VIRUS-LIKE PARTICLE VACCINES AGAINST BK AND JC POLYOMAVIRUSES

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Nearly all healthy adults are asymptotically infected with human polyomaviruses. In immunosuppressed individuals, the infection can reactivate and cause disease. BK polyomavirus (BKV) frequently damages transplanted kidneys and causes severe bladder disease in bone marrow transplant patients. JC polyomavirus (JCV) causes a lethal brain disease, PML, in individuals on various immnosuppressive therapies. PML also affects immunodeficient individuals, including AIDS patients.

The outer capsid proteins of polyomaviruses are structurally similar to the capsids of human papillomaviruses (HPVs). Building on the success of the NCI’s HPV virus-like particle (VLP) vaccine technologies, we have developed VLP vaccines targeting BKV and JCV. Preclinical testing in a monkey model indicates that the BKV and JCV VLP vaccines share the HPV vaccines’ exceptionally potent immunogenicity. Given our knowledge of the role that antibodies play in ameliorating polyomavirus pathologies, the new VLP vaccines are likely to protect at-risk patients against the development of BKV-induced urinary tract disease and JCV-induced brain disease. Each year, roughly 30,000 Americans join wait-lists for kidney transplantation. Additionally, roughly 300,000 Americans per year are diagnosed with diseases that might be treated with bone marrow transplantation. Emerging evidence indicates that antibody-producing plasma cells elicited by the BKV vaccine will persist after bone marrow transplantation and the vaccine should thus provide protection against post-transplant hemorrhagic cystitis.

The highly effective multiple sclerosis therapy Tysabri (natalizumab) is associated with up to 2% risk of PML side effects. Rituxan (rituximab), which is used for treatment of rheumatoid arthritis and certain types of lymphoma, carries a black box warning for PML and a dozen additional immunosuppressive therapies are also known or suspected to have PML side effects. The JCV vaccine should be a useful preventive adjunct for these popular immunotherapies.

Since there are currently no effective treatments for BKV or JCV diseases, the candidate vaccines seem likely to qualify for FDA’s Accelerated Approval Program. The NCI is currently seeking industry partners.