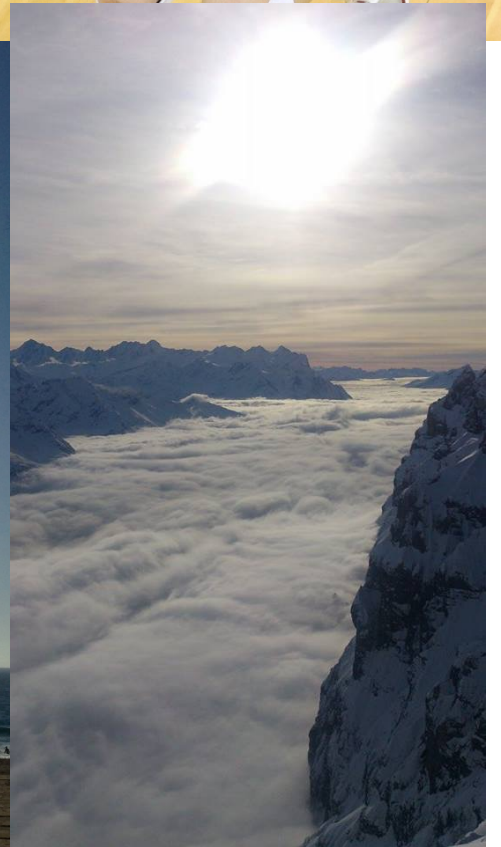


# Protective Immune Responses during Epstein Barr Virus (EBV) Infection

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# What is Epstein Barr Virus (EBV)?

- EBV is a “common human  $\gamma$ -herpesvirus that persistently infects more than 90% of the human adult population.”<sup>1</sup>
- Individuals, who are infected with the virus early in life, acquire and carry the virus usually without symptoms; however, 20-30% of Europeans and North Americans are infected later during adolescence and a high proportion of these will experience symptoms during primary infection.<sup>1</sup>



# Infectious Mononucleosis (IM)

- EBV is the virus that causes IM, which is often referred to as “The Kissing Disease”, because it is transferred through saliva.
- The reason why some acquire EBV with IM at increased age is still unclear, but it is thought that inefficient innate immune control might allow the virus to replicate to a higher level.<sup>1</sup>





