EBV Antibody Responses before, during and after Infectious Mononucleosis

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ABSTRACT

Epstein-Barr virus (EBV) is a common human herpesvirus that infects 90% of adults worldwide and is most commonly known for causing infectious mononucleosis (mono). From our work studying EBV in a university setting since 2002, we know that college freshmen who have never been infected are at a high risk for mono. Having access to this population, we conducted a study to measure antibody responses to EBV antigens, such as BZLF1, p54 and EBNA-1, before, during and after EBV infection. Our results illustrate trends in antibody responses to these key EBV antigens that are consistent with our understanding of their activities during the different periods of infection. From this observation, we were able to better estimate the number of days since the start of primary EBV infection. These findings form the basis for further research on the variability of antibody responses between individuals with different severities of illness.

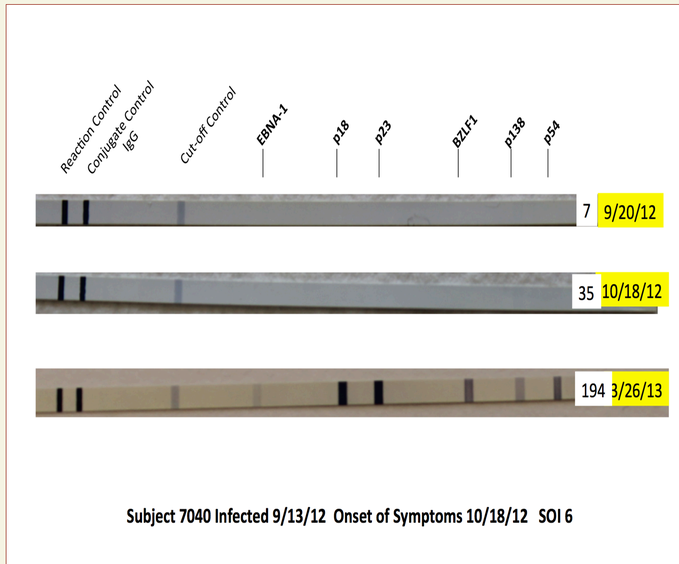
METHODS

Samples were collected from EBV naïve freshmen students at the University of Minnesota during the 2012-2013 academic school year. Antibody and antigen testing confirmed primary EBV infections. Of 87 subjects enrolled, 14 subsequently developed mononucleosis and 1 was completely asymptomatic. After EBV-positive subjects were identified, selective samples were tested using Mikrogen recomLine EBV IgG kits that detect for 6 EBV antigens associated with different stages of infection. Band intensity was assessed qualitatively and then scored as followed: 0 = no reactivity/negative. 1 = low band intensity/nonspecific cross reaction/negative. 2 = equivalent to the cutoff band/likely positive. 3 = high intensity/positive. 4 = strong intensity/strong positive.

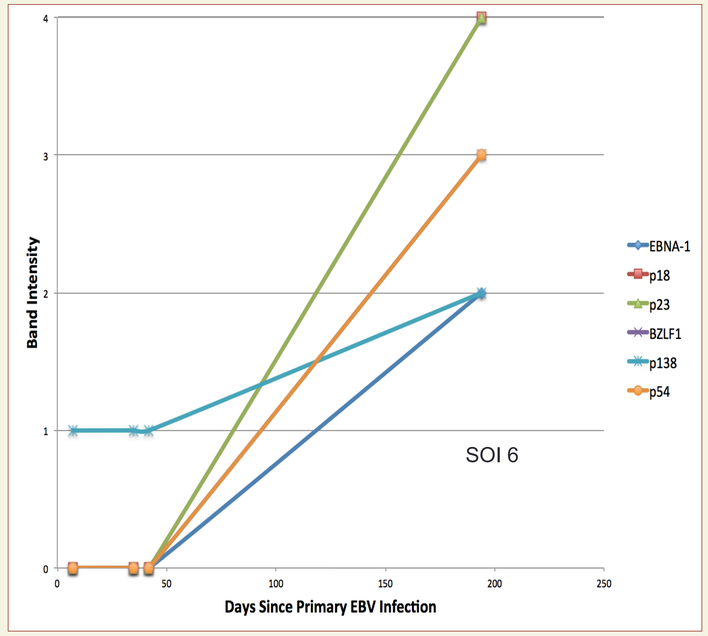
DISCUSSION AND CONCLUSION

We tested 15 subjects who subsequently developed primary EBV infection and from their incubational samples we were able to see immune responses prior to onset of symptoms. From our results we can see that antibody responses to VCA antigen p23 appear earlier than those to a different VCA antigen, p18. Subject 7141 is a good example of this finding, as we see the development of these bands before the subject is actually sick. For 7141, p23 and p54 develop at the same time, which is strongly indicative of an acute infection. Because of these early immune responses, we were able to better determine an estimate for when the subject became infected with EBV. From the results and insight gained from this study we are planning to look at how rapidity and intensity of antibody responses correspond to severity of illness.

