DEVELOPMENT OF A VACCINE TO INTERCEPT ORAL CANCER

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Background Oral cavity cancer is diagnosed in more than 300,000 people each year worldwide and approximately half of these will die within five years despite standard treatment. These cancers are often preceded by the appearance of a premalignant dysplastic lesion, which offers a unique opportunity to identify patients at high risk of developing cancer and offer them a vaccine that may prevent development of this non-viral malignancy. Lesions can be removed but because of a 'field effect' their entire oral mucosa is at risk – thus the vaccine. Recent studies have identified genes that are differentially expressed during progression from normal tissue to oral cancer providing a roadmap to developing a preventative vaccine [PMID: 27027432]

Methods We have manufactured and performed initial characterization of a DC-targeted microvesicle vaccine, DPV-007, made specifically to intercept the progression of oral dysplasia to oral cancer. DPV-007 is manufactured using platform vaccine technology that is in the clinic. This technology captures short-lived and non-canonical proteins that make up the dominant epitopes presented by HLA and packages them in microvesicles containing DAMPs and molecular chaperones. Characterization of DPV-007 included molecular, proteogenomic, biochemical and functional assessments. Preclinical studies were performed evaluating prevention of tumor development in the 4NQO-induced tumor model.

Results The DPV-007 microvesicle vaccine contains more than 200 proteins for genes that are upregulated in oral dysplasia and oral cancer. Preliminary data suggests that the vaccine may contain as many as 30 somatic variants identified as somatic mutations in the COSMIC Database. Additionally, the vaccine contains at least 11 NCI prioritized cancer antigens and has agonist activity for TLR 2, 3, and 9. In the 4NQO preclinical model, vaccination including relevant antigens and agonist activity, provided significant (p<0.02) protection from lesion onset and tumor outgrowth.

Conclusions The identification of genes associated with the progression of pre-cancerous lesions to cancer provides targets for active immunotheraphy of this disease. In preclinical models we have shown that this vaccine strategy is effective in both protection and therapy studies' [PMID: 21810919; PMID: 27874054; PMID: 31747946]. A clinical trial of a similar vaccine, DPV-001, administered as a single agent as adjuvant therapy for NSCLC, documented induction of immunity to a large number of cancer antigens contained in the vaccine and did not identify serious adverse events. Based on data summarized above, we propose to vaccinate patients with dysplastic lesions and investigate whether vaccination reduces lesion recurrence.

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Ethics Approval The Institutional Animal Care & Use Committee of the Earle A. Chiles Research Institute approved the above noted studies. Protocol 55.