**	ns
CL264			ns	ns	ns	ns	ns
GS-9620				*	**	**	ns
CL413					*	ns	ns
CL531						**	ns
CL572							ns

Supplemental Table 5. Supplemental Table 4. Statistical analysis of the ability of the different TLR agonists to induce IL-10 secretion. *P < 0.05, **P < 0.01, and ***P < 0.001, by two-tailed Wilcoxon matched-pairs signed-ranks.

Supplemental Table 6. IFN-γ

versus	Pam2CSK4	CL264	GS9620	CL413	CL531	CL572	PMA/ION
Media	*	ns	**	**	**	**	**
Pam2CSK4		ns	ns	**	ns	*	**
CL264			*	**	**	**	**
GS-9620				ns	*	**	**
CL413					ns	ns	**
CL531						**	**
CL572							**

Supplemental Table 6. Supplemental Table 4. Statistical analysis of the ability of the different TLR agonists to induce IFN-γ secretion. *P < 0.05, **P < 0.01, and ***P < 0.001, by two-tailed Wilcoxon matched-pairs signed-ranks.

Supplemental Table 7. IL-22

versus	Pam2CSK4	CL264	GS9620	CL413	CL531	CL572	PMA/ION
Media	**	ns	ns	*	**	**	**
Pam2CSK4		*	*	*	**	**	**
CL264			ns	*	**	**	**
GS-9620				*	**	**	**
CL413					**	ns	**
CL531						ns	**
CL572							**

Supplemental Table 7. Statistical analysis of the ability of the different TLR agonists to induce IL-22 secretion. *P < 0.05, **P < 0.01, and ***P < 0.001, by two-tailed Wilcoxon matched-pairs signed-ranks.

Supplemental Table 8. IFN-α

versus	Pam2CSK4	CL264	GS9620	CL413	CL531	CL572	
Media	*	*	***	**	**	***	
Pam2CSK4		ns	ns	ns	ns	*	
CL264			*	ns	ns	*	
GS-9620				*	ns	ns	
CL413					ns	**	
CL531						ns	

Supplemental Table 8. Statistical analysis of the ability of the different TLR agonists to induce IFN-α secretion. *P < 0.05, **P < 0.01, and ***P < 0.001, by two-tailed Wilcoxon matched-pairs signed-ranks.