Main symptoms of

# Infectious mononucleosis

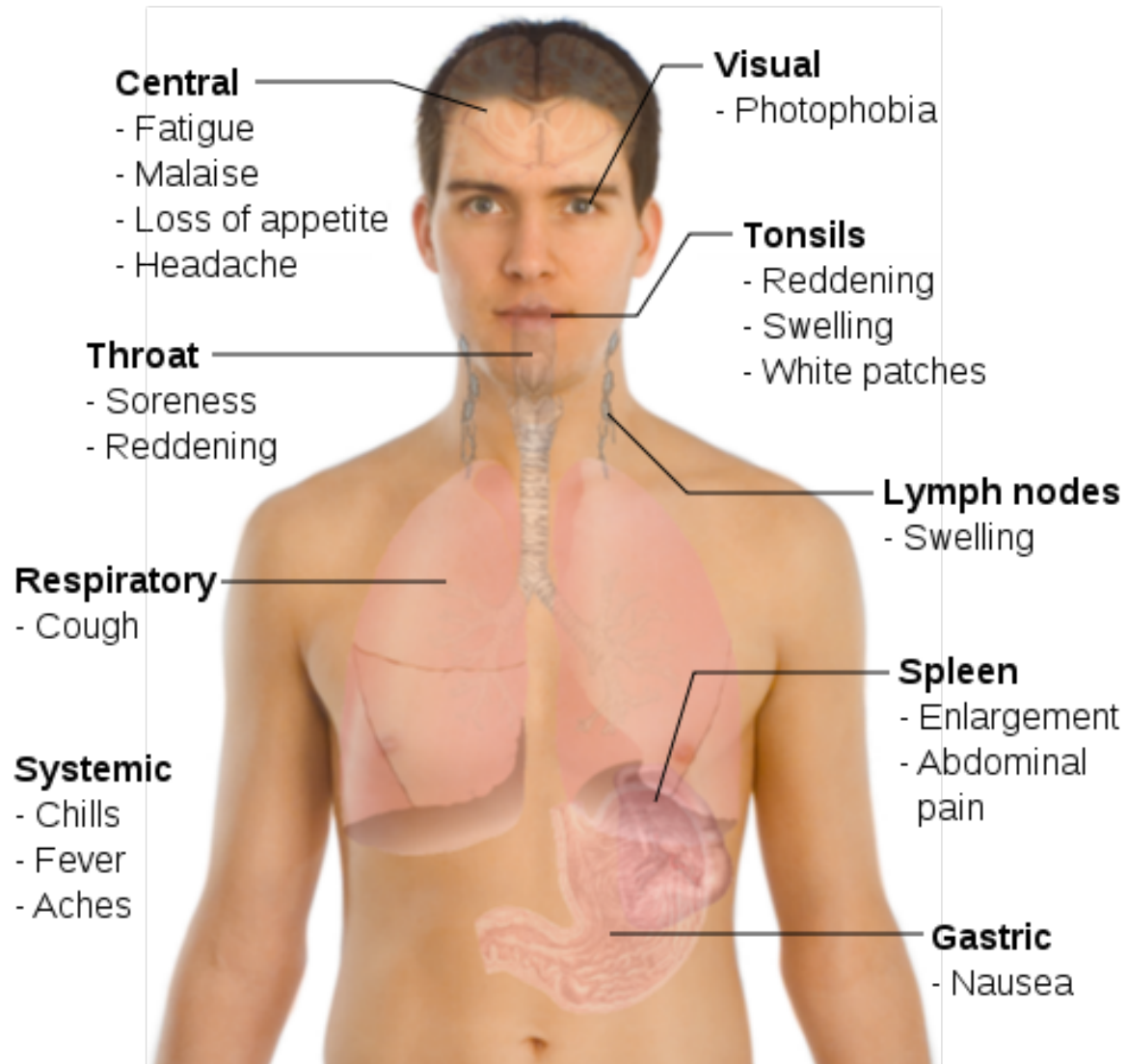


Image from "Epstein-Barr Virus: Infectious Mononucleosis."

# Natural Killer (NK) Cells

- NK cells are lymphocytes that were originally discovered for their spontaneous cytolytic potential against tumor cells.<sup>1</sup>
- As part of the innate immune system, NK cell recognize altered components of the infected or transformed cell surface that indicate cellular stress like DNA damage or an unfolded protein response.<sup>1</sup>
- “They are antibody-independent killers of tumor cells and also can participate in antibody-dependent cell-mediated cytotoxicity.”<sup>3</sup>



# Natural Killer (NK Cells)

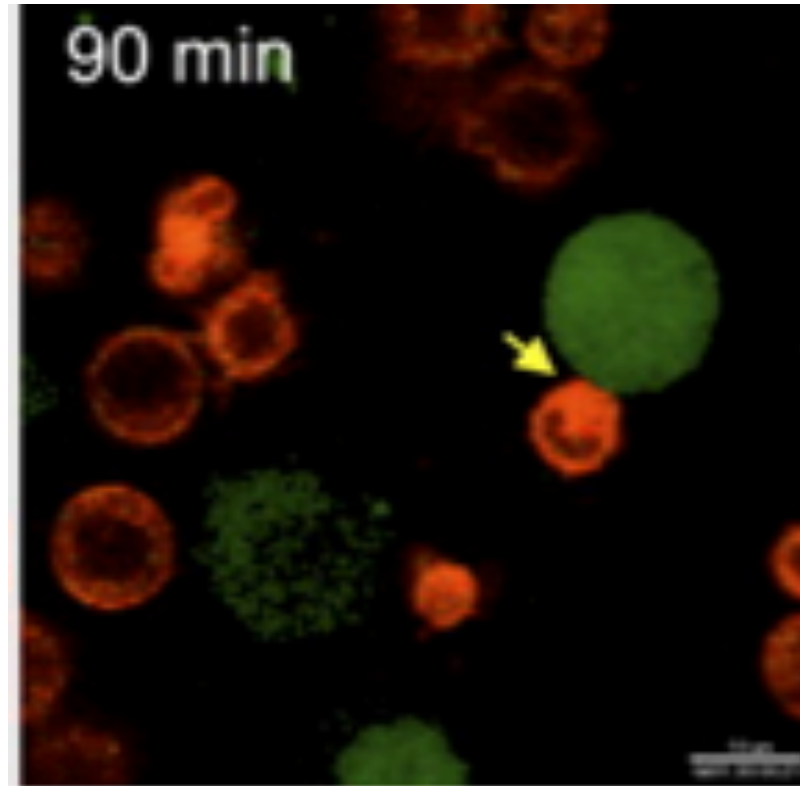


Image from Silva, et al., *Blood* (2011)