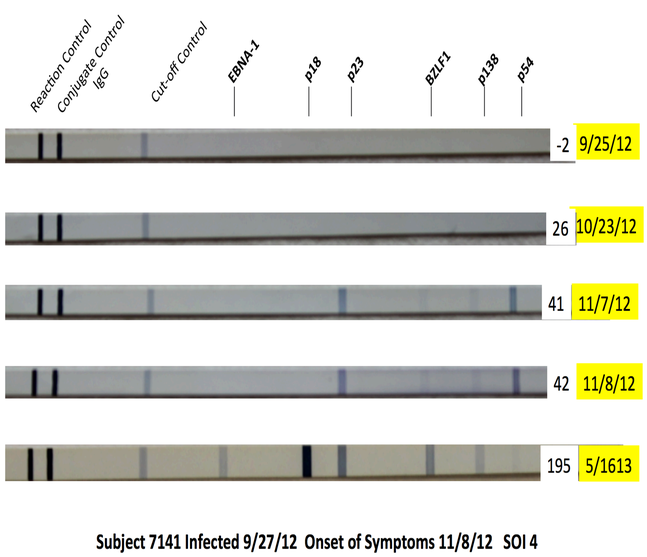
RESULTS



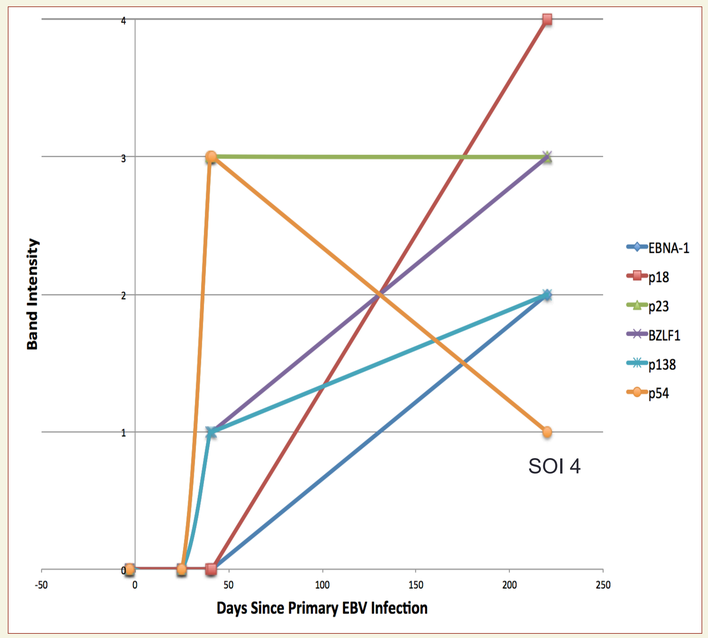
Subject 7040 Infected 9/13/12 Onset of Symptoms 10/18/12 SOI 6



Subject 7040 was one of our sickest subjects. From their immunoblot we see that they don't illicit any antibody responses during the first 35 days of their incubational period. However, during latency they have developed the full spectrum of EBV antibodies.



Subject 7141 Infected 9/27/12 Onset of Symptoms 11/8/12 SOI 4

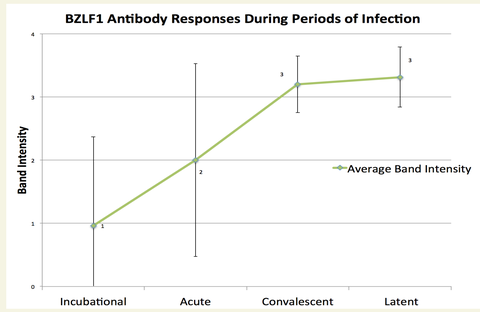


Subject 7141 developed an acute EBV infection on 11/8/12 and from their immunoblot we can see the development of immune response to early EBV antigens from 10/23/12 up until the time they show symptoms.

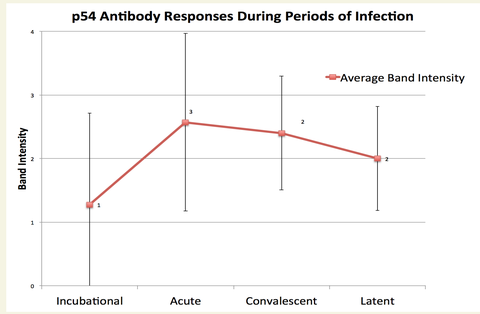
EBV antibody responses to antigen during different stages of infection

These graphs (below) represent the antibody responses to 3 EBV antigens – BZLF1, p54 and EBNA-1 – from our 15 EBV positive subjects. The x-axis represents time blocks of the different stages of infection as we define below:

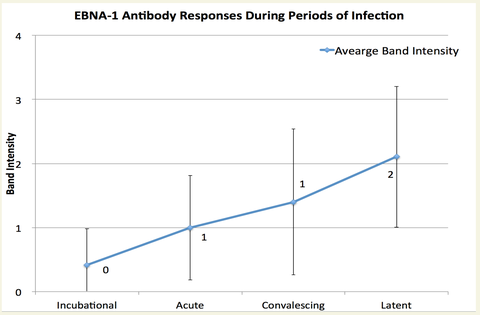
- **Incubational:** start of infect, no symptoms. Days 0-42
- **Acute:** symptoms develop and last 2-4 weeks. Days 43-57
- **Convalescent**: symptoms end. Days 58-93
- **Latent**: viral infection ongoing but inactive. Days 94 onward



BZLF-1 is an immediate early antigen (IEA) that is first detectable during the incubational and acute phases of infection.



p54 is an early antigen (EA) that is a marker for acute infection



EBNA-1 is the last to develop and confirms past EBV infection

REFERENCES

1. Balfour HH Jr et al. J Infect Dis 2013; 207: 88-8
2. Odumade O et al. Clin Microbiol Rev 2011; 24: 193-209