

Preface

We celebrated the 50th anniversary of the discovery of Epstein Barr virus (EBV) in Burkitt's lymphoma last year. During these 50 years of research on EBV, this first human candidate tumor virus has been found associated with many more malignant diseases in addition to Burkitt's lymphoma, including Hodgkin's lymphoma, nasopharyngeal carcinoma, a subset of gastric carcinomas, rare T/NK cell lymphomas, and many more. However, not only malignant diseases, but also some autoimmune diseases and the lymphocytosis of infectious mononucleosis have been found to be linked to EBV. In addition, we have learned to appreciate that continuous cell-mediated immune control prevents these EBV associated diseases, but cannot inhibit persistent infection, which the virus establishes in more than 90 % of the human adult population. Thus, EBV serves both as a paradigm for viral oncogenesis in humans and life-long immune control of chronic infection at the same time. The changes in the viral host cell and the host's immune control that determine the switch between these two states, continue to fascinate us and new experimental developments allow us to address this question in much more detail. Our ability to sequence EBV genomes faster and at lower cost allows us to explore the genetic diversity of EBV and its possible disease association for the first time. The recombinant EBV system allows us to generate mutant viruses to address the functional relevance of this diversity and new *in vivo* models of EBV infection, tumorigenesis, and immune control provide valuable insights into the pathologic relevance of the EBV characteristics that we have mapped during the last 50 years. With these tools in hand we should be able to unravel many more secrets that this human tumor virus keeps and develop vaccines against some of the EBV associated diseases in the next 50 years.

This exciting journey is summarized in the two book volumes in front of you. It starts with personal accounts of the discovery, tumor association, and immune control by pioneers of EBV research (Anthony Epstein, George Klein, Vivianne Lutzky, and Dennis Moss). It then continues with the knowledge on EBV genetics and epigenetics that has been gained (Paul Farrell, Paul Lieberman, Wolfgang Hammerschmidt, Regina Feederle, Olaf Klinke, Anton Kuthikin, Remy Poirey, Ming-Han Tsai, and Henri-Jacques Delecluse). An overview of EBV associated

diseases ranging from infectious mononucleosis and primary immune deficiencies to EBV associated tumors and autoimmune diseases completes the first volume (David Thorley-Lawson, Kristin Hogquist, Samantha Dunmire, Henri Balfour, Jeffrey Cohen, Ann Moormann, Rosemary Rochford, Paul Murray, Andrew Bell, Jane Healy, Sandeep Dave, Nancy Raab-Traub, Kassandra Munger, and Alberto Ascherio). In the second volume individual latent EBV gene products are then discussed (Lori Frappier, Bettina Kempkes, Paul Ling, Martin Allday, Quentin Bazot, Robert White, Arnd Kieser, Kai Sterz, Osman Cen, Richard Longnecker, Rebecca Skalsky, and Bryan Cullen). Viral entry and exit complete the virology chapters (Lindsey Hutt-Fletcher, Luidmila Chesnokova, Ru Jiang, Jessica McKenzie, and Ayman El-Guindy). The remainder of volume two is dedicated to the EBV specific immune response (Martin Rowe, Anna Lünemann, David Nadal, Jaap Middeldorp, Andrew Hislop, Graham Taylor, Maaïke Rensing, Michiel van Gent, Anna M. Gram, Marjolein Hooykaas, Sytse Piersma, and Emmanuel Wiertz), in vivo models of EBV infection (Fred Wang, Janine Mühe, and Christian Münz), and EBV specific therapies (Stephen Gottschalk, Cliona Rooney, Corey Smith, Rajiv Khanna, Jennifer Kanakry, and Richard Ambinder). The resulting picture of 32 chapters on EBV biology will hopefully inspire many more young scientists to join research on this paradigmatic human tumor virus.

Indeed we might just have now the toolbox in hand not only to transfer discoveries in preclinical infection models to EBV, but also use EBV itself as a human model pathogen to learn more about the human immune system, viral dynamics in the human population, and the intricacies of EBV infection.

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