# The immune response to primary EBV infection: a role for natural killer cells

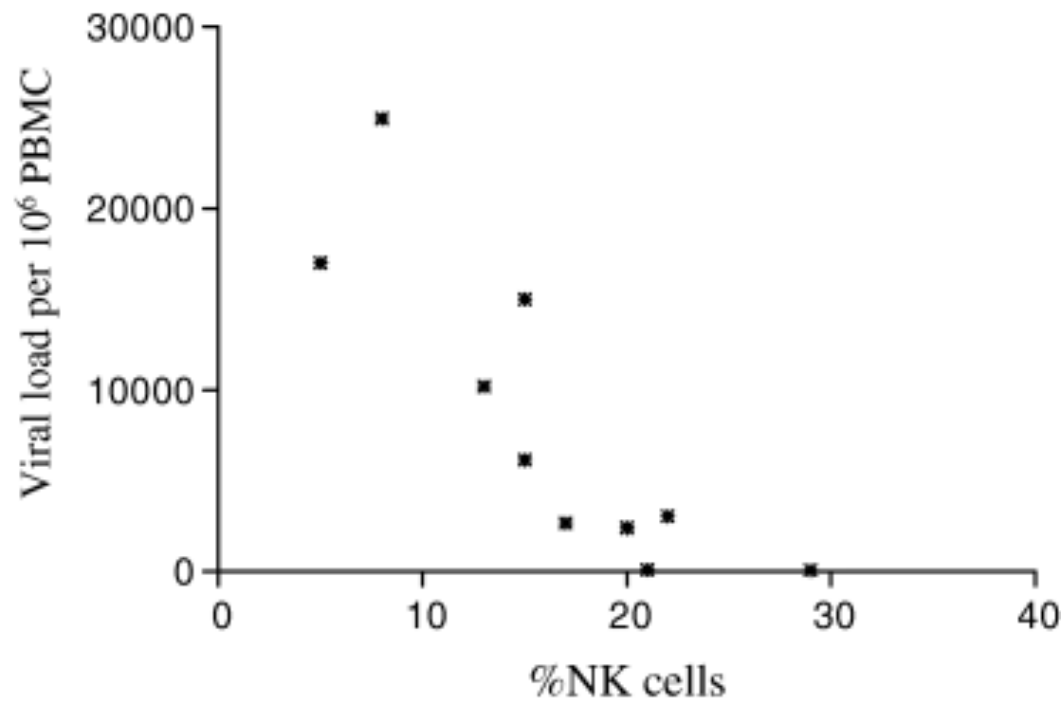


Image from Williams, *British Journal of Haematology* (2005).



# Methodology of the Experiments

- Human Natural Killer cell lines NKL, NK-92, and Nishi will be exposed to EBV-infected cells.
- Using antibodies and a confocal microscope, “SP5,” the synapse between the cells will be imaged to view the interaction between the cells and the recruited receptors and their ligands.



# Aim of the Experiments

- One receptor has been identified in the specific EBV protective NK cell subset (CD94/NKG2A).
- Through imaging, I will identify other receptors and ligands that are recruited to the interaction between NK cells and EBV infected cells.
- NK receptor candidates: NKG2D and DNAM-1.



