

Supplementary Table 3. Previous studies of CMV-specific immune monitoring using ELISPOT or Quantiferon-CMV in organ transplant patients to predict cytomegalovirus infection

Study	Population	CMV serostatus	Monitoring frequency	Method, antigen	Findings
Abate et al. (2010) [26]	85 KT recipient 27 Pretransplant	R+ (70/85, 82%) D+/R- (13/85, 15%) D-/R- (2/85, 2%)	Pre-TPL, and 1, 2, 3, 6, 12 months post-TPL	ELISPOT, pp65 peptide pool	Patients with CMV viremia had significantly lower INF- γ expression level in the 2 months prior to the episode than those without viremia ($p < 0.001$).
Chierighin et al. (2010) [38]	10 Bowel/multivisceral TPL recipients	R+ (100%)	Monthly from time of TPL	ELISPOT, pp65, IE1 peptide pool	Early (< 1 month) restoration of the T-cell response tended to be associated with asymptomatic or mild CMV infections with lower viral loads compared with late restoration.
Costa et al. (2011) [39]	24 Lung TPL	R+ (21/24, 81%), D+/R- (1/24, 4%), D-/R- (2/24, 8%)	At 2 time points > 1 year post-TPL	ELISPOT, CMV peptides mix	Responders (ELISPOT > 5 SFU/200,000 cells) had lower CMV viral loads in BAL than non-responders ($p = 0.02$); of 3 patients with high viral loads, 2 responders achieved negative conversion for CMV DNA vs. 1 non-responder who developed CMV pneumonia and died.
Abate et al. (2012) [27]	48 Heart TPL	R+ (100%)	Within 100 or after 100 days post-TPL	ELISPOT, pp65	Early high responders were able to control CMV viremia, and maintained stable high immune levels after 100 days post-TPL; thus, there was an inverse correlation between viremia level and immune recovery.
Patel et al. (2012) [40]	9 Pediatric SOT; 1 Stem cell TPL vs. 8 healthy control, 14 children > 1 year post-TPL	R+ (6/10, 60%) D+/R- (1/10, 10%) D-/R- (3/10, 30%)	1, 3, 6 Months post-TPL	ELISPOT, anti-CD3mAb, CMV pp65	Monitoring of ELISPOT in pediatrics is feasible, and may be useful for predicting risk of CMV disease; very limited numbers.
Bestard et al. (2013) [41]	137 KT	R+ (109, 80%), D+/R- (28, 20%)	Pre-TPL, and 6 months post-TPL	ELISPOT, IE1, pp65 peptide pool	Patients who developed post-TPL CMV infections had lower pre-TPL IE1 specific T-cell responses than those that did not ($p < 0.005$).
Costa et al. (2014) [42]	328 KT	R+ (289, 88%), D+/R- (30, 9%), D-/R- (9, 3%)	201 Monitored in the 1 year post-TPL 127 With a single test at > 1 year	ELISPOT, CMV peptides mix	More responders than non-responders had no episode of CMV infection ($p < 0.005$); the CMV-free period was also longer in responders ($p < 0.001$).
Ritta et al. (2015) [43]	80 KT	R+ (71/80, 89%), D+/R- (7/80, 9%), D-/R- (2/80, 3%)	Pre-TPL	ELISPOT, CMV peptides	Patients exhibiting ≥ 1 episode of CMV viremia at 12 months post-TPL had lower pre-TPL ELISPOT values than those without ($p = 0.08$).

Supplementary Table 3. Continued

Study	Population	CMV serostatus	Monitoring frequency	Method, antigen	Findings
Westall et al. (2008) [33]	39 Lung TPL	R+ (24, 62%), D+/R- (8, 21%), D-/R- (7, 18%)	0.5, 1, 2, 3, 6, 9, 12, and 18 months post-TPL	Quantiferon-CMV	Levels of IFN- γ at one time point did not predict CMV reactivation.
Lochmanova et al. (2010) [34]	14 KT	R+ (12, 86%), D+/R- (2, 14%)	Pre-TPL, and subsequently according to predefined schedule (75–840 days after TPL)	Quantiferon-CMV	Higher IFN- γ responders had a lower risk of CMV infection than lower responders.
Kumar et al. (2009) [29]	108 SOT	R+ (73/108, 68%), D+/R- (35/108, 32%)	Pre-TPL, and 1, 2, 3 months post-TPL	Quantiferon-CMV (cut-off: 0.1 IU/mL)	Patients with detectable IFN- γ at the end of CMV prophylaxis, had a lower CMV disease incidence ($p = 0.038$).
Weselslindtner et al. (2012) [35]	67 Lung TPL	R+ (39, 58%), D+/R- (17, 25%), D-/R- (11, 16%)	For 1 year post-TPL with mean monitoring interval 26 days (range, 2–95)	Quantiferon-CMV	A negative response was associated with higher levels of CMV DNA-emia ($> 1,000$ copies/mL) than a positive response ($p = 0.046$); high-level CMV DNAemia might also be linked to fluctuations in IFN- γ response.
Lisboa et al. (2012) [30]	37 SOT (with low level CMV viremia)	R+ (34/37, 92%), D+/R- (3/37, 8%)	Shortly after the onset of viremia	Quantiferon-CMV (cut-off: 0.2 IU/mL)	Spontaneous viral clearance was more common in patients with positive tests than in those with negative tests ($p = 0.004$); absolute IFN- γ production was higher in patients undergoing spontaneous viral clearance vs. progression.
Cantisan et al. (2013) [36]	23 Lung TPL 32 KT	R+ (44/55, 80%), D+/R- (8/55, 15%), D-/R- (3/55, 5%)	Pre-TPL, and 3 or 6 months post TPL (according to transplanted organ)	Quantiferon-CMV (cut-off: 0.2 IU/mL)	Pre-TPL nonreactive recipients were more likely to experience post-TPL CMV replication than those with pre-TPL reactive assays.
Manuel et al. (2013) [32]	124 SOT	D+/R- (100%)	End of prophylaxis discontinuation, and 1, 2 months later	Quantiferon-CMV (cut-off: 0.1 IU/mL)	Patients with positive results at anytime had a lower cumulative incidence of CMV disease at 12 months than those with negative or indeterminate results ($p < 0.001$).
Abate et al. (2013) [28]	120 KT 39 Healthy control	R+ (100/120, 83%) D+/R- (20/120, 17%)	-	Quantiferon-CMV vs. ELISPOT	The results of the two assays were positively correlated, and negatively correlated with CMV DNAemia; positive assays were associated with protection from CMV infection.

CMV, cytomegalovirus; ELISPOT, enzyme-linked immunospot; KT, kidney transplant; R+, positive recipient CMV immunoglobulin G (IgG); D+, positive donor CMV IgG; R-, negative recipient CMV IgG; D-, negative donor CMV IgG; TPL, transplant; IFN- γ , interferon γ ; IEI, immediate-early; SFU, spot forming unit; BAL, bronchoalveolar lavage; SOT, solid organ transplant of various types.