VIRAL IMMUNOBIOLOGY

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SUMMARY & MISSION STATEMENT

We try to understand the comprehensive immune control against the human oncogenic γ-herpesviruses EBV and KSHV. We aim to re-install this immune control in patients with the respective virus-associated malignancies by vaccination and to harness the components of this immune control against other tumors.

OVERVIEW

The human oncogenic γ-herpesviruses EBV and KSHV are each associated with around 1-2% of all tumors in patients. Their seroprevalence in the adult human population is, however, much higher with close to 100% for EBV worldwide and more than 50% for KSHV in regions of Subsaharan Africa. The tumorigenicity of these oncogenic viruses is immune controlled in most persistently infected individuals for life, constituting paradigms of comprehensive cell-mediated immune control of cancer cells.

We have characterized protective antigens of EBV that are now widely used in the currently tested vaccine candidates, implicated autophagy in the processing of these antigens for MHC presentation and established *in vivo* infection models for these two exclusively human lymphotropic viruses that recapitulate key features of tumor formation and immune control.

Our future studies aim to refine our understanding of the molecular mechanisms that ensure near perfect immune control of EBV and KSHV in most infected individuals, which of these components fail, when virus associated malignancies emerge and how comprehensive immune control could be re-installed in the respective cancer patients by vaccination. We aim to apply the lessons from these studies to immunotherapies of other human cancers.

SELECTED CANCER RELATED PUBLICATIONS

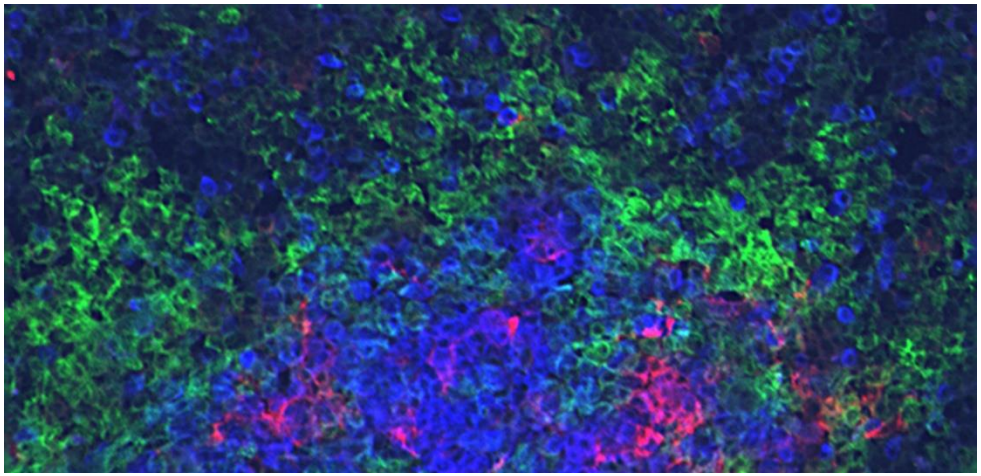
Human dendritic cells activate resting NK cells and are recognized via the NKp30 receptor by activated NK cells. Ferlazzo G, Tsang ML, Moretta L, Melioli G, Steinman RM, Münz C. **J Exp Med.** 2002 Feb;195(3):343-51.

Endogenous MHC class II processing of a viral nuclear antigen after autophagy. Paludan C, Schmid D, Landthaler M, Vockerodt M, Kube D, Tuschl T, Münz C. **Science.** 2005 Jan;307(5709):593-6.

Priming of protective T cell responses against virus-induced tumors in mice with human immune system components. Strowig T, Gurer C, Ploss A, Liu YF, Arrey F, Sashihara J, Koo G, Rice CM, Young JW, Chadburn A, Cohen JI, Münz C. **J Exp Med.** 2009 Jun;206(6):1423-34.

Natural killer cells prevent infectious mononucleosis features. Chijioke O, Müller A, Feederle R, … Moretta A, Hassan R, Boyman O, Niedobitek G, Delecluse HJ, Capaul R, Münz C. **Cell Rep.** 2013 Dec;5(6):1489-98.

Persistent KSHV infection increases EBV-associated tumor formation in vivo via enhanced EBV lytic gene expression. McHugh D, Caduff N, Barros MHM, … White RE, Allday M, Niedobitek G, Blackbourn D, Grundhoff A, Münz C. **Cell Host Microbe.** 2017 Jul;22(1):61-73.



Splenic white pulp area of a mouse with reconstituted human immune system components. Human B cells are stained for CD20 in green, human T cells for CD3 in blue and human dendritic cells (DCs) for DEC-205 in red (Meixlsperger et al., Blood 2013).