# Expected Results

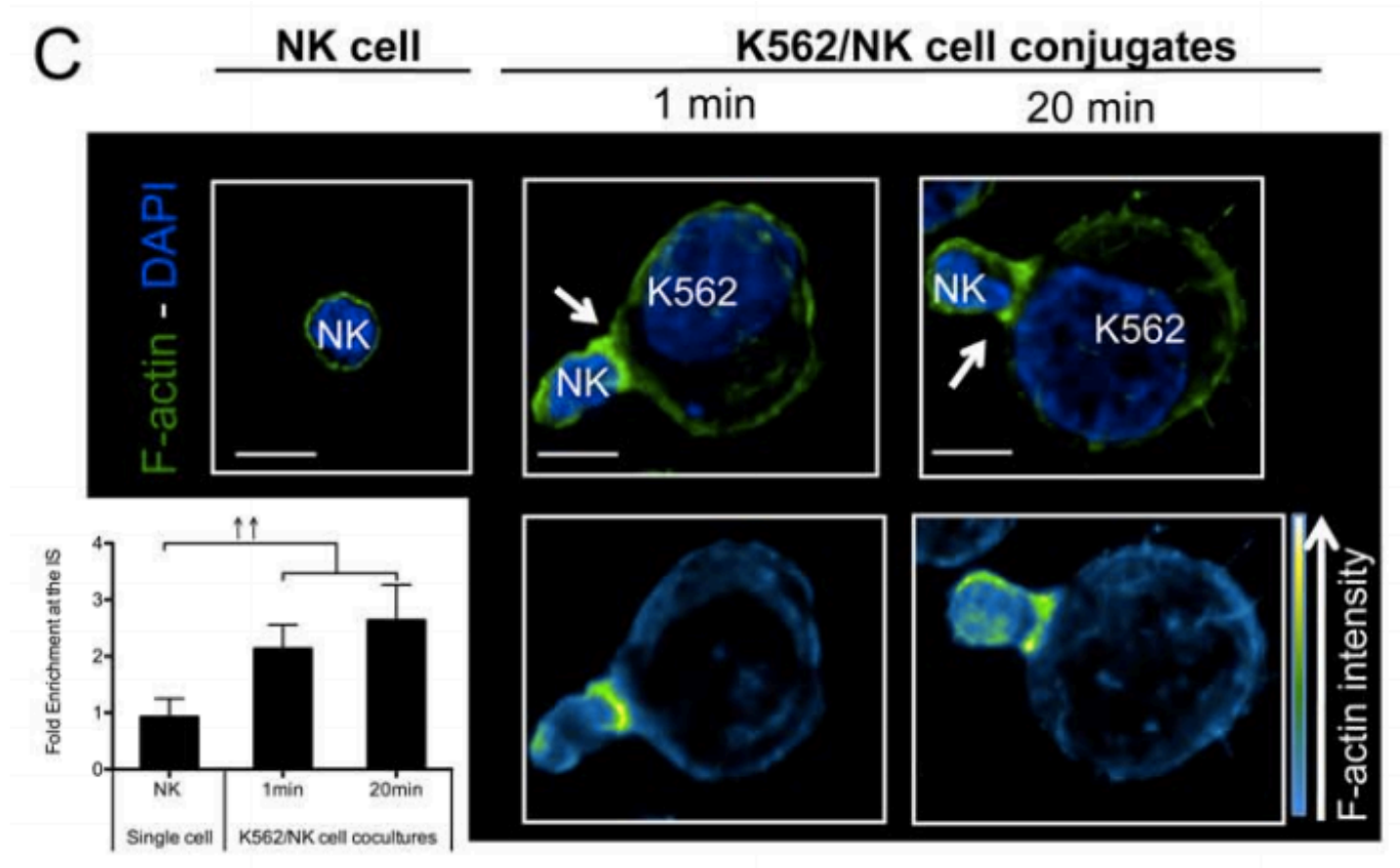


Image from Silva, et al., *Blood* (2011).

# Why is this important?

- Not much is known about the role of NK cells in primary EBV infection.
- Monitoring the human NK cell compartment could allow us to identify adolescents at risk for IM, which could benefit from EBV specific vaccination.<sup>1</sup>



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# References

1. Münz, Christian. "Role of Human Natural Killer Cells during Epstein-Barr Virus Infection." *Critical Reviews in Immunology* 6.34 (2014): 501-07. Print.
2. Epstein-Barr Virus: Infectious Mononucleosis. (n.d.). Retrieved March 3, 2015, from [http://bioweb.uwlax.edu/bio203/s2009/weisser\\_mich/diseasepathology.html](http://bioweb.uwlax.edu/bio203/s2009/weisser_mich/diseasepathology.html)
3. Kindt, T., & Goldsby, R. (2007). *Kuby immunology* (6th ed.). New York: W.H. Freeman.
4. Silva, R., Graf, C., & Munz, C. (2011). Cytoskeletal stabilization of inhibitory interactions in immunologic synapses of mature human dendritic cells with natural killer cells. *Blood*, 6487-6498.
5. Robertson, M., Cochran, K., Cameron, C., Le, J., Tantravahi, R., & Ritz, J. (1995). Characterization of a cell line, NKL, derived from an aggressive human natural killer cell leukemia. *Experimental Hematology*, (24), 406-415.
6. Chijioke, Obinna, Anne Müller, Regina Feederle, Mario Henrique M. Barros, Carsten Krieg, Vanessa Emmel, Emanuela Marcenaro, Carol S. Leung, Olga Antsiferova, Vanessa Landtwing, Walter Bossart, Alessandro Moretta, Rocio Hassan, Onur Boyman, Gerald Niedobitek, Henri-Jacques Delecluse, Riccarda Capaul, and Christian Münz. "Human Natural Killer Cells Prevent Infectious Mononucleosis Features by Targeting Lytic Epstein-Barr Virus Infection." *Cell Reports* (2013): n. pag. Web.
7. Williams, H., Mcaulay, K., Macsween, K., Gallacher, N., Higgins, C., Harrison, N., ... Crawford, D. (2005). The immune response to primary EBV infection: A role for natural killer cells. *British Journal of Haematology*, 266-274.
8. Vivier, E., Ugolini, S., Blaise, D., Chabannon, C., & Brossay, L. (2012). Targeting natural killer cells and natural killer T cells in cancer. *Nature Reviews Immunology*, 239-252.