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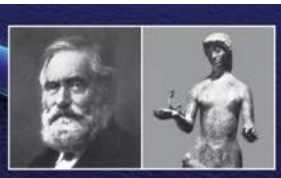

Monitoring the Cytomegalovirus-specific cellular immunity in lung transplant recipients: A comparative analysis of two assay systems

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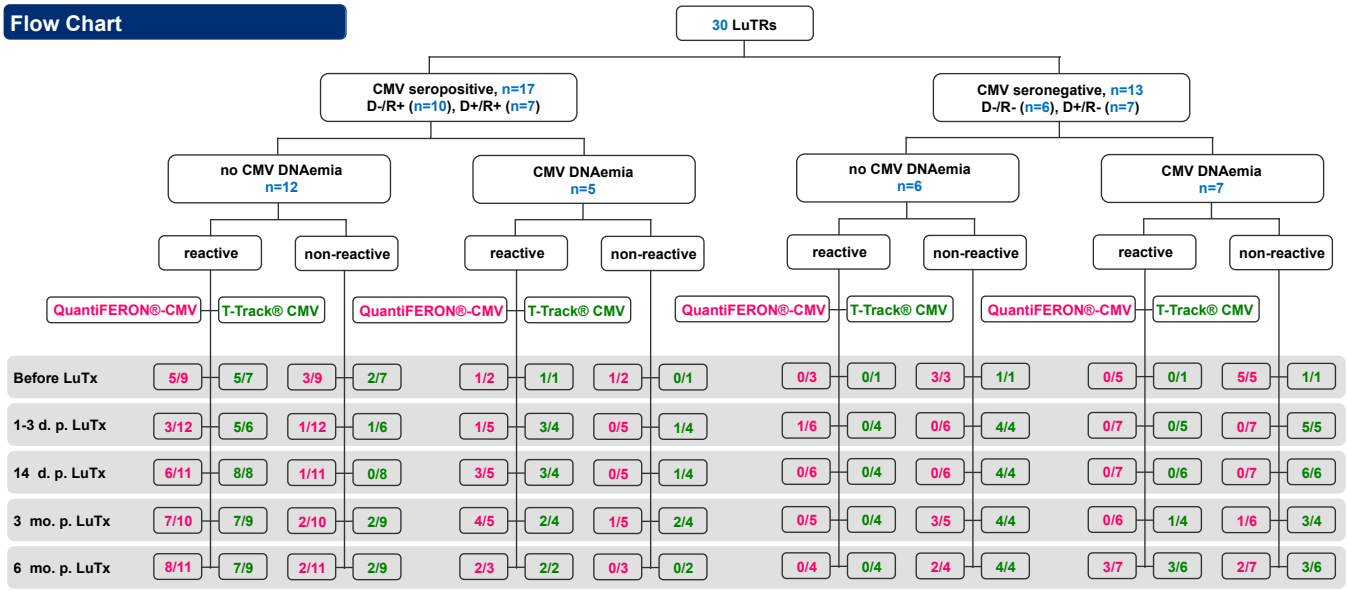
Objective. Monitoring the cellular immunity for Cytomegalovirus (CMV) in organ transplant recipients is a promising tool to support prevention strategies for posttransplant CMV infection or reactivation. Commercially available in vitro test systems differ substantially in their capacity to stimulate subpopulations of T-lymphocytes. We compared two assays for CMV immune monitoring in respect of their clinical practicability and significance.

Methods. Blood samples of 30 lung transplant recipients (LuTRs) were examined before transplantation and over a period of six months afterwards with T-Track® CMV (Lophius Biosciences GmbH, Regensburg) and QuantiFERON®-CMV (Cellestis GmbH, Darmstadt). The T-Track® CMV is based on ELISpot-technology, allowing quantification of interferon-gamma (IFNγ) secreting CD4+ and CD8+ T-cells after specific stimulation. Contrarily, the QuantiFERON®-CMV assay is restricted to detection of IFNγ secreted by CD8+ T-lymphocytes with ELISA. The data are evaluated in the context of transplant outcome and determination of viral load in plasma by qPCR.

Results and Conclusion. Both approaches provide similar results while exhibiting certain advantages and limitations. Early during immune suppressive therapy, QuantiFERON®-CMV generates often indeterminate results as depletion of T-cells is not taken into account. Although a comparatively large volume of blood is required, T-Track® CMV circumvents this drawback. In addition, T-Track® CMV reaches a higher sensitivity prior to LuTx and shortly after onset of immunosuppression.

Flow Chart



Flow chart describing 30 lung transplant recipients (LuTRs) with respect to CMV serostatus prior to transplantation (LuTx), the occurrence of CMV DNAemia during follow-up of 6 months post LuTx (>150 copies/mL blood plasma) and the respective results of CMV immune monitoring kits **QuantiFERON®-CMV** and **T-Track® CMV** performed before LuTx and at four timepoints during follow-up. The sample size of both tests can vary due to handling restrictions of T-Track® CMV, while QuantiFERON®-CMV often delivers indeterminate results especially early during immune suppressive therapy.

Statistical Characteristics

A. Patient Characteristics (N=30)

Age, median (range)	48 (23-64)
Sex, n (%)	
Female	10 (33.3)
Male	20 (66.6)

B. Sensitivity and Specificity

Test results before LuTx in relation to CMV serostatus

	Sensitivity	Specificity
T-Track® CMV (n=10)	75 %	100 %
QuantiFERON®-CMV (n=18)	60 %	100 %

C. Concordance of both assay results at final timepoint

D-/R-	D+/R-	R+
2/4 (50 %)	5/6 (83.3 %)	9/11 (81.8 %)

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Conclusions

- Both commercially available kits for monitoring the cellular CMV immunity deliver similar results to our in-house quantification of CMV-specific T-cells via intracellular cytokine staining, although there are some individual differences in the capacity of T-cell stimulation
- **T-Track® CMV**
  - \+ Input of a constant amount of cells compensates for negative effect of immune suppressive therapy
  - \+ T-Track® CMV shows higher sensitivity before LuTx (75%) compared to QuantiFERON®-CMV (60%)
  - \- Sample processing protocol requires a tight organization plan between attending physician and diagnostic laboratory; 15 mL blood volume needed
- **QuantiFERON®-CMV**
  - \+ Low blood volume (3 mL); stimulation protocol and ELISA read-out easily integrable into diagnostics routine
  - \- Often indeterminate results until 3 - 6 months after induction of immune suppressive therapy due to fixed blood volume
- In retrospective, monitoring the cellular CMV immunity in addition to surveillance of viral load in plasma could affect the decision about antiviral therapy, especially for patients at medium risk of CMV infection (R+)