# Novel targets for paediatric brain tumour immunotherapy

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Project Synopsis and Aims

Every year more than 170 Australian children are diagnosed with brain cancer. Diffuse Intrinsic Pontine Glioma (DIPG) is the most aggressive childhood brainstem tumour with no cure and median survival of only nine months post - diagnosis. Cancer vaccination is an emerging approach for untreatable cancers. The fundamental mechanism of the immune system for combating cancer is recognition of peptides exclusively presented on the tumour surface in complex with Human Leukocyte Antigen (HLA) molecules. However, selecting the right antigen and corresponding peptide-HLA complex (p-HLA) is the most challenging part of any vaccination strategy.

Generation and presentation of p-HLAs is a dynamic process within the cell. Therefore, intra and extracellular factors can affect the composition of the immunopeptidome (the array of peptides presented by a given HLA molecule). In the case of DIPG, two mechanisms can generate or potentiate DIPG tumour exclusive p-HLAs: 1) As the only, and first line of management of DIPG, radiotherapy not only causes tumour cell death, releasing antigen for subsequent presentation by professional antigen-presenting cells and the initiation of further immune responses; but can also increase the expression of p-HLA on the surface of resistant tumour cells rendering them more susceptible to immune attack. 2) Methylation/ mutation of the Histone3 gene are epigenetic signatures of DIPG. Recently, it has been discovered that these two signatures turn on the expression of particular endogenous retroviruses (ERV) in DIPG tumours. These viral antigens can also form novel targets of immune responses.