positive NK cells that expand independent of the MHC haplotype (see figure). Barao and colleagues next investigated whether the emergence of Ly49G2 single-positive NK cells would occur in the context of host stress induced through inflammatory cytokines and/or infection. Consistent with results observed in recipients of HSCT, treatment with IL-2 or infection with *Listeria monocytogenes* induced a significant expansion of Ly49G2 single-positive NK cells. Taken altogether, these data suggest Ly49G2 single-positive NK cells represent a first responder NK-cell population that does not require licensing to mediate innate immunity against infection or cytotoxicity against tumors.

Several studies have investigated the acquisition of Ly49 receptors during NK-cell development. Two principal models (2-step and sequential) are used to describe how NK-cell receptor repertoires are shaped by interactions with cognate MHC class I molecules.  


**REFERENCES**


**LYMPHOID NEOPLASIA**

Comment on Pancaldi et al, page 7099

**Opening new roads for MCPyV**

**Axel zur Hausen**  
**MAASTRICHT UNIVERSITY MEDICAL CENTER**

In this issue of *Blood*, Pancaldi et al report on the latent presence of large T antigen (L.Tag) sequences of the Merkel cell polyomavirus (MCPyV) in buffy coats of healthy individuals.  

The recent discovery of MCPyV, which has been shown to be monoclonally integrated in Merkel cell carcinomas (MCCs), has contributed to a major degree to the understanding of the etiopathogenesis of MCC. The presence of MCPyV in approximately 80% of MCCs and
the identification of tumor-specific truncating mutations within the LTag closely link MCPyV to the etiopathogenesis of MCC and identified MCPyV as a new human tumor virus.3

MCC patients are known to be at a significantly increased risk to develop chronic lymphocytic leukemia (CLL), which is the most common leukemia of adults in the Western world.3 In addition, it has been shown that CLL patients have a high risk to develop MCPyV positive MCCs.4 The detection of MCPyV in 22% of the buffy coats of healthy, thus immunocompetent, individuals reported by Pancaldi and colleagues suggests that MCPyV infects specific blood leukocyte cells in which it remains in latency. These data could provide evidence for a multistep transformation model that might be initiated by accumulating mutations of MCPyV in the context of progressive loss of immune surveillance.

This would also explain the low viral load of MCPyV as reported by Pancaldi et al and is also reflected by their technical approach of PCR reamplifications. Indeed it is remarkable that the prevalence of MCPyV sequences in the buffy coats of healthy individuals is almost identical to the recently independently reported prevalence of MCPyV in CLL ranging between 21% and 33%.5-7 Although initial studies could not link MCPyV to CLL, the presence of MCPyV in CLL cells has now been confirmed by FISH and in some MCPyV-positive CLL cases deletion mutants of the LTag have been found.5,8,9

Pancaldi and colleagues did not identify the specific leukocyte cell within the buffy coat that is infected by MCPyV. However, their data potentially close one gap of a multistep cascade between the presence of MCPyV in the buffy coats of immunocompetent individuals and a role for MCPyV in the etiopathogenesis in a significant subset of CLL. Furthermore, their data could possibly provide the basis to open new roads to broaden the spectrum of MCPyV-associated hematologic neoplasias. Because buffy coats contain a mixture of cells and it has already been shown that MCPyV is able to infect monocytic cells, it is very likely that there might be a role for MCPyV in other hematologic neoplasias.10 These days by far the most promising hematologic neoplasias to investigate for a role of MCPyV in their etiopathogenesis are myeloproliferative neoplasias such as essential thrombocythemia, polycythemia vera, and primary myelofibrosis.

Conflict-of-interest disclosure: The author declares no competing financial interests.

REFERENCES

Opening new roads for MCPyV

Axel zur Hausen