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**Validation of PASD1 as An Immunotherapeutic Target in Colorectal Cancer (CRC)**

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**ABSTRACT**

Colorectal cancer (CRC) is known to be the third most commonly diagnosed malignancy in Asia including Malaysia. Despite the advances in preventive screening, surgical removal or conventional therapies such as chemotherapy and radiotherapy, a significant proportion of CRC patients failed to achieve long term remission or are struggling with toxic side effects from the conventional therapies. The identification of immunogenic cancer testis antigens (CTAs) as immunotherapeutic targets represents one approach to improve treatment options for CRC patients. PASD1 [PAS (Per ARNT Sim) domain containing 1 (PASD1)], is a promising CTA that is expressed in a wide range of neoplasms. The aim of the present study was to investigate the expression of HLA-A\*2402 restricted PASD1 peptides and its CD8 T cells immune responses in CRC patients. About 35% of the CRC patients and 28% of healthy donors were determined to be HLA-A\*2402 positive by one-step polymerase chain reaction-sequence specific primer (PCR-SSP) typing in Malaysian population. The interferon (IFN) release was detected in all of the CRC patients tested (n=5) following short-term culture of their peripheral blood mononuclear cells (PBMCs) stimulated with four HLA-A\*2402-restricted PASD1 peptides. We tested 4 different subtypes of PASD1, the IFN-y responses from PASD1(4) pulsed PBMCs of CRC patients was the highest, followed by PASD1(3), PASD1(1) and PASD1(2) subtype. The RNA expression of PASD1 was only detected in SW480 but none was detected in CCD-112, COLO205, HCT116, HT29 and SW48 cell lines. Hence, the screening of the HLA-A\*2402 restricted PASD1 peptides suggest the possibility of designing peptide-based immunotherapeutic approaches that might prove the potential in the treatment option for PASD1-positive neoplasms.