MOUSE MODELS OF EBV ASSOCIATED DISEASE, FROM UNDERSTANDING MECHANISM TO PRE-CLINICAL MODEL

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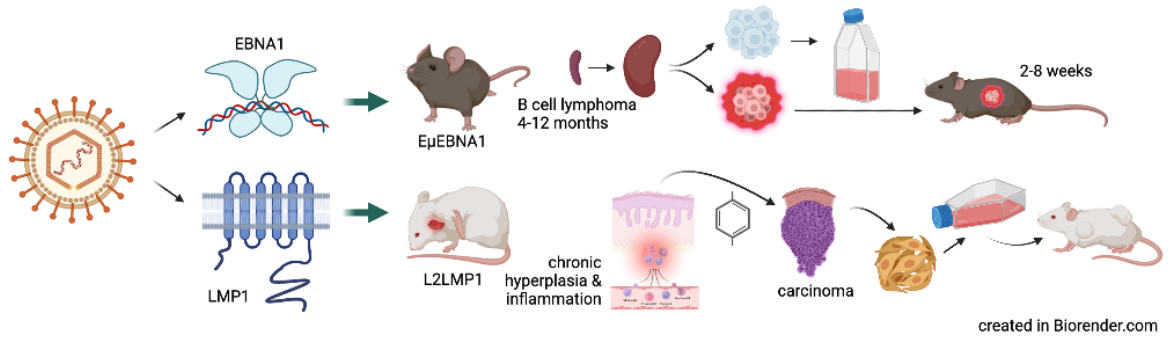
Mouse models that have been used to study EBV associated disease include human tumour ectopic xenografts (with immunocompromised mice), orthotopic models using human or mouse tumour cells engrafted into the appropriate tissue in mice, induction of viral disease in humanised mice, genetically engineered models, and autochthonous mouse models (eg chemically induced cellular mutations). A model is, by definition, only an approximation of reality and each of these present with advantages and limitations. Collectively, these mouse models provide a rounded understanding of disease mechanism *in vivo* and are crucial in drug development (from toxicology to clinically relevant parameters), using the most appropriate model at the right stage of study. As such, all of the models can provide valuable insights in different ways. We have been using transgenic mouse models, with mice expressing viral genes in the tissues of interest. Two that have proven particularly useful are the EμEBNA1 mice which succumb to B cell lymphoma and mice expressing LMP1 in the epidermis (PyLMP1 and L2LMP1), which develop chronic and progressive hyperplasia and inflammation.



The affected tissues, the primary tumours, the primary tumour cells, and the resulting cell lines permit an analysis of viral gene mechanism and have led to a greater understanding (with some surprises) of the role of these viral genes in tumourigenesis *in vivo* (for example, [1], [2], [3], [4]). Cell lines have been developed from the tumours from both series and these are growth-dependent upon the expression of the viral gene, allowing the consequences of inhibition of the viral gene product to be specifically examined [3,5]. Treatment modalities for the LMP1 induced inflammatory phenotype can be explored directly in the mice, in addition, tumours arising from both series are transplantable into syngeneic strains (mice that are not immunocompromised), permitting an analysis of new therapeutic or vaccine regimens [6,7]. In this presentation, these valuable resources will be described, with the aim of making them widely available to the research community, to colleagues who might find them useful to their studies.

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