

# CRT Licensing Opportunity



## PASD1: a Novel Tumour Specific Antigen

- Immunotherapy target for a range of haematological and solid cancers
- Proof of concept achieved using proprietary PASD1 immunogenic peptides
- Adaptability to a variety of platform vaccine technologies
- Opportunity for rapid progression into the clinic

BIOLOGICAL THERAPEUTICS | *In Vivo* Proof of Principle

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### Opportunity

First identified as an antigen associated with Diffuse Large B Cell Lymphoma (DLBCL) (1,2) and Acute Myeloid Leukaemia (AML) (3), PASD1 has been established as a novel tumour specific cancer testis antigen (CTA) with a wide cancer expression profile. PASD1 expression has been documented in a variety of haematological malignancies, including DLBCL, AML, follicular lymphoma, mantle cell lymphoma, MALT lymphoma, Burkitt's lymphoma, Hodgkin's lymphoma, T-acute lymphoblastic lymphoma and multiple myeloma (4, 5), as well as solid tumours such as melanoma, lung, head and neck and colorectal carcinoma (1,3). Due to its restricted expression in normal tissues, other than the testis (an immune-privileged site), PASD1 is expected to have little chance of inducing autoimmune toxicity in an immunotherapy setting. The above features combined with the proven immunogenicity of PASD1 peptides, make this antigen an attractive candidate for cancer vaccine development.

### Expertise

The lead researchers, Dr Alison Banham, Dr Karen Pulford (University of Oxford) and Dr Barbara Guinn (University of Southampton, King's College London), have been working with the PASD1 antigen since 2001 and are actively engaged in its further development as a cancer vaccine candidate in lymphomas, leukaemias and solid tumours.

### Application

PASD1 can be incorporated into a variety of cancer vaccine approaches, among others: i) non-viral delivery DNA/peptide vaccine, ii) viral delivery DNA/peptide vaccine, iii) PASD1-stimulated DC infusion, iv) TCR gene therapy and/or iv) PASD1-stimulated donor lymphocyte infusion.

### Proof of Principle - Immunogenic Peptides

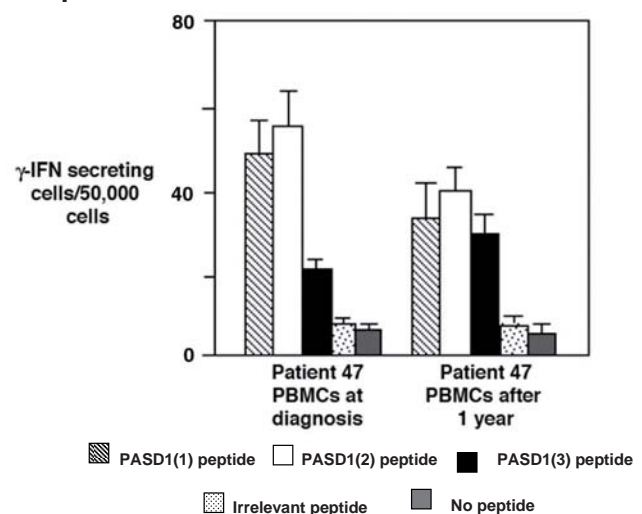


Figure 1: A significant gamma-IFN response to PASD1 peptides in a patient with de novo DLBCL at diagnosis and after one year in remission

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The major effector cell in tumour immunity is the cytotoxic CD8+ T cell (CTL), which recognises and kills tumour cells in an MHC-class I dependent manner. PASD1-specific peptides predicted to be immunogenic in the context of the MHC class I HLA-A\*0201 allele have been identified and validated in two primary indications, DLBCL and AML. In both malignancies a high percentage of patients relapse following treatment, therefore there is an urgent need to improve patient outcome and immunotherapy offers an exciting treatment option. Further validation work in solid tumours is also underway.

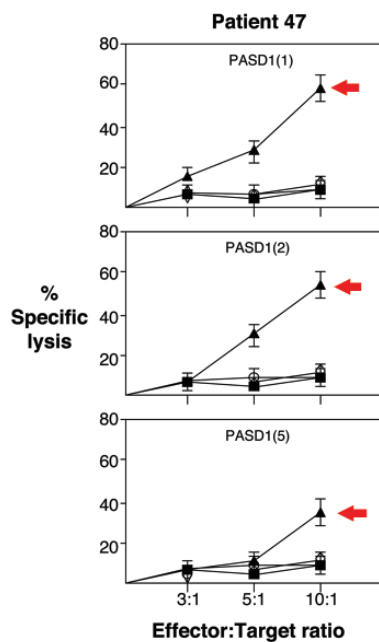


Figure 2: CTL cell lines from the same patient were able to recognise and lyse the HLA-A\*0201+/PASD1+ Thiel (myeloma) cell line (arrowed). No lysis was observed in the SUDHL-6 (DLBCL; HLA-A\*0201+/PASD1-) or the OCI-Ly3 (DLBCL) and KM-H2 (HL; HLA-A\*0201-/PASD1+) cell lines

A significant CTL response (as measured by  $\gamma$ -IFN release) was detected in a high percentage of HLA-A\*0201 positive DLBCL patient samples, following stimulation with the PASD1 peptides (6). The response correlated with PASD1 protein expression in the majority of DLBCL cases (6). Moreover, patient response persisted for at least a year, suggesting the presence of a pool of memory PASD1-specific CTLs that could be restimulated in a vaccine approach (6). When further stimulated with peptide, CTL cell lines from responding patients demonstrated the ability to recognise and lyse tumour cells endogenously expressing and processing PASD1 (6). Of importance, the percentage of CTLs recognising PASD1 peptides was comparable to that observed for other antigens currently in clinical development, such as MAGE-A3 (6).

Similar results have been seen using AML patient samples and normal donor samples, suggesting an available repertoire of PASD1-responsive T cells in humans. Peptide-specific *in vitro*

stimulation of human T cells from AML patients and normal donors can expand PASD1-specific CTLs, which are active (release  $\gamma$ -IFN) and demonstrate a cytolytic effect against PASD1 expressing tumour cells.

Interestingly, CD4+ T helper ( $T_H$ ) responses (MHC-class II-dependent) to PASD1 peptides have also been detected and specific peptides identified that are envisaged to be able to elicit coordinated CTL and  $T_H$  responses. This latter finding is extremely important in view of the accumulating evidence that  $T_H$  cells play a vital role in the maintenance of CTLs. Work on PASD1 MHC-class II-specific peptides is ongoing.

*In vivo* exemplification work on PASD1 as an immunotherapy target is underway using a clinically validated DNA vaccine technology.

The level and persistence of PASD1 specific CTL responses seen in patients and the possibility of selecting a responsive patient population through screening for PASD1 expression support the potential of raising therapeutically relevant immune responses in the clinic.

## Commercial Opportunity

This technology is being co-marketed by CRT and Isis Innovation, who are seeking a commercial partner for further development of PASD1-based immunotherapy under a license to the PASD1 patents.



## Intellectual Property

Patents on the PASD1 antigen and proprietary PASD1 immunogenic peptides are available for licensing and/or collaborative development.

Additional information on the opportunity can be made available under confidentiality agreement.

## References

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